Malignant, borderline and benign ovarian masses: the added diagnostic value of ADC measurement and correlation with histopathology. Preliminary results.

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Aims and objectives

Background

The prevalence of adnexal masses in the general population is 0.17%- 5.9% in asymptomatic women and 7.1%- 12% in symptomatic women in the United States [1]. Ovarian cancer is the leading cause of death from gynecologic cancers among women in the United States [2].

Ultrasonography (US), Computed Tomography, and Magnetic Resonance Imaging (MRI) are currently used to evaluate ovarian tumors. US is the first-line imaging investigation for suspected adnexal masses [3]. When US findings are nondiagnostic or equivocal, MRI can be a valuable problem solving tool, an adjunctive modality for evaluating adnexal lesions, useful to give also surgical planning information without radiation exposure [4]. MRI has a fundamental role in revealing morphologic characteristics of ovarian masses, such as papillary projections, nodularity, septa, solid portions and signal intensity on T1- and T2-weighted images, but the imaging findings are frequently nonspecific and accurate characterization can remain difficult.

In recent years, the quality of diffusion-weighted imaging (DWI) in body regions has improved remarkably, due to the development of fast imaging techniques such as echo-planar imaging and the parallel imaging technique [5].

Previous studies have demonstrated that qualitative assessment of DWI with the Apparent Diffusion Coefficient (ADC) measurement can contribute to the discrimination of ovarian lesions, because ADC has been shown to be decreased by increased tumor cellularity [6-9].

The ADC reflects the random thermal motion of protons and it has been introduced to compare diffusivity between lesions. As cancer tissue generally tends to have high cell densities and abundant intercellular membranes, it is generally lower in cancer tissue than in noncancerous tissue [10-11].

Ovarian masses present a special diagnostic challenge when imaging findings cannot be categorized into benign or malignant pathology [12].

Therefore the use of ADC can be useful in the characterization of an ovarian lesion, in association with morphological assessment. This is important in order to avoid unnecessary surgery and for the preoperative description of complex solid and cystic adnexal mass, that was crucial for possible surgical strategies [13].

Aim of the study
The aim of our retrospective study was to verify the diagnostic performance of the mean apparent diffusion coefficient (mADC) using MRI with DWI in discriminating malignant, borderline and benign ovarian masses. DWI and mADC in non-homogenous T2-weighted solid components of ovarian lesions were especially evaluated. Histopathology was taken as a reference standard.

**Methods and materials**

**Patients**

The RIS-PACS system of our Institute of Radiology (Radiological Informatics System: Imagoweb-El.Co.S.r.l. Savona Italy; Picture Archiving and Communication Systems: Carestream Health Genova Italy) was used for the search. Filters were: interval time: 2012-2013; technique: MRI; UDC (cost diagnostic unit): Gynecology; ULD (hospital logistic unit): Dysfunctional Gynecological Unit and Gynecologic Oncology Unit (Gynecology Specialized Endometriosis and Oncologic Unit).

In this way, females submitted to MRI within the past 1 year by suspect of adnexal mass could be identified. Then, the medical history in case sheets was investigated for surgery and histopathology.

The inclusion criteria were:

- a) patients with adnexal masses on MRI examination completed with DWI sequences and
- b) surgery.

Database research, medical history investigation and histopathology correlation were made by a radiologist different from those examining MRI findings.

Radiologists examining MRI data were not aware of specific clinical symptoms and patient's outcome. This study was based on T2-weighted and DWI-MRI findings. Thirty-nine patients with adnexal masses were included in the study.

**MRI Technique**

The MRI protocol applied in our Department in clinical doubt of ovarian mass is performed at 1.5-T superconducting magnet (Signa Excite; GE Medical Systems, Milwaukee, USA) using phased array coil. Patients are requested to fast for 3-4 hours before the examination.
To limit intestinal peristalsis, to attenuate uterine contractions and to improve visualization of the adnexa and peritoneal surfaces, patients receive an intramuscular injection of 1 mg of hyoscine Nbutylbromide (Buscopan, Schering, Berlin, Germany) 10 minutes before the examination.

Technical details are shown in Table 1.

Image analysis

The MR images were retrospectively reviewed by two radiologists who had 10 and 5 years of experience in MR imaging for gynecological pathologies, in consensus, having carefully reviewed all images.

We focused on hypointense T2 weighted ovarian lesions and hypointense components whitin non-homogenous T2 weighted ovarian masses.

The signal intensity of solid components on T2-weighted MR images was defined as hypo- or hyperintense compared to that of the outer myometrium.

The solid components, according to a previously established classification by Timmerman et al. [14] included thickened septa, vegetation (papillary projection) and solid portions that showed enhancement post-injection. The solid components of the lesions were identified on T2-weighted images and were matched on ADC maps.

DWI at b value 0-800 s/mm² were analysed qualitatively, referring to the signal intensity of ovarian lesions, for the presence of areas with higher signal intensity than the serous fluid (urine in the bladder or cerebrospinal fluid). Then a quantitative analysis on the ADC map was made.

For image analysis, data were transferred to a GE Advantage Workstation (Horizon Advantage GE Medical System) and analysed using the Functool dynamic analysis tool (GE, Waukesha, Wis, USA). ADCs were calculated on a pixel-by- pixel basis to generate ADC maps. A region-of-interest (ROI), with diameters ranging between 20 and 40 mm², was manually drawn around each solid ovarian component showing restriction on DWI. At least three measurements were obtained and an averaged ADC value was acquired (mADC).

Data analysis

All variables considered in our study showed a distribution that was not different from the normal one according to Kolmogorov-Smirnov test. Comparisons among groups of mADC were done by analysis of variance (ANOVA). In cases of global statistical significance, between groups comparisons were done by unpaired t test with statistical
The results of multiple comparisons corrected by Bonferroni rule. Data are reported as mean ± SD. A 2-tailed p value <0.05 was considered statistically significant.

**Images for this section:**

<table>
<thead>
<tr>
<th>Weighting And Plane</th>
<th>Axial T1W</th>
<th>Axial T2W</th>
<th>Sagittal T2W</th>
<th>Coronal T2W</th>
<th>Axial T1W</th>
<th>Axial DWI</th>
<th>Axial LAVA</th>
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<td>FRFSE</td>
<td>FRFSE</td>
<td>FRFSE</td>
<td>Out of phase</td>
<td>DWI body no asset b800</td>
<td>3D LAVA</td>
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<td>15</td>
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</table>

**Table 1:** FSE: Fast Spin Echo; FRFSE: Fast Recovery Fast Spin Echo; SPGR: Spoiled Gradient Echo; NEX: Number of Excitations; LAVA: Liver Acquisition with Volume Acceleration.
Results

39 patients satisfied inclusion criteria of this study (median age: 40±15 years; age range 16-73 years). Each patient presented an ovarian mass.

Using histopathology as reference standard, three groups of patients were identified:

- 12 with malignant tumors (3 clear cell carcinomas, 6 endometrioid G2 carcinomas, 3 granulosa cell tumors);
- 9 with borderline tumors (3 serous borderline tumors, 3 mucinous borderline cystadenomas, 3 endocervical-like mucinous borderline) and
- 15 with benign lesions (3 mucinous cystadenofibromas, 6 endometrioid cysts, 3 ovarian thecomas, 3 mature cystic teratomas).

The histopathological results are shown in figures 1 and 2.

The mADCs were:

- $0.97 \pm 0.22 \times 10^{-3} \text{mm}^2/\text{s}$ in malignant masses;
- $1.26 \pm 0.57 \times 10^{-3} \text{mm}^2/\text{s}$ in borderline lesions and
- $1.31 \pm 0.32 \times 10^{-3} \text{mm}^2/\text{s}$ in benign masses (see Table 2).

Using mADC, a statistically significant difference was found between the malignant and benign groups ($p=0.003$) but neither between the benign and borderline ($p=0.76$) nor between the borderline and malignant masses ($p=0.12$); (Figures 3 and 4).

Images for this section:
Fig. 1

Overall Population

- 46% Benign
- 31% Borderline
- 23% Malignant
Histopathology

- clear cell carcinomas
- endometrioid G2 carcinomas
- granulosa cell tumors
- serous borderline tumors
- mucinous borderline cystadenomas
- endocervical-like mucinous borderline tumors
- endometriod cysts
- mucinous cystadenofibromas
- ovarian tecomas
- mature cystic teratomas
- fibromas
# Results

<table>
<thead>
<tr>
<th></th>
<th>mADC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant</td>
<td>0.97±0.22x10⁻³mm²/s</td>
</tr>
<tr>
<td>Borderline</td>
<td>1.26±0.57x10⁻³mm²/s</td>
</tr>
<tr>
<td>Benign</td>
<td>1.31±0.32x10⁻³mm²/s*</td>
</tr>
</tbody>
</table>

*p=0.003 malignant vs benign

Table 2
Fig. 3
Fig. 4
Conclusion

In our series:

- mADC was statistically lower in malignant (Fig. 5-7) as compared to benign masses (Fig. 8-9) but mADC could not discriminate borderline (Fig. 10-11) from benign or malignant lesions.
- Teratomas and endometriomas showed lower mADC values as compared to other benign masses.

The restricted Brownian movement of water molecules within the keratinoid substance or fat in mature cystic teratomas and thick proteinaceous or bloody products in endometrial cysts results in a high signal on DWI and a low ADC values [15-18].

- Also fibromas (Fig. 12) and thecomas (Fig. 13-14), in our patients, presented low mADCs but no restriction of proton diffusion on DWI, as Zhang et al. [11] just reported.

Infact the majority of malignant ovarian tumors, mature cystic teratomas, and almost half of the endometriomas exhibited abnormal signal intensity on DWI, whereas most fibromas and other benign lesions did not [16]. Therefore the solid component within the complex adnexal mass with low signal intensity on T2 weighted and DWI sequences are invariably benign [11]. However, the assessment of morphology and contrast-enhancement yielded correct diagnosis.

Currently, there is no gold standard for the diagnosis of a benign versus malignant ovarian tumor prior to surgery, especially when the tumor has both solid and cystic components. Predictors of ovarian malignancies include lesion size (>6 cm), thickness of the walls and septa (>3 mm), and the detection of internal structures including papillary projections, nodularity, various degrees of solid components, necrosis, haemorrhage, or regions of striking enhancement following administration of contrast medium [19-22]. But these imaging parameters have been found to overlap for benign and malignant ovarian lesions. Therefore, as proposed by Katayama [23] and Thomassin-Naggara et al. [24-25], the abovementioned parameters are not always the most accurate predictors of ovarian malignancies.

Thus, the addition of DWI to conventional T1-weighted and T2-weighted MRI protocols may increase the accuracy of distinguishing ovarian benign and malignant tumors with solid components. The advantage of using DWI include also that it is a non-invasive technique, it does not cause a patient significant discomfort, and it does not require exposure to ionizing radiation or injection of contrast materials [26].
In conclusion, **DWI and the corresponding measurements of ADC values, could integrate the morphological and dynamic findings in discriminating malignant from benign ovarian masses.**

Nevertheless, further studies with a larger number of cases are needed to support these findings.

**Images for this section:**

**Fig. 5:** A 38-years-old woman with a clear cell carcinoma. A) Axial T1-weighted image shows an ovarian mass with a non-homogenous hypointensity; B) Axial T2-weighted image reveals an ovarian mass with a wall thickness of about 3 mm, largely fluid with thin septum on the right and peripheral nodules; C) Axial T2-weighted reference image; D) Axial DWI shows a high signal intensity of the the hypointense nodule (circle 1); E) ADC map (ADC=1.21 x 10^{-3} mm^2/s).
Fig. 6: A 44-years-old woman with a granulosa cell tumor. A) Axial pre-contrast T1-weighted image shows a right ovarian mass with hypointensity; B) Axial T2-weighted image confirms a hypointense ovarian mass; C) Axial T2-weighted reference image; D) Axial DWI shows a high-intermediate signal intensity of the mass (circle 1); E) ADC map (ADC=0.44 x 10-3mm2/s).
Fig. 7: Granulosa cell tumor. Axial post-contrast gradient-echo T1-weighted image with fat saturation shows progressive enhancement of the right ovarian mass (yellow arrow) respectively at 30 sec (A), 60 sec (B) and 120 sec (C).
Fig. 8: A 50-year-old woman with a cystoadenofibroma. A) Axial pre-contrast T1-weighted image shows a right ovarian hypointense mass; B) Axial T2-weighted image better reveals multiple hyperintense areas due to cystic components with a hypointense peripheral lesion. C) Axial T2-weighted reference image; D) Axial DWI shows high signal intensity (circle 1); E) ADC map (ADC=1.70 x 10^-3 mm^2/s).
Fig. 9: Cystoadenofibroma. Axial post-contrast gradient-echo T1-weighted image with fat saturation shows progressive enhancement within the right lateral aspect of mass (yellow arrow) respectively at 30 sec (A) and 60 sec (B) and 120 sec (C).
Fig. 10: A 16-years-old woman with a serous borderline tumor. A) Axial pre-contrast T1-weighted image shows a left ovarian mass with hypointensity; B) Axial T2-weighted image reveals a cystic ovarian mass with hypointense solid components; C) Axial T2-weighted reference image; D) Axial DWI shows high signal intensity on the solid components (circle 1); E) ADC map (ADC=1,50 x 10^-3 mm²/s).
Fig. 11: Serous borderline tumor. Axial post-contrast gradient-echo T1-weighted image with fat saturation shows progressive enhancement within the solid components on the left aspect of the mass (yellow arrow) respectively at 30 sec (A) and 60 sec (B) and 120 sec (C).
Fig. 12: A 47-years-old woman with a right ovarian fibroma. A) Axial T1-weighted image shows a hypointense right ovarian mass; B) Axial T2-weighted image reveals a markedly hypointense right ovarian mass with cystic areas; C) Axial T2-weighted reference image; D) Axial DWI shows no restricted diffusion of the lesion (circle 1); E) ADC map (ADC=0,25x 10^-3 mm^2/s).
Fig. 13: A 51-years-old woman with a thecoma. A) Axial pre-contrast T1-weighted image shows a left ovarian mass with a slightly hyperintensity; B) Axial T2-weighted image reveals a non-homogeneously hypointensity; C) Axial T2-weighted reference image; D) Axial DWI shows a low signal intensity (circle 1); E) ADC map (ADC=0,564 x 10^{-3}mm^2/s).
Fig. 14: Thecoma. Axial post-contrast gradient-echo T1-weighted image with fat saturation demonstrates a progressive enhancement of the mass (yellow arrow) respectively at 30 sec (A), 60 sec (B) and 120 sec (C).
Personal information

References


