A Simple and Clinically Applicable Decision Tree for Accurate Classification of Complex Adnexal Masses Based on Quantitative DCE-MRI

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Target Audience: Radiologists, physicists and surgeons with an interest in gynecological DCE-MR imaging

Introduction: Dynamic contrast enhanced (DCE-) MRI has shown to be a potent screening tool in providing predictive biomarkers of ovarian tumor malignancy, especially in sonographically indeterminate complex ovarian masses [1]. In this light, objective identification of sensitive and specific quantitative DCE-MRI parameters could play a key role for a reliable and definitive diagnosis. However, quantification of DCE-MRI becomes challenging in presence of motion artifacts, which further complicates accurate classification of benign and malignant complex ovarian masses. Motion compensation in dynamic imaging is frequently carried out using demanding non-rigid registration techniques, which is usually not feasible in routine clinical practice. This matter calls for devising an automated classifier, which could perform optimally in presence of motion while it increases the liability of an expert's reading in a simple and clinically-feasible framework. In this work, we exploit an automated classification algorithm, which allows for investigating the optimal predictor parameters unbiased to any prior or expert knowledge about the parameter cutoff values. Regarding the selected parameters, an automated classification decision-tree is proposed for accurate differentiation of malignant from benign complex ovarian tumors feasibly and easily for routine clinical applications.

Materials and Methods: Data Acquisition: DCE-MR images of thirty-four patients with histopathologically proven complex ovarian masses (18 benign, 16 malignant, 14-70 years, mean age = 35.9) were acquired on a 3T MR scanner (Siemens MAGNETOM Tim TRIO) using a surface phased-array coil before and immediately after injection of 0.2*m*L/kg of Gadolinium (DOTAREM; Guerbet, Aulnay, France), followed by injection of 20cc normal saline solution with 3*m*L/min injection rate. The imaging parameters were *TE*/*TR* = 1.74/5*m*sec, flip angle = 60°, image matrix = 156×192, FOV = 23×23cm^2, slice thickness = 5*m*m, number of measurements = 52 at 6 sec/volume, number of slices = 16. Data Quantification: For each examination, two regions-of-interest (ROIs) were placed on the solid part of tumors and within the adjacent psoas (as the internal reference). The signal intensity-time curves of tumor ROIs were normalized to the average signal intensity, within the ROI selected on psoas, to create relative signal intensity curves. Several semi-quantitative parameters were calculated for further analysis, namely: SI_{max} = maximum absolute enhancement, TTP: Time-to-Peak, Wash-in-Rate (WIR) = (SI_{max}-SI_0)/TTP, $IAUC_{60}$ = initial area under the time-intensity curve during the first 60 seconds. Classification: Comparison of the mean values of the parameters between benign and malignant groups was performed by Student's *t*-test, by assuming equality of variances for independent samples. Using each of descriptive parameters and all their possible combinations, classification was performed by linear discriminant analysis (LDA) classification technique. The performances of the designed classifiers were assessed using leave-one-out cross-validation method.

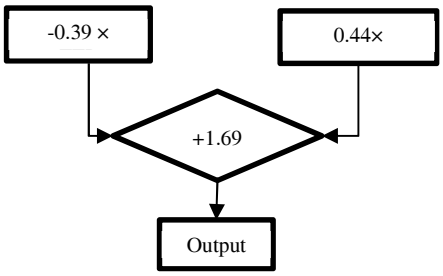
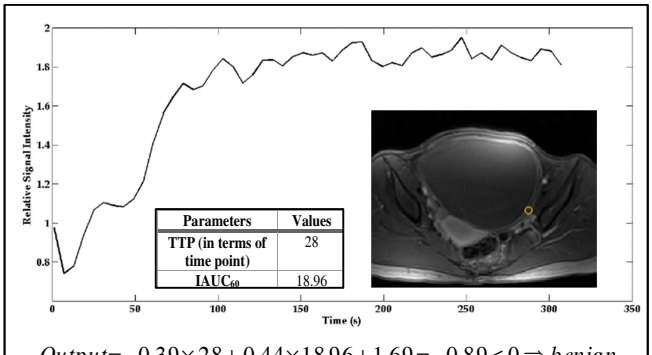
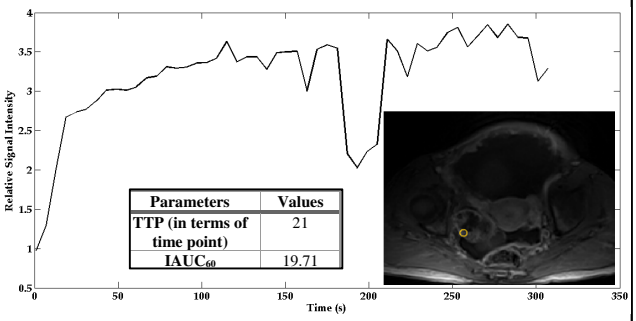


Fig. 1 Decision tree for classifying complex ovarian cancers (Output>0: malignant tumor, Output<0: benign tumor).

Results and Discussion: Using the proposed normalization approach, a statistically significant difference in the mean value of SI_{max} (P<0.05), TTP (P<0.0001), WIR (P<0.05), and $IAUC_{60}$ (P<0.0001) was found between the benign and malignant groups. Among all possible combinations of the aforementioned parameters (composed of two, three and four quantitative parameters), a statistically significant difference was demonstrated between the two groups of benign and malignant cancers (P<0.05 for combination of SI_{max} and WIR, and P<0.0001 for all other parameter sets). The diagnostic performance of LDA classification technique after cross-validation, using the selected parameter sets was calculated. It was shown that TTP and $IAUC_{60}$ are the most sensitive (100%), and WIR and TTP are the most specific single classifiers (94.4% and 88.9% respectively). In several studies, the early enhancement (TTP) is confirmed to be an indication of malignancy, and WIR is shown to be correlated with the expression of vascular endothelial growth factor (VEGF) [2]. Although there are no data on the relevance of $IAUC_{60}$ in characterizing ovarian tumors, this parameter is proven to be accurate for classification of complex ovarian cancers [2] and to be robust for assessment of early enhancement in presence of motion [3]. By adding $IAUC_{60}$ or SI_{max} parameters to TTP, the accuracy of classification reached 97%. This performance could be no further improved by any other combinations of parameters. The optimum classifier was regarded as the one that achieves the highest accuracy with the least number of parameters. Here, we selected the parameter set composed of TTP and $IAUC_{60}$ in order to construct a decision tree for accurate differentiation of benign and malignant complex ovarian cancers, which is indicated in **Fig.1**. Based on the equation given by $output = -0.39 \times TTP + 0.44 \times IAUC_{60} + 1.69$, the cancer should be classified as malignant if the output of this classifier is positive; otherwise, it should be regarded as benign.



$$Output = -0.39 \times 28 + 0.44 \times 18.96 + 1.69 = -0.89 < 0 \Rightarrow benign$$



$$Output = -0.39 \times 21 + 0.44 \times 19.71 + 1.69 = 2.17 > 0 \Rightarrow malignant$$

Fig. 2 Characterization of the tumor types based on the proposed decision tree for a (upper) benign and a (lower) malignant complex ovarian cases.

Conclusions: In this work, we assessed different semi-quantitative parameters, extracted from DCE-MR images of patients with complex ovarian cancer, both individually and in different combinations with each other through an automated classification approach. It was demonstrated that high sensitivity and specificity of an individual parameter could be lost when combined with inappropriate feature. The results recommend that optimizing the decision approach could compensate for misalignment of data, which is essentially important where employing complicated pulse sequences are costly or not feasible, and an accurate and fast registration software is not available or applicable in a clinical diagnosis setting. In conclusion, we proposed an accurate, clinically easy and feasible decision tree classifier, which 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 tumors.

References: **[1]** Spencer, J. A et al. ESUR guidelines for MR imaging of the sonographically indeterminate adnexal mass: an algorithmic approach. *Eur Radiol* 2010, 20(1), 25-35. **[3]** Thomassin-Naggara, I., et al. Dynamic contrast-enhanced magnetic resonance imaging: A useful tool for characterizing ovarian epithelial tumors. *Magn Reson Imaging*, 2008, 28(1), 111-120. **[4]** Hamy, V. et al. Respiratory motion correction in dynamic MRI using robust data decomposition registration– Application to DCE-MRI. *Med Image Anal*, (2014),18(2), 301-313.