Semiquantitative Dynamic Contrast-Enhanced MRI for Accurate Classification of Complex Adnexal Masses

Anahita Fathi Kazerooni, MSc,1,2 Mahrooz Malek, MD,3,4 Hamidreza Haghighatkah, MD,5 Sara Parviz, MD,3 Mahnaz Nabil, PhD,6 Leila Torbati, MD,3 Sanam Assili, MSc,1 Hamidreza Saligheh Rad, PhD,1,2 and Masoumeh Gity, MD3,4*

Purpose: To identify the best dynamic contrast-enhanced (DCE) magnetic resonance imaging (MRI) descriptive parameters in predicting malignancy of complex ovarian masses, and develop an optimal decision tree for accurate classification of benign and malignant complex ovarian masses.

Materials and Methods: Preoperative DCE-MR images of 55 sonographically indeterminate ovarian masses (27 benign and 28 malignant) were analyzed prospectively. Four descriptive parameters of the dynamic curve, namely, time-to-peak (TTP), wash-in-rate (WIR), relative signal intensity (SIrel), and the initial area under the curve (IAUC60) were calculated on the normalized curves of specified regions-of-interest (ROIs). A two-tailed Student’s t-test and two automated classifiers, linear discriminant analysis (LDA) and support vector machines (SVMs), were used to compare the performance of the mentioned parameters individually and in combination with each other.

Results: TTP ($P = 6.15E-8$) and WIR ($P = 5.65E-5$) parameters induced the highest sensitivity (89% for LDA, and 97% for SVM) and specificity (93% for LDA, and 100% for SVM), respectively. Regarding the high sensitivity of TTP and high specificity of WIR and through their combination, an accurate and simple decision-tree classifier was designed using the line equation obtained by LDA classification model. The proposed classifier achieved an accuracy of 89% and area under the ROC curve of 93%.

Conclusion: In this study an accurate decision-tree classifier based on a combination of TTP and WIR parameters was proposed, which provides a clinically flexible framework to aid radiologists/clinicians to reach a conclusive preoperative diagnosis and patient-specific therapy plan for distinguishing malignant from benign complex ovarian masses.

J. MAGN. RESON. IMAGING 2016;00:000–000.

An accurate differentiation of sonographically indeterminate benign and malignant complex ovarian masses preoperatively is clinically important.1 Traditionally, women with indeterminate ovarian masses were scheduled for radical surgery, which is no longer an appropriate option: patients with benign masses may be treated through a conservative procedure or with minimal resection, while women with malignant masses require radical surgery and reliable specialist referral.2,3 In this context, magnetic resonance imaging (MRI) plays a key role as a problem-solving imaging modality.1,4

Conventional MRI examination based on morphological and signal intensity appearances is proven to generate higher accuracy compared with ultrasound.2 Yet nonspecific imaging features and dependence on experience of the reader restricts the liability of conventional MRI. Therefore, quantitative MRI techniques, such as dynamic contrast-enhanced (DCE) MRI, which allow for less dependence on...
the expertise of the reader, may offer greater predictive value in differential diagnosis of ovarian masses.\textsuperscript{5,6}

Thus far, determination of ovarian mass categories based on DCE-MRI has been carried out through two common approaches: 1) subjective inspection of curve shape types and attempting to attribute them to benign, uncertain, and malignant ovarian masses;\textsuperscript{7–9} or 2) applying threshold criteria on the extracted semiquantitative or pharmacokinetic (PK) parameters.\textsuperscript{6,7,10,11} Similar to morphological criteria, curve shape assessment is qualitative, susceptible to unintended user bias, and may assign many masses to the "uncertain" category. Therefore, analytical methods that generate quantitative curve shape descriptors, ie, a semiquantitative approach, or provide physiological parameters, ie, PK modeling, are beneficial to provide objective indicators of tumor malignancy. Nonetheless, threshold criteria on analytical parameters must be computed for each specific protocol or scanner and cannot be generalized.

Presumably, for classification of benign and malignant complex ovarian masses based on DCE-MRI, where there are diverse suggestions about the potential features according to different protocols/scanners/quantification techniques,\textsuperscript{7,10–13} diagnostic decision support machines or models can be devised through computerized pattern-based approaches to objectively aid the radiologists to reach a more certain diagnosis. The pattern recognition or machine-learning methods learn and quantify the patterns and regularities of given data and construct a model of selected features, and if designed correctly, these techniques are likely to be generalized.

PK analysis methods impose several complications and limitations which make the semiquantitative analysis more attractive\textsuperscript{14}: 1) the compartmental model must be consistent with the underlying physiology; 2) accurate selection of arterial input function (AIF) is limited by temporal and spatial resolutions; and 3) prior \( T_1 \)-mapping is necessary for calculating accurate concentration–time curves.\textsuperscript{15,16} Evidently, such complexities, if not attentively managed, do not facilitate automated differentiation of benign from malignant lesions, and may lead to erroneous decisions.

The purpose of this study was to devise a computer-aided model for automatic classification of benign and malignant complex ovarian cancers based on patterns of descriptive DCE-MR semiquantitative parameters.

Materials and Methods

Patients

Study approval was obtained from the Institutional Review Board (IRB), and patients were included only if they provided written informed consent. Fifty-four patients were prospectively enrolled in this study. Prior to MRI examination, all study subjects had undergone transvaginal ultrasound evaluation and ultrasound score (U-score) estimation, with each U-score point being added if any of the following features existed: multilocular cyst, solid components, bilateral lesions, metastases, and ascites. Patients with a U-score of 1 or more were enrolled in the study.

The MR experiment was carried out if the patient did not show any contraindications for MRI or receiving contrast agent. All included patients were scheduled for surgical removal of suspicious ovarian masses and postoperative histopathological assessment within 2 weeks of MRI exam.

MRI Protocol

MR images were acquired on a 3T scanner (Magnetom Tim Trio, Siemens, Erlangen, Germany), with patients placed in a phased-array coil in the supine position. The patients were asked to fast for 3 hours and for each patient 20 mg of Hyoscine Butylbromide (Buscopano) antispasmodic drug was injected intravenously to reduce bowel peristalsis immediately prior to MRI acquisition.

Morphologic MR sequences included a sagittal \( T_2 \)-weighted fast spin-echo image from one femoral head to the other, an axial fat-suppressed \( T_2 \)-weighted fast spin-echo images from the renal hilum to the symphysis pubis, an axial \( T_1 \)-weighted gradient-echo with breathhold, and pre- and postcontrast axial fat-suppressed spoiled \( T_1 \)-weighted gradient-echo.

DCE-MRI was applied with 3D Turbo FLASH \( T_1 \)-weighted fat-suppressed gradient echo pulse sequence with 50 measurements and a temporal resolution of 6 s/frame. The acquisition was performed before and immediately after injection of 0.2 mL/kg of gadolinium (Dotarem; Guerbet, Aulnay, France) followed by injection of 20 cc normal saline solution with 3 mL/min injection rate. Parameters for all sequences are provided in Table 1.

Image Analysis and Quantification

MORPHOLOGICAL CRITERIA. Two experienced radiologists in abdominal imaging (H.H. with 15 years of experience in pelvic MRI and M.G. with 20 years of experience in female imaging involving 10 years of experience in pelvic MRI), who were blinded to the clinical and histopathological information of the patients and interpretations of each other, independently reviewed and interpreted the anatomical images. The radiologists were asked to define at least three 2D polygonal regions of interest (ROIs) larger than 3 mm on DCE-MR images of ovarian masses being cross-linked and carefully compared with morphological (\( T_1 \), \( T_1 \)C, and \( T_2 \)) images on INFINITT PACS Software (INFINITT Healthcare, South Korea).

It was preferable to define the ROIs within the solid portions of the adnexal lesions, identified subjectively based on morphological images by comparing the signal intensity of the solid portion with that of myometrium, and identified when it appeared equal to high-signal intensity on \( T_2 \)w images and low- to equal-signal intensity on \( T_1 \)w images, as compared with myometrium. In cases of multiple solid components, the radiologists selected the most enhancing area after inspection of the complete dataset. In multiloculated cystic lesions (like endometrioid cysts), the ROIs were defined on the thickest septa (more than 2 mm) or where the septa crossed each other and were thickened; otherwise, when the mass was purely cystic with no thickened septa or if identifying a solid portion was difficult, at least three ROIs were placed on the cyst
wall and with smallest possible dimensions to avoid partial volume or misregistration effects.

**DCE-MRI QUANTIFICATION.** Signal intensity–time courses of the ROIs were generated over all timeframes to interrogate the enhancement patterns of benign and malignant lesions through calculations of their descriptive parameters. In each patient, among the selected ROIs, the ones with highest signal intensity were chosen for analysis. To reduce interscanner variation, a similarly sized ROI was placed on the psoas muscle, as an internal reference. The signal intensity of the muscle (SI\textsubscript{psoas}) was calculated and time–intensity curves were normalized to their corresponding SI\textsubscript{psoas}. Semiquantitative enhancement parameters, including maximum relative enhancement (SI\textsubscript{rel}), initial area under the curve in the first 60 seconds (IAUC\textsubscript{60}), wash-in-rate (WIR), and time-to-peak (TTP), were calculated from the signal intensity–time curves using an in-house software implemented in MATLAB. Definitions of the investigated descriptive parameters are summarized in Table 2.

Comparisons of the mean values of all descriptive parameters among benign and malignant groups were performed by a two-tailed independent Student’s t-test, by assuming nonequality of variances for independent samples. As multiple comparisons were made, and by considering Bonferroni correction, a P-value of less than a level of 0.0125 was considered statistically significant.

**CLASSIFICATION OF BENIGN AND MALIGNANT LESIONS.** Classification was performed using each of the semiquantitative parameters and different sets of their combinations. The performances of two pattern classification methods were investigated in discriminating benign and malignant complex ovarian masses: linear discriminant analysis (LDA) with Fischer’s discriminant rule, and nonlinear support vector machines (SVM). LDA classifier exploits the simplest classification model where the separating line is obtained purely based on the inherent capability of each feature set in discriminating the two groups of patients. Thus, in this work LDA was applied to individual features and all their possible combinations to test the performance of the features (not the classifier). Consequently, SVM model was implemented to devise an accurate classifier that can optimally differentiate the lesion classes and aid the decision making process.

**LINEAR DISCRIMINANT ANALYSIS (LDA).** In LDA, a linear transformation is searched in a way such that the ratio of between-class variance to the within-class variance is maximized in the data-set; thus, the maximum linear discrimination would be

---

### TABLE 1. Parameters of MR Sequences

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SE T2-w</th>
<th>SE T2-w Fat Saturated</th>
<th>GRE FLASH T1-w Axial</th>
<th>GRE Spoiled Fat Saturated T1-w (pre- and post- contrast)</th>
<th>3D Turbo FLASH T1-w DCE-MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plane</td>
<td>Coronal and/ or Sagittal</td>
<td>Axial</td>
<td>Axial</td>
<td>Axial</td>
<td>Axial</td>
</tr>
<tr>
<td>TR (msec)</td>
<td>4000</td>
<td>5910</td>
<td>773</td>
<td>832</td>
<td>1.74</td>
</tr>
<tr>
<td>TE (msec)</td>
<td>100</td>
<td>96</td>
<td>11</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Flip angle (°)</td>
<td>120</td>
<td>120</td>
<td>70</td>
<td>70</td>
<td>60</td>
</tr>
<tr>
<td>Field of view (mm(^2))</td>
<td>200 × 250</td>
<td>214 × 350</td>
<td>214 × 350</td>
<td>214 × 350</td>
<td>230 × 230</td>
</tr>
<tr>
<td>Slice thickness (mm)</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Gap (mm)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Matrix</td>
<td>320 × 260</td>
<td>256 × 256</td>
<td>256 × 256</td>
<td>256 × 256</td>
<td>156 × 192</td>
</tr>
</tbody>
</table>

---

### TABLE 2. Description of Semiquantitative Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>SI\textsubscript{rel}</td>
<td>Relative enhancement amplitude: (SI\textsubscript{max}-SI\textsubscript{0})/SI\textsubscript{0}, where SI\textsubscript{max} represents the maximum absolute enhancement and SI\textsubscript{0} denotes the signal intensity at the initial time point.</td>
<td>(Ratio)</td>
</tr>
<tr>
<td>IAUC\textsubscript{60}</td>
<td>Initial area under the time-intensity curve over the first 60 seconds after gadolinium injection, normalized to that of psoas muscle</td>
<td>(Ratio)</td>
</tr>
<tr>
<td>TTP</td>
<td>Time-to-Peak: the time to the peak enhancement (located within 95% of the maximum enhancement)</td>
<td>s</td>
</tr>
<tr>
<td>WIR</td>
<td>Wash-in-Rate = (SI\textsubscript{max}-SI\textsubscript{0})/TTP</td>
<td>a.u./s</td>
</tr>
</tbody>
</table>
guaranteed. This classifier is optimal for the classes with Gaussian distribution that have equal covariance matrices. As real datasets are not essentially of Gaussian distribution, finding an optimal linear transformation cannot be ideally achieved. Hence, the aim is to seek the transformation that returns the least overlap among the classes.

**SUPPORT VECTOR MACHINES (SVM).** An SVM model is a mapping of the input space to a higher-dimensional feature space, where the optimum hyperplane or a set of hyperplanes is constructed in such a way that it has the largest distance to the nearest training data point of any class. Thereby, the generalization errors in SVMs usually tend to be lower than LDA classifiers. The SVM model can be constructed based on a variety of kernel functions, such as linear, Gaussian, or radial basis functions. The most common choice for the kernel function is the radial basis function (RBF), which was selected for our work too. The performance of an SVM-RBF classifier depends on two parameters, \( c \) (representing the cost function that controls the trade-off between the penalty of the model variable and error margin) and \( \gamma \) (RBF kernel parameter).

**CROSSVALIDATION AND CLASSIFIER ADJUSTMENTS.** To fine-tune the SVM classifier, the parameter space was exhaustively searched for values of \( 10^{-7} \leq c \leq 10^7 \) and \( 10^{-7} \leq \gamma \leq 10^7 \), first with steps of 0.1 and when the search was approaching the approximate range of parameter values, the step size was reduced to 0.001 for achieving the most accurate parameter values. For each parameter set, the classifier was trained on all data samples excluding one of them, and tested on the excluded sample. This was repeated for all data samples. The optimum parameter set was chosen once the classification performance, denoted by the area under the ROC curve (AUC) for the included data samples, reached its maximum.

For both LDA and SVM, the predictive performance and robustness of classification using different feature sets were assessed by the leave-one-out crossvalidation method in 100 iterations to decrease the possible bias generated by the outlier samples. All statistical and classification procedures were carried out in R statistical software environment (R 3.0.2, R Foundation for Statistical Computing, Vienna, Austria).

**Results**

**Postoperative Assessment of Patients**

Postoperative histopathological assessment of a total of 54 recruited patients (mean age, 38.4; age range, 15–71 years), revealed the presence of benign lesions in 27 patients (50%), low malignant potential (borderline) lesions in three patients (5.6%), and malignant tumors in 24 patients (44.4%). Regarding the histopathology results, four patients were eliminated from further analysis (three borderline masses were excluded due to their small prevalence for being considered as a separate tumor category; and the data of one malignant patient was discarded as the imaging was carried out with few timepoints and over a short duration due to patient discomfort). Fifty women were included in the quantification, 27 with benign and 23 with malignant complex ovarian masses (five with bilateral masses), resulting in a total of 28 malignant masses and overall 55 adnexal masses. The histologic findings of the 50 enrolled patients are detailed in Table 3.

**Quantitative Image Analysis**

The diagnostic performance of qualitative analysis for discrimination of benign from malignant masses based on morphological criteria was assessed between the two radiologists. Of the selected 50 patients, reader 1 correctly diagnosed 21 patients as benign (TN) and 18 patients as malignant (TP), while six benign patients were incorrectly classified as malignant (FP), and five malignant patients were mistakenly diagnosed as benign (FN), resulting in overall sensitivity of 78.3%, specificity of 77.7%, and accuracy of 78.0%. Evaluating the interpretation of reader 2 indicated the following results: TP = 16, TN = 18, FP = 9, and FN = 7, yielding an overall sensitivity of 64%, specificity of 72%, and accuracy of 68.0%.

**Semiquantitative Image Analysis**

 Significant differences were observed in the mean values of TTP \( (P = 6.15E-8) \), WIR \( (P = 5.65E-5) \), and IAUC \( 60 (P = 0.00043) \) between the benign and malignant groups,
but for $SI_{rel}$ there was no significant difference ($P = 0.15$). For all possible combinations of the aforementioned parameters (composed of permutations of two, three, and four quantitative parameters), statistically significant differences were demonstrated between the two groups of benign and malignant ovarian classes ($P < 0.0001$). The ROC curves of each of these four parameters are illustrated in Fig. 1.

**Classification of Benign and Malignant Lesions**

The performances of the classification frameworks in terms of sensitivity, specificity, accuracy, and the area under the ROC curve are presented in Table 4.

Assessment of diagnostic performance of LDA classification after crossvalidation revealed that TTP is the most sensitive (89%), and WIR is the most specific (92%) single classifiers, with both having almost equal AUC (89%). Intuitively, the combination of the most sensitive and the most specific descriptive features would result in the best classification accuracy among the sets of two features, which was confirmed when TTP and WIR were combined (AUC = 93%). By adding each of IAUC$_{60}$ or SI$_{rel}$ parameters to TTP, the AUC increased slightly and showed no significant added value. By carefully scrutinizing the SVM classification outcome in comparison with LDA, it can be

![Figure 1: The receiver operating characteristic (ROC) curves of all four descriptive parameters of time-intensity curves: (A) IAUC$_{60}$, (B) SI$_{rel}$, (C) TTP, and (D) WIR.](image-url)
inferred that employing a more complicated model could not remarkably refine the ultimate performance of the classification framework, implying the inherent potential of the DCE-derived descriptive features in differentiation of benign and malignant complex ovarian lesions.

**DCE-MRI Decision Tree**

A combination of TTP and WIR, the most sensitive and specific DCE-MRI features, with the LDA method was used to construct an accurate decision-tree classifier. As LDA tries to fit an optimum line that best discriminates benign and malignant classes based on the selected feature set, the equation of the adjusted line with formulation of \( \text{Output} = -0.025 \times \text{TTP} + 0.511 \times \text{WIR} + 1.5 \), as depicted in Fig. 2, can be used as the desired pattern classifier or the decision tree (accuracy \( \sim 89\% \) and AUC \( \sim 93\% \)). The resulting negative output values in the proposed formula are highly suggestive of benign masses and positive values are most probably indicative of malignant lesions. Two examples of the proposed decision tree on malignant and benign cases are illustrated in Figs. 3 and 4, respectively.

**Discussion**

In the work presented here we signified the feasibility of pattern-based classification approaches in providing objective and quantitative insights about the potency of DCE-MRI-derived semiquantitation for discriminating benign and malignant complex ovarian masses features, and its superiority over reader-dependent morphological criteria (89% of accuracy vs. 68–78%). These diagnostic models have not previously been investigated in the context of classifying ovarian masses. Regarding the existence of diverse suggestions about potential semiquantitative features, our proposed

---

**TABLE 4. Classification Performance Evaluation**

<table>
<thead>
<tr>
<th>Feature Set</th>
<th>LDA Sens.</th>
<th>LDA Spec.</th>
<th>LDA Acc.</th>
<th>LDA AUC</th>
<th>SVM Sens.</th>
<th>SVM Spec.</th>
<th>SVM Acc.</th>
<th>SVM AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAUC_{60}</td>
<td>58.6</td>
<td>74.1</td>
<td>66.2</td>
<td>78.4</td>
<td>51.7</td>
<td>64.7</td>
<td>58.9</td>
<td>78.4</td>
</tr>
<tr>
<td>SI_{rel}</td>
<td>55.5</td>
<td>55.6</td>
<td>56.2</td>
<td>62.1</td>
<td>60.9</td>
<td>40.7</td>
<td>51.8</td>
<td>62.0</td>
</tr>
<tr>
<td>TTP</td>
<td><strong>89.2</strong></td>
<td>74.3</td>
<td>81.9</td>
<td>89.7</td>
<td><strong>96.5</strong></td>
<td>55.1</td>
<td>76.3</td>
<td>89.8</td>
</tr>
<tr>
<td>WIR</td>
<td>66.8</td>
<td><strong>92.9</strong></td>
<td>79.6</td>
<td>89.6</td>
<td>30.0</td>
<td><strong>100.0</strong></td>
<td>64.4</td>
<td>89.5</td>
</tr>
<tr>
<td>IAUC_{60}, SI_{rel}</td>
<td>58.0</td>
<td>74.1</td>
<td>65.9</td>
<td>78.4</td>
<td>66.9</td>
<td>62.8</td>
<td>65.4</td>
<td>76.2</td>
</tr>
<tr>
<td>IAUC_{60}, TTP</td>
<td>89.0</td>
<td>82.3</td>
<td>85.7</td>
<td>91.5</td>
<td>90.8</td>
<td>72.5</td>
<td>81.9</td>
<td>92.2</td>
</tr>
<tr>
<td>IAUC_{60}, WIR</td>
<td>60.5</td>
<td>85.3</td>
<td>72.7</td>
<td>87.9</td>
<td>51.7</td>
<td>100.0</td>
<td>75.6</td>
<td>87.2</td>
</tr>
<tr>
<td>SI_{rel}, TTP</td>
<td>92.9</td>
<td>77.7</td>
<td>85.5</td>
<td>94.3</td>
<td>100.0</td>
<td>53.2</td>
<td>77.2</td>
<td>93.0</td>
</tr>
<tr>
<td>SI_{rel}, WIR</td>
<td>65.4</td>
<td>91.0</td>
<td>78.2</td>
<td>88.5</td>
<td>32.2</td>
<td>98.1</td>
<td>64.6</td>
<td>85.2</td>
</tr>
<tr>
<td>TTP, WIR</td>
<td><strong>89.0</strong></td>
<td><strong>87.8</strong></td>
<td><strong>88.6</strong></td>
<td><strong>92.9</strong></td>
<td><strong>88.6</strong></td>
<td><strong>87.4</strong></td>
<td><strong>88.0</strong></td>
<td><strong>93.0</strong></td>
</tr>
<tr>
<td>IAUC_{60}, SI_{rel}, TTP</td>
<td>95.8</td>
<td>80.4</td>
<td>88.3</td>
<td>94.0</td>
<td>95.0</td>
<td>74.0</td>
<td>84.7</td>
<td>93.3</td>
</tr>
<tr>
<td>IAUC_{60}, SI_{rel}, WIR</td>
<td>59.0</td>
<td>82.4</td>
<td>70.5</td>
<td>87.5</td>
<td>57.1</td>
<td>94.8</td>
<td>75.6</td>
<td>85.5</td>
</tr>
<tr>
<td>IAUC_{60}, TTP, WIR</td>
<td>89.2</td>
<td>88.8</td>
<td><strong>89.0</strong></td>
<td>92.7</td>
<td>87.7</td>
<td>92.6</td>
<td>90.1</td>
<td>94.3</td>
</tr>
<tr>
<td>SI_{rel}, TTP, WIR</td>
<td>89.5</td>
<td>88.2</td>
<td><strong>88.9</strong></td>
<td>95.3</td>
<td>91.6</td>
<td>83.6</td>
<td>87.8</td>
<td>95.0</td>
</tr>
<tr>
<td>IAUC_{60}, SI_{rel}, TTP, WIR</td>
<td>89.7</td>
<td>87.9</td>
<td>88.8</td>
<td>95.3</td>
<td>90.4</td>
<td>89.3</td>
<td>89.9</td>
<td>94.6</td>
</tr>
</tbody>
</table>

Sensitivity (Sens., %), Specificity (Spec., %), Accuracy (Acc., %), and the Area Under the Receiver Operating Curve (AUC, %) obtained by leave-one-out cross-validation using Linear Discriminant Analysis (LDA) and Support Vector Machines (SVM) classifiers and various feature sets. The dataset consists of 27 benign and 28 malignant lesions.

*The values in bold type indicate higher sensitivities/specificities/accuracies.*

---

**FIGURE 2:** Decision tree with accuracy of 89% and AUC of 93%, obtained with TTP and WIR features for classifying benign and malignant complex adnexal masses using the equation \( \text{Output} = -0.025 \times \text{TTP} + 0.511 \times \text{WIR} + 1.5 \).
approach may pave the road to reach more generalized and conclusive suggestions about the determinant DCE-MRI indicators of ovarian tumor malignancy.

As mentioned earlier, we employed a semiquantitative analysis method, because, unlike a PK modeling approach, it can be efficiently incorporated with routine clinical analysis.

FIGURE 3: A 22-year-old patient histopathologically confirmed with PNET (malignant tumor): (A) Sagittal T₂-w image; (B) Fat-saturated Axial T₂-w image; (C) Precontrast fat-saturated axial T₁-w image; (D) Postcontrast fat-saturated axial T₁-w image; (E) Axial DCE-MR image with the ROI selected on the solid part of the tumor tissue in a sample slice of DCE-MR image of the patient; the ROI is presented in black and an arrow indicates the location of the ROI. (F) The signal intensity–time curve on the selected ROI: the diamonds represent the data points. (G) The table indicates the parameter calculations. Using the decision tree proposed in Fig. 2 on the calculated relative TTP and WIR parameters, the output returns a negative value, indicating that the lesion is malignant, which is compatible with the histopathological finding of the patient.

\[
\text{output} = -0.025 \times 56 + 0.511 \times 2.7 + 1.5 = 1.5 > 0 \Rightarrow \text{malignant}
\]
FIGURE 4: A 51-year-old patient histopathologically confirmed with hemorrhagic cyst (benign lesion): (A) Sagittal $T_2$-w image; (B) Fat-saturated axial $T_2$-w image; (C) Precontrast fat-saturated axial $T_1$-w image; (D) Postcontrast fat-saturated axial $T_1$-w image; (E) Axial DCE-MR image with the ROI selected on the cyst wall in a sample slice of DCE-MR image of the patient; the ROI is presented in black and an arrow indicates the location of the ROI. (F) the signal intensity–time curve on the selected ROI: the diamonds represent the data points. (G) The table indicates the parameter calculations. Using the decision tree proposed in Fig. 2 on the calculated relative TTP and WIR parameters, the output returns a negative value, indicating that the lesion is benign, which is compatible with the histopathological finding of the patient.
practice. This is mainly due to its independence from AIF selection, prior $T_1$-mapping, and optimal fitting of the PK model to the tissue under investigation.

It was shown that early enhancement features, ie, TTP as the most sensitive (~90%) and WIR as the most specific single classifier (~93%), can best describe the properties of ovarian masses. The relationships of these two parameters with physiological biomarkers of ovarian tumor malignancy have been confirmed previously.5,7,12 The relevance of these two parameters to the pathophysiological properties of tumors can be explained by the highly permeable tumor neovasculature that is aggravated when the tumor advances into a malignant form.2,25 Therefore, by inspecting DCE-MRI curves in malignant lesions, a steep slope of enhancement, ie, higher wash-in-rate and smaller initial time to enhancement peak, denoting the time by which the contrast agent has permeated into the microvasculature, can be observed. This finding is consistent with several related studies where WIR and/or TTP (with other equivalent terminologies) have been reported as helpful indicators for discriminating benign and malignant ovarian masses.7,10,12

In our study, IAUC60 showed a significant difference in the mean values among benign and malignant masses, while no significant differences existed for SIrel. These two parameters did not return satisfactory sensitivity and/or specificity. This was not consistent with a few related works,7,9 due to differences in the acquisition protocol and the size and variety of the study population, and as the normalization strategy in the past works was dependent on the myometrium tissue,9 which is absent in patients with prior hysterectomy and large curve variations exist within the myometrium. The aforementioned normalization approach was not followed in other studies followed by the same researchers and other groups.5,8,12

Comparison of the performances of LDA and SVM classifiers in this study recommends that optimizing the decision approach with the most sensitive and specific parameters overrules the complexity of the classification model. Thus, it can be perceived that the DCE-MRI features are inherently accurate in such a way that without the requirement of imposing a complicated classification model, a combination of WIR and TTP can sufficiently characterize the curves and lesion types. Based on TTP and WIR parameters, a simple decision tree with diagnostic performance of 93% is proposed to aid preoperative decision making for complex ovarian masses.

Some limitations of this study must be addressed. First, our study was performed on a relatively small number of patients with complex masses and may not be applied to all ovarian masses. Second, manual ROI selection is a subjective procedure and is susceptible to unintended reader bias. However, the subjectivity of this procedure may be reduced by standardizing image acquisition in terms of voxel size, contrast and coverage, aiding the radiologists through computer-aided systems to select and segment the tissue of interest, and carefully training the radiologists for optimal placement of the ROIs. Third, borderline ovarian tumors were excluded from our study, due to their small number ($n = 3$) for being considered as a separate tumor category (besides benign and malignant categories). As these tumors frequently occur in young women wishing to preserve fertility, it is valuable to include a larger number of borderline tumors and attempt to identify their distinctive features accurately to prescribe the most appropriate therapeutic strategy for these patients. Finally, the proposed method is validated for one vendor and the derived formula may not be generalized for different MR scanners and protocols. A multicentric assay is mandatory to confirm broad applicability of this method.

In conclusion, by investigating the potential DCE-MRI indicators of malignancy through an automatic classification scheme, we proposed a decision-tree classifier that is unbiased to the threshold values of the parameters and provides a more flexible framework for increasing the positive prediction rate for distinguishing malignant from benign complex ovarian masses.

References

Kazerooni et al.: Classification of Complex Adnexal Masses


