Ultrasonography compared with magnetic resonance imaging for the diagnosis of adenomyosis: correlation with histopathology

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BACKGROUND: The objective of this study was to compare the accuracy of transabdominal (TAUS) and transvaginal sonography (TVUS) and magnetic resonance imaging (MRI) for the diagnosis of adenomyosis, and to correlate imaging with histological findings. METHODS: In a prospective study, 120 consecutive patients referred for hysterectomy underwent TAUS, TVUS and MRI. Results of these examinations were interpreted blindly to histopathological findings. RESULTS: Histological prevalence of adenomyosis and leiomyomas was 33.0 and 47.5% respectively. Adenomyotic uteri were accompanied by additional pelvic disorders in 82.5% of cases. Sensitivity, specificity, and positive and negative predictive values of TAUS and TVUS were 32.5 and 65.0%, 95.0 and 97.5%, 76.4 and 92.8%, and 73.8 and 88.8% respectively. Myometrial cyst was the most sensitive and specific TVUS criterion. In MRI, the presence of a high-signal-intensity myometrial spot was as specific but less sensitive than a maximal junctional zone thickness (JZmax) >12 mm and a JZmax to myometrial thickness ratio >40%. Sensitivity, specificity, and positive and negative predictive values of MRI were 77.5, 92.5, 83.8 and 89.2% respectively. No difference in accuracy was found between TVUS and MRI, but sensitivity was lower with sonography in women with associated myomas. CONCLUSIONS: TVUS is as efficient as MRI for the diagnosis of adenomyosis in women without myoma, while MRI could be recommended for women with associated leiomyoma.

Key words: adenomyosis/leiomyoma/MRI/ultrasound/uterus

Introduction

Adenomyosis is a common gynaecological disorder defined by the presence of ectopic endometrial glands and stroma within the myometrium (Zaloudek and Norris, 1994). Two distinct forms, diffuse and focal, have been described. In the diffuse form, foci of adenomyosis are distributed within the myometrium (Azziz, 1989; McCausland and McCausland, 1996). In the focal form, nodules of hypertrophic myometrium and ectopic endometrium (so-called adenomyoma) are observed. The histological frequency of adenomyosis ranges from 5–70% according to the series, depending on the historical criteria and the number of sections examined (Azziz, 1989; Siegler and Camilien, 1994; Ferencyz, 1998).

Adenomyosis is a cause of uterine enlargement, menorrhagia and dysmenorrhea. Clinical diagnosis of adenomyosis is difficult, because of the non-specific nature of symptoms. Furthermore, leiomyomas are frequently associated with adenomyosis, hindering the differential diagnosis. Transabdominal (TAUS) and transvaginal ultrasound examination (TVUS) have been recommended for the diagnosis of adenomyosis (Walsh et al., 1979; Bohlman et al., 1987; Siedler et al., 1987; Fedele et al., 1992; Arnold et al., 1995; Reinhold et al., 1995, 1996). The reported sensitivity and specificity of TAUS or TVUS are 53–89% and 50–89% respectively (Fedele et al., 1992; Ascher et al., 1994; Reinhold et al., 1995, 1996). The sensitivity and specificity of magnetic resonance imaging (MRI) have been reported to be as high as 88–93 and 67–91% respectively (Ascher et al., 1994; Reinhold et al., 1996). Few studies have compared sonographic and MRI accuracy rates for the diagnosis of adenomyosis (Ascher et al., 1994; Reinhold et al., 1996). Reinhold et al. reported similar diagnostic efficiencies with TVUS and MRI (Reinhold et al., 1996). In contrast, Ascher et al. suggested that MRI was the diagnostic modality of choice in this setting (Ascher et al., 1994). However, MRI diagnostic criteria for adenomyosis are controversial (Mark et al., 1987; Togashi et al., 1988; Hricak et al., 1992; Ascher et al., 1994; Reinhold et al., 1996).

The aims of this prospective study of a large series of patients were: (i) to determine the diagnostic performance of sonography and MRI for histologically proven adenomyosis, (ii) to compare their accuracy, and (iii) to identify the most specific sonographic and MRI features for adenomyosis.
Materials and methods

Patients
From January 1996 to April 1998, 167 patients referred for hysterectomy to the Gynecology Department of Hôpital Tenon, Paris, had pre-operative sonographic and MRI examinations. Forty-seven patients were excluded from the study for various reasons, including a lack of ultrasound and/or MRI findings due to technical reasons or patient-related factors (n = 26), cancelled surgery (n = 4), or conservative surgery including myomectomy (n = 5) and endometrial resection (n = 9). The study population thus consisted of 120 women, with a mean age of 51 years (range 30–88). The indications for surgery were menorrhagia and/or metrorrhagia (n = 61), post-menopausal bleeding (n = 17), adenexal masses (n = 15), cervical intraepithelial neoplasia (n = 12), pelvic pain (n = 16), genital prolapse (n = 11) and miscellaneous (n = 3). Eighty-three women were premenopausal (69%) and 37 post-menopausal (31%). Among the premenopausal women, 20 were on progestin and three were on GnRH analogues. Two of the 37 post-menopausal women were undergoing hormone replacement therapy.

All patients had TAUS, TVUS and MRI examinations.

Ultrasound examination
Sonographic examinations were performed with an Ultramark HDI 3000 unit (ATL, Bothell, WA, USA). Pelvic TAUS was performed using a wide-band 2- to 4-MHz transducer, and TVUS examination with a wide-band 5- to 9-MHz transducer. Colour Doppler examination was performed using a pulse repetitive frequency of 1000–1500 Hz, a wall filter of 50 Hz and a high-priority colour setup. Each examination was interpreted in real time and videotaped. During each sonographic examination, the uterine borders (regular or irregular), uterine size, myometrial echotexture and the presence of associated abnormalities (including myomas) were noted.

Diagnosis of adenomyosis by TAUS was based on criteria including an enlarged regular uterus with no evidence of leiomyoma and/or presence of myometrial cysts. For TVUS, in accordance with previous studies (Fedele et al., 1992; Reinhold et al., 1995), criteria for adenomyosis were as follows: myometrial cyst, distorted and heterogeneous myometrial echotexture, poorly defined focus of abnormal myometrial echotexture, and a globular and/or asymmetric uterus. Myometrial cyst was defined as a round anechoic area of 1–7 mm diameter (Fedele et al., 1992; Reinhold et al., 1995). Heterogeneous myometrium was defined by the presence of an indistinctly marginated myometrial area with decreased or increased echogenicity (Brosens et al., 1995b; Reinhold et al., 1995). Globular and/or asymmetric uterus was defined as a regular enlarged uterus with possible myometrial asymmetry unrelated to leiomyoma. Adenomyosis was not diagnosed if these criteria were not met.

Colour Doppler was used to distinguish between myometrial cyst and a vascular component, and between supposed leiomyoma and focal adenomyosis. Localized adenomyomas were characterized by the absence of flow or by the presence of straight vessels traversing a hypertrophic myometrium.

Adenomyosis was classified according to its uterine location and size, and the depth of myometrial involvement.

MRI examination
MRI was performed on a 1.5-T system (Gyroscan, Philips, Eindhoven or Magnetom Vision, Siemens, Erlangen, Germany) with T2-weighted spin-echo or T2-weighted turbo spin-echo (TSE) sequences in sagittal, oblique axial or coronal planes, and T1-weighted spin-echo in sagittal or axial planes. Using abdomen compression, MRI sections were acquired every 5 mm with a gap of 1 mm. Data were collected in a 256×256 matrix and a 300 mm field of view. In addition, 34 patients underwent two breath-hold fast T2-weighted pulse sequences (TruFsp and Tirm) in the sagittal and/or axial planes. Patients were required to fast for 3 h before MRI. Antispasmodic drugs were not used.

MRI results were interpreted by two independent observers. Four criteria were evaluated on T2-weighted sequences: (i) borders, size and uterine symmetry, (ii) maximal junctional zone (JZmax) thickness and/or presence of an ill-defined, relatively homogeneous, low-signal-intensity myometrial area (IDMA), (iii) maximal JZ thickness to myometrial thickness ratio (ratioJZmax), using the maximal thickness of the JZ and the corresponding thickness of the entire myometrium obtained at the same level, and (iv) high-intensity spots within the myometrium. Leiomyomas, adenexal masses, and endometrial or cervical abnormalities were also recorded.

Adenomyosis was defined by: (i) a large, regular, asymmetric uterus without leiomyomas, (ii) JZmax of at least 12 mm and/or an ill-defined, low-signal-intensity myometrial area distinguished from well-circumscribed masses related to myoma, (iii) ratioJZmax >40% and (iv) punctate high-intensity myometrial foci (Reinhold et al., 1996). Small hypointense spots within the myometrium on contrast-enhanced (gadolinium injection) T1-weighted images were attributed to adenomyosis.

Adenomyosis was classified according to its uterine location and size, and the depth of myometrial involvement.
Histopathological findings

Histopathological examinations were all performed by the same pathologist, who was blinded to sonographic and MRI data. Gross and microscopic histopathological examinations were performed according to Molitor’s method (Molitor, 1971). Specimens were orientated by a fixed mark on the anterior uterine wall. Uterus weight, macroscopic appearance and associated pathologic abnormalities were recorded. Fundal, anterior, posterior, right and left maximal uterine wall thicknesses were measured.

Macroscopically, adenomyosis was diagnosed as an enlarged uterus, a globular and/or asymmetric uterus, and a dense anechogenic fasciculated unlimited myometrium with small cavities (0.5–10 mm). Focal adenomyosis was defined by the presence of (i) adenomyoma (circumscribed nodular lesion) mimicking intramural myoma, or (ii) when lesions were restricted to one uterine wall (localized adenomyosis). In other cases, adenomyosis was defined as diffuse pathology.

Block sections were taken from the fundal, anterior, posterior, right and left uterine walls, and from macroscopically abnormal areas. The number of slides ranged from 5–15 depending on myometrial thickness.

Histopathological criteria used for the diagnosis of adenomyosis included the presence of ectopic endometrial tissue within the myometrium, located 2.5 mm beyond the endometrial-myometrial junction (Figure 1). Smooth-muscle cells surrounding ectopic endometrial areas were noted. Adenomyosis was graded according to the depth of myometrial involvement. Grades 1, 2 and 3 corresponded respectively to adenomyotic involvement of the inner third (superficial adenomyosis), two-thirds and entire myometrium (deep adenomyosis). Adenomyosis was also graded as mild, moderate or severe according to the number of endometrial islets observed (1–3, 4–9 and ≥10 foci respectively).

Statistical analysis

Statistical analysis was performed using Student’s t-test and Mann–Whitney test for parametric and non-parametric continuous variables respectively, and the $\chi^2$ test or Fisher’s exact test, where appropriate, for categorical variables. A $P$ value < 0.05 was considered statistically significant.

Results

Histopathological findings

Uterine bleeding was the main indication for hysterectomy (65%), and was due to various uterine diseases, including leiomyomas ($n = 57$), adenomyosis ($n = 40$), uterine carcinoma ($n = 32$), adnexal tumours ($n = 16$) and miscellaneous causes ($n = 7$). The histological prevalence rates of adenomyosis and leiomyomas were 33 and 47.5% respectively. Adenomas were found in seven patients (3.8%). Adenomyotic uteri were accompanied by additional pelvic disorders in 82.5% of cases. Thirty-one women were premenopausal (77.5%) and nine postmenopausal (22.5%).

Gross examination

Adenomyosis was recognized only after opening the uterine specimens. All cases but one were related to diffuse adenomyosis without leiomyoma. Seven adenomyomas had a macroscopic aspect resembling that of a leiomyomatous tumour. The sensitivity, specificity and positive and negative predictive values of gross examination for the diagnosis of adenomyosis were 47.5, 100, 100 and 79.2% respectively. Using systematic microscopic evaluation, we found an overall rate of adenomyosis of 47.5% in symptomatic women, even in the absence of macroscopic evidence. A significant difference in mean uterine weight was noted between adenomyotic uteri without leiomyomas (167 g) and non-adenomyotic uteri without leiomyomas (63 g) ($P < 0.01$).

Microscopic examination

The adenomyosis was fundal in 26 cases, posterior in 21 cases, anterior in 19 cases, right-sided in 12 cases and left-sided in 10 cases.

Twenty-three patients (57.5%) had diffuse adenomyosis, including two patients with associated adenomyoma.

Seventeen cases of focal adenomyosis were diagnosed (42.5%), comprising five adenomyomas and 12 cases of localized adenomyosis. Two patients had isolated adenomyoma. All cases of focal adenomyosis were of grade 1 or 2, and were located in the fundus in eight cases, the anterior wall in three cases and the posterior wall in six cases.

Adenomyosis was grade 1 in 13 cases, grade 2 in 15 cases and grade 3 in 12 cases; in other words, there were 13 cases of superficial adenomyosis and 27 cases of deep adenomyosis. The degree of adenomyosis was minimal in six cases, moderate in 19 cases and severe in 15 cases.

A hyperplastic muscular myometrium surrounding ectopic endometrial islets was observed in 32 cases (80%), in 30 premenopausal and two post-menopausal women. The preval-

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<th>US findings</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accuracy (%)</th>
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<td>95.0</td>
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<td>90.0</td>
<td>33.8</td>
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<td>97.5</td>
<td>93.8</td>
<td>86.6</td>
<td>88.3</td>
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PPV = positive predictive value; NPV = negative predictive value.
Figure 2. Sagittal transvaginal sonography demonstrates myometrial anechoic lacunae specific of adenomyosis involving the ventral and the dorsal myometrium (A). Transversal transabdominal examination shows a very large asymmetric uterus with thickening of the dorsal myometrium. Note the decreased echogenicity and heterogeneity of the dorsal myometrium not related to leiomyoma. There is poor definition of the endo-myometrial junction. All these findings suggest diffuse adenomyosis (B). Transvaginal sonography demonstrates diffuse adenomyosis involving the ventral myometrium and a dorsal subserous leiomyoma. Distinguishing features of adenomyosis include poor definition of lesion borders and lack of mass effect on the endometrium. In contrast, the leiomyoma has a round shape with well-defined borders and edge shadowing (C). Sagittal T2-weighted magnetic resonance image through the uterus shows numerous high-intensity spots in the inner myometrium, thickening of junctional zone (JZ) (13 mm) and ratio_max ≥40% (D). Axial T2-weighted magnetic resonance image demonstrates diffuse thickening of JZ both ventrally and dorsally, consistent with severe adenomyosis. Numerous foci of high signal representing the heterotopic endometrium are present (E). Sagittal T2-weighted magnetic resonance image through the uterus (F): there is an ill-defined mass centred around the endometrium. Several foci of increased signal consistent with heterotopic endometrium are present in the inner myometrium without mass effect on the endometrial cavity. In contrast, leiomyoma is very hypointense and has well-defined borders (F).

ence of a hyperplastic muscular reaction was higher in premenopausal women ($P < 0.01$). Differences in the prevalence of hyperplastic reactions according to the grade of the disease were not statistically significant.

Sonography

TAUS yielded a diagnosis of adenomyosis in 17 women. The sensitivity, specificity and positive and negative predictive values of TAUS for the diagnosis of adenomyosis were 32.5,
95.0, 76.4 and 73.8% respectively (Table I). The accuracy of TVUS was 74.1%.

If we used only myometrial cysts and focal heterogeneous myometrial areas as firm diagnostic criteria for adenomyosis, TVUS was diagnostic of adenomyosis in 28 women. The sensitivity, specificity and positive and negative predictive values of TVUS for the diagnosis of adenomyosis were 65.0, 97.5, 92.8 and 88.8% respectively. The accuracy of TVUS was 86.6%. The most sensitive and specific criterion for adenomyosis was the presence of a myometrial cyst (Figure 2A). Two cases of adenomyosis were missed by TVUS in enlarged abdomino-pelvic uteri without associated myoma (Figure 2B). Combined TAUS and TVUS increased the diagnostic yield of adenomyosis, with a sensitivity, specificity, positive and negative predictive values and accuracy of 70.0, 97.5, 93.8, 86.6 and 88.3% respectively (Table I).

The sensitivity and specificity of TVUS for the diagnosis of adenomyosis in the patients with and without leiomyomas were respectively 33.3 and 78.0%, and 97.8 and 97.1% (Figure 2C).

The sonographic location of adenomyosis concurred with histopathological findings in the 26 true-positive cases. However, no correlation was found between sonography and histopathology regarding the grade or degree of adenomyosis. Sonographic and histopathological grading concurred in only 15 cases (57%), while sonography underestimated the grade in seven cases (27%) and overestimated it in four cases (15%) relative to histopathology. Likewise, the degree of adenomyosis estimated sonographically concurred with histopathological findings in six cases (23%) and was underestimated in 20 cases (77%).

**MRI findings**

The sensitivity, specificity, positive and negative predictive values and accuracy of MRI criteria for adenomyosis are given in Table II. On TSE-T2, JZ was not visible in 36 women (30%). The most specific MRI criteria on TSE-T2 were high-signal-intensity myometrial spots, a visible JZ with a threshold value >12 mm and/or presence of an ill-defined low-signal-intensity myometrial area (IDMA), and ratio_max >40% (Figure 2D, E). Combination of these three criteria had a diagnostic accuracy for adenomyosis of 87.5%.

The sensitivity and specificity of MR imaging for the diagnosis of adenomyosis in patients with and without leiomyomas were respectively 66.6 and 82.1%, and 86.7 and 100% (Figure 2F).

The location of adenomyosis on T2-weighted MR images concurred with histopathological findings in 27 cases (91%) and disagreed in four cases (13%). The degree of myometrial involvement concurred with histopathological findings in 20 cases (65%), was underestimated in five cases (16%) and overestimated in six cases (19%).

**Unenhanced T1-weighted images**

T1-weighted images showed increased signal intensity in four patients (10%) with local haemorrhage confirmed by histological examination.

**Contrast-enhanced T1-weighted images**

Eighty-one (67.5%) of the 120 women had contrast-enhanced T1-weighted images. Of these, 27 (33.3%) had adenomyosis on pathological examination and 54 (66.6%) had no evidence of disease. The sensitivity, specificity, positive and negative predictive values and accuracy of contrast-enhanced T1-weighted MRI for adenomyosis were 35.7, 96.4, 83.3, 75.0 and 76.2% respectively.

**Discussion**

Adenomyosis refers to endometrial glands and stroma located deep within the myometrium (Ferenczy, 1998). In this study, we found that the accuracy of gross examination for the diagnosis of adenomyosis was low. This may explain the wide range of prevalence rates of adenomyosis observed in previous studies (Azziz, 1989; Siegel and Camillien, 1994; Ferenczy, 1998). In addition to endometrial glands and stroma located within myometrium, Bird et al. suggested that the diagnosis of adenomyosis required the identification of a smooth-muscle hyperplasia reaction (Bird et al., 1972). We observed such a reaction in 80% of women with adenomyosis. Furthermore, smooth muscle hyperplasia was more frequent in premenopausal women. These results are in keeping with those of previous studies showing the absence of this reaction in uteri from post-menopausal and pregnant women (Hendrickson and Kempson, 1990). Moreover, in contrast to previous studies, but in accordance with Emge, adenomyotic lesions were mainly
located in the fundus and were observed with a similar prevalence in the posterior and anterior uterine walls (Einge, 1962).

In our study, the accuracy of TAUS for the diagnosis of adenomyosis was low. Our results contrast with those of Siedler et al. showing a high accuracy of TAUS (Siedler et al., 1987): in a retrospective study of TAUS for the diagnosis of adenomyosis, Siedler reported sensitivity and specificity values of 63 and 97% respectively (Siedler, 1987). The low sensitivity obtained in our study could be explained by the inclusion of patients with associated disorders such as leiomyoma. Furthermore, our data are in keeping with those of Reinhold et al. suggesting that TAUS resolution is insufficient to reproduce detect subtle sonographic features of adenomyosis (Reinhold et al., 1998).

We found that TVUS allowed the diagnosis of adenomyosis with high accuracy. In accordance with a previous report (Hricak, 1998), our accuracy rate was influenced by associated disorders. Among the sonographic criteria, myometrial cyst was the most sensitive and specific. Fedele et al. were the first to report the diagnostic value of myometral anechoic lakes for adenomyosis (Fedele et al., 1992). In their experience, in women without leiomyoma or endometrial disease, the sensitivity and specificity values of this sonographic feature were 80 and 74% respectively. Despite the inclusion of patients with other disorders in addition to adenomyosis, the specificity of myometrial cyst remained high in our study, possibly because of an improvement in sonographic resolution. This reinforces the diagnostic value of myometrial cysts for adenomyosis.

It is difficult to compare our data with those of previous studies, in which the main criterion used for adenomyosis was an alteration of myometrial echotexture, not myometrial cyst (Ascher et al., 1994; Brosens et al., 1995b; Reinhold et al., 1995, 1996; Vercellini et al., 1998). Interestingly, those studies reporting a high accuracy of TVUS excluded women with distorted uteri related to leiomyomata or endocavitary lesions (Fedele et al., 1992; Ascher et al., 1994; Brosens et al., 1995b; Reinhold et al., 1995, 1996; Vercellini et al., 1998). Myometrial heterogeneity has been correlated with a smooth-muscle hypertrophic-hyperplasia reaction (Atri et al., 2000). However, in contrast to previous studies (Ascher et al., 1994; Brosens et al., 1995b; Reinhold et al., 1995, 1996; Vercellini et al., 1998), indistinctly heterogeneous myometrial areas had poor accuracy for the diagnosis of adenomyosis in the present study.

The sensitivity and specificity of MRI for the diagnosis of adenomyosis was 77.5 and 92.5% respectively. These results are in accordance with previous studies (Ascher et al., 1994; Reinhold et al., 1996). Nevertheless, even in women without myoma, regular homogeneous uterine enlargement was unreliable as an MRI criterion for adenomyosis. In contrast, a JZ of at least 12 mm and/or an ill-defined myometrial area, \( r_{\text{max}} > 40\% \) and high-signal-intensity myometrial spots had similar high accuracy rates. However, the JZ was not measurable in nearly one-third of our population, in which 22.5% of women had proven adenomyosis. These results contrast with those of Reinhold et al., who reported no cases of adenomyosis when the JZ was not visible (Reinhold et al., 1996). In previous reports the JZ was not visible in nearly 50% of post-menopausal patients (48.5% in our series) or women with gonadotrophin releasing-hormone analogue therapy (Brosens et al., 1995a; Byun et al., 1999). Foci of high signal intensity have been correlated with non-bleeding endometrial tissue (Togashi et al., 1988). However, in our experience and that of others (Reinhold et al., 1996), this MRI feature has low sensitivity. Our results suggest the possibility of using these imaging modalities to evaluate the incidence of adenomyosis in symptomatic and non-symptomatic women.

Fast spin-echo images and Trufisp and TIRM sequences appeared to have comparable yields in the diagnosis of adenomyosis. However, a formal analysis is necessary to determine whether these breath-hold rapid T2 sequences can routinely replace fast spin-echo sequences. As previously reported by Hricak et al. the use of contrast-enhanced T1-weighted images in our series did not improve the diagnostic yield for adenomyosis (Hricak et al., 1992). A particular diagnostic value of perfusion abnormalities on dynamic early-phase gadolinium-enhanced images has been reported in this setting (Outwater et al., 1998), but further studies are necessary to confirm these preliminary results.

In our experience, in women free of associated disorders, transvaginal sonography allows the diagnosis of adenomyosis with a similar accuracy to MRI. In contrast, in women with myomas, the accuracy of transvaginal sonography is lower than that of MRI. Ascher et al. suggested that MRI was the modality of choice for the diagnosis of adenomyosis, whereas Reinhold et al. recommended transvaginal sonography (Ascher et al., 1994; Reinhold et al., 1996). In accordance with Wood our results underline the limitations of sonography for the diagnosis of adenomyosis in women with uterine fibroids (Wood, 1998). Furthermore, our study shows a lack of correlation between histopathology and both sonography and MRI regarding the grade and degree of adenomyosis.

In conclusion, our results suggest that transvaginal sonography and MRI have similar accuracy rates for the diagnosis of adenomyosis. However, decreased sonographic accuracy was found in women with associated disorders. Therefore, MRI can be recommended for the diagnosis of adenomyosis in women with additional lesions.

References
Ultrasonography versus magnetic resonance imaging in adenomyosis


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