ORIGINAL ARTICLE

# The Effectiveness of Hyoscine-N-Butylbromide (Buscopan) in Reducing Physiological Bowel Uptake in 18F-FDG PET/CT

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## ABSTRACT

**Introduction:** Positron Emission Tomography-Computed Tomography (PET-CT) was introduced over four decades ago as an imaging tool to evaluate functional and anatomical aspects of disease such as malignancy. Besides pathological uptake, PET-CT also shows physiological uptake, especially in the gastrointestinal system, thus impacting diagnostic accuracy in these cases. There are many conditions that can attribute to increasing physiological uptake in PET-CT including microbial activity and drugs. Therefore, certain anti-spasmodic agents have been introduced to help reduce physiological uptake during scanning such as Hyoscine-n-butylbromide (Buscopan). This study aims to establish its effectiveness in reducing physiological bowel uptake on 18F-FDG PET-CT scan. **Methods:** 133 subjects were recruited in random for this study and divided into hyoscine (68 subjects) and control groups (65 subjects), respectively. Subjects in control group not given any anti-spasmodic medications and both groups received intravenous 18F-FDG according to body weight. PET-CT scan and images were interpreted by experienced nuclear medicine physician who scored the images according to the degree of bowel uptake and difficulty of image interpretation. **Results:** There were no statistical difference in bowel uptake based on SUV mean of the bowel and bowel-to-liver ratio between hyoscine and control groups. **Conclusion:** There was no significant effect of Hyoscine-n-butylbromide in reducing physiological bowel uptake in PET-CT scan.

**Keywords:** PET-CT, physiological uptake, Hyoscine-n-butylbromide, malignancy

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## INTRODUCTION

Positron Emission Tomography (PET) imaging was introduced in the field of nuclear medicine since 1974 with the capability of assessing functional/physiological status of a disease by using radioisotope. Over the years, its use especially in oncology cases has been widely accepted (1). However, it was limited due to lack of anatomical localisation (2) due to poor spatial resolution (3,4).

Computed tomography (CT) on the other hand has the ability to demonstrate good anatomy localisation but lack in functional evaluation. In view of that, new advancement has been introduced in 1998 by combining PET imaging and CT imaging to form a hybrid imaging called PET-CT. The ability of PET-CT imaging to evaluate the functional and anatomical findings has helped in improving diagnostic accuracy (5). Furthermore, PET-CT scan also enables evaluation of physiological 18F-FDG uptake. This is important because some uptake appears to be physiological in PET but CT evaluation found evidence of pathology at the uptake site (6). The ability to evaluate pathological and physiological findings has significantly helped to improve patient management (7).

In the gastrointestinal tract, there are several conditions attributed to high 18F- FDG uptake such as malignancy and other benign or physiological conditions. Other than smooth muscle activity or peristalsis, other benign condition in the bowel may also take up 18F-FDG. These conditions include inflammatory process such as colitis and duodenitis, infection such as viral and *H. pylori* infection, bleeding and microbial activity. The normal flora in the bowel takes up 18F-FDG that is excreted into the bowel lumen (8). Other than that, drug such as metformin also causes high 18F-FDG uptake in the bowel (9). Metformin is responsible for the activation of glucose transporter proteins or GLUT-2 on the mucosal surface of the bowel that causes higher avidity of glucose in the bowel (10). Patient in hyperglycemic state during 18F- FDG injection will have lower 18F-FDG uptake by the tumor. Insulin administration to lower down the glucose level can be done provided that the 18F-FDG

injection is delayed few hours later to avoid generalised muscle uptake during PET-CT scan (11).

Normal peristaltic activity of the bowel may cause 18F-FDG uptake in PET-CT and usually demonstrates variable uptake depending on sites. Diffuse low level of uptake usually observed in the small bowel. Colon demonstrates a more heterogenous uptake especially at the ileo-caecal junction, ascending colon and rectum (12). This is attributed to the activity of the sphincter and peristaltic activity. Besides that, the higher 18F-FDG uptake in the caecum and right colon was also attributed to the abundance of lymphocytes in that region (13). Other study also proposed that high 18F-FDG uptake in ascending colon was also related to the presence of lymphocytes (14).

Other conditions that can cause increase bowel activity will also cause higher 18F-FDG uptake. Patients with bowel related illness such as diarrhoea or constipation during the scan time might exhibit high 18F-FDG uptake in the bowel. However, some 18F-FDG uptakes are difficult to interpret such as physiological uptake in the smooth muscles of the bowel. Gastrointestinal tract uptake among others is the commonest site of uptake in PET-CT. High 18F-FDG uptake in the bowel might be due to active bowel movement. In view of this, it may mask any underlying bowel related pathology.

It is more challenging to interpret the image when the primary lesion originated from the bowel or any organ adjacent to the bowel. As a result, the use of antispasmodic agent such as Hyoscine-n-butylbromide (Buscopan) was introduced. Hysocine-n-butylbromide is a spasmolytic agent that has effect on the smooth muscles of gastrointestinal tract, genitourinary tract as well as biliary tract. It does not cross into the central nervous system as it in the form of quarternary ammonium derivative. Therefore, anticholinergic effects of central nervous system do not occur. However peripherally, it exerts anticholinergic action as a result from ganglionic blocking action within the visceral wall and antimuscarinic effect.

Studies looking into the use of these agents prior to PET-CT scan have noted reductions in the physiological 18F-FDG uptake in the bowel. However, in Malaysia there is no consensus as to whether the use of this drug helped in definite and resolute interpretation of the scan. Therefore, the aim of this study is to assess the effectiveness of this drug in reducing the physiological uptake in the bowel by comparing SUVmean of bowel and bowel-to-liver ratio among patients receiving Hyoscine and control group, comparing the degree of bowel uptake and difficulty of image interpretation among patients receiving Hyoscine and control group; and determining the relationship between the degree of bowel uptake and difficulty of image interpretation between these two groups.

## MATERIALS AND METHODS

Institutional review board approval was obtained prior to this study. The study was conducted between September 2016 and February 2017 in which 500 patients registered for PET-CT scan in PET/CT unit, Department of Nuclear Medicine, Hospital Pulau Pinang during the patient recruitment period. Systematic random sampling was done followed by simple random sampling was done to nominate the members of groups A (received Buscopan) and B (control). This was achieved by using random number table available in statistical reference book (15). Therefore, 70 patients were put in every group before further inclusion and exclusion criteria were evaluated.

After considering the exclusion criteria, from the total of 70 patients nominated in each group; 68 patients were recruited in hyoscine group and 65 patients were in the control group. The remaining patients who were not selected into this study were diabetic on metformin therapy and another 5 gave history of diarrhoea a week before the scan.

### Scanning protocol

Patients were fasted for at least 6 hours prior to 18F-FDG injection. Patients' weight and fasting blood glucose were recorded upon arrival. The acceptable glucose level for all patients was 8.0 mmol/L or lower. Hyoscine group patients were given oral Hyoscine-n- butylbromide 10mg 30 minutes before 18F-FDG injection. The patients in control group were given not given any anti-spasmodic medication and received intravenous 18F-FDG only. The dose of 18F-FDG is based on body weight ranging from 10-20 mCi (370-740 MBq).

PET-CT scanning was done 45 minutes to 1 hour after 18F-FDG injection using a dedicated PET-CT scanner (Discovery ST, General Electric Medical Systems, Waukesha, WI, USA). The scanner used Bismuth Germanium Oxide (BGO) crystals, detector field of view (DFOV) of 50 cm with 24 PET ring-detectors. The scan was done covering from the skull to mid-thigh. A contemporaneous low dose non-contrasted CT was also done by the same scanner with 100 mA and 120 kV. CT scan speed at 0.8 s per revolution with 3.75 mm slice thickness. Meanwhile PET acquisition was obtained at 6- 8 beds position with overlap of 3.270 mm and 3 minutes emission scan for each bed position. Images were reconstructed using an iterative ordered-subsets expectation maximisation (OSEM) algorithm with CT attenuation correction.

An experienced nuclear medicine physician who was blinded of the clinical data of the patients reviewed the images. The revision was done using GE Advantage Workstation (General Electric Medical Systems, Waukesha, WI, USA). The interpreter used visual analysis to evaluate the degree of bowel uptake and difficulty of image interpretation (Fig. 1, Fig. 2). The

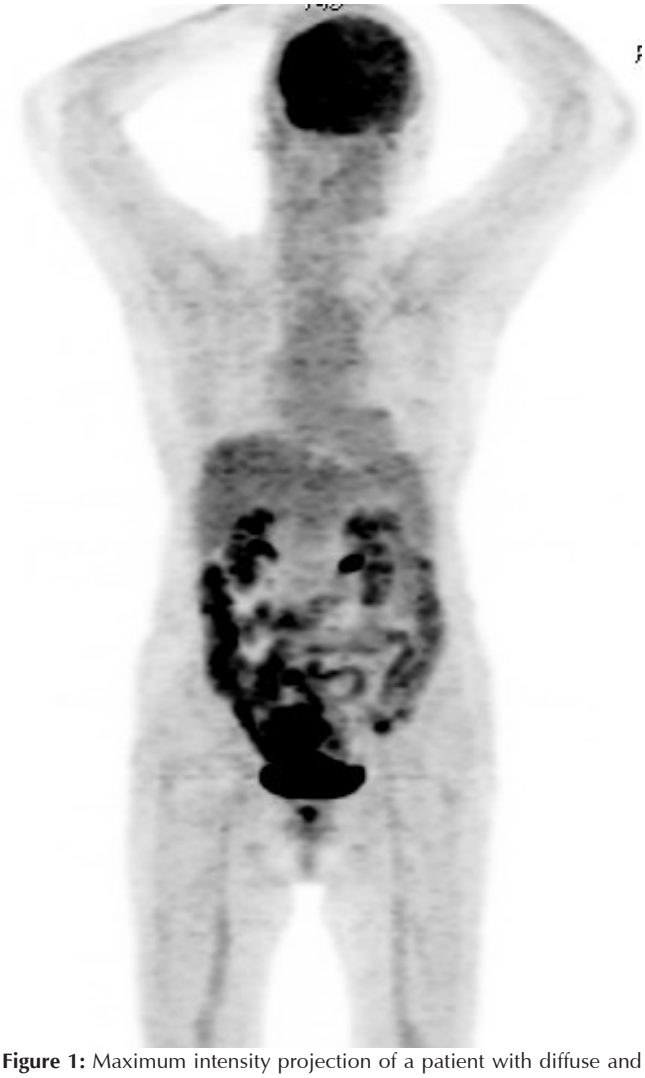

**Figure 1:** Maximum intensity projection of a patient with diffuse and intense uptake in the bowel with lower uptake in the liver. The interpreter scored 2 for degree of bowel uptake but scored 0 in the difficulty of bowel interpretation. This uptake was more likely physiological rather than pathological. This patient was from the control group.

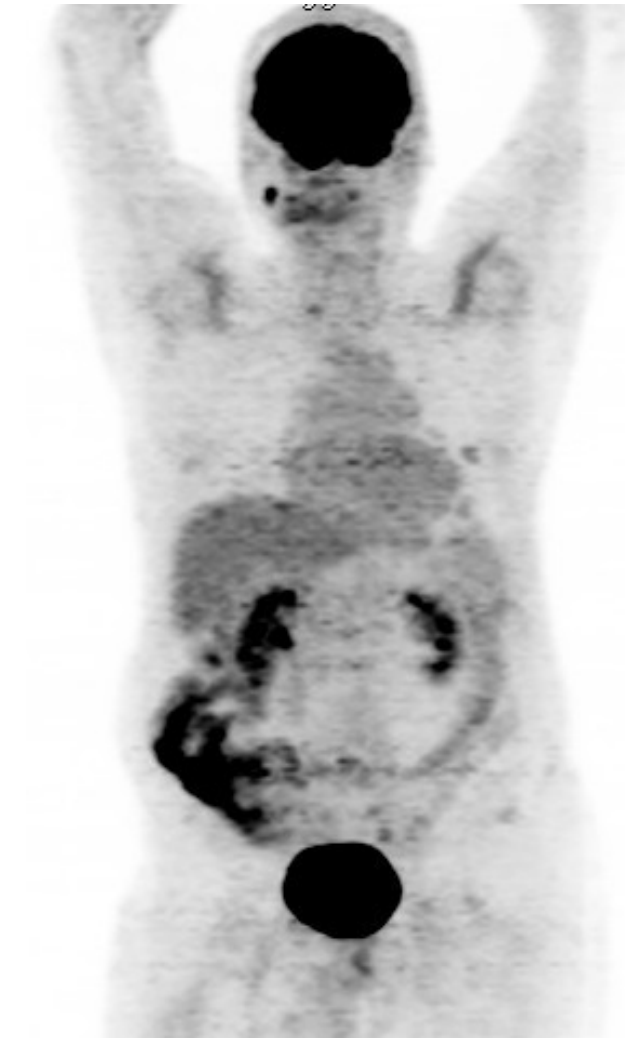

**Figure 2:** Maximum intensity projection showing a diffuse high uptake at the ascending colon area, which was higher than the liver uptake. The interpreter scored 2 for degree of bowel uptake and 2 for difficulty of image interpretation. This patient was from hyoscine group.

interpreter scored each aspect with number 0 to 2 scale (Table I and Table II).

The differences in means SUVmean of bowel and Bowel-to-Liver ratio among the two groups were tested using One-Way ANOVA. Meanwhile, the associations on the degree of bowel uptake and difficulty of image interpretation among the two groups were tested using Pearson Chi-square test and Fisher's Exact test respectively. The relationship between degree of bowel uptake and difficulty of image interpretation was determined by computing the Pearson correlation coefficient (r). A *p*-value of less than 0.05 was accepted as significant.

Semiquantitative subanalyses were also carried out. The data from patients with colorectal and gynaecological cancer was excluded in these subanalyses. Independent t- test was used for the subanalyses of differences in mean SUVmean of bowel and Bowel- to-Liver ratio of patients in hyoscine versus control group. A *p*-value of less than 0.05 was accepted as significant.

**Table I: Scoring scale in visual analysis on the degree of bowel uptake**

| Score | Description |
|---|---|
| 0 | No significant bowel uptake compared to background liver uptake |
| 1 | Mild bowel uptake compared to background liver uptake |
| 2 | Severe bowel uptake compared to background liver uptake |

**Table II: Scoring scale in visual analysis on the difficulty in image interpretation**

| Score | Description |
|---|---|
| 0 | No difficulty to interpret as physiological uptake |
| 1 | Slight difficulty to interpret as physiological uptake |
| 2 | Most difficult to interpret as physiological uptake |

## RESULTS

A total of 133 patients were recruited into this study. 55 male and 78 female patients were involved in this study. Majority of the patients were Malay (46.7%, n=62), followed by Chinese (43.1%, n=57), Indian (8.7%, n=12) and others (1.5%, n=2). The youngest patient was 19 years old and the eldest was 80 years old.

In hyoscine group, colorectal cancer accounted the highest number of patients (47.1%, n = 32) and no thyroid cancer patient in this group. Only one patient (1.5%) of lung cancer recruited in this group. Meanwhile, in control group the highest number of patients was lymphoma (32.3%, n = 21). The number of patient with colorectal cancer was the least (4.6%, n = 3).

### Semiquantitative analysis of bowel uptake in the two groups based on SUVmean of bowel

This study showed that hyoscine group has lower value of lowest SUVmean of bowel (0.50g/mL) in comparison to control group (0.70g/mL). The values of highest SUVmean hyoscine group was relatively lower (4.70g/mL) than the control group (7.20g/mL). However, the mean SUVmean of hyoscine group was higher (1.90g/mL) than the control group (1.60g/mL). This reflected a fairly equal effect between the control group and the hyoscine group (Table III).

**Table III: The value of lowest, highest and mean $SUV_{mean}$ of each group**

| Group | Lowest SUVmean (g/mL) | Highest SUVmean (g/mL) | Mean SUVmean (g/mL) |
|---|---|---|---|
| Hyoscine | 0.50 | 4.70 | 1.90 |
| Control | 0.70 | 7.20 | 1.60 |

One-way ANOVA analysis showed that the value of mean SUVmean of bowel among the two groups was statistically not significant. Post-hoc multiple comparison test Bonferroni's procedures were carried out to compare the means between hyoscine versus control. There was no significant difference in mean SUVmean of bowel in between hyoscine group and control group ($p$ = 0.215).

### Semiquantitative analysis of bowel uptake in the two groups based on Bowel-to-Liver ratio (B/L ratio)

Table IV shows that hyoscine group has the lowest value of lowest Bowel-to-Liver ratio (B/L ratio) among the two groups. The values of highest B/L ratio of hyoscine group were lower than the control group. However, this was not reflected in term of mean B/L ratio whereby hyoscine group showed higher mean B/L ratio compared to Control group. This reflected a fairly equal effect between the hyoscine group and control group (Table IV).

One-way ANOVA found that the value of mean B/L ratio among the two groups was not statistically significant. Post-hoc multiple comparison test Bonferroni's procedures were carried out to compare the mean B/L ratio between hyoscine versus control. There was no significant difference in mean B/L ratio in between hyoscine group and control group ($p$=0.064).

**Table IV: The value of lowest, highest and mean B/L ratio of each group**

| Group | Lowest B/L ratio | Highest B/L ratio | Mean B/L ratio |
|---|---|---|---|
| Hyoscine | 0.28 | 2.24 | 0.81 |
| Control | 0.21 | 3.13 | 0.65 |

## DISCUSSION

Most of the patients referred for PET-CT scan during the study period were diagnosed with lymphoma (25.6%, n=34) followed by colorectal (20.5%, n=27) and gynaecological (16.9%, n=23) malignancies. The demographic data collected in this study was in accordance to local Penang Cancer Registry and Malaysian National Cancer Registry report (16). PET-CT is widely accepted as imaging modality for lymphoma as it is superior in lesion detection, ability to characterise the residual mass post therapy and in prognosis of patient after chemotherapy (17).

In the control group, this study found that the lowest SUVmean of bowel was 0.70 g/mL. This value was not much different from the lowest SUVmean values for hyoscine group. The highest SUVmean of bowel in the control group was higher than the other group. However, the mean SUVmean of bowel among the two groups were not much different among each other. The results showed that the two groups had a fairly equal effect in term of reduction of physiological bowel uptake. The statistical analyses also observed non-significant difference in means of SUVmean of bowel among the two groups.

Similarly, for the value of B/L ratio, the hyoscine group showed not much difference in mean of B/L ratio compared to the control group. These findings reflected that the two groups were having fairly equal effect in reducing physiological bowel uptake. The mean B/L ratio of hyoscine group was slightly higher among the two groups. Since the hyoscine group showed less effect on this study, it might be related to its slightly poor gastrointestinal absorption (18) as compared to other drugs such as Mebeverine.

A study with 2290 patients was conducted in a nuclear medicine centre in Spain in 2015, where patients were subjected to PET and PET-CT scans without prior pretreatment with any drugs or substance. Only 27 patients were found to have focal colorectal 18F-FDG uptake. Although several methods of decreasing bowel uptake in PET-CT had been studied, no technique has been found to be consistently reduced bowel uptake (19).

Besides peristaltic activity, there was another possible explanation of increased 18F-FDG uptake in the bowel. The 18F-FDG was excreted into the lumen of bowel and subsequently used by the normal flora along the luminal wall (8). Therefore, antispasmodic agent such as hyoscine did not cause any significant effect on 18F-FDG bowel uptake. Excessive peristaltic activity in the bowel was probably not the cause of 18F-FDG uptake during PET-CT. Jadvar et al. (20) hypothesised that the bowel uptake in 18F-FDG PET-CT was probably not due to peristaltic activity. The hypothesis was tested by comparing the level of 18F-FDG uptake in the bowel in the patients before and after administering two different drugs (Atropine and Sincalide) in separate occasions. Atropine has the antiperistaltic effect while Sincalide increases peristaltic activity. They found that there was no significant different in the level of 18F-FDG uptake before and after administration of both drugs.

Meanwhile, the statistical analysis also showed that in between hyoscine and control groups, there was no significant difference in means SUVmean and B/L ratio. This study found that hyoscine has higher mean SUVmean compared to control group. B/L ratio of hyoscine group was also higher than the control group. In contrast to these findings, there was a study by Emmott et al. (21), evaluating the effects of hyoscine on bowel uptake during 18-F FDG PET-CT. They found that hyoscine was effective in reducing bowel uptake when comparing between patients received hyoscine and control group. Furthermore, qualitative analysis showed statistically significant contribution of bowel uptake on confidence of reporting between two independent observers.

Besides poor gastrointestinal absorption of hyoscine, the above findings can be attributed to the shorter effect of hyoscine. Ideally, hyoscine has to be given 30 minutes before 18F-FDG injection (22). The effect of the drug achieved maximum at around 2 hours after ingestion. The strict timing was difficult to follow in this study because the 18F-FDG was brought from Hospital Putrajaya (estimated 4-5 hours' journey to Hospital Pulau Pinang). In between scans, there were unscheduled delays due to various reasons such as repeat scan and machine breakdown. Efforts had been made to minimise this problem such as recording strictly time of hyoscine administration. The attending radionuclear pharmacists were also helpful by getting the daily departure time of 18F-FDG from Hospital Putrajaya. Therefore, the arrival time was estimated and time of hyoscine administration could be scheduled.

Besides that, other confounding factor may need to be considered is patients' medications. Several drugs were noted to interact with hyoscine. The examples of commonly consumed drugs were antihistamine, baclofen, antipsychotics, metoclopramide, thiazide diuretics, tramadol and antidepressants. These drugs reduced the efficacy of hyoscine as an antispasmodic agent. Detail drug history need to be carried out in order to reduce the drug-drug interactions. Unfortunately, some of patients were not able to give a good drug history being the majority of study samples were aged above 60 years old.

The measurement of SUVmean was dependent on the method of region of interest (ROI) selection for SUVmean measurement and other factors such as body habitus, bowel related disease, patients' medications and blood sugar level (23). The 18F- FDG uptake in tumor was considerably affected by the blood glucose level. However, 18F-FDG uptake in the bowel was not related to blood sugar level (24). The measurement of SUVmean was operator dependent. The size of region of interest (ROI) might differ in one sample to another. This is particularly important in patients with diffuse and high bowel uptake. Other than that, a large focal bowel uptake was also affected by ROI. Some patients also had surgery done to bowel that changed the normal anatomy of bowel. Examples were like patient with colostomy or ileal conduit. The same size of ROI in the bowel as well as in the liver was used. As far as possible, the interpreter had tried to avoid putting the ROI box near a non-bowel structure.

The computer used for SUVmean measurement normalised the calculated value to the patients' body weight. This might affect the SUVmean measurement in the larger body weight patient. The increased of body fat fraction caused overestimation of SUV measurement (25). The avidity of different tissues in the body was also different. This caused variability of SUVmean measurement by the computer. For example, fatty tissues had the lowest 18-F FDG uptake while for changes in body weight between 50 kg to 100 kg; normal liver uptake varied almost 40-50% (23). Even though correctional methods were available, many studies omitted this issue when reporting SUV value. Most of the time, ratio of the measured SUV value to background uptake of liver or skeletal muscles were used.

The standard practice in our centre was to start scanning the patient 45 minutes to one hour after 18F-FDG injection. The time for rapid FDG uptake differed from patient to patient due to various uncontrollable factors. SUV value might differ when the patient had longer uptake duration (26). Meanwhile, plasma glucose level was also important factor affecting the SUV value. Doubling the plasma glucose level might cause a fall in SUV value up to 40% (27). The liver uptake was also affected by the fasting plasma glucose. The variability of uptake in the liver was associated with higher blood glucose level (28). In this study, the 18F-FDG uptake time was controlled as strict as possible. However, there were occasions whereby the duration was violated due to unforeseen circumstances. The upper value of fasting blood sugar was set not to exceed 8.0 mmol/L.

Our study however has some limitations. The distribution of diagnoses within each group was unequal despite proper randomisation. The hyoscine group had the highest number of patients with colorectal cancer reaching almost half of its population (47.1%, n=32). Another 13 patients (19.1%) were diagnosed with gynaecological cancer in this group. In contrast, gynaecological cancer accounted to 20.0% (n=13) in the control group with only 3 patients (4.6%) diagnosed with colorectal cancer. This situation might explain the findings of high mean SUVmean of bowel and Bowel-to-Liver ratio in hyoscine group as the majority of patients in this group were diagnosed with colorectal and gynaecological cancers. There was no significant difference of mean SUVmean and bowel-to-liver ratio compared to the control group. Further subanalyses between hyoscine and control group after excluding patients with colorectal and gynaecological cancers were carried out to test the effect in reduction of bowel uptake. The subanalyses found that the control group has significantly lower mean SUVmean of bowel and B/L ratio ($p$=0.025 and $p$=0.002 respectively). It showed that the control group has lower 18F-FDG uptake compared to hyoscine group. These results were in contrast to the study conducted by Emmot et al. (21). We hypothesised the factors contributing to these results were due to many causes of poor 18F-FDG uptake such as presence of bowel flora, presence of pathological tissue within the gastrointestinal system that might caused different uptake level on PET-CT.

Various factors were considered upon making the conclusion. Among others, pattern of 18-F FDG uptake provided a clue to the underlying cause. Diffuse uptake was likely due to physiological while focal uptake were more suggestive of pathological (30). Therefore, focal suspicious uptake in the bowel warrants further evaluation (7).

Other than the pattern of bowel uptake, correlation with CT findings was helpful as well. Calcification, surgical sites, streakiness, bowel mass, thickening of bowel wall, adjacent enlarged lymph nodes among the CT findings related to pathology. Besides that, correlation with clinical data was also important to decide the likelihood of pathology.

PET-CT has high sensitivity to detect bowel malignancy, however it has lower specificity due to the potential pitfalls from bowel motility as well as low- attenuating lesions mimicking bowel uptake (31). It showed high 18F-FDG uptake in primary and recurrent colorectal cancer (32) with the smallest focal size of the primary lesion detected measuring 1.4cm (33). The most common cause for false positive interpretation of PET findings was physiological 18F-FDG uptake in displaced pelvic organs (34). There were many pitfalls detected in patients with known pelvic pathology including ovarian and endometrial diseases (35).

## CONCLUSION

Based on our study, there was no significant effect of Hyoscine-n-butylbromide in reducing physiological bowel uptake during 18F-FDG PET-CT in this study. Further study of involving other antispasmodic agents might be beneficial to be conducted to look for their effect on physiological bowel uptake during 18F-FDG PET-CT.

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## REFERENCES

1. Rohren EM, Turkington TG, Coleman RE. Clinical Applications of PET in Oncology. Radiology. 2004;231(2):305-32.
2. Hausegger K, Lind P, Reinprecht P, Igerc I, Beyer T. Advantages and limitations of FDG PET in the follow-up of breast cancer. Eur J Nucl Med Mol Imaging. 2004;Suppl 1:S125-34.
3. Moses WW. Fundamental limits of spatial resolution in PET. Nucl Instruments Methods Phys Res Sect A Accel Spectrometers, Detect Assoc Equip. 2011;648 Supplement 1: S236–S240.
4. Beyer T, Townsend DW, Brun T, Kinahan PE, Charron M, Roddy R, et al. A combined PET/CT scanner for clinical oncology. J Nucl Med. 2000;41(8):1369–79.
5. Von Schulthess GK, Steinert HC, Hany TF. Integrated PET/CT: Current Applications and Future Directions. Radiology. 2006;238(2):405–22.
6. Kostakoglu L, Hardoff R, Mirtcheva R, Goldsmith SJ. PET-CT Fusion Imaging in Differentiating Physiologic from Pathologic FDG Uptake. RadioGraphics. 2004;24(5):1411-31.
7. Bar-Shalom R, Yefremov N, Guralnik L, Gaitini D, Frenkel A, Kuten A, et al. Clinical performance of PET/CT in evaluation of cancer: additional value for diagnostic imaging and patient management. J Nucl Med. 2003;44(8):1200–9.
8. Moadel RM, Feng J, Freeman LM. PET/CT in the evaluation of colorectal carcinoma. Appl Radiol [Internet]. 2008. Available from: https://appliedradiology.com/articles/pet-ct-in-the-evaluation-of-colorectal-carcinoma.
9. Gontier E, Fourme E, Wartski M, Blondet C, Bonardel G, Le Stanc E, et al. High and typical 18F-FDG bowel uptake in patients treated with metformin. Eur J Nucl Med Mol Imaging. 2008;35(1):95-9.
10. Walker J, Jijon HB, Diaz H, Salehi P, Churchill T, Madsen Kl. 5-Aminoimidazole-4-carboxamide riboside (AICAR) enhances GLUT2-dependent

jejunal glucose transport: a possible role for AMPK. Biochem J. 2005;385(Pt 2): 485–491.
11. Boellaard R, Delgado-Bolton R, Oyen WJG, Giammarile F, Tatsch K, Eschner W, et al. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. Eur J Nucl Med Mol Imaging. 2014;42(2):328–54.
12. Blake MA, Rcsi FFR, Singh FA, Bindu N. Pearls and Pitfalls in Interpretation of Abdominal and Pelvic. 2006;1335–54.
13. Abouzied MM, Crawford ES, Nabi HA. 18F-FDG imaging: pitfalls and artifacts. J Nucl Med Technol. 2005;33(3):145-55.
14. Lee JC, Hartnett GF, Hughes BGM, Ravi Kumar AS. The segmental distribution and clinical significance of colorectal fluorodeoxyglucose uptake incidentally detected on PET-CT. Nucl Med Commun. 2009;30(5):333-7.
15. Chua YP. Kaedah dan Statistik Penyelidikan: Kaedah Penyelidikan. 2nd ed. Shah Alam: McGraw-Hill Education; 2011.
16. Azizah AM, Nor Saleha IT, Noor Hashimah A, Asmah ZA, Mastulu W. Malaysian National Cancer Registry Report 2007-2011, Malaysia Cancer Statistics, Data and Figure. Natl Cancer Institue. 2016;16:203.
17. Schoder H, Larson SM, Yeung HWD. PET/CT in oncology: integration into clinical management of lymphoma, melanoma, and gastrointestinal malignancies. J Nucl Med. 2004 Jan;45 Suppl 1:72S–81S.
18. Ripley B, Murdoch D. BUSCOPAN Tablets and Ampoules. 2008;96782(10):3–7.
19. Fuertes J, Montagut C, Bullich S, Coma MI, Mestre-Fusco A, Su6rez-Picera M, et al. Incidental focal uptake in colorectal location on oncologic FDG PET and PET/CT studies: Histopathological findings and clinical significances. Rev Esp Med Nucl Imagen Mol. 2015;34(2):95–101.
20. Jadvar H, Schambye RB, Segall GM. Effect of Atropine and Sincalide on the Intestinal Uptake of F-18 Fluorodeoxyglucose. Clin Nucl Med. 1999;24(12).
21. Emmott J, Sanghera B, Chambers J, Wong WL. The effects of N-butylscopolamine on bowel uptake: an F-FDG PET study. Nucl Med Commun. 2008;29(1):11-6.
22. Tytgat GN. Hyoscine Butylbromide A Review of its Use in the Treatment of Abdominal Cramping and Pain. Drugs. 2007;67(9):1343–57.
23. Keyes JWJ. SUV: standard uptake or silly useless value? J Nucl Med. 1995 Oct;36(10):1836–9.
24. De Groot M, Meeuwis APW, Kok PJM, Corstens FHM, Oyen WJG. Influence of blood glucose level, age and fasting period on non-pathological FDG uptake in heart and gut. Eur J Nucl Med Mol Imaging. 2005;32(1):98-101.
25. Kim CK, Gupta NC, Chandramouli B, Alavi A. Standardized uptake values of FDG: body surface area correction is preferable to body weight correction. J Nucl Med. 1994;35(1):164-7.
26. Hamberg LM, Hunter GJ, Alpert NM, Choi NC, Babich JW, Fischman AJ. The dose uptake ratio as an index of glucose metabolism: useful parameter or oversimplification? J Nucl Med. 1994;35(8):1308-12.
27. Langen KJ, Braun U, Rota Kops E, Herzog H, Kuwert T, Nebeling B, et al. The influence of plasma glucose levels on fluorine-18-fluorodeoxyglucose uptake in bronchial carcinomas. J Nucl Med. 1993;34(3):355-9.
28. Kubota K, Watanabe H, Murata Y, Yukihiro M, Ito K, Morooka M, et al. Effects of blood glucose level on FDG uptake by liver: a FDG-PET/CT study. Nucl Med Biol. 2011;38(3):347–51.
29. Murphy R, Doerger KM, Nathan MA, Lowe VJ. Pretreatment with diphenoxylate hydrochloride/atropine sulfate (Lomotil) does not decrease physiologic bowel FDG activity on PET/CT scans of the abdomen and pelvis. Mol Imaging Biol. 2009;11(2):114-7.
30. Culverwell AD, Scarsbrook AF, Chowdhury FU. False-positive uptake on 2-[18F]-fluoro-2-deoxy-D-glucose (FDG) positron-emission tomography/computed tomography (PET/CT) in oncological imaging. Clin Radiol. 2011;66(4):366–82.
31. Prabhakar HB, Sahani D V, Fischman AJ, Mueller PR, Blake MA. Bowel hot spots at PET-CT. Radiographics. 2007;27(1):145-59.
32. Yasuda S, Fujii H, Nakahara T, Nishiumi N, Takahashi W, Ide M, et al. 18F-FDG PET detection of colonic adenomas. J Nucl Med. 2001;42(7):989-92.
33. Abdel-Nabi H, Doerr RJ, Lamonica DM, Cronin VR, Galantowicz PJ, Carbone GM, et al. Staging of primary colorectal carcinomas with fluorine-18 fluorodeoxyglucose whole-body PET: correlation with histopathologic and CT findings. Radiology. 1998;206(3):755-60.
34. Even-Sapir E, Parag Y, Lerman H, Gutman M, Levine C, Rabau M, et al. Detection of Recurrence in Patients with Rectal Cancer: PET/CT after Abdominoperineal or Anterior Resection. Radiology. 2004;232(3):815–22.
35. Subhas N, Patel P V, Pannu HK, Jacene H a, Fishman EK, Wahl RL. Imaging of pelvic malignancies with in-line FDG PET-CT: case examples and common pitfalls of FDG PET. Radiographics. 2005;25(4):1031-43.