Differentiation of incidental intestinal activities at PET/CT examinations with a new sign: Peristaltic segment sign

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A B S T R A C T
Purpose: The aim of this study was to present the effect of the peristaltic segment sign for the differential diagnosis between malignant, physiological and gastrointestinal focal fluorodeoxyglucose (FDG) uptakes as an alternative method to maximum standardized uptake value (SUVmax).

Materials and methods: Gastrointestinal tract (GIT) sections of 823 FDG positron emission tomography/computed tomography (FDG-PET/CT) performed in our center were reviewed retrospectively. Images of these cases that have been reported for positive intestinal focal FDG uptake areas were included. Through the sectional images, any accompanying segment expanded with air just after or before the uptake area was marked as “positive peristaltism sign”. The cases were confirmed with endoscopy plus biopsy (n:42), endoscopy (n:5), laparotomy (n:1), transabdominal biopsy (n:1), enteroclysis (n:1), CT-colonoscopy (n:5), rectal contrast enhanced CT (n:4). Distinguishing features of the sign were analyzed statistically compared to the conventional method for differentiation of malignancy.

Results: Localized FDG uptake was reported in 59 of 823 cases. A SUVmax greater than 2.5 with intestinal wall thickening allowed the diagnosis of malignancy with sensitivity 33%, specificity 65%, positive predictive value 69% and negative predictive value 46%. The peristaltic segment sign, considered as a benign finding, increased the statistical values to 68%, 80%, 82% and 65%, respectively.

Conclusion: In case of gastrointestinal increased focal FDG uptake, the new parameter of peristaltic segment sign may differentiate the physiologic uptakes from the malignant ones more accurately than the conventional SUVmax.

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S I G N O   d e l   s e g m e n t o   p e r i s t á l t í c o:   u n   n e w  s i g n   d e l   e x a m e n   P E T / T A C    p a r a   e l   d i a g n ó s i t i c o   d i f e r e n c i a l   d e   l a s   a c t i v i d a d e s   i n t e s t i n a l e s   i n c i d e n t a l e s

R E S U M E N
Objetivo: El objetivo de este estudio fue presentar el efecto del signo del segmento peristáltico en el diagnóstico diferencial, maligno o fisiológico, de las captaciones focales de FDG detectadas en el tracto gastrointestinal (GIT) como un nuevo parámetro alternativo al SUVmax.

Material y métodos: Se revisaron retrospectivamente las secciones del GIT de 823 estudios PET/TC con FDG en los que se informaron la presencia de una captación focal intestinal de FDG. Se identificó como “signo peristáltico positivo” cualquier segmento intestinal que contuviera aire antes o después del área de captación de FDG. Los casos se confirmaron por endoscopia con biopsia (42), endoscopia (5), laparotomía (1), biopsia transabdominal (1), enteroclysis (1), colonoscopía virtual (5) y TAC abdominal con contraste rectal (4). Los rasgos característicos del signo se analizaron estadísticamente comparados al método convencional para diferenciar malignidad.

Resultados: La captación localizada de FDG se informó en 59 de los 823 casos. Un SUV mayor de 2.5 con engrosamiento de la pared intestinal permitió el diagnóstico diferencial de malignidad con sensibilidad 33%, especificidad 65%, valor predictivo positivo 69% y valor predictivo negativo 46%. El signo del segmento peristáltico, considerado como un hallazgo benigno, aumentó significativamente los valores a 68%, 80%, 82% y 65%, respectivamente.

Conclusión: Cuando se detecta un aumento focal de captación de FDG en el GIT, el signo del segmento peristáltico, como un nuevo parámetro, puede diferenciar la captación fisiológica de la captación maligna de forma más exacta que el SUV.

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Introduction

Physiological uptakes of $^{18}$F-FDG in the brain, myocardium, muscular tissues, pharyngeal mucosal surfaces and palatine tonsils can be recognized due to their various characteristics defined in the literature. However, activity uptakes in intestinal traces are more heterogeneous and require more information for discrimination. FDG is excreted in part through the gastrointestinal tract (GIT), with uptake in the distal esophagus, stomach, small intestine, and large intestine representing normal patterns of tracer distribution. GIT-originated physiological uptakes, which are frequently encountered on FDG-PET/CT examinations, are likely to cause mistakes during evaluations.

It is difficult to interpret positron emission tomography images in the absence of correlative anatomical images. FDG uptake may occur in some anatomical localization even without malignancy. FDG uptake traces can be localized by the anatomical information obtained from correlative CT sections. Such discriminations can be made more definitely by multimodality advanced evaluations or biopsies, particularly in the oncologic cases.

Diffuse increased FDG uptake in the GIT can be defined as physiologic and unrelated to the malignant process with relatively high certainty. These physiologic or benign sites of FDG uptake may be falsely attributed to a cancerous etiology. A focal, well-circumscribed intra-abdominal area of increased FDG uptake may, however, be interpreted as equivocal or suggestive of malignancy with an unclear location. Also, increased tracer activity in malignant lesions may be erroneously interpreted as unrelated to cancer.

Previous large-scale studies showed no significant difference between FDG uptake rates in terms of SUVmax of underlying malignant, premalignant and benign lesions in the focal uptake cases which occurred in unexpected localizations in GIT. Intense focal uptakes in the intestinal traces are seen by 1.3–3% among the cases that undergo FDG-PET/CT. These uptakes may be physiological or may occur due to the inflammatory, benign, premalignant or malignant lesions as well. Physiological uptakes are those which occur due to peristalsism and originate from the wall composed of smooth muscle, whereas non-peristaltic uptakes may originate particularly from the reactive uptake in the mural lymphatic tissue that spreads over the cecum and ileum traces.

This analysis included PET studies showing a single site of focally increased abdominal FDG uptake that was more intense than liver uptake and was localized by fused PET/CT to the GIT. The patients had no previous malignant involvement and no clinical or imaging suspicion of abnormalities in the same areas. Different from previous studies, in the present study, we additionally aimed to investigate the efficacy of a special sign, the so-called “intestinal peristalsism sign”, in discriminating physiological uptake from malignancy in the focal intestinal uptakes on PET/CT imaging.

This study was initiated by a series of cases in which focal intra-abdominal FDG uptake that had been localized by PET/CT to the GIT, which had no previously known morphologic lesions, was proven on follow-up to be of malignant or premalignant etiology. The purpose of the present study was to evaluate the effect of the peristaltic segment sign in differentiation of the malignant and physiologic localized FDG uptakes through the GIT as a new parameter.

Material and methods

The GIT traces of 823 patients (577 males and 246 females), who had undergone FDG-PET/CT examination because of malignancy in a special health center, were reviewed. The mean age of the cases was 49 years (ranged from 11 to 89 years). Distribution of the tumor types among cases was as follows: 396 pulmonary tumor, 135 lymphoma, 84 colorectal carcinoma, 37 laryngeal tumor, 27 nasopharyngeal tumor, 23 cervical tumor, 13 ovarian tumor, 9 esophageal tumor, 8 melanoma, 6 soft tissue sarcoma, 5 urine bladder tumor, 4 endometrial tumor, 4 non-pulmonary carcinoid tumor, 4 breast tumor, 2 small intestine tumor with reported pathologic FDG uptake and another 66 cases reported to have normal level of FDG uptake thorough the body. On the images of these cases, the foci that FDG uptake had been identified and the reported intestinal foci were retrospectively evaluated. Being aware of the diagnoses of the cases, reviews were performed retrospectively on multi-display workstations with multi-planar reformatting focusing on the GITs that display abnormal uptake on minimum intensity projection. After reviewing the images and reports of all patients, the cases with localized activation in the stomach, duodenum, jejunum, ileum and colon traces were recorded. Focal activities shorter than a segment in the stomach and duodenum, non-longitudinal, nonlinear focal uptakes in the jejunum and ileum, and focal uptakes limited to maximum one centimeter of the cecum, ascendant colon, hepatic flexure, transverse colon, splenic flexure, descending colon, sigmoid colon, and rectum segments in the colon were considered as localized activity and included in the study.

Long segmental uptakes, focal or linear uptakes, and the activities that did not show superposition with the intestinal wall on CT fusion images were excluded from the study. The field with increased FDG activity was taken into consideration if it was of a more intense nature than the liver and if the SUVmax value was higher than 2.5 units.

This low SUVmax value, although being nonspecific, is selected with the purpose of highly sensitive detection of malignant foci.

The “peristalsism sign” was considered positive (for benignity) in the presence of a bowel loop which has been expanded with air and located just proximal or distal to the focused (FDG-affinitive) segment (Fig. 1).

Standard protocol that was applied to all cases investigated for malignancy

- Colon opacification was provided with 1000 ml of 1500 ml oral contrast solution prepared using 40 ml nonionic contrast that was given 12 h before the procedure.
- The stomach and the small intestine were opacified with 500 ml oral contrast solution given an hour before the procedure.
- Intravenous injection of 13–15 mCi FDG 40–60 min before the procedure.
- The patient rested under normal conditions 1 h before the examination.
- CT scan: cranio-caudal, with a section thickness of 3.75 cm, 1.75 pitch, 10 mm collimation, 120 peak kV, and 100–120 mA.
- PET study direction was adjusted as caudo-cranial 2D.

System

- PET and 16-detector CT (Discovery ST PET/16 slice CT fusion system HPOWER 60; General Electric Medical Systems, Milwaukee, WI).
- A section thickness of 3.75 mm, 2D-PET.
- Multi-display workstations: multiplanar reconstruction (MPR), maximum intensity projection (MIP), PET/CT fused images could be simultaneously evaluated.

The presence or absence of the sign was investigated within the uptake trace in the GITs of 59 cases. Intestinal foci, showing an uptake more intense than the liver localized and measured. And foci with a SUVmax ≥ 2.5 were included in the study. Endoscopic evaluation (n=47) and endoscopic biopsy (42 of 47 cases) data of the cases were available with gastric-duodenal-colonic uptakes, exploratory laparotomy data of a case diagnosed with small
The obtained data by testing according to the presence or absence of the “peristaltic segment sign” was used; the sensitivity, specificity, PPV, NPV, and accuracy of the sign in discriminating malignant from benign intestinal uptake by itself were found 68%, 80%, 82%, 65%, and 73% respectively (Table 3).

Discussion

PET/CT imaging provides useful data in detecting malignant diseases and in the discrimination of malignant vs. benign lesions. \(^3\)\(^,\)\(^9\)

It is known that lesions with increased FDG uptakes with high SUV\(_{\text{max}}\) values that mimic malignancies are likely to occur in various localizations in the body. \(^2\)\(^,\)\(^7\)\(^,\)\(^8\) The GIT is one of the localizations in which local incidental uptakes are frequently detected. \(^5\)\(^,\)\(^8\)–\(^11\)

Although the majority of focal gastric and small intestinal uptakes are associated with benign physiological activities, further evaluation is required in colonic focal uptakes. \(^5\)\(^,\)\(^8\)\(^,\)\(^11\)

In the present study, we tried to discriminate malignant focal FDG uptakes from the benign ones, which were retrospectively investigated throughout the entire intestinal system and were well localized via “peristaltism sign” benefiting from the multislice characteristic of the fused CT system. In this context, focal activities throughout the intestinal system were considered as localized activity and included in the study. The “peristaltism sign” was considered positive in the presence of a bowel loop which had been expanded with air and located proximal or distal to the pathologic (FDG-affinitive) intestinal segment.

Colonoscopies of the cases with incidental, focal colonic FDG activity revealed organic pathologies (mucosal abnormalities, adenoma, or carcinoma) in various rates ranging from 71% to 95%. \(^6\)\(^,\)\(^8\)–\(^8\)

Increments in localized peristaltism due to partial obstruction caused by the lesion may be responsible for the focal uptake in the colon and concurrent peristaltism sign. Kamel et al. evaluated the probability of an organic pathology in overall incidental focal uptakes of the GIT, which could change the future diagnostic and therapeutic steps. He found organic pathology in 28% of the cases with intestinal focal uptake detected on PET/CT. \(^7\)

The rate was also consistent with the rate (27%) defined in our study. In literature, there are studies about the efficacy of SUV\(_{\text{max}}\) measurements in the differentiation of etiological factors of focal uptake. \(^5\)\(^,\)\(^12\)

whereas there are also studies emphasizing that discrimination of malignant vs. benign lesions could not be made properly by
measuring uptake value alone and that further evaluation is required.\(^{13}\) Moreover, Isreal et al. in their review displayed that there was no statistically significant difference between physiological uptake and incidental uptake occurring due to premalignant–malignant lesions in terms of SUVmax values of incidental uptake in the intestinal trace. This has shown that SUVmax has no efficacy in discriminating malignity in a focal incidental uptake.\(^{5}\) The number of cases with benign lesions that have substantially high SUVmax is not low at all. In the present study, substantially low SUVmax values were included. Matched sections of peristalsis sign were found, superposed, and accordingly, the definite discrimination of intestinal vs. non-intestinal uptakes has been made.

It is known that intestinal uptakes exist in a wide spectrum including diffuse, segmental and focal uptake. Unifocal uptakes are seen mostly in Barret’s esophagus and tubulovillous adenomas, whereas multifocal, segmental or diffuse intestinal uptake is seen in inflammatory bowel diseases.\(^{14-18}\) Several studies emphasized that long segmental uptakes are caused by benign entities (physiological or inflammatory or post RT colitis).\(^{9,10}\) Therefore, recent studies have been targeted to discriminate malignity via new parameters taking the cases with focal uptakes into consideration.\(^{19}\) Gluecker et al. reported that dependent intestinal mucosal–mural FDG uptake occurs frequently due to contact with stool and irritation. The same study emphasized that nondependent incidental focal intestinal uptakes are more meaningful and require further evaluation.\(^{20}\) Because discrimination of dependent vs. non-dependent methods might be unable to define the origin of an FDG shining focus in the presence of uptake in the collapsed small intestine or in colonic loop trace, we did not use it as a criterion.

Artefactual uptakes in the GIT may be reduced by lowering the amount of swallowing and providing colon cleansing with iso-osmotic solution.\(^{21}\) In order to eliminate luminal or mural pathology of the colon, methods that discriminate the wall from the lumen are required. For this procedure, the lumen and the wall can be clearly exposed with a rectal contrast enema that would expand the entire colon. Otherwise, peristaltic segments or the segments with insufficient filling might not be visualized optimally. Since rectal contrast use is unlikely during PET/CT imaging, it can be used just in the suspected cases, if required, as the next evaluation step. Additional late phase imaging protocols may be needed especially for gastric lesions. Gastric focal uptakes could not be differentiated from the activities in the same lodge such as pancreatic tile uptake and lymph node uptake of the splenic medial pole.\(^{2}\)

The present study revealed an underlying malignancy by a high rate such as 27% at these incidental intestinal uptake foci, and discriminated the malignancies more sensitively than the conventional method (33% vs. 68%). In general, literature revealed that endoscopic correlation is required to eliminate malignancy in the cases of esophageal uptakes. As a result, histopathological sampling is in question to eliminate premalignant lesions even for benign activities, in which uptake occurs at Barret’s point.\(^{9,22}\) We already have excluded the esophagus for the indicator of sign, since an active peristalsis would not be in question except for nutrition.

In the present study, we investigated the presence of a peristaltic segment sign for the stomach and duodenum considering the existence of low-grade adenocarcinomas, which are likely to have low SUVmax rates. We had high rates of false negativity (approximately 60%) in the cardia. This was attributed to the point’s being the Barret’s point, and peristalsis–associated changes’ being unable to be visualized on CT sections, despite the presence of premalignant and malignant lesions. Since neither the cardia nor the distal segment of the esophagus could be evaluated in terms of presence or absence of peristalsis because of the same problem, such a high false negativity has been considered as directive, rather than a handicap, for endoscopy to eliminate the premalignant lesions.

In the small-intestine-related uptakes, the peristalsis sign was used efficiently in 12 cases where the focal uptakes in the jejunoileal segments have been evaluated, except for a case with false positive and another case with false negative, for the discrimination of malignant vs. benign conditions.\(^{9,23,24}\)

### Table 1

<table>
<thead>
<tr>
<th>Distribution of the findings in the gastrointestinal system according to the criteria defined in the methodology.</th>
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<tbody>
<tr>
<td><strong>Gastro-Duodenal</strong> (n = 19)</td>
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<tr>
<td>Cardio-esophageal junction (n = 5)</td>
</tr>
<tr>
<td>Antrum (n = 11)</td>
</tr>
<tr>
<td>Duodenal bulbus (n = 2)</td>
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<tr>
<td>2nd duodenal segment (n = 1)</td>
</tr>
<tr>
<td>Malignant: 7 (Adenocarcinoma)</td>
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<tr>
<td>Benign: gastritis, duodenitis, hypertrophic rugae</td>
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### Table 2

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<th>Data obtained from the evaluation by measuring the SUVmax levels (conventional method).</th>
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<tr>
<td><strong>Suspicious malignity and advice for further evaluation in case of measuring &gt; 2.5 SUVmax values</strong></td>
</tr>
<tr>
<td>Prediagnoses</td>
</tr>
<tr>
<td>Benign: 20</td>
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### Table 3

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<th>Sensitivity values of the special sign (peristalsism sign), which has been used in the discrimination of malignant vs. benign uptakes.</th>
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<tr>
<td><strong>True positive</strong></td>
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<tr>
<td><strong>False positive</strong></td>
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<tr>
<td>---</td>
</tr>
<tr>
<td>Antrum (n = 1)</td>
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<tr>
<td>Ileocecal valve (n = 1)</td>
</tr>
<tr>
<td>Jejunum (n = 1)</td>
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<tr>
<td>Sigmoid colon (n = 2)</td>
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</table>
FDG activity within the colon is typically heterogeneous. There is higher uptake within the cecum and right colon due to the higher concentration of lymphoid tissue in this region. Diffuse uptake is usually associated with infectious or inflammatory colitis. Focally increased FDG uptake within the bowel has been described for both malignant and benign processes. PET-CT findings in these cases may be diagnostic, since the CT manifestations of these entities are well described in the literature as appendicitis, diverticulitis or nonspecific uptakes. On the other hand, although FDG-PET has been shown to be highly sensitive in detecting colorectal cancer it has low specificity because of physiological uptakes as well as inflammatory causes.

Among the present cases, the discrimination of malignant vs. benign lesions could be made in a total of 28 focal colonic uptake cases, except for three false positive and six false negative cases, regardless of the frequency of malignant or benign underlying pathologies. Discrimination of malignant vs. benign lesions could be achieved in 19 of 28 cases (seven malignant and 21 benign) via the sign without using any other auxiliary method or modality.

False negativity means both sign and malignancy positive, secondary to the increased peristalsim probably caused by partial obstruction. On the other hand, false negativity means absence of the malignity and the sign together. In our study, the false positivity rate of the sign was more common in the GIT except the colon, whereas the false negativity rate was higher in the colon, likely due to less peristalsism. The water-soluble iodine-based hyperosmolar contrast agent, which had taken a night before to provide intestinal luminal opacification might have increased the rate of false negativity by inducing the increment in the peristalsism.

Some limitations of this study are: (1) the retrospective feature; (2) limited number of the cases; (3) the absence of dynamic imaging (early + late phase); and (4) uptake images caused by the attenuation difference (pseudo-uptake) emerged from the iodine content of the oral contrast agents. These artifacts could be easily solved correlating with CT section. One major controversy of our study was the decrease in peristaltic movements at the localization of the malignancy. The transmural expansion of malignancy and invasion of neurogenic plexus leads to a decrease in peristaltism in these affected segments. We can use the peristaltism sign conversely in these cases.

We could not found dynamic study results of the all cases in this retrospective study. But, we believe that addition of the dynamic examination to the protocol will increase the sensitivity of our sign in detecting the pathologic FDG foci. In the other hand, although selecting very low SUVmax value with the purpose of sensitive detection of malignant foci may increase the number of false positive cases, we did not accept it as a serious limitation. In our study, for 2 cases, the presence of intraluminal air density in small bowel helped us to evaluate the peristaltism sign. But it may be a problem to find air thorough the small intestines in all examinations. Expansion of lumen by liquid contents may also be used as marker of the peristaltism sign instead of luminal air.

In summary, PET/CT examination, focal FDG uptakes may be in question throughout the entire GIT. In the present study, discrimination of malignancy can be achieved by 33% sensitivity and by 65% specificity when the focal uptake accompanied by pathological wall thickening on CT sections was considered as a criterion; in contrast, the sensitivity and specificity have been increased up to 68% and 80% respectively when the peristaltism sign was used. In case of detecting focal-segmental FDG uptakes in the GIT, even incidental, SUVmax exceeding 2.5 but which has not been accompanied by the peristalsism sign, should certainly be further evaluated by endoscopic tests.

As a conclusion, the peristaltic segment sign is in favor of benignity, and is more sensitive than the methods used for benign–malignant differentiation such as SUVmax and luminal wall thickening.

Conflict of interest

The authors have no conflict of interest to declare.

References