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# Role of Diffusion Weighted Magnetic Resonance Imaging at 3-T in Staging of Endometrial Cancer and Correlation to Histopathology

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***Authors' contributions***

*This work was carried out in collaboration between all authors. Authors GQD and JCW contributed equally to this work. Authors GQD and JCW designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors KD and HS managed the analyses of the study. Author KD managed the literature searches. All authors read and approved the final manuscript.*

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## ABSTRACT

**Aim:** To investigate the value of diffusion weighted imaging (DWI) at 3-T MR in staging of endometrial cancer and the correlation to histopathology.
**Study Design:** A retrospective study.
**Place and Duration of Study:** CT-MR Division, Qianfoshan Hospital Affiliated to Shandong University. Department of Radiology, Affiliated Hospital of Jining Medical College. From June 2013 to June 2014
**Methodology:** 30 patients with histologically proved endometrial cancers were analyzed retrospectively. The staging diagnosis of DWI was compared with pathologic results. The ADC values in different histologic types and different differentiated of endometrial cancers were also compared. $P<0.05$ was considered statistically significant.
**Results:** The staging accuracy of DWI was 83.3%. The ADC value in 30 patients of endometrial cancer was $(0.856\pm0.080)\times10^{-3}$ $mm^2/s$. There was no statistically significant difference in different

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histologic types (t=1.093，P=0.284). In different differentiated endometrial cancers, there was significant difference (F=97.246，P=0.000).
**Conclusion:** DWI has considerable value in staging of endometrial cancer. The ADC values can demonstrate the grade malignancy of tumors initially. So diffusion weighted sequences can be included in routine MR protocols for tumor assessment.

*Keywords: DWI; endometrial cancer; histopathology; neoplasms by histologic type; stage.*

## 1. INTRODUCTION

Endometrial cancer is the fourth most common malignancy in females and the most common malignancy of the female reproductive tract [1]. Magnetic resonance (MR) imaging is essential for the preoperative staging of endometrial cancer because it can accurately depict the depth of myometrial invasion, which is the most important morphologic prognostic factor. Furthermore, some other factors including histologic type, tumor grade and presence of lymph node metastases may influence overall patient survival [2]. Diffusion weighted magnetic resonance imaging (DWI) is a functional imaging technique whose contrast derives from the random motion of water molecules within tissues. DWI is a useful adjunct to standard morphologic imaging and may improve overall staging accuracy [3,4]. DWI can also provide values of apparent diffusion coefficient (ADC) of tissues under investigation. The ADC value of tissue is influenced by nuclear-to-cytoplasmic ratio (NCR) and cellular density [5-7]. It is known that the ADC values of malignant neoplasm are lower than those of normal tissues and benign lesions in many organs [8-13]. The ADC values of endometrial cancer have also been proved much lower than normal endometrium and benign lesions in uterine endometrial cavity [14,15]. Most of the literatures focused on the differentiation of endometrial malignancies from benign endometrial lesions and the improvement of staging accuracy. Few studies paid close attention to the correlation with endometrial cancer to histopathology which is another important prognostic factor. Our purpose of this study was to determine the feasibility of DWI at 3-T in staging of endometrial cancer and to investigate whether the ADC values of endometrial cancers have correlation to histopathology.

## 2. MATERIALS AND METHODS

### 2.1 Patient Population

This retrospective study was performed under an institutional review board protocol and complied with the Declaration of Helsinki. From June 2013 to June 2014, 30 female patients (age range, 29-76 years; mean age, 54.2 years) pathologically confirmed endometrial cancer underwent preoperative assessment with MR of the pelvis. A professional gynecological doctor was responsible for dealing with the cases. 24 patients were postmenopausal women and the other 6 patients were premenopausal female. Informed consent was obtained from all patients or their legal representatives before MR examination. All patients underwent panhysterectomy and pelvic lymphadenectomy within one week after MR examination.

### 2.2 MR Technique

MR imaging was performed using a 3-T MR system (Siemens Magnetom Skyra 3-T) with an 8-channal torso phased-array coil. Routine pelvic MR imaging were acquired as follows: (a) T2-weighted fast spin echo imaging in the sagittal oblique plane with fat saturation (repetition time [TR]/echo time [TE], 6210.0/86.0 milliseconds; slice thickness, 4mm; field of view, 32-40 cm; matrix size, 320×216; number of excitation, 2 ); (b) T2-weighted fast spin echo imaging in the axial plane (TR/TE, 5300.0/85.0 milliseconds; slice thickness, 4mm; field of view, 32-40 cm; matrix size, 256×256; number of excitation, 2); (c) T1-weighted fast spin echo imaging in the axial plane with fat saturation (TR/TE, 788.0/20.0 milliseconds; slice thickness, 4mm; field of view, 32-40 cm; matrix size, 320×218; number of excitation, 2).

Axial DW images were obtained. DWI sequence was used for fat suppression in a spin echo type and single-shot echo planar imaging (EPI) sequence, with free breathing during acquisition. Imaging parameters for DWI was as follows: TR/TE, 4400.0/87.0 milliseconds; b factors, 0 and 800 s/mm$^2$; slice thickness, 4mm; field of view, 32-40 cm; matrix size, 160×122; numbers of excitation, 5; acquisition time, approximately 2.5 min.

### 2.3 Image Analysis

The ADC map of each DW image was produced automatically. Then all of the DW images and ADC map were sent to a workstation (SYGNO VE40A, Siemens). According to the images, the evaluation of tumor staging was made by 2 radiologists with more than 5 years' experience in genitourinary radiology, respectively. The criterion of tumor staging was complied with International Federation of Gynecology and Obstetrics (FIGO) system revised in 2009 [16]. If the two radiologists had different diagnosis, they could find an amicable solution through the consultation process.

The ADC values of endometrial cancers were performed on the ADC maps that contained the largest tumor cross-section. The region of interest (ROI) could not be placed to involve necrosis within the tumor in reference with T1- and T2-weighted images. For each case, the ADC values were measured 3 times in different regions, and the mean measurement values were computed.

### 2.4 Histopathology

The histologic types and tumor grades were performed by a senior and experienced pathologist. Because most of the tumors were endometrioid adenocarcinomas, the other histologic types included adenocarcinoma with squamous differentiation, uterine sarcomas and adenosquamous carcinoma. So in this study, we only divided all the tumors into two groups according to histologic types: group of endometrioid adenocarcinomas and group of non- endometrioid adenocarcinomas. The tumor grades included highly differentiated, moderately differentiated and poorly differentiated grade.

### 2.5 Statistical Analysis

Statistical analysis was done on SPSS 19.0 software. The staging accuracy of DWI was calculated with the golden standard of pathological staging. ADC values were recorded as the format—'mean±standard deviation' ( $\bar{x}\pm s$). ADC values were calculated by independent samples T test between two groups of histologic types and analysis of variance (ANOVA) in different groups of tumor grades. $P<0.05$ was considered statistically significant.

## 3. RESULTS

### 3.1 DWI Staging

The results of DWI and pathological staging of endometrial cancers were showed in Table 1. The tumors of stage $\overline{A}$ were misdiagnosed for 2 cases (one case was overestimated stage $\overline{B}$, one case was overestimated stage $\alpha$). One case of stage $\overline{B}$ was underestimated stage $\overline{A}$. There were another two cases of stage $\alpha$ underestimated stage $\overline{B}$. The total staging accuracy of DWI was 83.3% (Figs. 1 and 2).

### 3.2 The Correlation of ADC Values to Histopathology

The mean ADC value of total 30 cases of endometrial cancers was $(0.856\pm0.080)\times10^{-3}$ $mm^2/s$. The results of different histologic types and tumor grades were showed in Table 2 and 3. There was no significant difference between group of endometrioid adenocarcinomas and group of non- endometrioid adenocarcinomas ($P>0.05$). No significant difference was found between highly differentiated and moderately differentiated groups ($P>0.05$). The ADC values of poorly differentiated group were lower than highly and moderately differentiated groups with significant difference ($P<0.05$). There was significant difference among the three groups of different differentiated ($P<0.05$) (Figs. 1 and 2).

**Table 1. The results of DWI and pathological staging (number of cases)**

| | DWI | Pathology |
|---|---|---|
| I A | 9 | 10 |
| I B | 10 | 8 |
| II | 8 | 9 |
| III | 2 | 2 |
| IV | 1 | 1 |

## 4. DISCUSSION

Uterine endometrial cancer is one of the common cancers in female. In many countries, it is the most common gynecologic malignancy [17]. Preoperative assessment of the depth of myometrial invasion is very important because it closely correlates with the prevalence of lymph node metastasis and the patient's prognosis [18,19]. Surgical staging of endometrial cancer was first proposed in 1988, and the staging system was updated in 2009 [16]. Key changes incorporated into the 2009 FIGO staging system

include simplification of stage Ⅰ disease and removal of cervical mucosal invasion as a distinct stage.

**Table 2. ADC values of different histologic types**

| Group | n | ADC value ($\times10^{-3}$ $mm^2/s$) |
|---|---|---|
| Endometrioid adenocarcinomas | 26 | 0.862±0.082 |
| Non-endometrioid adenocarcinomas | 4 | 0.815±0.055 |

**Table 3. ADC values of different differentiated grades**

| Group | n | ADC value ($\times10^{-3}$ $mm^2/s$) |
|---|---|---|
| Highly differentiated | 11 | *0.912±0.020 |
| Moderately differentiated | 9 | +0.901±0.019 |
| Poorly differentiated | 10 | 0.751±0.042 |

**P=0.000, compared to poorly differentiated; +P=0.000, compared to poorly differentiated; P=0.000 (F=97.246): comparison of three groups*

Magnetic resonance (MR) imaging is essential for the preoperative staging of endometrial cancer because of its fine soft tissue contrast resolution. It can accurately help assess the depth of myometrial invasion, whereas histologic grade can be determined with endometrial sampling. However, some pathologic factors, such as myometrial thinning due to polypoid tumor, coexisting leiomyoma or adenomyosis, and congenital anomalies, may cause incorrect MR diagnosis of myometrial invasion [20]. DWI with ADC measurement yields quantitative information reflecting tissue cellularity, and may be helpful in differentiating relatively hypercellular endometrial cancer from normal edometrium and benign endometrial lesions. Shen et al. [21] found that DWI could highlight the location and extent of endometrial cancer, and detect some unconspicuous lesions in routine MRI. Thus DWI can improve the staging accuracy before operation. In our study, the staging accuracy with DWI was 83.3%. It can depict the myometrial invasion clearly.

Besides the preoperative staging, histologic type and tumor grade are also prognostic factors which can influence the patient's overall survival [22,23]. The histologic types of endometrial cancer include endometrioid adenocarcinoma, clear cell carcinoma, serous papillary adenocarcinoma, squamous carcinoma, mucinous carcinoma , undifferentiated carcinoma and mixed carcinoma. Among the various kinds of endometrial tumors, most tumors belong to endometrioid adenocarcinoma accounting for 80%-90%. In our study, the endometrioid adenocarcinoma accounted for 86.7% (26/30), with the consistency of literatures. The ADC values in endometrioid adenocarcinomas had no significant difference compared with that in non-endometrioid adenocarcinomas. This is also consistent with literatures [24].

DWI is a recent new imaging technique which depicts tissue characteristics based on diffusion motion of water molecules. It visualizes a random microscopic motion of molecules and that is how it provides a tissue contrast different from that of conventional T1 and T2 weighted images. The ADC relates to the molecular translational movement of water molecules. This movement is limited in an environment that contains structures such as cell membranes [25]. Therefore, with increasing tumor cellularity and architectural distortion, there is a reduction in extracellular space, which also becomes increasingly tortuous. These changes are reflected by a reduced ADC value. In general, malignant tumors have a higher cellularity than normal tissues and benign lesions [26]. High-grade adenocarcinomas typically have high cellular density and so would be expected to have lower ADC values. A trend toward lower ADC values in higher-grade endometrial cancers was noted by Tamai et al. [27] although this trend did not achieve statistical significance in their study. Now we systematically evaluated the correlation between ADC values and tumor grades. Our study showed that ADC values were statistically different in tumors with various pathologic grades. The ADC values of poorly differentiated tumors were lower than highly and moderately differentiated tumors with significant difference. While no significant difference was found between highly differentiated and moderately differentiated tumors. The results demonstrate that in similar differentiated tumors, such as highly differentiated and moderately differentiated, ADC values exist no difference. Maybe the cellular density and cell structure are little changed from highly differentiated to moderately differentiated. However, since the cellularity is changed so much, ADC values can reflect the difference, such as poorly differentiated and highly differentiated.

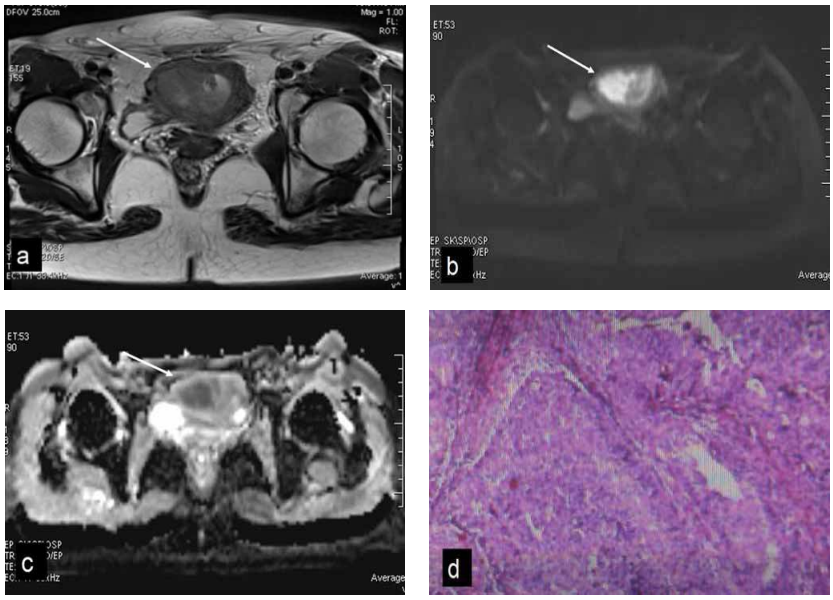


**Fig. 1. Endometrial cancer stage IA (arrow). a. T2WI image demonstrates a hyperintense mass. b. DWI image demonstrates the hyperintense mass with superficial myometrial invasion. c. ADC map demonstrates the hypointense mass with ADC value of $0.638\times10^{-3}$ $mm^2/s$. d. Pathological image of poorly differentiated endometrioid adenocarcinoma (HE, ×100)**

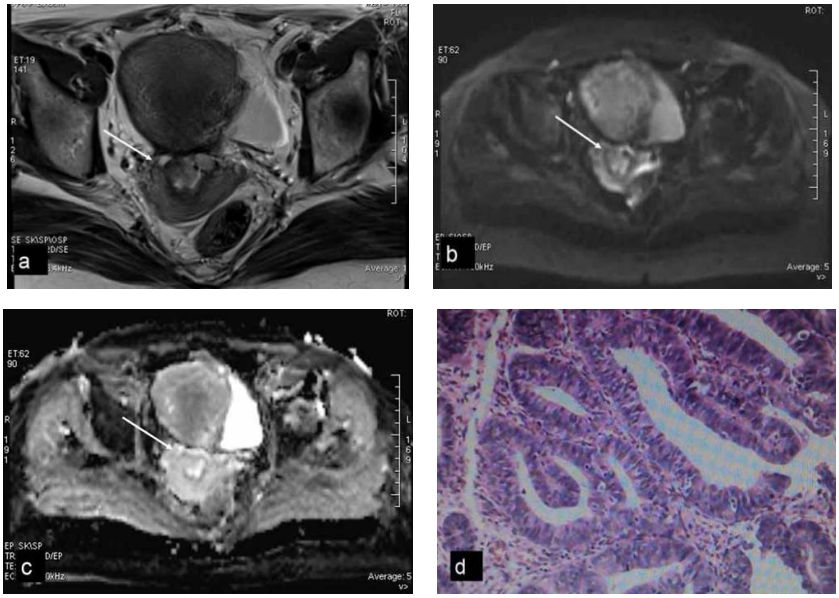


**Fig. 2. Endometrial cancer stage II (arrow). a. T2WI image demonstrates a slightly hyperintense mass with uterine junction zone broken in cervical level. b. DWI image demonstrates the slightly hyperintense mass. c. ADC map demonstrates the slightly hypointense mass with ADC value of $0.932\times10^{-3}$ $mm^2/s$. d. Pathological image of highly differentiated endometrioid adenocarcinoma (HE, ×100)**

This study has some limitations. First, the number of patients cases used in this study was too few to properly classify the diagnostic efficiency in each stage of tumors. This study only evaluated the effectiveness of the whole staging. Despite the small number of cases, the primary importance of DWI in the staging would be to conduct more conservative surgery in

patients with stage IA, in which the realization of pelvic lymphadenectomy is unnecessary. A larger population of the patients may be required in the future. Second, in this study we had not compared DWI results with those in wide-used T2WI with / without contrast enhanced T1WI. Further studies should be continued in the future.

## 5. CONCLUSION

DWI can make a decision about the staging of endometrial cancer accurately. It can initially demonstrate the grade malignancy though measurement of ADC values. Meanwhile, no contrast medium injection is required, so that diffusion weighted sequences can be included in routine MR protocols for tumor assessment.

## ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the ethics committee of Qianfoshan Hospital Affiliated to Shandong University and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Beddy P, O'Neill AC, Yamamoto AK, Addley HC, Reinhold C, Sala E. FIGO staging system for endometrial cancer: Added benefits of MR imaging. Radiographics. 2012;32(1):241-254. [PubMed: 22236905].
2. Dogan D, Inan N, Sarisoy HT, Gumustas S, Akansel G, Muezzinoğlu B, et al. Preoperative evaluation of myometrial invasion in endometrial carcinoma: diagnostic performance of 3T MRI. Abdom Imaging. 2013;38(2):388-396. [PubMed: 22722382].
3. Li HM, Qiang JW, Xia GL, Zhao SH, Ma FH, Cai SQ, et al. Primary ovarian endometrioid adenocarcinoma: Magnetic resonance imaging findings including a preliminary observation on diffusion-weighted imaging. J Comput Assist Tomogr. 2015;39(3):401-405. [PubMed: 25978592].
4. Ren C, Xue HD, Li S, Zhang J, Pan WD, Sun ZY, et al. Clinical application of magnetic resonance imaging in preoperative evaluation of endometrial cancer. Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2012;34(5):455-460. [PubMed: 23134820].
5. Gallego JC, Porta A, Pardo MC, Fernández C. Evaluation of myometrial invasion in endometrial cancer: Comparison of diffusion-weighted magnetic resonance and intraoperative frozen sections. Abdom Imaging. 2014;39(5): 1021-1026. [PubMed: 24699937].
6. Inoue C, Fujii S, Kaneda S, Fukunaga T, Kaminou T, Kigawa J, et al. Apparent diffusion coefficient (ADC) measurement in endometrial carcinoma: Effect of region of interest methods on ADC values. J Magn Reson Imaging. 2014;40(1):157-161. [PubMed: 24677497].
7. Uhl M, Altehoefer C, Kontny U, Il'yasov K, Büchert M, Langer M. MRI-diffusion imaging of neuroblastomas: First results and correlation to histology. Eur Radiol. 2002;12(9):2335-2338. [PubMed: 12195491].
8. Kartalis N, Lindholm TL, Aspelin P, Permert J, Albiin N. Diffusion-weighted magnetic resonance imaging of pancreas tumors. Eur Radiol. 2009;19(1):1981-1990. [PubMed: 19687725].
9. Bogner W, Gruber S, Pinker K, Grabner G, Stadlbauer A, Weber M, et al. Diffusion-weighted MR for differentiation of breast lesions at 3.0 T: How does selection of diffusion protocols affect diagnosis? Radiology. 2009; 253(2):341-351. [PubMed: 19703869].
10. Zhang J, Tehrani YM, Wang L, Ishill NM, Schwartz LH, Hricak H. Renal masses: Characterization with diffusion weighted MR imaging: A preliminary experience. Radiology. 2008;247(2):458-464. [PubMed: 18430878].
11. Kilickesmez O, Bayramoglu S, Inci E, Cimilli T. Value of apparent diffusion coefficient measurement for discrimination of focal benign and malignant hepatic masses. J Med Imagin Radiat Oncol. 2009; 53(1):50-55. [PubMed: 19453528]

12. Kiliçkesmez O, Cimilli T, Inci E, Kayhan A, Bayramoğlu S, Taşdelen N, et al. Diffusion-weighted MRI of urinary bladder nd prostate cancer. Diagn Interv Radiol. 2009; 15(2):104-110. [PubMed: 19517380].
13. Chen J, Zhang Y, Liang B, Yang Z. The utility of diffusion weighted MR imaging in cervical cancer. Eur J Radiol. 2009;74(3): e101-106.
14. Fujii S, Matsusue E, Kigawa J, Sato S, Kanasaki Y, Nakanishi J, et al. Diagnostic accuracy of the apparent diffusion coefficient in differentiating benign from malignant uterine endometrial cavity lesions: Initial results. Eur Radiol. 2008; 18(2):384-389. [PubMed: 17917730].
15. Masroor I, Zeeshan M, Afzal S, Ahmad N, Shafqat G. Diffusion weighted MR imaging (DWI) and ADC values in endometrial carcinoma. J Coll Physicians Surg Pak. 2010;20(11):709-713. [PubMed: 21078241].
16. Creasman W. Revised FIGO staging for carcinoma of the endometrium. Int J Gynaecol Obstet. 2009; 105(2):109. [PubMed: 19345353].
17. Ma X, Zhao LG, Sun JW, Yang Y, Zheng JL, Gao J, et al. Association between breastfeeding and risk of endometrial cancer: A meta-analysis of epidemiological studies. Eur J Cancer Prev. 2015 Aug 7. [Epub ahead of print] [PubMed: 26258808].
18. Andreano A, Rechichi G, Rebora P, Sironi S, Valsecchi MG, Galimberti S. MR diffusion imaging for preoperative staging of myometrial invasion in patients with endometrial cancer: A systematic review and meta-analysis. Eur Radiol. 2014;4(6): 1327-1338. [PubMed: 24668009]
19. Koplay M, Dogan NU, Erdogan H, Sivri M, Erol C, Nayman A, et al. Diagnostic efficacy of diffusion-weighted MRI for pre-operative assessment of myometrial and cervical invasion and pelvic lymph node metastasis in endometrial carcinoma. J Med Imaging Radiat Oncol. 2014;58(5): 538-546 [PubMed: 25046775].
20. Utsunomiya D, Notsute S, Hayashida Y, Lwakatare F, Katabuchi H, Okamura H, et al. Endometrial carcinoma in adenomyosis: Assessment of myometrial invasion on T2-weighted spin-echo and gadolinium enhanced T1-weighted image. Am J Roentgenol. 2004;182(2):399-404. [PubMed: 14736670].
21. Shen SH, Chiou YY, Wang JH, Yen MS, Lee RC, Lai CR, et al. Diffusion-weighted single-shot -planar imaging with parallel technigue in assessment of endometrial cancer. AJR Am J Roentgenol. 2008; 190(2):481-488. [PubMed: 18212236].
22. Kodama J, Seki N, Nakamura K, Hongo A, Hiramatsu Y. Prognostic factors in pathologic parametrium-positive patients with stage I B- II B cervical cancer treated by radical surgery and adjuvant therapy. Gynecol Oncol. 2007;105(3):757-761. [PubMed: 17433424].
23. Kisu I, Banno K, Lin LY, Ueno A, Abe T, Kouyama K, et al. Preoperative and intraoperative assessment of myometrial invasion in endometrial cancer: Comparison of magnetic resonance imaging and frozen sections. Acta Obstet Gynecol Scand. 2013;92(5):525-535. [PubMed: 2316348 0].
24. McVeigh PZ, Syed AM, Milosevic M, Fyles A, Haider MA. Diffusion weighted MRI in cervical cancer. Eur Radiol. 2008;18(5): 1058-1064. [PubMed: 18193428].
25. Nakamura K, Joja I, Fukushima C, Haruma T, Hayashi C, Kusumoto T, et al. The preoperative SUVmax is superior to ADCmin of the primary tumour as a predictor of disease recurrence and survival in patients with endometrial cancer. Eur J Nucl Med Mol Imaging. 2013;40(1): 52-60. [PubMed: 22968401].
26. Woo S, Cho JY, Kim SY, Kim SH. Histogram analysis of apparent diffusion coefficient map of diffusion-weighted MRI in endometrial cancer: A preliminary correlation study with histological grade. Acta Radiol. 2014;55(10):1270-1277. [PubMed: 24316663].
27. Tamai K, Koyama T, Saga T, Umeoka S, Mikami Y, Fujii S, et al. Diffusion-weighted MR imaging of uterine endometrial cancer. J Magn Reson Imaging. 2007;26(3):682-687. [PubMed: 17729360].



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