

Optimal Decision Tree for Classification of Benign and Malignant Ovarian Masses Based on DCE-MRI Quantitative Parameters Employing Hierarchical Clustering Approach

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

Introduction:

Accurate characterization of benign and malignant ovarian cancers plays a critical role in decision making about the therapeutic strategy, treatment monitoring, and could highly affect the treatment outcome. In this context, dynamic contrast enhanced (DCE-) MRI has evolved into a helpful imaging technique in distinguishing complex adnexal masses by providing noninvasive and quantitative biomarkers of tumor progression. Reliable prediction of malignancy in complex adnexal masses depends on proper selection of quantitative DCE-MRI descriptive parameters and their cutoff points, which the latter is commonly carried out by threshold criteria [1]. In this work, we exploited an unsupervised, non-parametric clustering algorithm, which does not require any prior or expert knowledge about the thresholds to select the optimal predictor parameters, followed by introducing a classification decision-tree for accurate differentiation of malignant from benign ovarian tumors.

Materials and Methods:

Data Acquisition: Twenty-two patients diagnosed with solid or solid/cystic complex ovarian masses (12 benign and 10 malignant as identified with histological assessment) underwent DCE-MR imaging on a 3T MR scanner (Siemens MAGNETOM Tim TRIO) using a surface phased-array coil, $TE/TR = 1.74/5\text{msec}$, flip angle = 60° , image matrix = 156×192 , FOV = $23 \times 23\text{cm}^2$, slice thickness = 5mm , number of measurements = 52 at 6 sec/volume, number of slices = 16. The acquisition was performed before and immediately after injection of 0.2mL/kg of Gadolinium (DOTAREM; Guerbet, Aulnay, France), followed by injection of 20cc normal saline solution with 3mL/min injection rate. **Pre-processing:** All images were corrected for motion artifacts, using an efficient non-rigid image registration approach in a groupwise setting [2]. **Data Quantification:** The regions-of-interest (ROIs) were placed on the solid part of tumors and within the adjacent psoas (as an internal reference). Several semi-quantitative parameters were used for further analysis and clustering of the signal intensity curves: SI_{max} = maximum signal intensity of tumor to that of psoas, TTP: Time-to-Peak, Wash-in-Rate (WIR) = $(SI_{\text{max}} - SI_0)/TTP$, $IAUC_{60}$ = initial area under the time-intensity curve during the first 60 seconds in tumor to that of psoas. **Clustering:** Clustering was performed for each descriptive parameters, using unsupervised Hierarchical Clustering (HC) with Ward's linkage method, before and after registration, to both determine the best descriptive parameters for diagnosing malignant from benign tumors and evaluate the effects of registration on the outcome of diagnosis.

Results and Conclusions:

Fig. 1 illustrates the box-and-whisker plots for TTP, SI_{max} , WIR, and $IAUC_{60}$ for both benign and malignant tumors. TTP and WIR parameters led to none and small overlaps between enhancement characteristics of benign and malignant tumors, respectively, suggesting their reliability in distinguishing cancer types. The sensitivity and specificity of each parameter in diagnosing malignancy in complex ovarian cancers are summarized in **Table 1**. As it can be inferred, WIR parameter returns a sensitivity of 100% in distinguishing malignant tumors (both before and after registration), and TTP produces the best specificity in comparison with SI_{max} and $IAUC_{60}$ parameters. In several studies, the early enhancement (TTP) is confirmed to be an indication of malignancy [3], and WIR is shown to be correlated with the expression of vascular endothelial growth factor (VEGF) [4]. Also, it can be observed that registration can significantly improve the outcome of tumor characterization, in the sense that the parameters would become more reliable to characterize the cancer malignancy. Regarding these results, WIR and TTP were combined to develop a decision tree

for classification of malignant from benign tumors (**Fig. 2**), which generated promising results on the data with 95% of accuracy before and 100% after registration. This result recommends that optimizing the decision approach could compensate for misalignment of data, which is essentially important when proper registration software is not available or feasible in a clinical diagnosis setting.

In conclusion, we proposed a decision tree classifier developed through an unsupervised clustering approach, 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] Bernardin P *et al.*, *EUR Radiol* 22, 880 (2012). [2] Kia E *et al.*, submitted to ISMRM 2014, submission number . [3] Sohaib SA *et al.*, *AJR Am J Roentgenol* 180, 1297–1304 (2003). [4] Thomassin-Naggara I *et al.*, *Radiol* 248 (1), 148-59 (2008).

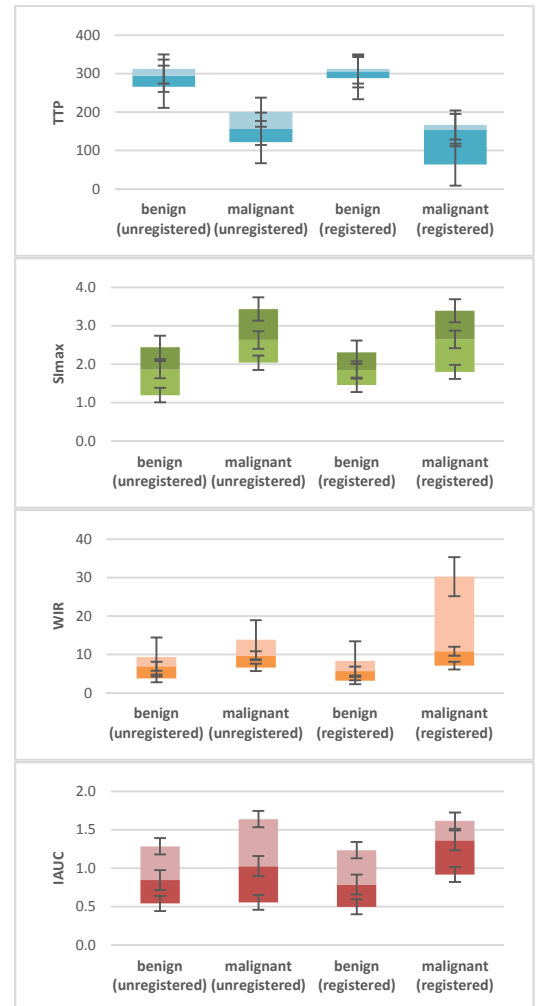


Fig. 1 Box-and-whisker plots for TTP, SI_{max} , WIR, and $IAUC_{60}$ for both benign and malignant tumors

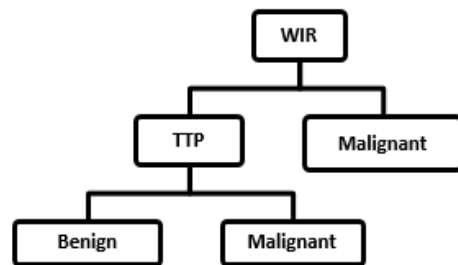


Fig. 2 Decision Tree for classifying complex ovarian cancers.

Table 1 Sensitivity and specificity of parameters for malignancy prediction before and after registration

	Sensitivity (unregistered)	Specificity (unregistered)	Sensitivity (registered)	Specificity (registered)
TTP	80 %	83 %	83 %	100 %
SI_{max}	54 %	67 %	50 %	63 %
WIR	100 %	60 %	100 %	66 %
$IAUC_{60}$	63 %	65 %	60 %	75 %