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Value of the intraoperative assessment of the depth of myometrial invasion in endometrial carcinoma

Wartość makroskopowej oceny głębokości nacieku nowotworowego mięśnia macicy w raku *endometrium*

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Abstract

Objectives: *The aim of the study was to evaluate the value of intraoperative assessment of depth of myometrial invasion in patients with FIGO stage I of the endometrial carcinoma.*

Material and methods: *A total number of 112 patients with FIGO stage I of the endometrial carcinoma undergoing surgery were enrolled in the study. All patients had undergone intraoperative assessment of the depth of myometrial invasion performed by a surgeon. The depth was determined as more or less than 50% of myometrial thickness according to FIGO classification. Gross visual estimation of the depth of myometrial invasion at the time of the operation was compared with the final histopathological report. Sensitivity, specificity and positive and negative predictive values of the method were determined by means of statistical analyses.*

Results: *The depth of the myometrial invasion was accurately determined by the surgeon in 82.1% of cases. Sensitivity and specificity were 68% and 82.1%, respectively. The accurate prediction rate of the myometrial invasion in the group of patients with well differentiated (G1) endometrial carcinoma was higher (88,4%) than in group with moderately and low differentiated tumour (78,3%).*

Conclusions: *The accuracy of macroscopic evaluation of myometrial invasion is high and reaches up to 82,1%. The accurate determination rate increases if the differentiation of tumour is higher.*

Key words: **endometrial carcinoma** / **myometrium-invasion** /

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Streszczenie

Cel: *W pracy podjęto próbę określenia wartości śródoperacyjnej makroskopowej oceny głębokości nacieku nowotworowego mięśnia macicy w raku endometrium.*

Materiał i metody: *Prospektywnym badaniem objęto 112 pacjentek leczonych operacyjnie z powodu raka endometrium FIGO I. U każdej z nich przeprowadzono śródoperacyjną makroskopową ocenę głębokości nacieku nowotworowego, który odpowiednio do klasyfikacji FIGO określano jako mniejszy lub większy niż połowa grubości warstwy mięśniowej ściany macicy. Ocenę makroskopową porównano z wynikiem badania histopatologicznego preparatu pooperacyjnego. Obliczono czułość, specyficzność i wartości predykcyjne metody.*

Wyniki: *Głębokość nacieku mięśnia macicy została prawidłowo makroskopowo oceniona w 82,1% przypadków. Czułość i specyficzność metody wyniosły odpowiednio 68% i 83,78%.*

Odsetek prawidłowych rozpoznań u pacjentek z dobrze zróżnicowanym (G1) rakiem endometrium – 88,4% – był wyższy niż u kobiet ze średnio i nisko zróżnicowanymi (G2 i G3) nowotworami - 78,3%.

Wnioski: *Trafność diagnostyczna makroskopowej oceny głębokości nacieku mięśniówki macicy w raku endometrium jest wysoka i wynosi 82,1%.*

Dokładność makroskopowej oceny infiltracji mięśnia macicy rośnie wraz ze wzrostem zróżnicowania nowotworu.

Słowa kluczowe: **rak *endometrium*** / **naciek mięśniówki** /

Introduction

Currently endometrial carcinoma is the most common female genital tumour [1-4]. Treatment of choice in stage I endometrial carcinoma involves simple hysterectomy with bilateral adnexectomy [5-8].

In certain clinical conditions surgical treatment also involves pelvic and paraaortic lymphadenectomy. There is a widespread opinion that pelvic lymphadenectomy should be performed in cases of moderately and poorly differentiated tumours (G2, G3) that infiltrate more than half of myometrial thickness (FIGO IC) and certain histological types (e.g. squamous adenocarcinoma, clear cell carcinoma) [1, 5, 6, 8-11].

Ultrasound evaluation of the depth of tumour invasion features high sensitivity but low specificity [12-14]. Other currently used imaging methods (CT, MRI) provide very detailed assessment of local progression of endometrial carcinoma; however, they are applied rarely in clinical practice. Depth of myometrial invasion by endometrial carcinoma is usually determined by macroscopic visual assessment. Literature data concerning predictive value of this method are inconsistent and require verification [8, 15-18].

Objective

The aim of the study was to determine diagnostic value of intraoperative assessment of the depth of myometrial invasion in endometrial carcinoma on the basis of the authors' own material.

Material and methods

The prospective study involved 112 patients in stage I endometrial carcinoma, who were admitted to the Department of Obstetrics and Gynaecology, Provincial Specialised Hospital in Rzeszów in years 1998-2001. Mean age of the patients was 63.1 years (range 38-85 years). The majority of the toumors were adenocarcinoma (72.3%).

The detailed list of histological types of endometrial carcinoma in the study group shows Table I.

Table I. Distribution of histological types of endometrial carcinoma in the study group.

Histological type	No. of patients	%
Adenocarcinoma	81	72.3
Papillary serous adenocarcinoma	8	7.1
Adenocarcinoma with squamous metaplasia	8	7.1
Squamous adenocarcinoma	7	6.3
Clear cell carcinoma	5	4.5
Poorly differentiated carcinoma	2	1.8
Squamous cell carcinoma	1	0.9
Total	112	100

Moderately differentiated carcinomas (G2) were the most common (50 patients), while poorly differentiated carcinomas (G3) comprised the smallest group (19 patients). Exact percentages of particular differentiation grades in the material examined are presented in Table II.

Table II. Histological differentiation of endometrial carcinoma in the study group.

Grade of histological differentiation	No. of patients	%
G1	43	38.4
G2	50	44.6
G3	19	17.0
Total	112	100

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Basic type of surgery in the endometrial carcinoma patients examined was simple hysterectomy with bilateral adnexectomy. At the patient's request, in two cases laparoscopically assisted vaginal hysterectomy was performed. According to current guidelines, in some patients additionally pelvic lymphadenectomy was performed. All the procedures performed are presented in Table III.

Table III. Types of surgery performed in the study group.

Type of surgery	No of patients
Simple hysterectomy with bilateral adnexectomy	31
Simple hysterectomy with bilateral adnexectomy and lymphadenectomy	79
Laparoscopically assisted vaginal hysterectomy	2
Total	112

In each case the removed uterus was open, and visual estimate of depth of myometrial invasion was recorded by the surgeon. According to FIGO classification the infiltration was determined as less (Figure 1) or more than 50% of myometrial thickness (Figure 2).

Macroscopic assessment was compared with the final histopathologic report. Histopathological specimens were routinely stained with haematoxylin and eosin (Figures 3 & 4). Additionally Masson trichrome staining for collagen fibres was performed (Figures 5 & 6).

The latter staining method is not routinely used is histopathological determination of endometrial carcinoma. It was applied under the study protocol for the sake of better visualisation of the contrast between myometrium and carcinoma infiltration within the specimen. The blue colour of the myometrium results from fibrous stromal tissue, while carcinoma infiltration in the specimen is apparently pink, which colour is related to pink discoloration of carcinoma cellular cytoplasm. Contrary to regular myometrium, the tumour tissue contains small amount of fibrous stroma.

Sensitivity, specificity, positive and negative predictive values of the method were calculated assuming cut-off value of infiltration more than half of myometrial thickness. Moreover, correctness of diagnosis in relation to the degree of tumour differentiation was assessed.

Results

The depth of myometrial infiltration was accurately determined by macroscopic assessment in 92 (82.1%) patients. In 16 cases local progression of the tumour was underestimated, while in four patients diagnosis was false positive (Table IV).

Sensitivity and specificity of the method were 68% and 83.78%, respectively. Values of other selection criteria of diagnostic tests are presented in Table V.

Percentage of correct diagnosis in patients with well-differentiated endometrial carcinoma (88.4%) was higher than in patients with moderately and poorly differentiated tumours (78.3%) (Tables IV & VII).

Due to the small size of particular subgroups, values of selection criteria for diagnostic test were not calculated.

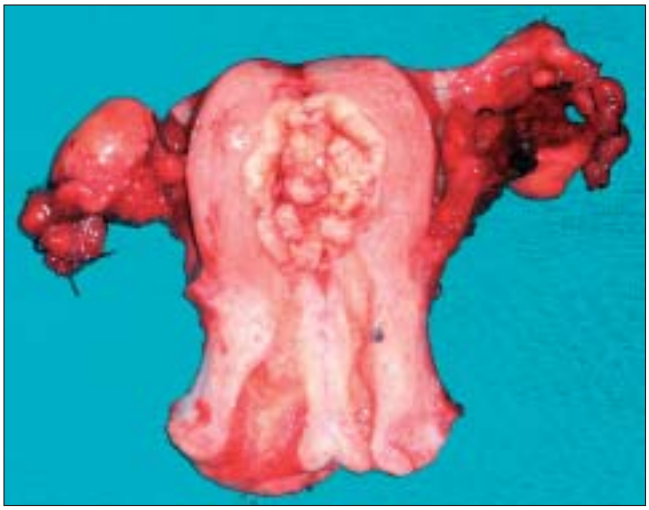

Figure 1. Longitudinal section of uterus in stage FIGO IB endometrial carcinoma.

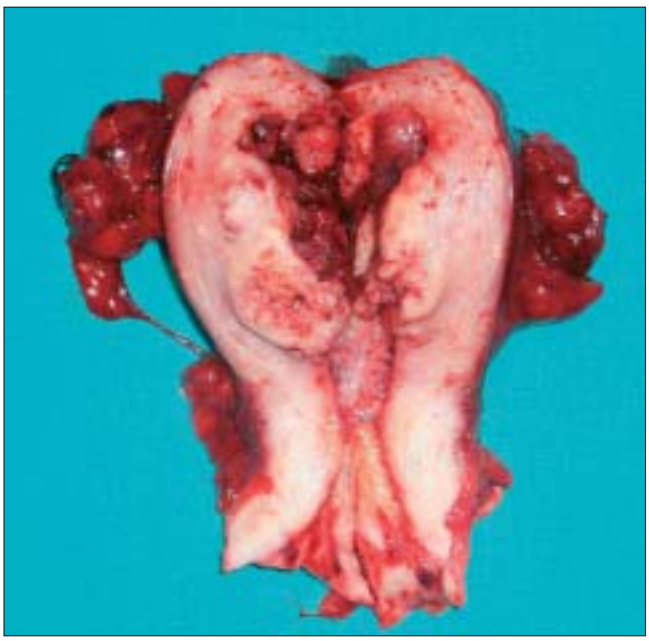

Figure 2. Longitudinal section of uterus in stage FIGO IC endometrial carcinoma.

Discussion

Since 1988, the spread of endometrial carcinoma has been assessed according to surgical and pathological staging system FIGO [19]. One of major element of the system is determination of the depth of tumour infiltration of the myometrium. The parameter, together with histological type and differentiation, is one of the most important risk factors for lymph node metastases. Probability of lymph node involvement is significantly higher, when myometrial infiltration exceeds 50% of its thickness (FIGO IC) [15, 17, 20, 21].

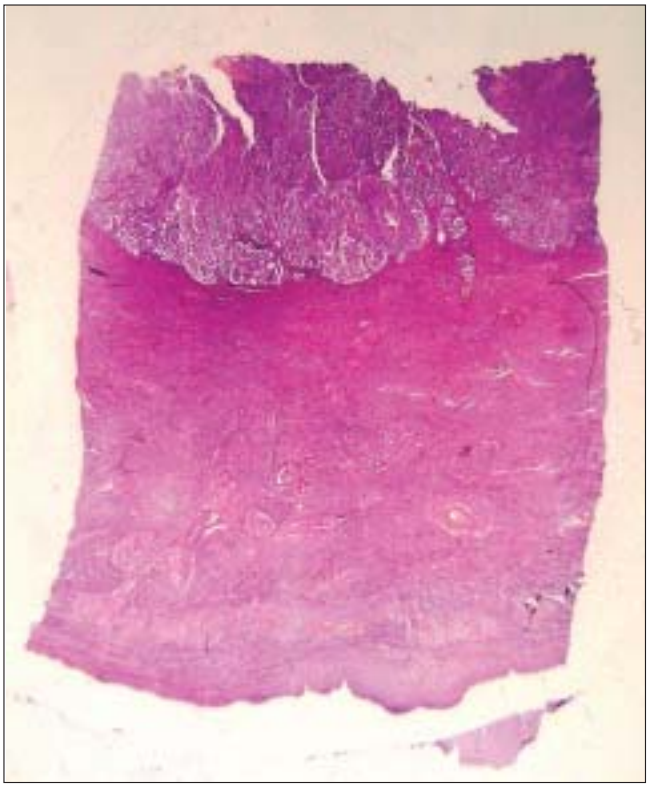

Figure 3. Histopathological specimen of H&E stained in stage FIGO IB endometrial carcinoma. Tumour infiltration involves 1/3 (upper) of myometrium.

Figure 5. Histopathological specimen of FIGO IB endometrial carcinoma stained for collagen fibres (Masson trichrome staining). Tumour infiltration involves 1/3 (upper) of myometrium.

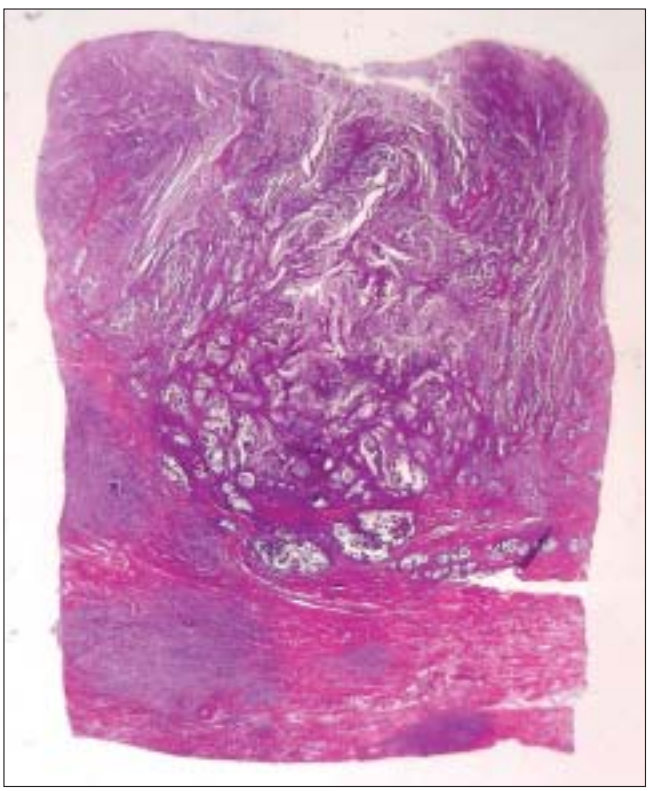

Figure 4. Histopathological specimen of H&E stained in stage FIGO IC endometrial carcinoma. Tumour infiltration involves 3/4 (upper) of myometrium.

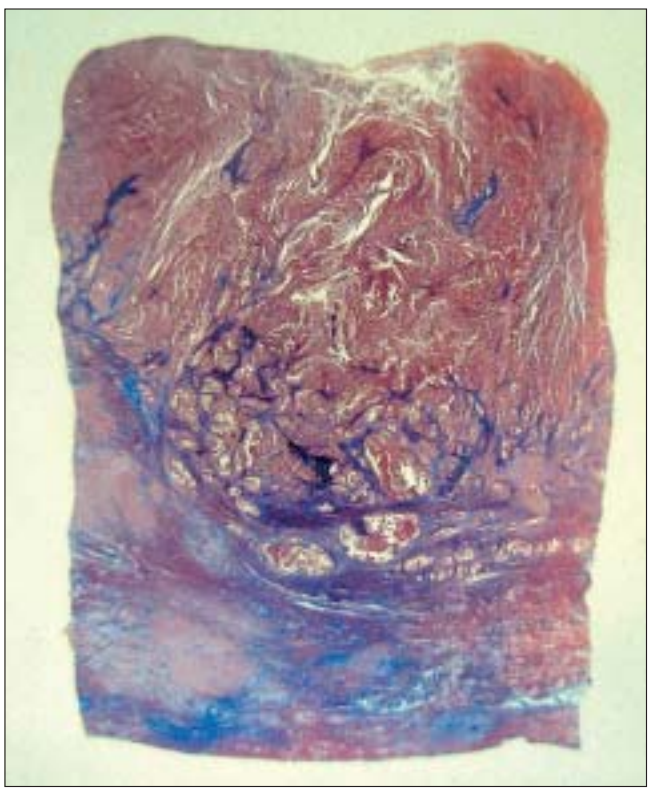

Figure 4. Histopathological specimen of FIGO IC endometrial carcinoma stained for collagen fibres (Masson trichrome staining). Tumour infiltration involves 3/4 (upper) of myometrium.

Table IV. Comparison of macroscopic and microscopic assessment of the depth of myometrial infiltration in endometrial carcinoma.

Macroscopic assessment	Microscopic assessment			Total
	endometrium only	< ½ thickness	> ½ thickness	
< ½ thickness	7	51	16	74
> ½ thickness	0	4	34	38
Total	7	55	50	112

Table V. Values of selection criteria of diagnostic test related to macroscopic assessment of depth of myometrial infiltration in endometrial carcinoma.

Sensitivity	**68%**
Specificity	**83.78%**
Negative predictive value	**93.55%**
Positive predictive value	**89.47%**
Accuracy	**82.14%**

Table VI. Comparison of macroscopic and microscopic assessment of the depth of myometrial infiltration in subgroup of patients with well differentiated (G1) tumours.

Macroscopic assessment	Microscopic assessment			Total
	endometrium only	< ½ thickness	> ½ thickness	
< ½ thickness	4	30	4	38
> ½ thickness	0	1	4	5
Total	4	31	8	43

Table VII. Comparison of macroscopic and microscopic assessment of the depth of myometrial infiltration in subgroup of patients with moderately and poorly differentiated (G2 and G3) tumours.

Macroscopic assessment	Microscopic assessment			Total
	endometrium only	< ½ thickness	> ½ thickness	
< ½ thickness	3	21	12	36
> ½ thickness	0	3	30	33
Total	3	24	42	69

In the case of well differentiated (G1) adenocarcinoma the parameter is the only criterion indicating the need for lymphadenectomy [22].

According to current standard of care [8, 17, 23], an attempt of assessment of local progressions of endometrial carcinoma should be made as early as during preoperative diagnostics. The simplest method of determination of the depth of tumour infiltration is transvaginal ultrasound. Sensitivity of this method is relatively high, varying from 86% to 100%; however, it features relatively low specificity of 65-73% [12-14]. Up to 16% of the results are overestimated, according to Randelzhofer. Predictive value of transvaginal ultrasound in determination of the depth of myometrial infiltration is 80-87% [24].

Other method of determination of the depth of myometrial infiltration in endometrial carcinoma is computed tomography (CT); the method features higher specificity (82-93%) but lower sensitivity (77-88%), as compared with ultrasound [25].

Magnetic resonance imaging (MRI) is not considered a routine preoperational examination of endometrial carcinoma patients [23]; however, it features numerous advantages (e.g. lack of radiation exposure, good contrast of soft tissues), which result in its increasing importance in determination of staging of female genital tumours [26]. MRI is also used in planning of primary radiotherapy [23]. However, results of assessment of myometrial infiltration by MRI vary significantly. According to various authors, sensitivity of the method is 40-100%, and specificity varies from 50-95% [12, 13, 16, 26-29]. Diagnostic accuracy of MRI in the assessment of staging of endometrial carcinoma is the highest among all the imaging methods [30].

Sensitivity of macroscopic assessment of the depth of myometrial infiltration varies from 53 to 83.7%, while specificity of the method is 90.6-96% [15, 31-33].

Results obtained from the authors' own studies are similar to those quoted in the literature. Percentage of correct diagnosis was higher in patients with well-differentiated endometrial carcinoma (88.4%) than in ones with moderately and poorly differentiated tumours (78.3%). The results conform to findings by other authors [34]. According to Fanning et al., accuracy of macroscopic assessment of the depth of myometrial infiltration is significantly higher when associated with intraoperative histopathological examination. Sensitivity and specificity of the method are 87% and 99%, respectively [35].

Conclusion

1. Predictive value of macroscopic assessment of the depth of myometrial infiltration by endometrial carcinoma is high and amounts to 82.1%.
2. Accuracy of macroscopic assessment of the depth of myometrial infiltration is more reliable as the differentiation of tumour increases.

Piśmiennictwo

1. DiSaia P, Creasman W. Ginekologia onkologiczna. Tom I. Lublin: *Czelej,* 1999, 169-208.
2. Greenlee R, Murray T, Bolden S, [et al.]. Cancer statistics, 2000. *CA Cancer J Clin.* 2000, 50, 7-33.
3. Horn L. Das Endometriumkarzinom – von der molekularen Pathogenese über die Histomorphologie zur individualisierten Therapie. *Zentralbl Gynäkol.* 2002, 1, 1-2.
4. Vizza E, Galati G, Corrado G, [et al.]. Role of pelvic lymphadenectomy in the management of stage I endometrial cancer: our experience. *Eur J Gynaecol Oncol.* 2003, 24, 126-128.
5. Emerich J. Leczenie raka błony śluzowej trzonu macicy. W: Rak błony śluzowej trzonu macicy. Red. Markowska J. Warszawa: *Springer PWN,* 1998, 153-164.
6. Kurzgefasste interdisziplinare AGO-Leitlinien für die Diagnostik und Therapie des Endometriumskarzinoms. *Zentralbl Gynäkol.* 2002, 1, 58-62.
7. Zieliński J. Nowotwory kobiecego narządu płciowego. W: Zasady rozpoznawania i leczenia nowotworów zalecane przez Centrum Onkologii w Warszawie. Red. Kułakowski A, Towpik E. Warszawa: *Wydawnictwo Polskiej Fundacji Europejskiej Szkoły Onkologii,* 1997, 41-65.

8. Tropé C, Alektiar K, Sabbatini P, [et al.]. Corpus: Epithelial Tumors. W: Principles and practice of gynecologic oncology. Ed. Hoskins W, Perez C, Young R, [et al]. Philadelphia: *Lippincott Williams & Wilkins,* 2005, 823-872.

9. Baker T. Rak endometrium. W: Podręcznik onkologii ginekologicznej. Red. Piver M. Warszawa: *PZWL,* 1999, 197-222.

10. Dreher E, Hänggi W. Basisrichtlinien zur Behandlung des Korpuskarzinoms. *Arch Gynecol Obstet.* 1991, 249, 95-98.

11. Łapińska-Szumczyk S, Emerich J. Kliniczna wartość usuwania węzłów chłonnych miednicy mniejszej w leczeniu operacyjnym raka błony śluzowej trzonu macicy. *Ginekol Pol.* 2002, 73, 976-979.

12. DelMaschio A, Vanzulli A, Sironi S, [et al.]. Estimating the depth of myometrial involvement by endometrial carcinoma: Efficacy of transvginal sonography vs MR imaging. *Am J Roentgenol.* 1993, 160, 533-538.

13. Gordon A, Fleischer A, Dudley B. Preoperative assessment of myometrial invasion of endometrial adenocarcinoma by sonography (US) and magnetic resonance imaging (MRI). *Gynecol Oncol.* 1989, 34, 175-179.

14. Prömpeler H, Madjar H, du Bois A, [et al.]. Transvaginal sonography of myometrial invasion depth in endometrial cancer. *Acta Obstet Gynecol Scand.* 1994, 73, 343-346.

15. Kolben M, Höss C, Oberlechner E, [et al.]. Operative Therapie des Endometriumskarzinoms. In: Manual Malignome des Corpus uteri. 3th.Ed. Dannecker C, Kolben M, Kürzl R. München: *Zuckschwerdt GmbH Verlag,* 2007, 28-35.

16. Cunha T, Felix A, Cabral I. Preoperative assessment of deep myometrial and cervical invasion in endometrial carcinoma: Comparison of magnetic resonance imaging and gross visual inspection. *Int J Gynecol Cancer.* 2001, 11, 130-136.

17. Baltzer J, Meerphol H, Bahnsen J. Praxis der gynäkologischen Onkologie. 2th. Stuttgart-New York: *Georg Thieme Verlag,* 2000, 200-220

18. Bidziński M, Dańska-Bidzińska A, Derlatka P [et al.]. Ocena ryzyka nawrotu nowotworu u chorych leczonych z powodu raka błony śluzowej trzonu macicy w stopniu I wg klasyfikacji klinicznej FIGO. *Ginekol Pol.* 2007, 78, 471-475.

19. FIGO. Changes in gynecologic staging by the International Federation of Gynecology and Obstetrics. *Am J Obstet Gynecol.* 1990, 162, 610-611.

20. Morrow C, Bundy B, Kurman R. Relationship between surgical-pathological risk factors and outcome in clinical stage I and II carcinoma of the endometrium. A Gynaecologic Oncology Group Study. *Gynecol Oncol.* 1991, 2, 55-65.

21. Creasman W, Morrow C, Bundy B, [et al.]. Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Group Study. *Cancer.* 1987, 60, 2035-2041.

22. Sehouli J, Lichtenegger W. Management des Endometriumkarzinoms Standards und neue Trends. *Gynäkologe.* 2004, 37, 245-25.

23. Kürzl R. Prätherapeutische Diagnostik. In: Manual Malignome des Corpus uteri. 3th. Ed. Dannecker C, Kolben M, Kürzl R. München: *Zuckschwerdt GmbH Verlag,* 2007,11-15.

24. Randelzhofer B, Pohle M, Latterman U, [et al.]. Sonographische Bestimmung der Infiltrationstiefe beim Endometriumkarzinom. *Geburtsh Frauenheilk.* 1999, 59, 167-170.

25. Dore R, Moro G, D'Andrea F, [et al.]. CT evaluation of myometrium invasion in endometrial carcinoma. *J Comput Assist Tomogr.* 1987, 11, 282-289.

26. Hamm B, Pöllinger A. Radiologische Schnittbilddiagnostik beim Endometriumkarzinom. *Zentralbl Gynäkol.* 2002, 124, 27-31.

27. Yamashita Y, Harada M, Sawada T, [et al.]. Normal uterus and FIGO stage I endometrial carcinoma: Dynamic gadolinium-enhanced MR imaging. *Radiology.* 1993, 186, 495-501.

28. Yazigi R, Cohen J, Munoz A, [et al.]. Magnetic resonance imaging determination of myometrial invasion in endometrial cancer. *Gynecol Oncol.* 1989, 34, 94-97.

29. Kim S, Kim H, Song Y, [et al.]. Detection of deep myometrial invasion in endometrial carcinoma: Comparison of transvaginal ultrasound, CT and MRI. *J Comput Assist Tomogr.* 1995, 19, 766-772.

30. Frei K, Kinkel K, Bonel H, [et al.]. Prediction of deep myometrial invasion in patients with endometrial cancer: clinical utility of contrastenhances MR imaging-a meta-analysis and Bayesian analysis. *Radiology.* 2000, 216, 444-449.

31. Vorgias G, Hintipas E, Katsoulis N, [et al.]. Intraoperative gross examination of myometrial invasion and cervical infiltration in patients with endometrial cancer: decision-making accuracy. *Gynecol Oncol.* 2002, 85, 483-486.

32. Franchi M, Ghezzi F, Melpignano M, [et al.]. Clinical value of intraoperative gross examination in endometrial cancer. *Gynecol Oncol.* 2000, 76, 357-361.

33. Doering D, Barnhill D, Weiser E, [et al.]. Intraoperative evaluation of depth of myometrial invasion in stage I endometrial carcinoma. *Obstet Gynecol.* 1989, 74, 930-933.

34. Goff B, Rice L. Assesment of depth of myometrial invasion in endometrial adenocarcinoma. *Gynecol Oncol.* 1990, 38, 46-48.

35. Fanning J, Tsukada Y, Piver M. Intraoperative frozen section diagnosis of depth of myometrial invasion in endometrial adenocarcinoma. *Gynecol Oncol.* 1990, 37, 47-50.