# GYNECOLOGIC ONCOLOGY

# **Region-based diagnostic performance of multidetector CT** for detecting peritoneal seeding in ovarian cancer patients

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#### Abstract

*Purpose* To determine the accuracy of multi-detector CT (MDCT) compared with the surgical findings, such as peritoneal seeding and metastatic lymph nodes, in ovarian cancer patients.

*Methods* Fifty-seven FIGO stage IA–IV ovarian cancer patients, who underwent MDCT before primary surgery, were included in this study. Two radiologists evaluated the following imaging findings in consensus: the presence of nodular, plaque-like or infiltrative soft-tissue lesions in peritoneal fat or on the serosal surface; presence of ascites; parietal peritoneal thickening or enhancement; and small bowel wall thickening or distortion. We also evaluated the presence of lymph node metastases. To allow region-specific comparisons, the peritoneal cavity was divided into 13 regions and retroperitoneal lymph nodes were divided into 3 regions. Descriptive statistical data were thus obtained.

*Results* The MDCT sensitivity, specificity, positive predictive values, and negative predictive values were 45, 72, 46, and 72%, respectively, for detecting peritoneal seeding

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Department of Obstetrics and Gynecology, Konkuk University Hospital, Konkuk University, Seoul, Korea and 21, 90, 52, and 69%, respectively, for detecting lymph node metastasis.

*Conclusions* MDCT is moderately accurate for detecting peritoneal metastasis and lymph node metastasis in ovarian cancer patients.

**Keywords** Ovarian cancer · Peritoneal seeding · Multi-detector computed tomography

# Introduction

Ovarian cancer is a fifth most common cause of cancer death and a leading cause of death from gynecologic malignancy in women worldwide. Although the prognosis of FIGO stage I disease can indicate a better survival rate of 80-90%, currently 60-65% of patients present with stages III or IV disease at the time of diagnosis. This is the main reason that ovarian cancer is one of the most lethal cancers in female. For these advanced ovarian cancer patients, the optimal cytoreduction of tumor bulk to as less as possible and platinum- and taxane-based chemotherapy is the standard treatment. In this patient group, the amount of residual disease is the most important prognostic factor [1]. The presence of tumor in a specific location, such as suprarenal lymph node, porta hepatis, liver parenchymal metastasis, and small bowel mesenteric involvement can prohibit optimal cytoreduction in ovarian cancer patients [2]. For this reason, delineation of the precise location of the peritoneal implant is crucial in the management of advanced ovarian cancer patients.

CT has been extensively used in the preoperative diagnosis and postoperative surveillance of ovarian cancer patients. Several investigations have been performed to evaluate the diagnostic performance of CT for detecting peritoneal seeding in ovarian cancer patients [3–7]. In these studies, the reported sensitivity and specificity were 63–93 and 73–100%, respectively. However, these studies reported patient-based CT diagnostic performance for the detection of peritoneal seeding, and as far as we know there have been no studies reporting the region-based diagnostic performance of CT for detecting peritoneal seeding in ovarian cancer patients.

The aim of our study is to prospectively determine the diagnostic performance, i.e. sensitivity, specificity, positive predictive value, and negative predictive value of CT compared with the surgical findings for detecting peritoneal seeding and metastatic lymph nodes in primary ovarian cancer patients.

#### Materials and methods

#### Study population

This study used a prospectively collected database. It included 57 consecutive patients with histologically confirmed FIGO stages IA-IV ovarian cancer as determined by surgery; 6, 5, 38, and 8 patients were identified and comprised the current FIGO stages I, II, III, and IV groups, respectively. These patients were recruited between July 2006 and January 2008, were between 30 and 72 years of age (mean age 53.1 years), had no contraindications to the surgical procedure, and had an Eastern Cooperative Oncology Group performance state of 0-2 before surgery. Their serum CA-125 levels ranged from 12.3 to 8510 U/mL (mean 794.8 U/mL). The histology of our study patients' ovarian carcinoma is as follows: serous carcinoma (n = 38); mucinous carcinoma (n = 12); endometrioid carcinoma (n = 2); clear cell carcinoma (n = 2); transitional cell carcinoma (n = 1); and other (n = 2). Architecture grades 1, 2, and 3 tumors existed in 3 (10%), 14 (47%), and 13 patients (43%), respectively. All patients were classified into two groups according to the whether or not they had undergone neoadjuvant chemotherapy. Twenty-seven (47.4%) had undergone neoadjuvant chemotherapy before surgery and 30 patients (52.6%) had not. No statistical difference of the clinical variables was observed between the neoadjuvant group and the non-neoadjuvant patients group.

# CT technique

All CT data were obtained using a four-channel MDCT scanner (Mx 8000, Marconi Medical System, Israel). Preoperative CT scans were obtained at a single institution an average of 17.6 days before surgery (range 2–44 days). IV contrast material (Iopromide, Ultravist 300, Schering, Berlin) was administered via an antecubital vein using a mechanical injector (140 mL at 2.3 mL/s). Scanning began 70 or 80 s after the start of IV contrast injection (from the lower thorax to the lower pelvis). Scanning parameters included the following: detector array 1.25 mm  $\times$  4; beam pitch 1.35; section thickness 3.2 mm; and a reconstruction increment of 3 mm.

## Classification of regions

The peritoneal cavity was classified into 13 regions, i.e. right subdiaphragmatic area, left subdiaphragmatic area, porta hepatis, lesser sac, small bowel mesentery, splenic hilar area, omentum, right paracolic gutter, left paracolic gutter, right pelvic cavity, left pelvic cavity, sigmoid mesentery, and bladder dome area (Fig. 1).

Lymph nodes were classified into three groups: paraaortic (including right and left para-aortic lymph nodes), right pelvic, and left pelvic areas.

# Surgical technique

All patients underwent preoperative antibiotic bowel preparation for 2 days prior to surgery. Perioperative antibiotics, thromboembolic prophylaxis with lower molecular heparin, and pressure stockings were routinely used. Patients were placed in the Trendelenburg position with straight, extended legs, and gel pads were placed under their



**Fig. 1** Classification of the abdominopelvic cavity. *1* Right subdiaphragmatic area, 2 left subdiaphragmatic area, 3 porta hepatis, 4 lesser sac, 5 small bowel mesentery, 6 splenic hilar area, 7 omentum, 8 right paracolic gutter, 9 left paracolic gutter, 10 right pelvic cavity, 11 left pelvic cavity, 12 sigmoid mesentery, 13 bladder dome area

shoulders and heels. A midline vertical incision was made from the pubic symphysis to the xiphoid process.

All surgeries used the same instruments and techniques and were performed by experienced gynecologic oncologists assisted by a gynecology-board-certified fellow and a resident in training. First, the pelvic and abdominal organs and the peritoneal surfaces were thoroughly explored. Prior to dissection, peritoneal cytology samples were obtained from the abdominopelvic cavity. Cytoreductive surgery was performed from the upper abdomen to pelvic cavity. Omentectomy with resection of both gastro-epiploic vessels was usually the first cytoreductive procedure. Cytoreductive surgery was then performed in the upper abdomen. Subdiaphragmatic peritoneal stripping and/or diaphragmatic resection, hepatic resection, cholecystectomy, splenectomy, distal pancreatectomy, large and small bowel resection, appendectomy, and urinary tract resection and anastomosis were selectively performed as clinically indicated to minimize residual tumor. Then, tumor resection in the pelvis was performed, such as hysterectomy, bilateral salpingooophorectomy, low anterior resection, or pelvic peritonectomy. Lymph node dissection in the pelvis and para-aortic area was performed, and lastly, bowel anastomosis was performed. After the removal of all visible tumors, random peritoneal biopsies were obtained from the diaphragm, paracolic gutters, pelvic side walls, posterior cul-de-sac, bladder peritoneum, and from suspicious lesions or adhesions.

## Analysis and statistics

CT images were interpreted by consensus of two radiologists (C.H.J. and J.D.C.) with 7 and 5 years of clinical experience, respectively, in gynecologic imaging including CT. The two readers were unaware of any of the surgical results. Evaluated imaging findings for peritoneal seeding were as follows: 1, presence of a nodular, plaque-like or infiltrative soft-tissue lesion in the peritoneal fat or surface bowel serosa; 2, presence of ascites; 3, parietal peritoneal thickening or enhancement; and 4, small bowel wall thickening or distortion [3-5, 8]. The criterion for suspicion of malignancy on CT was a pelvic or para-aortic lymph node with a short-axis diameter >1 cm. All images were examined using the picture archiving and communication system. Information regarding the CT imaging was entered into a prospective database, and the surgical staging information was stored in a separate file.

Descriptive statistical data, including sensitivity, specificity, positive predictive value, and negative predictive value, were calculated. The  $\chi^2$  test was used to compare the sensitivity, specificity, positive predictive value, and negative predictive value. QuickCalc (GraphPad Software Inc)

software was used for analysis. A P value of 0.05 or less was considered to represent a significant difference.

# Results

Of the 57 patients with primary ovarian cancer, who underwent laparotomy and CT, peritoneal seeding was present in 50 of the 57 patients in the all-patient group (87%), in 25 of the 30 patients in the non-neoadjuvant group (83%), and in 25 of the 27 patients in the neoadjuvant group (93%) (Fig. 2a–g). The splenic hilar area was the most common site of peritoneal seeding, and both pelvic cavities were the least common sites of peritoneal seeding in the all-patient group. The distribution of peritoneal seeding is summarized in Table 1.

The diagnostic performance of CT for detecting peritoneal seeding and lymph node metastasis is summarized in Table 2. There were no statistical differences in the diagnostic performance of CT in the non-neoadjuvant and neoadjuvant groups. Sensitivity and specificity (35.1 and 68%) were lower for the detection of peritoneal seeding in patients with peritoneal implants smaller than 1 cm in maximum diameter compared with the detection of peritoneal implants 1 cm or larger (52.4 and 75%), and there was a statistically significant difference in sensitivities (p = 0.037) (data not shown). The region-specific diagnostic performance of CT in the non-neoadjuvant group, neoadjuvant group, and all-patient group are summarized in Table 3.

### Discussion

The presence of peritoneal seeding is an important prognostic factor in ovarian cancer patients as it is the most common pathway of dissemination in ovarian cancer and is found in approximately 70% of patients on their initial diagnosis. Although ovarian cancer patients are surgically staged with laparotomy according to the recommendations of the International Federation of Gynecology and Obstetrics (FIGO) [9], it is important for the proper triage of ovarian cancer patients who will be suboptimally resected to be placed in a more appropriate neoadjuvant chemotherapy group to detect peritoneal seeding preoperatively [10]. In addition, recognizing the location of peritoneal seeding is also important for predicting the possibility of optimal resection [11, 12]. For this reason, it is important to know the region-based diagnostic performance of CT for detecting peritoneal seeding in ovarian cancer patients. However, the moderate accuracy of MDCT in the current study still leaves much to be desired. To completely know whether the patients underwent optimal



Fig. 2 A 54-year-old woman with primary serous cystadenocarcinoma of the ovary. **a** Axial contrast-enhanced CT scan shows a heterogeneously enhancing solid mass (*arrow*) in the spleen, suggestive of a left subdiaphragmatic peritoneal implant with invasion of the spleen. Note the large amount of ascites (*asterisks*) in both subdiaphragmatic area. **b** Intraoperative photograph shows a *yellowish*, bulging mass in the spleen (*arrows*), which turned out to be splenic metastasis form ovarian cancer. Note the disseminated, subcentimeter-sized peritoneal implants (*arrowheads*) in the left subdiaphragmatic area. **c** Axial, contrast-enhanced CT scan shows a large amount ascites in both of the subdiaphragmatic areas without

cytoreduction or not, the current standard, exploratory laparotomy, should be performed. Image-based selection for neoadjuvant chemotherapy still remains experimental.

The primary purpose of our study was to prospectively evaluate the region-based diagnostic performance of postcontrast CT for the detection of peritoneal seeding in ovarian cancer patients. To date, some studies have been conducted based on the performance of CT for detecting peritoneal seeding in ovarian cancer patients [3–7]. However, all of these studies reported the patient-based diagnostic performance of CT. Tempany et al. [7] performed a multicenter prospective study and did a region-based comparison, but the obtained sensitivity (92%) and specificity (82%) of CT were based on patient-based diagnostic performance. On the other hand, in our study, the regionbased diagnostic performance of CT was assessed as we thought it would form a baseline study for the evaluation of the usefulness of CT for predicting optimal tumor resection and peritoneal seeding in ovarian cancer patients.

peritoneal implants (*asterisk*). Note the omental cake in the left anterior abdominal cavity (*arrow*). **d** Intraoperative photograph shows a disseminated, subcentimeter-sized peritoneal implant in the left subdiaphragmatic area. **e** Intraoperative photograph shows multiple, conglomerated, peritoneal implants forming an omental cake. **f** Axial, contrast-enhanced CT scan shows misty mesentery (*asterisk*), although no definite mass or implants are shown in the CT scan. Note the peritoneal thickening (*arrowheads*), omental cake (*arrow*), and large amount ascites. **g** Intraoperative photograph shows multiple peritoneal implants in the mesenteric root (*arrowheads*)

In our study, the sensitivity and specificity of CT for detecting peritoneal seeding were 45 and 72%, respectively. In time of evaluating the accuracy of CT for the peritoneal seeding especially in upper abdomen, we must consider the surgical aggressiveness and surgical extent. Because even if surgeons keep the principle of surgical approach for ovarian cancer, such as thorough exploration of the whole abdomen on inspection and palpation and careful biopsy of all suspicious tissues via lower midline incision from the sternum to the symphysis pubis, surgical extensiveness and approach for each area could be different [13]. Evaluation and/or biopsy for the area of porta hepatis, less sac, or diaphragm at hepatophrenic junction which has been firstly evaluated in the current study as far as we know may be performed or not according to surgeons' policy. This results in different outcomes in terms of evaluating the accuracy of CT. We did all our best to minimize the residual tumor adopting extensive cytoredutive surgical procedures such as intrathoracic debulking, diaphragmatic

Table 1	Distribution	of	detected	peritoneal	seeding
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Region	No $(\%)^a$ (non-neoadjuvant group) ( $n = 30$ )	No $(\%)^{a}$ (neoadjuvant group) ( $n = 27$ )	No $(\%)^{a}$ (all primary ovarian cancer patients) ( $n = 57$ )
Right subdiaphragmatic area	18 (60) <sup>b</sup>	17 (63)	35 (61)
Left subdiaphragmatic area	18 (60) <sup>b</sup>	16 (59)	34 (60)
Porta hepatis	7 (23)	3 (11)	10 (18)
Lesser sac	11 (37)	7 (26)	18 (32)
Small bowel mesentery	9 (30)	5 (19)	14 (25)
Splenic hilar surface	18 (60) <sup>b</sup>	20 (74) <sup>b</sup>	38 (67) <sup>b</sup>
Omentum	11 (37)	9 (33)	20 (35)
Right paracolic gutter	13 (43)	9 (33)	22 (39)
Left paracolic gutter	13 (43)	7 (26)	20 (35)
Right pelvic cavity	2 (7) <sup>c</sup>	2 (7) <sup>c</sup>	4 (7) <sup>c</sup>
Left pelvic cavity	5 (17)	3 (11)	8 (14)
Sigmoid mesentery	7 (23)	5 (19)	12 (21)
Bladder dome area	10 (33)	6 (22)	16 (28)

<sup>a</sup> Data are numbers of regions considered positive for peritoneal seeding

<sup>b</sup> Highest value in the column

<sup>c</sup> Lowest value in the column

 Table 2
 Summary of the diagnostic performance of CT for detecting peritoneal seeding and lymph node metastasis in primary ovarian cancer patients (anatomical-region-based comparison)

	Sensitivity (%)	Specificity (%)	PPV (%)	NVP (%)
Peritoneal seeding				
Primary ovarian cancer patients without neoadjuvant chemotherapy	49 (69/142)	69 (170/248)	47 (69/147)	70 (170/243)
Primary ovarian cancer patients with neoadjuvant chemotherapy	41 (45/109)	76 (185/242)	44 (45/102)	74 (185/249)
All primary ovarian cancer patients	45 (114/251)	72 (355/490)	46 (114/249)	72 (355/492)
Lymph node metastasis				
Primary ovarian cancer patients without neoadjuvant chemotherapy	24 (8/33)	88 (50/57)	53 (8/15)	67 (50/75)
Primary ovarian cancer patients with neoadjuvant chemotherapy	20 (5/25)	93 (52/56)	56 (5/9)	72 (52/72)
All primary ovarian cancer patients	22 (13/58)	90 (102/113)	54 (13/24)	69 (102/147)

stripping, partial gastrectomy, hepatectomy, cholecystectomy, adrenalectomy, splenectomy, distal pancreatectomy, colectomy, and small bowel resection [14–18]. Therefore, the sensitivity in the current study might low than previous studies because of more microscopic tumor in more resected area. In the future, the study on the accuracy of CT for the peritoneal seeding of ovarian cancer is recommended to include such information, such as surgical efforts, surgical extent, and degree of optimal cytoreduction for comparison with previous studies.

Although statistically insignificant, the higher sensitivity and lower specificity seen in the non-neoadjuvant group when compared with those in the neoadjuvant group was observed. As ascites is a common finding in patients with peritoneal seeding and it makes the other CT findings of peritoneal seeding, such as a nodular or plaque-like, enhancing, soft-tissue mass, more prominent, the absent or decreased ascites may obscure an accurate diagnosis of peritoneal seeding in the neoadjuvant patient group.

The region-based sensitivity and specificity of CT for detecting lymph node metastasis were 22, 90% in all included patients and 30, 60 and 38, 100% in the non-neoadjuvant and neoadjuvant groups, and there was no statistical difference in diagnostic accuracy between the neoadjuvant and non-neoadjuvant group. These were relatively lower than previously reported sensitivities and specificities (41–44 and 64–89%) in our study [7, 19, 20], however, as there was only a relatively small number of metastatic nodes, we believe that, in general, it is difficult to arrive at a definite conclusion regarding the diagnostic performance of CT for detecting metastatic lymph nodes in ovarian cancer patients.

Region	Non-neoadju	ıvant group (9,	(9		Neoadjuvan	tt group (%)			Neoadjuvant	t group and n	on-neoadjuvaı	it group (%)
	Se	Sp	ΡΡV	NVP	Se	Sp	ΡΡV	NVP	Se	Sp	Δdd	NVP
Right subdiaphragmatic area	72 (13/18)	83 (10/12)	87 (13/15)	67 (10/15)	35 (6/17)	80 (8/10)	75 (6/8)	42 (8/19) <sup>b</sup>	54 (19/35)	82 (18/22)	83 (19/23)	53 (18/34)
Left subdiaphragmatic area	61 (11/18)	92 (11/12)	92 (11/12)	61 (11/18)	31 (5/16)	91 (10/11)	83 (5/6) <sup>a</sup>	48 (10/21)	47 (16/34)	91 (21/23)	89 (16/18) <sup>a</sup>	54 (21/39)
Porta hepatis	29 (2/7)	100 (23/23) <sup>a</sup>	$100(2/2)^{a}$	82 (23/28)	0 (0/3) <sup>b</sup>	92 (22/24)	0 (0/2) <sup>b</sup>	88 (22/25) <sup>a</sup>	20 (2/10)	96 (45/47) <sup>a</sup>	50 (2/4)	85 (45/53)
Lesser sac	18 (2/11)	89 (17/19)	50 (2/4)	65 (17/26)	43 (3/7)	95 (19/20) <sup>a</sup>	75 (3/4)	83 (19/23)	28 (5/18)	92 (36/39)	63 (5/8)	74 (36/49)
Small bowel mesentery	11 (1/9)	90 (19/21)	33 (1/3)	70 (19/27)	40 (2/5)	95 (21/22) <sup>a</sup>	67 (2/3)	88 (21/24) <sup>a</sup>	21 (3/14)	93 (40/43)	50 (3/6)	78 (40/51)
Splenic hilar surface	67 (12/18)	50 (6/12)	67 (12/18)	50 (6/12) <sup>b</sup>	75 (15/20) <sup>a</sup>	57 (4/7)	83 (15/18) <sup>a</sup>	44 (4/9)	71 (27/38) <sup>a</sup>	53 (10/19)	75 (27/36)	48 (10/21) <sup>b</sup>
Omentum	18 (2/11)	63 (12/19)	22 (2/9)	57 (12/21)	44 (4/9)	56 (10/18)	33 (4/12)	67 (10/15)	30 (6/20)	59 (22/37)	29 (6/21)	61 (22/36)
Right paracolic gutter	77 (10/13)	24 (4/17) <sup>b</sup>	43 (10/23)	57 (4/7)	56 (5/9)	61 (11/18)	42 (5/12)	73 (11/15)	68 (15/22)	43 (15/35) <sup>b</sup>	43 (15/35)	68 (15/22)
Left paracolic gutter	69 (9/13)	47 (8/17)	50 (9/18)	67 (8/12)	29 (2/7)	75 (15/20)	29 (2/7)	75 (15/20)	55 (11/20)	62 (23/37)	44 (11/25)	72 (23//32)
Right pelvic cavity	$100(2/2)^{a}$	43 (12/28)	11 (2/18)	100 (12/12) <sup>a</sup>	0 (0/2) <sup>b</sup>	44 (11/25) <sup>b</sup>	0 (0/14) <sup>b</sup>	85 (11/13)	50 (2/5)	43 (23/53) <sup>b</sup>	6 (2/32)	92 (23/25) <sup>a</sup>
Left pelvic cavity	60 (3/5)	36 (9/25)	16 (3/19)	82 (9/11)	33 (1/3)	58 (14/25)	9 (1/11)	88 (14/16) <sup>a</sup>	50 (4/8)	47 (23/49)	13 (4/30)	85 (23/27)
Sigmoid mesentery	14 (1/7)	91 (21/23)	33 (1/3)	78 (21/27)	20 (1/5)	91 (20/22)	33 (1/3)	83 (20/24)	17 (2/12)	91 (41/45)	33 (2/6)	80 (41/51)
Bladder dome	0 (0/10) <sup>b</sup>	95 (19/20)	$0 (0/1)^{b}$	66 (19/29)	0 (0/6) <sup>b</sup>	95 (20/21) <sup>a</sup>	0 (0/1) <sup>b</sup>	77 (20/26)	0 (0/16) <sup>b</sup>	95 (39/41)	0 (0/2) <sup>b</sup>	70 (39/55)
Data are numbers of regions (	considered po	sitive for peri	toneal seeding									

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NPV negative predictive value, PPV positive predictive value, Se sensitivity, Sp specificity

<sup>a</sup> Highest value in the column

<sup>b</sup> Lowest value in the column

In our study, the common sites of peritoneal seeding were the splenic hilar surface (15%) and both subdiaphragmatic areas (right subdiaphragmatic area, 14%; left subdiaphragmatic area 14%) as these are the sites where peritoneum reflections and peritoneal fluid tend to remain longer [21]. In our region-based comparison, CT shows the highest sensitivity in the splenic hilar surface (71%, 27/38) and the lowest sensitivity in the bladder dome (0%, 0/16). As in our study, the coronary and sagittal reconstructions were not performed, and the lower sensitivity of CT for detecting peritoneal seeding in the bladder dome may be attributable to this factor. The sensitivity of CT for detecting peritoneal implants in the right and left paracolic gutter and right and left subdiaphragmatic area, was 77, 69, 72, and 61%, respectively, in the non-neoadjuvant group and 56, 29, 17, and 16%, respectively, in the neoadjuvant group. These decreased sensitivities may be due to the decreased or no longer existing ascites which may facilitate the detection of peritoneal implants.

Our study has some limitations. First, the number of patients involved was relatively small to be able to carry out a subgroup analysis, such as determining the difference in the diagnostic performance for detecting peritoneal seeding in the neoadjuvant and non-adjuvant groups. We believe that next study including a larger patient number may have resulted in a more reliable result on this issue. A second limitation of our study was that multi-planar reformatted images, which may facilitate the detection of peritoneal seeding [22], were not reconstructed.

In conclusion, although multi-detector CT is useful for detecting peritoneal implants and lymph node metastasis in ovarian cancer patients, it has only moderate, region-based diagnostic performance.

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**Conflict of interest statement** The authors have no conflict of interest to declare.

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