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Role of MRI in Diagnosis of Endometrial Cancer

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ABSTRACT

Background: the role of MRI in female pelvic imaging has been magnified nowadays by the aid of diffusion weighted magnetic resonance imaging (DW-MRI) and contrast enhanced imaging for better assessment of endometrial cancer. **Aim of the Work:** this study aimed to show MRI role in diagnosis of female patients with endometrial cancer for better evaluation, prognosis and treatment strategies according to preoperative MRI staging. **Patients and Methods:** this study carried out in Radiology Department of Ain Shams University Hospitals. This study included 25 patients. All patients were subjected to careful history taking, histologic diagnosis of endometrial carcinoma and pelvic MRI was done. **Results:** the diagnosis capability of the MRI in comparison to histopathology in patients with endometrial carcinoma was significant. **Conclusion:** MR imaging with the aid of contrast enhanced images, diffusion weighted images and ADC mapping, had a great role in diagnosis of endometrial cancer as part of pre-operative assessment for lesion characterization and staging of the disease, that improve overall survival rate of patients by choosing better treatment plan.

Keywords: Endometrial Carcinoma, MRI.

INTRODUCTION

Endometrial carcinoma is the most common malignancy of the female genital tract [(1)]. The disease occurs most frequently in women during the sixth and seventh decades of life [(2)]. It typically presents with abnormal uterine bleeding in 75% to 90% of patients [(3)]. MRI has been shown to be the best imaging modality in disease staging and treatment planning compared to endo-vaginal ultrasound and computed tomography, because of its contrast resolution and multi-planar capability [(4)]. The role of MRI in endometrial cancer includes the evaluation of depth of myometrial invasion, cervical invasion, and nodal metastasis. This greatly optimize the surgical procedure and therapeutic strategy[(1)]. Prognosis depends on patient's age, histological grade, depth of myometrial invasion, cervical invasion, and the presence of lymph node metastases [(4)]. Magnetic resonance imaging has proven to be an accurate tool for assessing the depth of myometrial invasion. It differentiates the presence of deep myometrial invasion from more superficial involvement. The depth of myometrial invasion could be identified on a T2-weighted image according to junctional zone invasion [(5)]. In postmenopausal women, the junctional zone may be poorly visible and the myometrium may be thinned due to uterine involution, making the presence and depth of myometrial infiltration more difficult to assess[(6)]. Endometrial cancer is usually demonstrated as thickened endometrium or mass displaying hypo-to-isointense on T1WI with an intermediate signal intensity on T2WI[(7)]. On MRI, lymph node metastases were diagnosed when the short-axis diameter of the LN was 10 mm or above and describing the characteristics of malignancy [(5)]. The histological grade of the tumor is well known as one of the most important prognostic factors regarding the lymph nodes metastasis and overall survival of the patient [(8)]. Diffusion-weighted imaging (DWI) with the aid of quantitative apparent diffusion coefficient (ADC) measurement is a unique, non-invasive modality that was shown to improve the radiological diagnosis of malignant tumors [(9)]. Areas characterized by high signal intensity (restricted diffusion) at DWI or by low values of the ADC generally correspond with foci of hypercellularity represents a malignant tissue [(10)]. Overall MRI helps in decreasing endometrial carcinoma mortality rate due to early diagnosis and pre-operative staging. Post-operative MRI of the pelvis helps in assessing tumor reduction and decrease recurrence rate by choosing proper postoperative management[(11)].

AIM OF THE WORK

The aim of this study was to show the MRI role in diagnosis of female patients with endometrial cancer.

PATIENTS AND METHODS

The current study is a cross sectional prospective study،patients were referred from the Gynecology Department to the Women's imaging Unit at Radio-Diagnosis Department ofAin Shams University Hospitals in the period from November 2017 to April 2018.**The study was approved by the Ethics Board of Ain Shams University and**

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an informed written consent was taken from each participant in the study. Study Population: Prior to MRI imaging all cases were subjected to full history taking. **Inclusion criteria:** The study includes 25 female patients with pre-menopausal abnormal vaginal bleeding or postmenopausal bleeding suspecting endometrial cancer. **Exclusion Criteria:** Patients who have absolute contraindications to MRI as: brain aneurysm clips, pacemakers, certain artificial heart valves, inner ear (cochlear) implants, recently placed artificial joints, some older types of vascular stents, orbital Foreign bodies. **Evaluation:** The standard reference for the study was the complete pathologic specimen following hysterectomy or curettage samples. **Study Tools:** All MRI studies weredone on 1.5-T MRI unit (Achieva, Philips medical system) with a pelvic phased-array coil. **Study Procedures:** Patients were fasting for at least 4 hours prior to the examination and void to empty the bladder before exam to avoid image artifacts. MR images of the pelvis were performed from the symphysis pubis up to the renal hilum while patients were lying in the supine position. **MRI Imaging Protocol:** This includes: Pre-contrast images with high-resolution fast spin echo sequences: Axial obliqueT1 WI (3 mm slice thickness), axial T2 WI (4 mm slice thickness), sagittal T2 WI (4 mm slice thickness), coronal T2WI (4 mm slice thickness). Diffusion study and ADC mapping: Axial oblique DWI was performed. Data acquisition was obtained by applying three different b factors of 0, 500, and 1000 s/mm with 4 mm slice thickness, DW images were utilized for calculation of the ADC values, ADC measurements were automatically calculated by drawing the largest possible region of interest (ROI) with focus on the solid component of the uterine carcinomas. ADC value was usually expressed in (x 10^{-3}) square millimeters per second. Post (Gadolinium-DTPA) contrast study: T1 fat saturation images were taken at 180 seconds after intra venous administration of the contrast material. **Image Interpretation:** MR images analysis for following parameters: Thickness of the endometrium, tumor size on T2WI on the sagittal images by measuring the longitudinal diameter of the tumor along the long axis of the endometrial cavity and the anteroposterior diameter, tumor signal intensity onT2-weighted image compared with that of adjacent myometrium, uterine enhancement pattern at post contrast images, myometrial invasion, extension of the tumor to cervix or vagina, extra uterine extension and distant metastasis, lymph node assessment, areas of restricted diffusion on DW MR Images, ADC value is lower in carcinoma than normal endometrium and polyps. The more lower the value, the more aggressive the tumor according to pathological grading. In this study we use a cut off ADC value = $1.2\times10^{-3}mm^2/s$. to distinguish endometrial carcinoma from benign lesions while normal endometrium measures (1.53 ± 0.10) ×10−3mm2/s. **Statistical Analysis:** The collected date were revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS 15.0.1 for windows; SPSS Inc., Chicago, IL, 2001). Data were presented as mean and standard deviation (± SD) for quantitative parametric data, and median and interquartile range for quantitative non parametric data. Frequency and percentage were used for presenting qualitative data. Suitable analysis were done according to the type of data obtained. Student T test or Mann Whitney test wereused to analyze quantitative data while chi square test and fisher exact test wereused to analyze qualitative (NS): $P<0.05$: Significant (S), $P<0.01$: Highly significant (HS). **Statistical Package:** Statistical package for Social Science (SPSS 15.0.1 for windows; SPSS Inc., Chicago, IL, 2001).

RESULTS

This study included (25) female patients with suspected endometrial carcinoma. They were sent for confirmation of diagnosis and pre-operative staging and histopathology. **Study group Age:** The patients age ranged from (39-78) years old and the mean age was 61.6 years (table 1)

Table (1): Age distribution among the study group.

Age (years)	No.	%
<=60 years	9	36
>60 years	16	64
Total	25	100
Mean	61.6	
Range	39-78	
SD	10.3	
Variance	106.5	

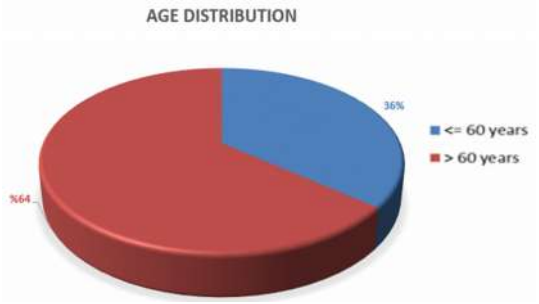

Chart (1): Age distribution in the study group.

Study group Symptoms

Table (2): Symptoms distribution in the study group distribution

Symptoms	No.	%
Menorrhagia	5	20
Post-menopausal bleeding	20	80
Total	25	100

5 Patients presented with menorrhagia and 20 patients with postmenopausal bleeding.

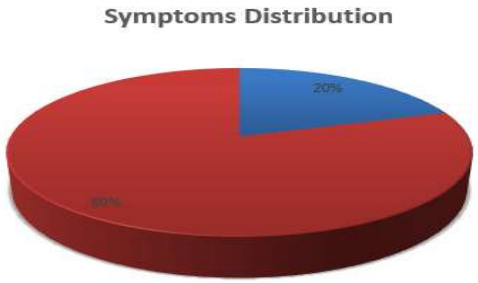

Chart (2): Symptoms distribution in the study group distribution.

Endometrial thickening

Table (3): Endometrial thickening

Endometrial thickness	No.	%
< = **20** mm	9	36
>20 mm	16	64
Total	25	100

Endometrial thickening was less or equal 20 mm in 9 patients and more than 20 in 16 patients.

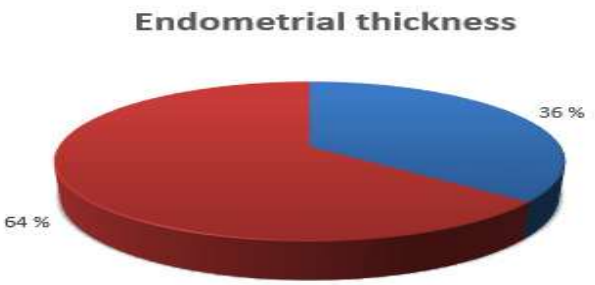

Chart (3): Endometrial thickening.

Histopathological findings: Histopathology was done for all patients postoperatively and the results were 22 patients with endometrial carcinoma and 3 patients with endometrial hyperplasia.

Table (4): Histopathological diagnosis of the study group

Diagnosis	Number	%
Endometrial carcinoma	22	88
Endometrial hyperplasia	3	12
Total	25	100%

Chart (4): Histopathological diagnosis of the study group.

Histological type distribution of adenocarcarcinoma: 21 case diagnosed histopathological as Endometrioid adenocarcinoma and only 1 case as serous adenocarcinoma

Table (5): Histological type distribution among the endometrial carcinoma cases

Histological type	Number	%
Endometrioid adenocarcinoma	21	95.5
Serous adenocarcinoma	1	4.5
Total	22	100%

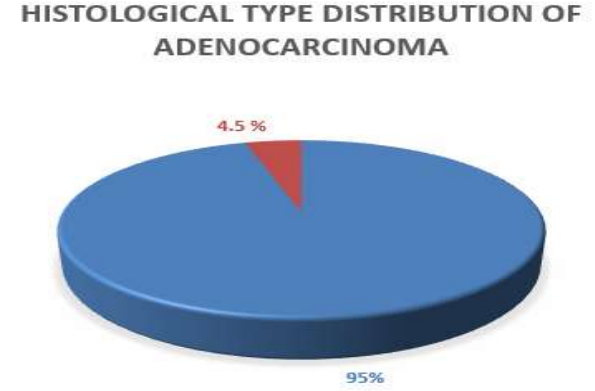

Chart (5): Histological type distribution among the endometrial carcinoma cases.

FIGO Grading distribution among endometrioid endometrial adenocarcinoma study cases: In this study population, 21 patients had endometrioid endometrial adenocarcinoma and are classified according to FIGO grading system to: ***Grade 1*** endometrioid adenocarcinoma (well differentiated) was seen in 10 cases by histopathology, ***Grade 2*** endometrioid adenocarcinoma (moderately differentiated) was seen in 6 of cases, ***Grade 3*** endometrioid adenocarcinoma (High Grade) in 5 patients.

Table (6): FIGO Grade distribution among endometrioid endometrial adenocarcinoma

Grade of tumor	Number	%
Grade 1 endometrioid adenocarcinoma (well differentiated)	10	47.6
Grade 2 endometrioid adenocarcinoma (moderately differentiated)	6	28.5
Grade 3 endometrioid adenocarcinoma (High grade)	5	23.8
Total	21	100%

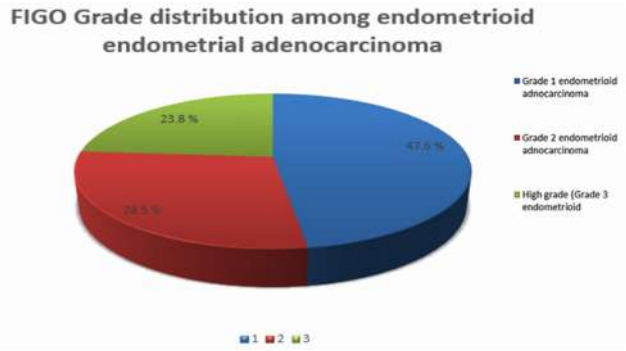

Chart (6): FIGO grade distribution among endometrioid endometrial adenocarcinoma.

Diagnosis of Endometrial carcinoma: MRI was performed for all patients preoperatively and we compared the results with our golden standard (surgical histopathology) postoperatively: by MRI 21 cases were diagnosed as endometrial carcinoma and 4 cases as endometrial hyperplasia, By Histopathology, 22were diagnosed as endometrial carcinoma and 3 as endometrial hyperplasia.

Table (7): Correlation of diagnosis between MRI and histopathological diagnosis of the study group.

Diagnosis	By MRI	%	By Histopathology	%
Endometrial carcinoma	21	84	22	88
Endometrial hyperplasia	4	16	3	12
Total	25	100%	25	100%

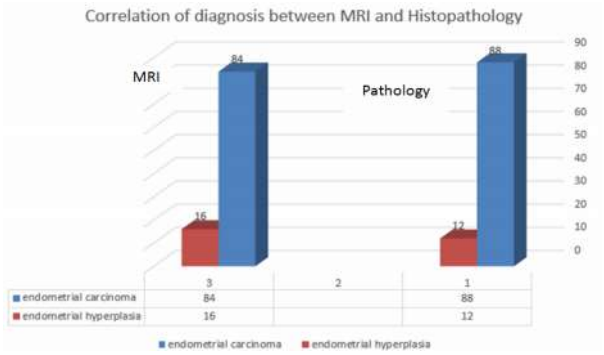

Chart (7): Correlation of diagnosis between MRI and Histopathology of the study group.

MRI signal characteristics in the study group: no case showed hypo-intense T2 signal, 9 cases showed iso-intense T2 signal and 16 cases showed hyper-intense T2signal, 7 Cases showed hypo-enhanced endometrium after contrast uptake, 3 cases showed homogenous contrast uptake and 15 cases showed heterogeneous contrast uptake, high signal intensity in DWI was registered in 24 cases and low signal intensity was seen in only 1 case of endometrial hyperplasia.The ADC values elicited from the corresponding ADC maps were calculated and found to be $<1.2\times10^{-3}mm^2/s$ in 21 cases and $>=1.2\times10^{-3}mm^2/s$ in 4 cases.

Table (8): MRI signal characteristics in the study group

		22 malignant (endometrial carcinoma)	3 benign (endometrial hyperplasia)	Total	%
		Number	Number		
T2 signal intensity in relation to myometrium	Hypointense	0	0	0	0%
	Isointense	8	1	9	36%
	Hyperintense	14	2	16	64%
Contrast uptake	Hypo-enhanced	7	0	7	28%
	Homogenous enhancement	0	3	3	12%
	Heterogeneous enhancement	15	0	15	60%
DWI	High signal intensity	22	2	24	96%
	Low signal intensity	0	1	1	4%
ADC value	$<1.2\times10^{-3}mm^2/s$	21	0	21	84%
	$>=1.2\times10^{-3}mm^2/s$	1	3	4	16%

Accuracy measures of cut off ADC value in discrimination between malignant and benign endometrial tumors: applying our cut off ADC value of 1.2×10^{-3} mm^2/s, achieved 95.5 % sensitivity, 100 % specificity, and 96 % to

differentiate between endometrial carcinoma and hyperplasia, the different ADC values elicited from the corresponding ADC maps were calculated and found statistical difference between the malignant and benign tumors with p-value 0.001 that was considered of statistical (HS) high significance.

Table (9): Accuracy measures of cut off ADC value in discrimination between malignant and benign endometrial tumors

ADC value ($\times10^{-3}$ mm^2/s)	By Histopathology		Sens.	Spec.	Accur.	p-value
	Endometrial carcinoma	Endometrial hyperplasia				
< 1.2	21 (93.7%)	0 (0%)	95.5%	100%	96%	<0.001 (HS)
>= 1.2	1 (6.3%)	3 (100%)				
Total	22 (100%)	3 (100%)				

Correlation between histological grade of endometrial carcinoma and the ADC value of each grade: The mean ADC values were 0.79 ± 0.09×$10^{-3}$$mm^2$/s for grade 1, 0.73± 0.13×$10^{-3}$$mm^2$/s for grade 2, and 0.75 ± 0.10×$10^{-3}$$mm^2$/s for grade 3 endometrial carcinoma.

Table (10): Correlation between histological grade of endometrial carcinoma and the ADC value.

Grade of tumor	Mean
Grade 1	0.79±0.09
Grade 2	0.73±0.13
Grade 3	0.71±0.11

Staging of Endometrial carcinoma:

Table (11): Correlation between MRI and Histopathology in FIGO staging of endometrial carcinoma.

FIGO stage	By MRI	Histopathology
Stage I A	6	5
Stage I B	3	3
Stage II	2	1
Stage III A	1	2
Stage IIIB	0	0
StageIIIC1	4	4
StageIIIC2	2	2
Stage IVA	0	1
Stage IVB	4	4
Total	22	22

FIGO staging by MRI was concordant with histopathology in 86.3% of cases. It was overestimated in 9 % and underestimated in 9 % of cases.

DISCUSSION

Prognosis of endometrial carcinoma depends on patient's age, histological grade, depth of myometrial invasion, cervical invasion, and the presence of lymph node metastases. [(1)].The histological grade of the tumor is one of the most important prognostic factors regarding overall survival of the patients [(8)]. MRI of the uterus represents up to now the sole imaging technique with scientific evidence of accurate pre-operative assessment of myometrial invasion [(12)]. Optimization of MR imaging protocols with the use of T2-weighted images, diffusion-weighted, and contrast-enhanced images improves staging and treatment planning in patients with endometrial cancer[(13)]. The European Society for Urogenital Imaging and the UK Royal College of Radiologists' cancer imaging guidelines also recommend MR imaging for staging of endometrial carcinoma[(14)]. This study was conducted at the Radiology Department at Ain Shams University Hospitals in November 2017 until April 2018.Our aim was to detect the role and sensitivity of magnetic resonance imaging in diagnosis of endometrial carcinoma, with histopathological diagnosis taken as a reference. The study included 25 females with pre-menopausal abnormal vaginal bleeding or postmenopausal bleeding. Their ages ranged from 39-78 years old. 9 patients (36%) were <=60 years and 16 patients (64%) were > 60 years with mean age 61.6 years. In our study, 95.5% of the cases were found to have endometrioid adenocarcinoma and 4.5% have serous adenocarcinoma. Diffusion weighted magnetic resonance imaging (DW-MRI) is now part of the standard imaging protocols for accurate diagnosis of uterine malignancies. The DW images should always be evaluated together with ADC maps in order to avoid potential pitfalls in image interpretation such as T2 shine-through, water restriction in normal and non-malignant tissues and lesions with low cellularity [(15)]. In our study, b 0, b 500, and b 800 DW images were obtained. We used the b 800 image in our interpretation. Many studies used b value of 800, other studies used b 1000 DW image and ***Beddy et al.*** [(15)]used b value of 500.According to ***Andreano et al.*** [(16)]. meta-analysis this difference in b values did not seem to affect the final results. ***Tamai et al.*** [(4)]performed a study on 30 female patients and concluded that The ADC values of endometrial cancers of higher grade

showed tendency to decrease compared to those of lower grade. According to their results; the mean ADC value of endometrial cancer was (0.88 ± 0.16), which was significantly lower ($P < 0.01$) than that of normal endometrium (1.53 ± 0.10). The mean ADC value for each histologic grade was 0.93 ± 0.16 (G1), 0.92 ± 0.13 (G2), and 0.73 ± 0.09 (G3). However, the diagnostic value of DWI with quantitative ADC in grading of the endometrial carcinoma has been controversial [17]. In 2011, Bharwani et al.[18]. performed a study on 23 female patients with histologically proved endometrial cancer aiming to correlate the ADC value with the histological tumor grade. The study concluded that there was considerable overlap and no statistically significant difference between tumor grades for mean ADC or minimal ADC values. In our study, our results were similar to ***Tamai et al.*** [4]where all cases of endometrial cancer demonstrated high signal intensity on DW images with mean ADC values for endometrial cancer equal 0.74± $0.11\times10^{-3}mm^2/s$. The mean ADC value for each histologic grade was 47.6% for grade (1), 28.5% for grade (2) and 23.8% for grade (3). In which the lower the ADC value the higher the grade of the tumor.In 2011, ***Motoshima et al.***[10]. used a DWI with a high b-value of 0 and 1,000 sec/mm^2 and a reversed and a cut-off ADC values of 1.15×10^{-3} mm^2/sec for endometrial carcinoma. In our study, we applied a cut-off ADC value of $1.2\times10^{-3}mm^2/s$ and the sensitivity, specificity, and accuracy in differentiation between malignant and benign lesions were 95.5%,100% and 96% respectively and the mean ADC value of endometrial carcinoma was 0.74±0.11. Our results showed that uterine cancer of higher grade tended to have lower ADC values as compared to cancer of lower grade. Post CE images were used for evaluation of the depth of myometrial invasion. They were obtained in the portal venous phase whereas the maximum tumor to myometrium contrast was achieved in the equilibrium phase (2 - 5 minutes, post injection), which was the most optimal phase of enhancement for assessment of the depth of myometrial invasion [14]. In our study, weacquired delayed post contrast T1 fat suppression enhanced images at 3 minutes post gadolinium injection. In 2012, ***Beddy et al.***[15]**.** showed that contrast-enhanced images, when read together with T2-weighted images, have a diagnostic accuracy up to 98% for assessing myometrial invasion. However, there is some controversy in the literature regarding the added value of dynamic contrast-enhanced MR imaging for overall FIGO staging: Although the majority of published studies showed an improvement in staging accuracy with dynamic contrast-enhanced MR imaging, some authors have found no benefit. In our study the sensitivity, specificity and accuracy of delayed CE-MRI in assessment of myometrial invasion were 91.6%, 100% and 93.7% respectively. The staging accuracy of diffusion-weighted MR imaging was superior to that of dynamic contrast-enhanced MR imaging [15]. The overall MR accuracy of the staging of endometrial carcinoma was 81% according to [19,20]. In our study, the overall staging accuracy by MRI was 86.3 % with 9 % overestimation and 9% underestimation of tumor staging.

CONCLUSION

MR imaging is highly sensitive and specific for depicting important prognostic factors of the endometrial carcinoma as depth of myometrial invasion, cervical invasion and the presence of lymph node metastases, which is essential for accurate pre-operative staging, which helps in treatment planning and improves overall patient survival. MRI had been shown to be the best imaging modality in disease staging and treatment planning compared to endo-vaginal ultrasound and computed tomography. The purpose of this study was to evaluate the role of magnetic resonance imaging in diagnosis of endometrial carcinoma, with histopathological diagnosis taken as the reference. Our study was conducted on twenty five patients, MRI correctly diagnosed 21 patients with endometrial carcinoma correlated with post-operative histopathological diagnosis. Combining T2-weighted imaging, contrast enhanced imaging and Diffusion-weighted MR imaging, improved morphologic imaging, depth of myometrial invasion and overall staging accuracy. Post Contrast Enhanced images are very useful for evaluation of the depth of the tumor.Endometrial carcinoma relatively showed weak contrast enhancement in comparison with intensely enhanced normal myometrium. Mean ADC value measurement could provide useful information for differentiation of benign and malignant endometrial lesions.Malignant tumors had significantly lower ADC values than benign lesions such as endometrial polyps and submucosal leiomyomas. Also, lower ADC values were associated with high grade endometrial tumors. The sensitivity, specificity and accuracy of ADC value

in discrimination between benign and malignant endometrial lesions by using a cut-off ADC value of $1.2\times10^{-3}mm^2/s$, were 95.5%, 100% and 96% respectively.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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