Accuracy of the ADNEX MR scoring system based on a simplified MRI protocol for the assessment of adnexal masses

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PURPOSE
We aimed to evaluate the ADNEX MR scoring system for the prediction of adnexal mass malignancy, using a simplified magnetic resonance imaging (MRI) protocol.

METHODS
In this prospective study, 200 patients with 237 adnexal masses underwent MRI between February 2014 and February 2016 and were followed until February 2017. Two radiologists calculated ADNEX MR scores using an MRI protocol with a simplified dynamic study, not a high temporal resolution study, as originally proposed. Sensitivity, specificity, positive and negative predictive values, likelihood ratios, and the area under the receiver operating characteristic curve were calculated (cutoff for malignancy, score ≥ 4). The reference standard was histopathologic diagnosis or imaging findings during >12 months of follow-up.

RESULTS
Of 237 lesions, 79 (33.3%) were malignant. The ADNEX MR scoring system, using a simplified MRI protocol, showed 94.9% (95% confidence interval [CI], 87.5%–98.6%) sensitivity and 97.5% (95% CI, 93.6%–99.3%) specificity in malignancy prediction; it was thus highly accurate, like the original system. The level of interobserver agreement on simplified scoring was high (κ = 0.91).

CONCLUSION
In a tertiary cancer center, the ADNEX MR scoring system, even based on a simplified MRI protocol, performed well in the prediction of malignant adnexal masses. This scoring system may enable the standardization of MRI reporting on adnexal masses, thereby improving communication between radiologists and gynecologists.

Adnexal masses are frequent findings in pelvic and abdominal imaging studies, such as those conducted with ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI) (1). Preoperative evaluation of these lesions and determination of the risk of malignancy are critical to define treatment. A lesion with a low risk of malignancy can be followed or treated with minimally invasive surgery performed by a general gynecologist. When the risk of malignancy is significant, the patient should be referred to a tertiary center for treatment by a multidisciplinary team that includes an oncologic gynecologist (2, 3).

Every year, about 240 000 women worldwide are diagnosed with ovarian cancer. The 5-year survival rate is less than 45%, and ovarian cancer is responsible for about 150 000 deaths annually. Thus, it is the seventh most common cancer and the eighth most common cause of cancer death among women (4).

US is the first-line modality for the assessment of suspected adnexal masses, with very accurate results (5). However, US examination yields indeterminate findings in approximately 20% of adnexal masses (6–8). Exophytic and large tumors, fatty components, clots that mimic vegetation, and fibrous tumors have morphologic characteristics that are difficult to interpret with US. Other imaging methods (e.g., MRI, CT, positron emission tomography–computed tomography [PET-CT]) are under investigation as stand-alone examinations or for use in combination with US in the evaluation of these masses (9–12). MRI has
the best potential for preoperative evaluation of adnexal masses. It has shown greater accuracy (88.9%) than transvaginal US (63.9%) in the characterization of adnexal masses as malignant, and better specificity (83.7% vs. 39.5%) (13). Systematic reviews showed that MRI has improved the preoperative evaluation of suspicious adnexal lesions. In the evaluation of ultrasound-indeterminate adnexal lesions, MRI could be considered as the gold standard, highlighting the high specificity of this imaging method in the characterization of benign lesions (13, 14).

Various MRI protocols have been used to evaluate ovarian lesions, and MRI reporting methods vary among institutions (15, 16). In an attempt to standardize imaging evaluation and reporting and to facilitate communication between gynecologists and radiologists, Thomassin-Naggar et al. (17) published the MRI scoring system for adnexal lesions (ADNEX MR scoring system) in 2013. This protocol has a structure similar to that of the Breast Imaging Report Data System (BI-RADS™), with a sensitivity of 93.5% and specificity of 96.6% in the detection of malignant adnexal masses (17). However, one of the main parts of the protocol is the acquisition and post-processing of perfusion-weighted magnetic resonance images obtained by using a dynamic contrast-enhanced T1-weighted gradient-echo sequence. This sequence is technically demanding, and the required temporal resolution for the originally proposed dynamic contrast-enhanced study is 2.4 s. Another great limitation is the lack of widespread use of perfusion MRI in current clinical practice, in some regions, recognized even by scoring authors (18). Also, some post-processing techniques can be complex, such as the semiquantitative analysis based on relative signal intensity of the curve, used to calculate the initial area under the curve (before 60 s) and different mathematic models used to obtain the enhancement amplitude, time of half rising, and maximal slope of the curve.

The objective of this study was to test the ADNEX MR scoring system, based on a simplified MRI protocol, using a simple dynamic study with high spatial resolution at 30, 60, 90, 120, and 150 s acquisitions. We believe that this scoring approach is promising for the standardization of MRI evaluation and reporting, which is urgently needed to improve team communication and has been performed successfully for other organs, such as the breast (BI-RADS™), prostate (Prostate Imaging Reporting and Data System; PI-RADS™), and liver (LIRADS™). We used histopathologic and long-term clinical follow-up data as the standard reference. To our knowledge, this study is the first to evaluate the ADNEX MR scoring system using a simplified MRI protocol, besides having the highest number of adnexal masses evaluated.

**Methods**

**Patients**

This prospective study was conducted at the Faculty of Medical Sciences of the State University of Campinas. All medical procedures and examinations were performed at the Women’s Prof. José Aristodemo Pinotti Women’s Hospital and Sumaré State Hospital, which are medical facilities that compose the healthcare area of Unicamp. The Women’s Hospital, also known as Caism, is a hospital with a gynecologic oncology reference unit of regional and national scope. Written informed consent was obtained from all patients. The study was approved by the university’s Research Ethics Committee (protocol nos. 1092/2009 and 008/2010).

Two hundred women who had been referred to the oncology clinic of Women’s Hospital due to the detection of adnexal masses between February 2014 and February 2016 were prospectively invited to participate. We randomly invited women referred to our hospital because of an adnexal mass, with the recruiter not knowing

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**Main points**

- ADNEX MR scoring system, based on a simplified MRI protocol, is a useful tool in the assessment of adnexal masses.
- This system helps the standardization of MRI reports for adnexal masses.
- Very high interobserver agreement was obtained using the simplified protocol.
- Borderline tumors remain a diagnostic challenge.

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**Figure 1.** Flow-chart depiction of patient selection.
clinical information (time of evolution, for example), laboratory tests (serum levels of CA-125) or imaging of the patient (pelvic US), trying to avoid any selection biases.

MRI examinations were performed after thorough pelvic examination. We included all women with adnexal masses for whom histologic results were available or who had been followed for at least 1 year (until February 2017), as proposed by Thomassin-Nagagara et al. (17). We also included women discharged from our oncology facility due to benign clinical findings, such as functional cysts, endometrioma or hydrosalpinx, and those whose adnexal masses had disappeared on follow-up examinations.

Fig. 1 illustrates patient allocation. In total, 200 women were evaluated using ADNEX MR scoring system based on simplified MRI protocol. Of these, 13 women were excluded because they had no medical indication for surgery or did not complete 12 months of follow-up after diagnosis of the adnexal masses. The adnexal masses were excised via laparoscopy or laparotomy for histopathologic assessment. For the 13 unresectable tumors encountered, pathologic specimens were obtained by percutaneous biopsy of the pelvic masses or from abdominal implants. In total, 164 adnexal masses (from 104 women with single masses, 27 women with two masses each, and 2 women with three masses each) were evaluated histologically.

Of 54 women with no surgical indication due to benign/functional characteristics of the adnexal masses, 39 women had single masses, 12 women had bilateral masses, 2 women had three masses each, and 1 woman had four masses (total, 73 masses). None of these women showed worsening on follow-up imaging studies for at least 12 months.

MRI protocol and evaluation

Patients fasted for 3 hours before undergoing MRI performed with a 1.5 Tesla device (GE Signa HDxt; General Electric) using an 8-channel pelvic phased-array coil. Table 1 details the technical parameters of the MRI sequences used. Axial, sagittal, and coronal T2-weighted fast spin-echo sequences, axial T2-weighted sequences with fat suppression, and T1-weighted sequences with and without fat suppression were performed. Diffusion-weighted images were acquired in the axial plane, with b values of 0, 500, and 1000 s/mm², as we routinely used in clinical practice. We used three-dimension-

al pre- and post-contrast (LAVA*) (TE, 2.1; TR, 4.3; FA, 12; slice thickness, 3.8 mm; intersection gap, 2.0 mm; FOV, 320×192). After intravenous gadolinium injection, the dynamic study was performed in 5 post-contrast phases with 30 s delay each. Gadolinium chelate (Omniscan, 0.2 mL/kg body weight; GE Healthcare*) was administered at a rate of 3.5 mL/s using a power injector (Medrad), followed by a 10 mL infusion of normal saline. In the postprocessing of images, regions of interest (ROI) were selected and qualitative criteria were performed for diffusion-weighted restriction, as proposed by Thomassin-Nagagara et al. (17), avoiding areas of necrosis. The postprocessing of the dynamic study included the absolute signal and the relative enhancement to build the dynamic curves.

Two radiologists (P.N.P. with 7 years of experience in body MRI, with an emphasis on gynecological pathologies and R.H.O.B. with 6 years of experience in body MRI, with an emphasis in gastrointestinal pathologies) independently evaluated MRI data from all patients and calculated ADNEX MR scores for all 237 adnexal masses. Interobserver agreement on these scores was evaluated. This was a prospective double-blind study, as the evaluators had no knowledge of the US reports, histologic and/or follow-up results.

ADNEX MR scores are based only on MRI parameters, as follows (17):

1. No adnexal mass;
2. Benign mass: purely cystic, with the presence of endometrioid or fatty masses; or absence of wall enhancement in masses without solid tissue; or low signal on diffusion- or T2-weighted images within solid tissue; or masses with solid tissue with curve type 2 or nonfeasible and absence of wall enhancement;
3. Probably benign mass: wall enhancement in masses without solid tissue or type 1 time-signal intensity curve within solid tissue;
4. Indeterminate mass: type 2 time-signal intensity curve within solid tissue and wall enhancement;
5. Probably malignant mass: peritoneal implants or type 3 time-signal intensity curve within solid tissue.

Reference standard

The reference standard was histopathologic diagnosis, following the Guidelines of the World Health Organization’s International Classification of Ovarian Tumors (19).

Borderline ovarian tumors were classified as malignant disease for statistical purposes. For adnexal masses not subjected to histopathologic examination, the criteria for benign disease were based on clinical and imaging monitoring for at least 12 months, following the usual clinical care protocols of the institution.

Statistical analysis

We analyzed data using a dedicated statistical software (R Environment for Statistical Computing software). The odds ratio (OR) and chi-squared test were used to examine associations between categorical variables. Statistical calculations were performed using 95% confidence intervals (CIs), with P values <0.05 considered to be statistically significant. Normally distributed data were presented as means and standard deviations (SDs).

We calculated the sensitivity, specificity, positive and negative predictive values, and area under the receiver operating characteristic (ROC) curve for ADNEX MR scores, using ≥4 as the cutoff for malignancy, as suggested by Thomassin-Nagagara et al. (17). Interobserver agreement on ADNEX MR scores was evaluated using unweighted and Fleiss kappa indices.

Results

Patients with malignant disease were older than those with benign lesions (mean age, 57.8±13.2 vs. 47.1±14.9 years). In addition, postmenopausal status predominated in patients with malignant disease compared with those with benign lesions (68.4% [54/79] vs. 37.4% [59/158]; P <0.001).

Table 2 shows final diagnostic data for the 237 adnexal masses. For 164 lesions (76.7%), final diagnoses were obtained by pathologic examination of surgical or percutaneous biopsy specimens. For 73 lesions (23.3%), diagnoses were based on at least 12 months of imaging follow-up. Ovarian tumors comprised most benign and malignant masses (80%), and most were of epithelial origin. Germ cell tumors were the second most frequent lesion type in women with benign disease, followed by endometriomas and stromal/functional tumors. In women with malignant tumors, serous adenocarcinoma was the most frequent diagnosis, followed by clear cell and metastatic tumors.

Table 3 shows results for all MRI parameters evaluated. Apart from tumor size (mean value of the orthogonal mass axes),
all parameters considered in scoring differed individually between malignant and benign masses. Type 3 time-signal intensity curves were associated strongly with malignant disease (35/58 malignant tumors) with respective ORs of 4.55 and 9.5 when compared with type 1 and 2 curves; and consistently ruled out benignity (only 1 in 20 women with benign disease presented this characteristic). Figs. 2, 3, and 4 illustrate three different types of adnexal masses and their respective enhancement curves.
Performance indicators for the ADNEX MR scoring system based on simplified MRI protocol are presented in Table 4. The originally proposed cutoff of ≥4 for malignant disease showed 94.9% (95% CI, 87.54%–98.60%) sensitivity and 97.5% (95% CI, 93.65%–99.31%) specificity, with accuracy of 96.62% (95% CI, 93.46%–98.53%). The positive and negative predictive values were 94.8% and 97.4%, respectively. The positive likelihood ratio was 37.5 (95% CI, 14.23–98.81) and the negative likelihood ratio was 0.05 (95% CI, 0.02–0.14). The four malignant adnexal masses that received a score of 3 (probably benign) were borderline tumors without solid tissue. The four benign adnexal masses that received a score of 4 were: one endometrioma with extensive pelvic adherences, one broad ligament leiomyoma, and two serous cystadenomas. The level of interobserver agreement on the final classification of lesions using the ADNEX MR scoring system based on simplified MRI protocol was high (κ = 0.91). The area under the ROC curve for ADNEX MR scores was 0.98 (95% CI, 0.96–0.99), demonstrating that ≥4 was the optimal cut-off point for malignancy (Fig. 5).

**Discussion**

This study showed that the ADNEX MR scoring system is of great value, even based on a simplified MRI protocol, as it combines optimum MRI parameters in the evaluation of malignancy probability in women with adnexal masses. In our sample of adnexal masses, this MRI scoring system had high performance indicators, such as sensitivity and specificity values exceeding 94%. Importantly, our study corroborates the results reported by the proponents of the original ADNEX MR scoring system (17), with the use of a simple dynamic contrast-enhanced curve that can easily be obtained in clinical practice. The use of a simplified MRI protocol can catalyze the use and dissemination of ADNEX MR scoring system in the adnexal masses assessment. We also obtained a very high level of agreement between readers, which demonstrates its reproducibility.

The standardization of preoperative imaging evaluation of adnexal masses is highly desirable, as misinterpretation of results and reporting bias can lead to severe consequences for patients, most notably, unnecessary surgery and/or delayed onset of the treatment of potentially lethal disease (20). Several attempts to address failures in imaging methods are currently underway; they range from the modelling of US evaluation and reporting, such as the simple rules of the International Ovarian Tumor Analysis group (6, 7), to the proposition...
### Table 3. MRI parameters of benign and malignant masses

<table>
<thead>
<tr>
<th>MRI parameters</th>
<th>Benign disease (n=158)</th>
<th>Malignant disease (n=79)</th>
<th>P</th>
<th>OR</th>
<th>95% CI</th>
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<tr>
<td>Size (cm)</td>
<td>9.11±6.5</td>
<td>9.16±6.5</td>
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<td>Septum</td>
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<td>0.0008</td>
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<tr>
<td>Single</td>
<td>25/54 (46.2)</td>
<td>3/35 (8.6)</td>
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<td>Two or more</td>
<td>29/54 (53.8)</td>
<td>32/35 (91.4)</td>
<td>9.2</td>
<td>2.50</td>
<td>33.69</td>
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<td>Septum thickness</td>
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<tr>
<td>Thin</td>
<td>37/54 (68.5)</td>
<td>2/35 (5.8)</td>
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<td></td>
<td></td>
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<tr>
<td>Thick</td>
<td>17/54 (31.5)</td>
<td>33/35 (94.2)</td>
<td>26.2</td>
<td>5.55</td>
<td>123.58</td>
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<td>T2-weighted signal intensity within solid tissue</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>17/23 (74.0)</td>
<td>2/70 (2.8)</td>
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<td></td>
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<tr>
<td>Medium/high</td>
<td>6/23 (26)</td>
<td>68/70 (97.2)</td>
<td>96.3</td>
<td>17.84</td>
<td>520.13</td>
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<td>b=1000 s/mm²–weighted signal intensity within solid tissue</td>
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<tr>
<td>Low</td>
<td>17/25 (68)</td>
<td>2/69 (2.9)</td>
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<tr>
<td>Medium/high</td>
<td>8/25 (32)</td>
<td>67/69 (97.1)</td>
<td>72.25</td>
<td>14.04</td>
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<td>42/42 (100)</td>
<td>69.68</td>
<td>4.17</td>
<td>1163.88</td>
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<td>Type 1</td>
<td>13/20 (65)</td>
<td>1/58 (1.7)</td>
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<tr>
<td>Type 2</td>
<td>6/20 (30.0)</td>
<td>22/58 (38)</td>
<td></td>
<td></td>
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<tr>
<td>Type 3</td>
<td>1/20 (5.0)</td>
<td>35/58 (60.3)</td>
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<td>Type 3 vs. type 1</td>
<td>&lt;0.0001</td>
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<td>455</td>
<td>26.47</td>
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<td>Type 3 vs. type 2</td>
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<td>9.5</td>
<td>1.07</td>
<td>84.71</td>
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<td>47.66</td>
<td>5.14</td>
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<td>Ascites</td>
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<td>134/158 (84.8)</td>
<td>26/79 (45.6)</td>
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<td>Yes</td>
<td>24/158 (15.2)</td>
<td>43/79 (54.4)</td>
<td>9.2</td>
<td>4.80</td>
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<td>40/79 (50.7)</td>
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<tr>
<td>Yes</td>
<td>0</td>
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<td>309.17</td>
<td>18.6</td>
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<td>158/158 (100)</td>
<td>73/79 (92.7)</td>
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<tr>
<td>Yes</td>
<td>0</td>
<td>6/79 (7.6)</td>
<td>28.03</td>
<td>1.55</td>
<td>504.30</td>
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</table>

Data are expressed as mean ± standard deviation or n/N (%). The denominators used to calculate percentages varied according to the availability of data. MRI, magnetic resonance imaging; OR, odds ratio; CI, confidence interval.
Figure 2. a–d. Right adnexal mass with irregular contour, undetermined by IOTA simple rules in a 74-year-old woman. Final ADNEX MR score of 2. Follow-up since 2015 shows stability of the findings. Axial T2-weighted spin-echo image (a) shows a well-defined, lobulated low signal intensity solid tumor. Axial contrast-enhanced study (b) demonstrates low level of enhancement of the mass (green circle ROI, uterus; red circle ROI, adnexal mass). Signal intensity curve (c) shows gradual increase in the signal intensity of the solid tissue on the dynamic contrast-enhanced images, without a peak (type 1 curve). Relative enhancement ratio (d) shows gradual increase in mass enhancement compared with the uterus, without a peak (type 1 curve).

Figure 3. a–d. Pelvic mass of undefined etiology in a 23-year-old woman. Final ADNEX MR score of 4. Right salpingo-oophorectomy plus omentectomy was performed; a borderline serous tumor of right ovary was the histologic diagnosis. Axial T2-weighted spin-echo image (a) demonstrates a cystic mass with solid components adhered to the right ovary. Axial contrast-enhanced study demonstrates inhomogeneous enhancement of the mass (green circle ROI, uterus; red circle ROI, adnexal mass). Signal intensity curve (c) shows moderate initial increase in the signal intensity of solid tissue, followed with a plateau (type 2 curve). Relative enhancement ratio (d) shows moderate initial increase in mass enhancement compared with the uterus, followed by a plateau.
evaluation of adnexal masses. However, both professionals were relatively seasoned radiologists with ≥6 years of professional activity. The inclusion of medical residents (inexperienced readers) in a further evaluation of score reproducibility would be desirable. Third, the sample included a limited number of borderline ovarian tumors, whose evaluation is most challenging. Fourth, we considered patients who were not operated, but were followed for at least 1 year with no sign of disease, to be “negative”; this interval may be short for some ovarian diseases, such as borderline tumors, which can evolve slowly.

In conclusion, at a tertiary cancer center, the ADNEX MR scoring system, even based on a simplified MRI protocol, was of great value in the standardization of MRI evaluation and reporting for adnexal masses. The system showed excellent performance in our institution, as it did in the original study. The next step is to test and refine the scoring system for application to masses that are difficult to evaluate using US and to further improve the parameters, enabling better identification of borderline ovarian tumors (e.g., with the use of the simplified system in combination with other imaging or laboratory methods).

Conflict of interest disclosure
The authors declared no conflicts of interest.

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