REVIEW ARTICLE

Present and future of FDG-PET/CT in ovarian cancer

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Abstract Integrated FDG-PET/CT has been used successfully for the diagnosis, staging, restaging, therapy monitoring and prognostic prediction of ovarian cancer as well as various other malignant tumors. Compared with conventional PET/non-contrast CT images, combined PET/ contrast-enhanced CT images with intravenous iodine contrast medium and sufficient radiation dose may contribute to a more accurate diagnosis with higher confidence. In the future, tracers other than FDG and integrated PET/ MRI will be realized. We herein review the place and role of FDG-PET/CT in the management of ovarian cancer, discussing its usefulness and limitations in the imaging of these patients.

Keywords FDG \cdot PET/CT \cdot Ovarian cancer \cdot Staging \cdot Restaging

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Introduction

Ovarian cancer is the second most common cancer of the female genital tract, but accounts for over half of all deaths related to gynecologic neoplasms [1]. The disease typically has vague symptoms that are often ignored, and it is therefore usually diagnosed at an advanced stage. Prognosis is strongly related to the stage of disease at initial diagnosis. The overall survival at 1 and 5 years is 75 and 45%, respectively [2]. The 5-year survival is 92% for the localized stage, but only 19% are detected at this stage; 71% are detected when there is regional spread, and 30% are detected when there are distant metastases [2].

In the late 1990s, positron emission tomography (PET) with 2-[¹⁸F]fluoro-2-deoxy-D-glucose (FDG), which exploits the increased utilization of glucose by malignant cells and their high uptake of glucose, opened a new field in clinical oncologic imaging. Originally, PET lacks anatomic information, and precise localization of any suspicious lesions may be difficult. Recently, integrated PET/ CT, in which a full-ring-detector clinical PET scanner and multidetector row helical CT scanner are combined, has made it possible to acquire both metabolic and anatomic imaging data using a single device in a single diagnostic session and provides precise anatomic localization of suspicious areas of increased FDG uptake [3]. In the clinical setting, FDG-PET/CT has achieved a significant improvement in diagnostic accuracy and exerted a considerable impact on patient management including diagnosis, staging, optimization of treatment, restaging, therapy monitoring, and prognostic prediction of various malignant tumors [4, 5]. We herein review the current and future role of FDG-PET/CT in the management of ovarian cancer, discussing its usefulness and limitations in the imaging of these patients.

Primary diagnosis/differentiation between malignant and benign ovarian tumors

At present, the diagnosis of primary ovarian cancer is principally based on gynecological examination, assay of specific serum tumor markers including CA125, and radiological imaging techniques such as transvaginal sonography (TVUS), CT and MRI. Contrast-enhanced MRI in the pelvis is an imaging modality with excellent spatial and contrast resolution and recently good diagnostic performance of 92–100% sensitivity and 76–94% specificity has been reported for differentiation between malignant and benign ovarian tumors [6, 7].

Three researchers reported a relatively good diagnostic accuracy of differentiating malignant and benign ovarian tumors by PET/CT showing 87-100% sensitivity, 74-100% specificity and 92-97% accuracy (Table 1) [8-10]. Although Nam et al. demonstrated that PET/contrastenhanced CT (PET/ceCT) with intravenous iodine contrast medium is superior to enhanced MRI and is useful in revealing metastatic ovarian cancer and other co-existing malignant tumors [10], more data are needed to better define the role of PET/CT in the primary diagnosis of ovarian cancer. PET/CT hardly detects low-grade and early adenocarcinomas and borderline tumors with small volume or low cellular density, and false-positive results also have been reported with serous cystadenoma, endometrioma, teratoma, and fibroma. These facts that FDG is a nonspecific radioactive tracer for ovarian cancer, even with the spatial limited resolution of currently available PET/CT systems, make detection of microscopic lesions still challenging.

Initial staging

Accurate staging at the time of diagnosis is extremely important in order to plan adequate therapy and is the most important prognostic factor in ovarian cancer [11]. Ovarian cancer is typically staged by exploratory laparotomy at the time of primary debulking in accordance with the recommendations of the International Federation of Gynecology and Obstetrics. For preoperative staging of ovarian cancer, MRI and CT have been accepted as being the most useful imaging techniques for the assessment of pelvis and chest/ abdomen, respectively. Ricke et al. reported that enhanced MRI had good accuracy for diagnosing pelvic and abdominal cancer spread in patients with ovarian cancer, showing 71–87% sensitivity and 44–87% specificity for peritoneal dissemination, and 64% sensitivity and 75% specificity for pelvic and para-aortic LN metastases [12].

Three researchers have reported that radiologic staging by PET/CT was consistent with surgical staging in 69-78% of patients [9, 10, 13]. Kitajima et al. [13] demonstrated that PET/ceCT had better initial staging than enhanced CT, and more data are needed to better define the role of PET/ ceCT in the initial staging of ovarian cancer. High-resolution MRI with contrast material and diffusion-weighted image (DWI) may remain to be the best imaging technique for initial primary tumor staging regarding invasion to the surrounding organs and dissemination at present. In combination with conventional MRI, DWI and apparent diffusion coefficient (ADC) findings provide additional information such as detecting tiny lesions and disseminated lesions in patients with ovarian cancer [14, 15]. So, FDG-PET/CT might be complementary to conventional staging procedures and not a replacement for MRI. Nevertheless, the assessment of retroperitoneal LN metastasis by PET/ CT may be superior to that of MRI. The limitation of the size-based characterization (the most accepted criterion is whether the short-axis diameter exceeds 10 mm or not) of MRI and CT is well known. PET is a functional method based on the increased glucose metabolism of cancer cells, regardless of node size, and PET/CT can often detect relatively tiny metastatic LN from 5 to 9 mm in size. Kitajima et al. reported that overall node-based sensitivity, specificity, and accuracy of enhanced CT alone for detection of pelvic and para-aortic LN metastases were 37.5, 100, and 86.5%, respectively, and those of PET/ceCT were 81.3, 96.6, and 93.2%, respectively [13].

Table 1 Results of the studies using FDG-PET/CT in evaluation of differentiation between malignant and benign ovarian tumors

Authors	Year	No. of patients	Sen (%)	Spe (%)	Acc (%)	Modality
Risum et al. [8]	2007	97 (M:57, B:40)	100	93	97	PET/ceCT
Castelluci et al. [9]	2007	50 (M:32, B:18)	87	100	92	PET/CT
			90	61	80	TVUS
Nam et al. [10]	2009	133 (M:108, B:25)	98	74		PET/ceCT
			95	46		Enhanced MRI
			90	53		TVUS

M malignant ovarian tumor (ovarian cancer), B benign ovarian tumor, Sen sensitivity, Spe specificity, Acc accuracy, TVUS transvaginal sonography, PET/ceCT PET/contrast-enhanced CT

Generally, the role of FDG-PET/CT in oncology has mainly been to assess LN (N) and distant metastasis (M), rather than to determine tumor extension and its relationship with surrounding tissues (T). PET/CT has an effective role in staging for patients with advanced stage, providing useful information on extrapelvic sites, such as supraclavicular LN, para-aortic LN metastasis, peritoneum, omentum, bone and muscle. An example of PET/ceCT images obtained for initial staging of a patient with ovarian cancer, peritoneal dissemination and para-aortic LN metastasis is shown in Fig. 1.

Tumor recurrence/restaging

Standard treatment of advanced ovarian cancer includes aggressive cytoreductive surgery followed by platinum- or taxane-based chemotherapy. Although neoadjuvant chemotherapy followed by surgical debulking has been used to

Fig. 1 A 57-year-old woman with primary ovarian cancer with peritoneal dissemination and retroperitoneal lymph node metastasis. Maximum intensity projection (MIP) of PET shows multiple uptakes in the pelvis and abdomen (a). PET/contrastenhanced CT shows a multilocated cystic ovarian mass with mural nodules and solid component showing intense FDG uptake of this solid component (b). PET/contrastenhanced CT can easily detect para-aortic LN metastases and multiple tiny peritoneal dissemination (c, d arrows)

improve the outcome, this can be achieved only in patients with complete or nearly complete response to neoadjuvant therapy [16].

In approximately 20–30% of patients with early-stage disease and 50–75% of those with advanced disease who obtain a complete response after first-line chemotherapy, disease will ultimately recur [17]. Few formal guidelines exist on the surveillance of these patients, and the type and timing of the examinations that should be performed. The clinical follow-up generally includes measurement of the serum cancer antigen CA-125 level, physical examination, and imaging examinations.

CT and MRI are the most commonly used imaging modalities in patients with suspected recurrent ovarian cancer, but small local recurrence, LN metastasis, small dissemination, and bone/muscle metastasis are difficult to detect with CT and MRI. Because PET/CT has high contrast between tumor and background, it has been reported to have better diagnostic accuracy in these clinical situations.



There have been many reports discussing the usefulness of FDG-PET/CT for restaging patients with ovarian cancer [18–34]. When the gold standard was clinical follow-up including radiological imaging, the diagnostic accuracy of PET/CT was very high with 73-100% sensitivity, 71-100% specificity, and 83-100% accuracy in patient-based analysis (Table 2) [18–29]. However, when the gold standard was histopathology by surgery, the diagnostic accuracy of PET/ CT tended to be poorer and it was reported that the sensitivity, specificity, and accuracy of patient-based analysis were 53-83, 40-86, and 63-82%, respectively, and those of lesion-based analysis were 41-78, 75-95, and 72-77%, respectively (Table 3) [30-34]. The discrepancies in these values between the clinical follow-up and the surgical histopathology as a gold standard may partly depend on the resolution of the PET/CT systems used and partly on the size of microscopically small lesions from which few positron/ gamma rays are emitted.

Three authors reported that the performance of PET/ ceCT is significantly superior to that of enhanced CT [18, 19, 26]. Kitajima et al. [18] demonstrated PET/ceCT to be slightly superior to PET/non-contrast CT for restaging. An example of PET/ceCT images obtained for restaging a patient with tiny peritoneal dissemination and tiny retrocaval LN metastasis is shown in Fig. 2. Generally, PET/CT provides useful information about patient management in various malignant tumors, because the findings of PET/CT resulted in a change of management by initiating an unplanned treatment, changing the treatment plan, or obviating the need for planned treatment. Several authors reported that the percentage of cases in which clinical treatment was changed on the basis of PET/ CT findings in patients with suspected recurrence/metastasis was 25–59% (Table 3). Kitajima et al. [18] reported that the findings of PET/ceCT resulted in a change of management for 39% of patients, and affected the management of 12% of patients diagnosed by enhanced CT and 2% of patients diagnosed by PET/non-contrast CT.

Because no standard recommendations have been issued on the use of diagnostic imaging, second-look laparotomy has sometimes been recommended to assess tumor status after initial debulking surgery and first-line chemotherapy. However, second-look laparotomy is an invasive and expensive procedure, and 35% of patients with negative findings experience recurrence within 1 year of the procedure [35] and the procedure is of no help in detecting distant metastasis except in the pelvic cavity. Therefore, there is a growing acceptance that noninvasive imaging evaluations of disease status provide better options. To date, PET/CT is the most accurate imaging modality for

 Table 2
 Results of the studies using FDG-PET/CT in evaluation of recurrence/metastases in patients with ovarian cancer with clinical follow-up including radiological imaging findings as the standard reference

Authors	Year	Ν	Location	Contrast medium	Sen (%)	Spe (%)	Acc (%)	Modality	Management (%)
Hauth et al. [19]	2005	19	Whole	Oral + IV	100	100	100	PET/ceCT	
					100	100	100	Enhanced CT	
					73	100	84	PET	
Nanni et al. [20]	2005	41	Whole	NA	88	71	85	PET/CT	
Simcock et al. [21]	2006	56			NA	NA	NA		57
Chung et al. [22]	2007	77	Whole	Oral	93	97	95	PET/CT	25
Mangili et al. [23]	2007	32	Abd	NA	91	NA	NA	PET/CT	44
					63	NA	NA	Enhanced CT	
Thrall et al. [24]	2007	34	Whole	NA	95	100	NA	PET/CT	
Kim et al. [25]	2007	36	Abd	NA	73	93	81	PET/CT	
Sebastian et al. [26]	2008	51	Whole	Oral + IV	97	80	92	PET/ceCT	
					92	60	83	Enhanced CT	
Iagaru et al. [27]	2008	43	Whole	NA	88	88	88	PET/CT	
Soussan et al. [28]	2008	29	Whole	Oral	93	NA	NA	PET/CT	34
					76	NA	NA	Enhanced CT	
Kitajima et al. [18]	2008	132	Whole	IV	79	91	85	PET/ceCT	
					74	91	83	PET/CT	
					61	85	73	Enhanced CT	
Fulham et al. [29]	2009	90	Whole	NA	NA	NA	NA	PET/CT	59

N number of patients, NA not available, Whole whole body was assessed, Abd abdomen and pelvis was assessed, IV intravenous contrast material is used for CT portion of PET/CT, Oral oral material is used for CT portion of PET/CT, Sen sensitivity, Spe specificity, Acc accuracy, PET/ceCT PET/contrast-enhanced CT

surgery	as the standard reference	ce			
surgery	as the standard reference	ce			

Authors	Year	No. of patients	Contrast medium	Sen (%)	Spe (%)	Acc (%)	Based-analysis
Makhija et al. [30]	2002	8	NA	62	NA	NA	Patient
Bristow et al. [31]	2003	22	NA	83	75	82	Patient
				61	95	72	Lesion
Sironi et al. [32]	2004	31	NA	53	86	68	Patient
				78	75	77	Lesion
Pannu et al. [33]	2004	16	NA	73	40	63	Patient
Bristow et al. [34]	2005	14	Oral	41	94	72	Lymph node

Number number of patients, NA not available, Oral oral material is used for CT portion of PET/CT, Sen sensitivity, Spe specificity, Acc accuracy



Fig. 2 A 61-year-old woman with recurrent lesions consisting of tiny peritoneal dissemination and tiny LN metastasis. MIP of PET shows two abnormal uptakes in the abdomen (a). Although the contrast-

restaging, especially for assessment of peritoneal dissemination, LN metastasis, local recurrence, and bone/muscle metastasis. Gu et al. reported a meta-analysis comparing techniques for detection of recurrence that PET/CT (sensitivity, 91%; specificity, 88%) performed better than CT (sensitivity, 79%; specificity, 84%) or MRI (sensitivity, 75%; specificity, 78%) [36]. Moreover, PET/CT can also evaluate the whole body in a single examination. PET/CT may have the greatest utility in the situation in which CA-125 levels are rising and conventional imaging studies show negative or equivocal findings. Smith et al. [37] used a simulation analysis to compare the cost of managing recurrent ovarian cancer with and without the use of FDG-PET. Evaluation of patients with FDG-PET decreased unnecessary laparotomies from 70 to 5% of patients. Cost savings per patient ranged from \$1,941 to \$11,766.

enhanced CT component of PET/contrast-enhanced CT cannot detect abnormal findings (**b**, **c**), PET/contrast-enhanced CT can easily detect tiny peritoneal dissemination (**d**) and tiny retrocaval LN metastasis (**e**)

Kim et al. [38] compared the prognosis of 55 patients evaluated either by FDG-PET or second-look laparotomy after cytoreductive surgery and adjuvant chemotherapy. PET had a prognostic value similar to that of second-look surgery. There was no significant difference in progressionfree interval (28.8 vs. 30.6 months) or disease-free interval in the PET-negative group (40.5 vs. 48.6 months). They suggested that FDG-PET can be used to replace secondlook laparotomy, but further investigations of larger groups of patients are needed.

Treatment monitoring

At present, conventional anatomical imaging is commonly used to evaluate the response to treatment by evaluating changes in tumor size as for other tumors. However, CT and MRI are limited in detecting the response early after the initiation of therapy because anatomic changes are usually seen only 2 or 3 months after therapy. Metabolic changes often precede morphologic changes in tumor response and therefore FDG-PET can demonstrate this response sooner than CT and MRI. FDG-PET is thought to be useful in that a non-responder to chemotherapy can be picked up at an earlier stage during chemotherapy. Identification of nonresponders would significantly improve patient management by reducing the use of ineffective therapies, preventing adverse effects, reducing the delay before administering more effective treatment and minimizing costs.

Nishiyama et al. demonstrated that FDG-PET derived parameters, including SUV and percentage change, have the potential to predict response to chemotherapy or chemoradiotherapy in patients with advanced gynecologic cancer (uterine cancer, n = 13; ovarian cancer, n = 8) [39]. Based on histopathologic analysis of the specimens obtained at surgery, 10 patients were found to be responders and 11 to be nonresponders. When an arbitrary SUV of 3.8 was taken as the cutoff for differentiating between responders and nonresponders after therapy, FDG-PET showed a sensitivity of 90%, a specificity of 63.6%, and an accuracy of 76.2%. When an arbitrary percentage change of 65% was taken as the cutoff, FDG-PET showed a sensitivity of 90%, a specificity of 81.8%, and an accuracy of 85.7%. An example of PET/ceCT images obtained for treatment monitoring patients with primary ovarian cancer and peritoneal dissemination before and after chemotherapy is shown in Fig. 3.

Prognostic prediction

The prognostic value of PET or PET/CT remains insufficiently investigated in ovarian cancer, and further evaluation in prospective clinical trials will be required to assess the prognostic value of PET/CT in ovarian cancer.

Avril et al. [40] demonstrated that FDG-PET may be promising for the early prediction of the response to chemotherapy and for prediction of the response after the completion of chemotherapy. They demonstrated a significant correlation between changes in tumor tracer after the first and third cycles of chemotherapy, but not with conventional clinical or CA-125 response criteria. A higher rate of complete tumor resections was achieved in metabolic responders [defined as >20% reduction in standard uptake value (SUV) after the first cycle and >50% after the third cycle] than in nonresponders, and macroscopically tumorfree surgery was achieved in 33% of metabolic responders, compared with only 13% of nonresponders. Metabolic responders had a longer median overall survival than did nonresponders. By using a threshold for decrease in SUV from baseline of 20% after the first cycle, median overall survival was 38.3 months in metabolic responders, compared with 23.1 months in metabolic nonresponders. At a threshold of 55% decrease in SUV after the third cycle, median overall survival was 38.9 months in metabolic responders, compared with 19.7 months in nonresponders.

Kurosaki et al. [41] demonstrated that the prognosis (2-year survival) of patients with positive FDG-PET findings was less favorable than that of patients with negative findings. However, over the mean extended observation period of about 2.5 years, no significant difference was seen between the 2 groups.

Risum et al. [42] demonstrated that when FDG-PET/CT is used for preoperative evaluation of patients with advanced ovarian cancer (stage III and IV), the number of patients diagnosed with stage IV increases and stage migration is likely to occur and that the median overall survivals of PET/CT stage III and stage IV were 30.5 and 29.9 months, respectively. They also reported that using univariate analysis, PET/CT stage IV (p = 0.03), complete debulking (no macroscopic residual tumor) (p = 0.002), and performance status (p = 0.04) were statistically prognostic variables, whereas using multivariate Cox regression analysis, complete debulking was the only statistically significant independent prognostic variable (p = 0.02).

PET/contrast-enhanced CT

Given the spatial resolution of 4-6 mm of currently available PET/CT systems, and the fact that FDG is a non-tumorspecific tracer, the detection of microscopic lesions remains challenging. To overcome these limitations of conventional PET/CT, more recently, PET/contrast-enhanced CT (PET/ ceCT) with intravenous iodine contrast medium and sufficient radiation dose has been gradually introduced in the clinical setting. The use of contrast-enhancement would be expected to increase diagnostic confidence, as differentiation between adjacent soft-tissue structures and accurate localization and extension of tumors is often difficult with unenhanced CT images. If there is a high index of suspicion by PET in the pelvis, contrast-enhanced and high-dose CT of inline PET/CT could accurately differentiate pathological uptake of FDG by LNs from physiological uptake by vessels, bowel, or ureter compared with unenhanced and low-dose CT. In fact, many of these fused images are used for the diagnosis of various malignant tumors including gynecologic cancer in our institutions [13, 18, 43–45]. Although the latest CT-based attenuation correction algorithms reduce the overestimation by de-emphasizing highdensity areas due to contrast medium, without significant errors in quantification [46], in many centers as well as our

Fig. 3 A 58-year-old woman with neoadjuvant chemotherapy Although MIP of PET before the chemotherapy shows multiple abnormal uptakes in the pelvis and abdomen (a), MIP of PET after the chemotherapy shows almost complete disappearance of abnormal uptake (d). Tiny uptake in the pelvis was proved to be physiological uptake of the bowel by PET/contrastenhanced CT (not shown). Although axial T2-weighted MRI before the chemotherapy shows an ovarian tumor with solid and cystic component and multiple peritoneal disseminations (b), T2-weighted MRI after the chemotherapy shows ovarian tumor that became smaller and lost its solid component and disappearance of peritoneal disseminations (e). Although PET/contrastenhanced CT before the chemotherapy shows the ovarian tumor and multiple peritoneal disseminations with intense FDG uptake (c), PET/ contrast-enhanced CT after the chemotherapy shows no FDG uptake of smaller ovarian tumor and disappearance of peritoneal disseminations (f), showing no viable tumor tissue





В

A

institution, an unenhanced and low-dose CT is performed for attenuation correction. After a routine PET/CT study, we performed a diagnostic CT study with iodine medium immediately with the patient in the same position.

Pitfalls or limitations of FDG-PET/CT

FDG is physiologically accumulated in the bowel and excreted through the urinary tract. This might interfere with the optimal evaluation of primary tumors in the abdomen and pelvis. Urinary bladder activity can be avoided by requesting that the patient to empty her urinary bladder at the beginning of the exam [47]. Other approaches are using a urinary catheter to drain continuously or using hydration with 1,000 ml of intravenous normal saline along with diuretics such as furosemide [48, 49].

Moreover, in the abdomen and pelvis, a large number of misregistrations can occur as a result of the physiologic uptake in bowel and bladder and as a result of bowel peristalsis; knowledge of these issues and careful review are required for accurate interpretation [50].

We should take care of some pitfalls in interpreting FDG-PET/CT: the accumulation of FDG in normal ovary and activated inflammatory cells. Kim et al. [51] demonstrated that physiological ovarian FDG accumulation could be found around the time of ovulation and during the early luteal phase of the menstrual cycle in premenopausal woman. The inflammatory focus accumulates FDG avidly, making differentiation between residual tumor and normal tissue response sometimes difficult [52]. This problem could be resolved by fusion PET/MRI.

FDG-PET/CT is limited in its ability to identify lesions <1 cm, in particular, those smaller than 5 mm, leading to a false-negative rate of 5–10% [50]. FDG-PET/CT can only detect lesions with a certain volume of malignant cells sufficient to change the observed glucose metabolism, and neither of these imaging modalities can detect tiny lesions. This inadequate PET and PET/CT performance is not surprising, because 5 mm corresponds to the mean value of spatial resolution of the PET components, which is in the range of 4–6 mm. This still limited spatial resolution of the PET component makes the presence of metastasis in small LNs hardly detectable [6, 8, 48, 52].

Future directions with PET

Other FDG tracers

Tracers other than FDG also have been evaluated in patients with ovarian cancer, but not many papers on this topic are available so far. Yoshida et al. [53] evaluated

whether 16α -18F-fluoro-17 β -estradiol(FES)-PET to detect estrogen receptors could provide information useful for assessing estrogen receptor status in advanced ovarian cancer. Torizuka et al. [54] compared ¹⁸F-FDG-PET with ¹¹C-choline PET in a population of 21 patients with 18 untreated patients with gynecological malignancies and 3 with suspected relapse and found that ¹¹C-choline PET detected lesions in a higher number than did ¹⁸F-FDG-PET. Ludemann et al. studied tumor oxygenation and perfusion in 27 patients with primary or recurrent pelvic tumors who underwent regional hyperthermia with H₂¹⁵O-PET, performing PET prior to and up to 1 h after regional hyperthermia, to quantitatively determine perfusion and partition coefficient. He demonstrated that heating under hyperthermia conditions significantly increased the partition coefficient for pelvic tumors (p = 0.005) [55].

Integrated PET/MRI

In recent years, there has been increasing interest in the development of integrated PET/MRI systems following the success of hybrid imaging with PET/CT. PET/MRI would have the following advantages: improved soft-tissue contrast; the possibility of performing truly simultaneous instead of sequential acquisitions; and availability of sophisticated MRI sequences, such as diffusion and perfusion imaging, functional MRI, and MR spectroscopy, which can add important information. Moreover, the use of PET/MRI would result in a significant decrease in radiation exposure, which is of foremost importance for serial follow-up and pediatric imaging.

A combined PET/MRI scanner would provide an alternative to a combined PET/CT scanner for whole-body oncologic imaging [56, 57]; improved accuracy could be achieved in the detection, staging, characterization, and functional therapy monitoring of several cancers. However, prototype designs for human whole-body PET/MRI systems are emerging with a number of technical and methodological difficulties needing to be overcome: these include the compatibility of both the PET and MRI components in an integrated system and merging two technologies whose signals are prone to distortion [58].

Conclusion

FDG-PET/CT has been used successfully for staging, restaging, and therapeutic monitoring of ovarian cancer. Compared with conventional PET/non-contrast CT images, combined PET/contrast-enhanced CT images with intravenous iodine contrast medium and sufficient radiation dose may contribute to a more accurate diagnosis with higher confidence. For initial staging, FDG-PET/CT has a limited role of assessing primary tumor extension in the pelvis, but it provides useful information about LN involvement and distant metastasis. Further evaluation in prospective clinical trials will be required to assess the prognostic value of FDG-PET in patients with ovarian cancer.

References

- Bristow RE, Duska LR, Lambrou NC, Fishmann EK, O'Neill MJ, Trimble EL, et al. A model for predicting surgical outcome in patients with advanced ovarian carcinoma using computed tomography. Cancer. 2000;89:1532–40.
- Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, et al. Cancer statistics, 2008. CA Cancer J Clin. 2008;58:71–96.
- 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;41:1369–79.
- von Schulthess GK, Steinert HC, Hany TF. Integrated PET/CT: current applications and future directions. Radiology. 2006;238: 405–22.
- Patel CN, Goldstone AR, Chowdhury FU, Scarsbrook AF. FDG PET/CT in oncology: "raising the bar". Clin Radiol. 2010;65: 522–35.
- Adusumili S, Hussain HK, Caoili EM, Weadock WJ, Murray JP, Johnson TD, et al. MRI of sonographically indeterminate adnexal masses. AJR Am J Roentgenol. 2006;187:732–40.
- Booth SJ, Turnbull LW, Poole DR, Richmond I. The accurate staging of ovarian cancer using 3T magnetic resonance imaging—a realistic option. BJOG. 2008;15:894–901.
- Risum S, Hogdall C, Loft A, Berthelsen AK, Hogdall E, Nedergaard L, et al. The diagnostic value of PET/CT for primary ovarian cancer—a prospective study. Gynecol Oncol. 2007;105: 145–9.
- Castelluci P, Perrone AM, Picchio M, Ghi T, Farsad M, Nanni C, et al. Diagnostic accuracy of ¹⁸F-FDG PET/CT in characterizing ovarian lesions and staging ovarian cancer: correlation with transvaginal ultrasonography, computed tomography, and histology. Nucl Med Commun. 2007;28:589–95.
- Nam EJ, Yun MJ, Oh YT, Kim JW, Kim JH, Kim S, et al. Diagnosis and staging of primary ovarian cancer: correlation between PET/CT, Doppler US, and CT or MRI. Gynecol Oncol. 2010;116:389–94.
- Omura GA, Brady MF, Homesley HD, Yordan E, Major FJ, Buchsbaum HJ, et al. Long-term follow-up and prognostic factor analysis in advanced ovarian carcinoma: the Gynecologic Oncology Group experience. J Clin Oncol. 1991;9:1138–50.
- Ricke J, Sehouli J, Hach C, Hanninen EL, Lichtenegger W, Felix R. Prospective evaluation of contrast-enhanced MRI in the depiction of peritoneal spread in primary or recurrent ovarian cancer. Eur Radiol. 2003;13:943–9.
- Kitajima K, Murakami K, Yamasaki E, Kaji Y, Fukasawa I, Inaba N, et al. Diagnostic accuracy of integrated FDG-PET/contrastenhanced CT in staging ovarian cancer: comparison with enhanced CT. Eur J Nucl Med Mol Imaging. 2008;35:1912–20.
- Namimoto T, Awai K, Nakaura T, Yanaga Y, Hirai T, Yamashita Y. Role of diffusion-weighted imaging in the diagnosis of gynecological diseases. Eur Radiol. 2009;19:745–60.
- Fujii S, Matsusue E, Kanasaki Y, Kanamori Y, Nakanishi J, Sugihara S, et al. Detection of peritoneal dissemination in

gynecological malignancy: evaluation by diffusion-weighted MR imaging. Eur Radiol. 2008;18:18–23.

- Chan YM, Ng TY, Ngan HY, Wong LC. Quality of life in women treated with neoadjuvant chemotherapy for advanced ovarian cancer: a prospective longitudinal study. Gynecol Oncol. 2003;88:9–16.
- Schwarz JK, Grigsby PW, Dehdashti F, Celbeke D. The role of ¹⁸F-FDG PET in assessing therapy response in cancer of the cervix and ovaries. J Nucl Med. 2009;50:64S–73S.
- Kitajima K, Murakami K, Yamasaki E, Domeki Y, Kaji Y, Fukasawa I, et al. Performance of integrated FDG-PET/contrastenhanced CT in the diagnosis of recurrent ovarian cancer: comparison with integrated FDG-PET/non-contrast-enhanced CT and enhanced CT. Eur J Nucl Med Mol Imaging. 2008;35:1439–48.
- Hauth EA, Antoch G, Stattaus J, Kuehl H, Veit P, Bosckisch A, et al. Evaluation of integrated whole-body PET/CT in the detection of recurrent ovarian cancer. Eur J of Radiol. 2005;56: 263–8.
- Nanni C, Rubello D, Farsad M, De Iaco P, Sansovini M, Erba P, et al. ¹⁸F-FDG PET/CT in the evaluation of recurrent ovarian cancer: a prospective study on forty-one patients. Eur J Surg Oncol. 2005;31:792–7.
- Simcock B, Neesham D, Quinn M, Drummond E, Milner A, Hicks RJ. The impact of PET/CT in the management of recurrent ovarian cancer. Gynecol Oncol. 2006;103:271–6.
- 22. Chung HH, Kang WJ, Kim JW, Park NH, Song YS, Chung JK, et al. Role of [¹⁸F]FDG PET/CT in the assessment of suspected recurrent ovarian cancer: correlation with clinical or histological findings. Eur J Nucl Med Mol Imaging. 2007;34:480–6.
- Mangili G, Picchio M, Sironi S, Vigano R, Rabaiotti E, Bornaghi D, et al. Integrated PET/CT as a first-line re-staging modality in patients with suspected recurrence of ovarian cancer. Eur J Nucl Med Mol Imaging. 2007;34:658–66.
- Thrall MM, DeLoia JA, Gallion H, Avril N. Clinical use of combined positron emission tomography and computed tomography (FDG-PET/CT) in recurrent ovarian cancer. Gynecol Oncol. 2007;105:17–22.
- Kim CK, Park BK, Choi JY, Kim BG, Han H. Detection of recurrent ovarian cancer at MRI: comparison with integrated PET/CT. J Comput Assist Tomogr. 2007;31:868–75.
- Sebastian S, Lee SI, Horowitz NS, Scott JA, Fischman AJ, Simeone JF, et al. PET-CT vs. CT alone in ovarian cancer recurrence. Abdom Imaging. 2008;33:112–8.
- Iagaru AH, Mittra ES, McDougall IR, Quon A, Gambhir SS. ¹⁸F-FDG PET/CT evaluation of patients with ovarian carcinoma. Nucl Med Commun. 2008;29:1046–51.
- Soussan M, Wartski M, Cherel P, Fourme E, Goupil A, Le Stanc E, et al. Impact of FDG PET/CT imaging on the decision making in the biologic suspicion of ovarian carcinoma recurrence. Gynecol Oncol. 2008;108:160–5.
- Fulham MJ, Carter J, Baldey A, Hicks RJ, Ramshaw JE, Gibson M. The impact of PET/CT in suspected recurrent ovarian cancer: a prospective multi-centre study as part of the Australian PET data collection project. Gynecol Oncol. 2009;112:462–8.
- Makhija S, Howden N, Edwards R, Kelley J, Townsend DW, Meltzer CC. Positron emission tomography/computed tomography imaging for the detection of recurrent ovarian and fallopian tube carcinoma: a retrospective review. Gynecol Oncol. 2002;85: 53–8.
- Bristow RE, Del Carmen MG, Pannu HK, Cohade C, Zahurak ML, Fishman EK, et al. Clinically occult recurrent ovarian cancer: patient selection for secondary cytoreductive surgery using combined PET/CT. Gynecol Oncol. 2003;90:519–28.
- 32. Sironi S, Messa C, Mangili G, Zangheri B, Aletti G, Garevaglia E, et al. Integrated FDG-PET/CT in patients with persistent

ovarian cancer: correlation with histologic findings. Radiology. 2004;233:433-40.

- Pannu HK, Cohade C, Bristow RE, Fishman EK, Wahl RL. PET-CT detection of abdominal recurrence of ovarian cancer: radiologic-surgical correlation. Abdom Imaging. 2004;39:398–403.
- Bristow RE, Giuntoli RL II, Pannu HK, Schulick RD, Fishman EK, Wahl RL. Combined PET/CT for detecting recurrent ovarian cancer limited to retroperitoneal lymph nodes. Gynecol Oncol. 2005;99:294–300.
- Rose PG. Surgery for recurrent ovarian cancer. Semin Oncol. 2000;27:17–23.
- Gu P, Pan LL, Wu SQ, Sun L, Huang G. CA125, PET alone, PET-CT, CT and MRI in diagnosing recurrent ovarian carcinoma: a systematic review and meta-analysis. Eur J Radiol. 2009;71:164–74.
- Smith GT, Hubner KF, McDonald T, Thie JA. Cost analysis of FDG PET for managing patients with ovarian cancer. Clin Positron Imaging. 1999;2:63–70.
- 38. Kim S, Chung JK, Kang SB, Kim MH, Jeong JM, Lee DS, et al. [¹⁸F]FDG PET as a substitute for second-look laparotomy in patients with advanced ovarian carcinoma. Eur J Nucl Med Mol Imaging. 2004;31:196–201.
- Nishiyama Y, Yamamoto Y, Kaneishi K, Ohno M, Hata T, Kushida Y, et al. Monitoring the neoadjuvant therapy response in gynecological cancer patients using FDG PET. Eur J Nucl Med Mol Imaging. 2008;35:287–95.
- 40. Avril N, Sassen S, Schmalfeldt B, Naehrig J, Rutke S, Weber WA, et al. Prediction of response to neoadjuvant chemotherapy by sequential F-18-fluorodeoxyglucose positron emission tomography in patients with advanced-stage ovarian cancer. J Clin Oncol. 2005;23:7445–53.
- 41. Kurosaki H, Oriuchi N, Okazaki A, Tamaki T, Uki A, Izuta M, et al. Prognostic value of FDG-PET in patients with ovarian carcinoma following surgical treatment. Ann Nucl Med. 2006;20: 171–4.
- 42. Risum S, Hogdall C, Loft A, Berthelsen AK, Hogdall E, Nedergaard L, et al. Does the use of diagnostic PET/CT cause stage migration in patients with primary advanced ovarian cancer. Gynecol Oncol. 2010;116:395–8.
- 43. Kitajima K, Murakami K, Yamasaki E, Kaji Y, Sugimura K. Accuracy of integrated FDG-PET/contrast-enhanced CT in detecting pelvic and paraaortic lymph node metastasis in patients with uterine cancer. Eur Radiol. 2009;19:1529–36.
- 44. Kitajima K, Murakami K, Yamasaki E, Domeki Y, Kaji Y, Morita S, et al. Performance of integrated FDG-PET/contrast enhanced CT in the diagnosis of recurrent uterine cancer: comparison with PET alone and enhanced CT alone. Eur J Nucl Med Mol Imaging. 2009;36:362–72.
- 45. Kitajima K, Suzuki K, Nakamoto Y, Onishi Y, Sakamoto S, Senda M, et al. Low-dose non-enhanced CT versus full-dose

contrast-enhanced CT in integrated PET/CT studies for the diagnosis of uterine cancer recurrence. Eur J Nucl Med Mol Imaging. 2010;37:1490–8.

- Bunyaviroch T, Turkington TG, Wong TZ, Wilson JW, Colsher JG, Coleman RE. Quantitative effects of contrast enhanced CT attenuation correction on PET SUV measurements. Mol Imaging Biol. 2008;10:107–13.
- Kumar R, Chauhan A, Jana S, Dadparvar S. Positron emission tomography in gynaecological malignancies. Expert Rev Anticancer Ther. 2006;6:1033–44.
- Koyama K, Okamura T, Kawabe J, Ozawa N, Torii K, Umesaki N, et al. Evaluation of ¹⁸FDG PET with bladder irrigation in patients with uterine and ovarian tumors. J Nucl Med. 2003; 44:353–8.
- Belhocine T, Thille A, Fridman V, Albert A, Seidel L, Nickers P, et al. Contribution of whole-body 18FDG PET imaging in the management of cervical cancer. Gynecol Oncol. 2002;87:90–7.
- Prakash P, Cronin CG, Blake MA. PET/CT in ovarian cancer. AJR Am J Roentgenol. 2010;194:W464–70.
- Kim SK, Kang KW, Roh JW, Sim JS, Lee ES, Park SY. Incidental ovarian 18F-FDG accumulation on PET: correlation with the menstrual cycle. Eur J Nucl Med Mol Imaging. 2005;32: 757–63.
- Domingues RC, Carneiro MP, Lopes FCR, Domingues RC, Fonseca LMB, Gasparetto EL. Whole-body MRI and FDG PET fused images for evaluation of patients with cancer. AJR Am J Roentgenol. 2009;192:1012–20.
- 53. Yoshida Y, Kurokawa T, Tsujikawa T, Okazawa H, Kotsuji F. Positron emission tomography in ovarian cancer: 18F-deoxyglucose and 16α -18F-fluoro-17 β -estradiol(FES) PET. J Ovarian Res. 2009;2:7–16.
- Torizuka T, Kanno T, Futatsubashi M, Okada H, Yoshikawa E, Nakamura F, et al. Imaging of gynaecologic tumor: comparison of 11C-Choline PET with 18F-FDG PET. J Nucl Med. 2003; 44:1051–6.
- Ludemann L, Sreenivasa G, Amthauer H, Michel R, Gellermann J, Wust P. Use of H¹⁵₂O-PET for investigating perfusion changes in pelvic tumors due to regional hyperthermia. Int J Hyperth. 2009;25:299–308.
- Antoch G, Bockisch A. Combined. PET/MRI: a dimension of whole-body oncology imaging? Eur J Nucl Med Mol Imaging. 2009;36:S113–20.
- 57. Pichler BJ, Kolb A, Nagele T, Schlemmer HP. PET/MRI: paving the way for the next generation of clinical multimodality imaging applications. J Nucl Med. 2010;51:333–6.
- Pichler BJ, Wehrl HF, Kolb A, Judenhofer MS. Positron emission tomography/magnetic resonance imaging: the next generation of multimodality imaging? Semin Nucl Med. 2008;38:199–208.