Value of diffusion-weighted imaging in the evaluation of adnexal tumors.

A Roussel (1), I Thomassin-Naggara (1), E Darai (2), C Marsault (1) and M Bazot (1)

Résumé
Évaluation de la séquence de diffusion pour l’étude des tumeurs annexielles
J Radiol 2009;90:589-96

Purpose. To determine the value of diffusion-weighted imaging (DWI) in the evaluation of adnexal tumors, especially to distinguish between malignant and benign tumors.

Materials and methods. Fifty-four patients with pelvic tumors (32 malignant and 22 benign) were referred for MRI of the pelvis. DWI was obtained in all patients. Histological correlation was available in all cases. The signal of solid and cystic tumor components was evaluated on T2W and b=1000 DWI, and ADC values were obtained.

Results. T2W hypointensity or absence of hyperintense signal on b=1000 DWI sequences was suggestive of a benign tumor. Hyperintensity on b=1000 DWI sequences was strongly correlated with malignant lesions. ADC values did not appear to discriminate between malignant and benign tumors. Also, the signal intensity of cystic tumor components on DWI sequences was not helpful to distinguish between malignant and benign tumors.

Conclusion. The evaluation of solid tumor components on DWI appears to be helpful for adnexal tumor characterization.


Abstract
Objectif. Évaluer l’apport de la séquence de diffusion pour l’exploitation des tumeurs annexielles gynécologiques, notamment pour distinguer les tumeurs malignes des tumeurs bénignes.


Résultats. Un hyposignal T2 ou l’absence d’hypersignal b1000 de la portion solide des tumeurs annexielles étaient en faveur de la bénignité. Un hypersignal b1000 de la portion solide était significativement corrélé à une histologie maligne. L’ADC n’apparaissait pas discriminant pour distinguer tumeurs malignes et bénignes. De même, l’étude en diffusion de la portion kystique ne permettait pas d’orienter le diagnostic vers sa nature maligne ou bénigne.

Conclusion. L’étude de la portion solide des tumeurs annexielles en séquence de diffusion semble être un élément utile pour différencier les lésions annexielles malignes et bénignes.

Key words: MRI. Diffusion-weighted imaging. Apparent diffusion coefficient. Ovarian cancer. Adnexal tumor.


The presence of an adnexal mass is one of the most frequent gynecological surgical indications. Treatment and prognosis of ovarian cancers depends on the FIGO (International Federation of Gynecology and Obstetrics) classification that evaluates the main prognostic factors. It relies mainly on clinical, surgical and histological findings, but presurgical imaging has become essential to optimize the management of these tumors.

US is a first line imaging study that allows characterization of multiple adnexal lesions. MRI without and with intravenous contrast is indicated for large tumors, complex tumors, or tumors that cannot be characterized on US. Some morphological MR imaging features are suggestive of malignancy and the overall accuracy of MRI for a diagnosis of malignant tumor is between 91 and 93% (1, 2).

Diffusion weighted imaging (DWI) is a recent technique based on evaluation of the movement of water molecules within tissues, or Brownian motion. Random intra-voxel movements within the magnetic field cause loss of signal (3). DWI provides tissue contrast based on water molecule motion, different from the signal provided by conventional T1W and T2W sequences.

The usefulness of DWI is well established in the evaluation of the CNS, especially in the diagnosis of acute ischemic stroke (4). Initially, use of DWI in the evaluation of solid intra-abdominal organs was considered difficult because it is very susceptible to motion artifacts. The availability of faster pulse sequences, such as echo planar imaging, and the recent addition of parallel imaging have considerably improved DWI pulse sequences and enabled their use for abdominal imaging (5, 6) and whole body for oncologic imaging (7).

Diffusion weighted sequences allow objective evaluation of random intra-voxel motion of water molecules, by calculating apparent diffusion coefficient (ADC) values that are closely correlated to structures at the molecular level. ADC values are especially reduced when
water motion in tissues is restricted. ADC values in solid tumors are related to several histological features including nuclear-cytoplasmic ratio and cell density. Some authors have reported that measurement of ADC values was useful in differentiating between malignant and benign tumors (8-10). For gynecological pathology, the value of DWI has previously been suggested for endometrial (11-14) and cervical (15-17) diseases.

The purpose of this study was to determine the value and limitations of DWI in the preoperative characterization of adnexal tumors.

**Materials and methods**

Between February 2006 and October 2007, 76 patients with adnexal tumors underwent pelvic MRI, including DWI. Twenty-two patients were excluded due to the lack of histological correlation (12 patients) or non-conforming (9 patients with b value different from 500 and 1000) or non-diagnostic (1 patient with hip prosthesis causing ferromagnetic artifacts rendering the images uninterpretable) DWI sequences. Endometriomas and mature cystic teratomas were also excluded. As reported by Nakayama, et al. (18), DWI is not helpful to characterize mature cystic teratomas since the diagnosis is easily suggested based on conventional T1W sequences without and with use of fat suppression confirming the presence of a fat component (19-22). However, it may at times be helpful for teratomas with very small fat content. DWI shows the presence of high signal with low ADC values in the keratinoid substance. Endometriomas are T1W hyperintense, and iso- to hyperintense relative to subcutaneous fat, persistent on fat-suppressed images (19, 20). Conventional sequences allow diagnosis of Endometriomas with a sensitivity of 90% and specificity of 98% (23). On DWI, Endometriomas usually are hyperintense with low ADC values due to the hemorrhagic content, but this provides little additional diagnostic information compared to conventional sequences that are usually sufficient to achieve a diagnosis (18).

A total of 54 patients were included, with a mean age of 53.3 years (range: 23 to 86 years). Histological confirmation was available in all cases, from surgery (49/54 patients or 90.7%) or laparoscopic biopsy (5/54 patients or 9.3%). The surgical procedures included tumorectomy (5 patients), unilateral salpingo-oophorectomy (6 patients), bilateral salpingo-oophorectomy (8 patients), hysterectomy with bilateral salpingo-oophorectomy, peritoneal biopsies, omentectomy and pelvic lymph node dissection (25 patients) and pelvectomy (5 patients).

The mean interval delay between MRI and surgery was 20 days (range: 1 to 70 days). The examinations were performed on a 1.5T MR unit (Vision, Siemens, Erlangen, Germany) using a dedicated multi-channel pelvic coil.

Patients were NPO 3 hours prior to examination. An abdominal belt was used to reduce abdominal wall respiratory motion artifacts. An anti-peristaltic agent (1 ml of glucagon) was slowly administered immediately before the MRI to reduce bowel motion. Saturation bands were placed anteriorly and posteriorly to reduce ghosting artifacts from subcutaneous fat.

The imaging protocol included the following sequences:

- Sagittal FSE T2W (TR/TE, 5050/121 ms) images from femoral head to femoral head and axial FSE T2W (TR/TE, 6790/89 ms) from renal hilum to symphysis pubis to assess the aorto-lumbar nodes (ETL: 15; slice thickness: 5 mm; interslice gap: 1 mm; FOV: 350-320 mm; number of excitations: 2; matrix: 512 × 276).
- Axial and sagittal breath-hold gradient-echo T1W images (TR/TE, 170/4.76 ms; flip angle 70°; number of excitation: 1; slice thickness: 5 mm; interslice gap: 1 mm; FOV: 370-275 mm; matrix: 256 × 145). Axial and sagittal breath-hold gradient-echo T1W images (TR/TE, 213-5.95, and similar parameters as described above), when spontaneous T1W hyperintensity was noted in the lesion.
- Axial fat-suppressed gradient-echo T1W images (TR/TE, 213-5.95, and similar parameters as described above), when spontaneous T1W hyperintensity was noted in the lesion.
- The morphology and signal characteristics of the solid (irregular thick septations, mural nodules, or soft tissue component) and cystic components of each adnexal tumor was analyzed, including the signal characteristics on T2W and b=1000 DWI sequences.

The signal intensity was compared to the signal of normal outer myometrium on T2W images. When the signal intensity of the lesion was lower compared to myometrium, the lesion was considered hypointense, whereas when it was superior, the lesion was considered hyperintense.

On the diffusion scan, tumor evaluation was performed on the b=1000 images, and the signal characteristics of the lesion previously analyzed on conventional T1W and T2W images was recorded. We have classified lesions as hyperintense or showing no detectable signal on the b=1000 diffusion images. In addition, quantitative ADC measurements were also obtained by placing an ROI over the solid and cystic components of the tumors on the ADC maps. The ROI was as large as possible, in a region demonstrating homogeneous signal, while excluding areas of necrosis and hemorrhage. The values were recorded in × 10-3 mm²/s.

Diffusion images at b=0 and b=500 were only used for ADC calculations. The signal intensity of lesions was never assessed due to the weaker diffusion weighting and increased T2 shine-through compared to images at b=1000. Images at b=1000 were chosen in order to obtain more heavily diffusion-weighted images, with less T2 shine through and...
Perfusion effects, two effects that may modify the signal intensity of tissues when using lower b values. In addition, this provided better suppression of signal from adjacent organs thus facilitating the detection of DWI hyperintensity within the tumor.

ADC values were correlated with histological findings. Statistical analysis was based on the continuous comparison of parametric variables with the Mann-Whitney test and categorical variables with Fisher’s exact test. A p value <0.05 was considered statistically significant. For some criteria, a descriptive statistical analysis (sensitivity, specificity, positive and negative predictive values, diagnostic accuracy), with corresponding 95% confidence interval, was performed.

**Results**

From a total of 54 adnexal tumors, 32 were malignant (59.3%) and 22 were benign (40.7%). Tumor histology and FIGO grades of the 32 malignant tumors are summarized in Table I. The histology of 22 benign tumors is summarized in Table II.

Two benign tumors corresponded to hydrosalpinx in the setting of chronic salpingitis; both lesions were diagnosed as ovarian tumors on MRI. Solid and cystic nature of adnexal tumors The cystic and/or solid nature of the adnexal tumors is summarized in Table III.

### Characteristics of cystic tumor components

A cystic component was present in 29/32 (90.6%) of malignant tumors and 13/22 (59.1%) of benign tumors. The T2W and DWI signal characteristics, ADC values and statistical analysis of the cystic component of adnexal tumors are summarized in Table IV. The mean ROI surface area for cystic components was 989.2 mm² for malignant tumors and 1393.1 mm² for benign tumors. The cystic component of most adnexal tumors was T2W hyperintense and DWI hypointense with high ADC values. There was no difference of signal on T2W and b=1000 diffusion images, and no significant difference of ADC values to allow distinction between malignant and benign tumors (fig. 1 and 2).

### Characteristics of solid tumor components

A solid component was present in 32/32 (100%) of malignant tumors and 12/22 (54.5%) of benign tumors. The T2W and DWI signal characteristics, ADC values and statistical analysis of the solid component of adnexal tumors are summarized in Table V. The mean ROI surface area for cystic components was 158.6 mm² for malignant tumors and 897.9 mm² for benign tumors. The sensitivity, specificity, positive and negative predictive values, diagnostic accuracy and 95% confidence intervals for the presence of T2W hypointensity within the solid component of adnexal tumors suggesting a benign etiology were respectively 50% (29.9%-61.5%), 93.8% (86.2%-98.1%), 75% (44.9%-92.3%), 83.3% (76.6%-87.2%) and 81.8% (70.9%-88.1%).

The sensitivity, specificity, positive and negative predictive values, diagnostic accuracy and 95% confidence intervals for the presence of b=1000 DWI hyperintensity within the solid component of adnexal tumors suggesting a malignant etiology were respectively 100% (93.3%-100%), 75% (57.2%-75%), 91.4% (85.3%-
Table IV

<table>
<thead>
<tr>
<th>Cystic component of adnexal tumors.</th>
<th>T2 Signal</th>
<th>b=1000 Signal</th>
<th>ADC (×10⁻³ mm²/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hypointense</td>
<td>Hyperintense</td>
<td>Hypointense</td>
</tr>
<tr>
<td>Malignant</td>
<td>0/29</td>
<td>29/29</td>
<td>27/29</td>
</tr>
<tr>
<td>n=29 (%)</td>
<td>(0)</td>
<td>(100)</td>
<td>(93.1)</td>
</tr>
<tr>
<td>Benign</td>
<td>0/13</td>
<td>13/13</td>
<td>12/13</td>
</tr>
<tr>
<td>n=13 (%)</td>
<td>(0)</td>
<td>(100)</td>
<td>(92.3)</td>
</tr>
<tr>
<td>p</td>
<td>NS¹</td>
<td>NS¹</td>
<td>NS³</td>
</tr>
</tbody>
</table>

Fisher’s exact test¹, Mann-Whitney test², NS: not significant.

91.4%), 100% (76.3%-100%) and 93.2% (83.5%-93.2%).
There was no significant difference (p=0.6)
between ADC values of the solid compo-
nent of malignant tumors (ADC=1.04 ± 0.23 × 10⁻³ mm²/s) and the ADC values
of the solid component of benign tumors
(ADC=1.16 ± 0.57 × 10⁻³ mm²/s) (fig. 3 and 4).

Discussion

Frequently, characterization of an ad-
nexal mass is achieved at US. However,
when the mass is large, complex or re-
mains indeterminate on US, MRI of the
pelvis is suggested to further assess.
Preoperative characterization of an ad-
nexal mass is relevant for surgical plan-
ning, either conservative or radical. So-
me pelvic MR imaging features of adnexal masses are suggestive of malig-
nancy: size over 6 cm, bilateral tumors,
tumor with solid and cystic compo-
nents, presence of vegetations, more
than 5 thick and irregular internal sep-
tations. The presence of peritoneal carci-
nomatosis, adenopathy, pelvic sidewall

© 2018 Elsevier Masson SAS. Tous droits réservés. - Document téléchargé le 15/12/2018 Il est interdit et illégal de diffuser ce document.
or adjacent organ invasion are strongly indicative of malignancy (1, 2).

We have assessed DWI to determine if it could be an additional criteria in the characterization of adnexal masses as benign or malignant.

To our knowledge, no published study describes the DWI signal characteristics of the solid tumor component of adnexal tumors on pelvic MRI. In our study, the solid component of malignant adnexal tumors was diffusion-weighted hyperintense in all cases (100%). On the other hand, the solid component of 3/12 (25%) benign tumors showed diffusion-weighted hyperintensity on b=1000 images. All 3 tumors were ovarian fibromas. One was complicated by torsion with diffuse hemorrhagic necrosis, probably the cause of extra-cellular water motion restriction. A diagnosis of ovarian fibroma was however easily achieved on T2W images.

The solid component of two malignant tumors (one ovarian metastasis and one borderline mucinous cystadenoma) showed T2W hypointensity, but the presence of hyperintensity on b=1000 diffusion-weighted images was helpful to correctly characterize these tumors as malignant. Diffusion-weighted imaging (b=1000) appears to be complementary to other conventional sequences and should probably be added to the routine MRI evaluation of adnexal pathology. The signal intensity on the DWI sequence may be an additional argument in the characterization of a mass as benign or malignant, when conventional sequences already are suggestive of one over the other, or provide a deciding element towards benign or malignant when other sequences are indeterminate. The presence of hyperintensity within the solid component of an adnexal tumor on b=1000 diffusion-weighted images should alert the radiologist to the possibility of a malignant tumor. However, this finding is not specific since some benign tumors may also be diffusion-weighted hyperintense. The absence of hyperintensity on DWI strongly supports a benign etiology.

Evaluation of the signal intensity on the DWI sequence should always be correlated to the imaging features on conventional sequences and the possibility of T2 shine through or hemorrhage as a cause of hyperintensity on b=1000 diffusion images should always be considered.

In our experience, analysis of ADC maps has proven to be disappointing. We were unable to demonstrate a significant difference (p=0.6) between ADC values in

<table>
<thead>
<tr>
<th>Table V</th>
<th>Solid component of adnexal tumors.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T2 Signal</td>
</tr>
<tr>
<td></td>
<td>Hypointense</td>
</tr>
<tr>
<td>Malignant</td>
<td></td>
</tr>
<tr>
<td>n=32</td>
<td>2/32</td>
</tr>
<tr>
<td>(%)</td>
<td>(6,3)</td>
</tr>
<tr>
<td>Benign</td>
<td></td>
</tr>
<tr>
<td>n=12</td>
<td>6/12</td>
</tr>
<tr>
<td>(%)</td>
<td>(50)</td>
</tr>
<tr>
<td>p</td>
<td>p=0.002 ¹</td>
</tr>
</tbody>
</table>

¹ Fisher’s exact test, ² Mann-Whitney test.
the solid component of malignant (ADC=1.04 ± 0.23 × 10⁻³ mm²/s) and benign (ADC=1.16 ± 0.57 × 10⁻³ mm²/s) adnexal tumors, even though ADC values tended to be lower in the solid component of malignant tumors. Some benign tumors (ovarian fibroma, serous cystadenofibroma, Brenner tumor) have solid components composed of hyalinized fibrous tissue, collagen and spindle cells (24, 25), responsible for restricted diffusion. ADC values for these tumors were low, and probably were responsible for the lack of significant statistical difference between ADC values of malignant and benign tumors. However, these tumors were not hyperintense on the b=1000 diffusion-weighted images, maybe to a “T2 dark-through” effect (26), correlating with the low T2W signal intensity on conventional images suggestive of a benign lesion.

The cystic component of ovarian tumors, benign or malignant, was nearly always T2W hyperintense and DWI hypointense, with no significant statistical difference in ADC values (ADC=2.47 ± 0.48 × 10⁻³ mm²/s for malignant tumors and ADC=2.46 ± 0.50 × 10⁻³ mm²/s for benign tumors).

Several authors have studied the ADC values of the cystic component of ovarian tumors. Some have reported that ADC values in the cystic component of malignant ovarian tumors were lower than ADC values in benign tumors (27-30), but with significant overlap in values between malignant and benign tumors, making the use of ADC values difficult in clinical practice to differentiate between malignant and benign ovarian tumor. Other authors reported no significant difference in ADC values between both groups of tumors (18, 31, 32).

The ADC value in a cyst relates to its viscosity, which varies based on the concentration of proteins, sugars, nucleic acids, and it decreases with increasing viscosity as occurs with mucinous or hemorrhagic contents (29). Lesions with complex cystic components. Also, hemorrhagic lesions have even lower ADC values due to the combination of high protein content and paramagnetic effect of methemoglobin (31-33).

ADC values are more related to the cyst content than to its histological nature, and ADC values are greatly variable within a same subgroup of tumors (32).

ADC value measurements of the cystic component of ovarian tumor do not appear to assist in distinguishing benign from malignant tumors.

There is a bias in our study with regards to ADC measurements on the ADC maps due to the small size of the ROI on the T2W images, with non-negligible risk of partial volume artifacts with surrounding structures that could result in inaccurate ADC values.

Also, we have not compared the value of DWI compared to other criteria routinely used on MRI in the characterization of adnexal tumors as benign or malignant.

Fig. 3: Left ovarian fibroma. The fibroma os T2W isointense, DWI hypointense, with ADC of 1,62 x 10⁻³ mm²/s.

a Axial T2W images.
b b=1000 diffusion-weighted image.
c ADC map.
Conclusion

Combined with conventional MR pulse sequences, DWI appears to provide additional information in characterizing adnexal tumors as benign or malignant. T2W hypointensity or the absence of hyperintensity on b=1000 diffusion-weighted images in the solid component of an adnexal tumor strongly suggest a benign etiology. On the other hand, the presence of hyperintensity on b=1000 diffusion-weighted images must be considered suspicious. DWI evaluation of the cystic component of adnexal tumors provides no additional diagnostic information.

References


