

# Handling missing DCE data in prostate cancer detection using multiparametric MRI

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**Introduction** – Prostate cancer (PCa) is one of the leading causes of morbidity and mortality for Canadian men with more than 23,000 diagnoses in 2013 [1]. Multiparametric MRI (mpMRI) is now widely used as a means of determining the need for prostate biopsy and for targeting prostate biopsies, with the aim of maximizing the rate of detection of clinically significant prostate cancer, while reducing the number of unnecessary biopsies [2]. Recently, Diffusion Tensor Imaging (DTI) MRI and Dynamic Contrast-Enhanced (DCE) MRI parametric maps were used to build a support vector machine (SVM) classifier for the detection of PCa with reported area under ROC curve (AUC) of 0.95 [3]. One problem with the mpMRI approach is that all MRI modalities might not be available for each patient. For example, the use of Gadolinium-based contrast agents in DCE-MRI results in allergic reactions in some patients with reported reaction rates as high as 19.8% and acute reactions in a small group [4,5]. Therefore, the objective of the work presented here is to design classifiers to detect cancer from MRI parametric maps with the capability of handling missing DCE parameters. We propose two different methods and show their effectiveness in maintaining high AUC while handling missing parameters.

**Materials and Methods** – *Data*: DTI and DCE MRI data, at 3T, of patients ( $n = 29$ ) with elevated prostate specific antigen (PSA) and/or palpable prostatic nodule (PSA range from 0.94 to 15 ng/mL) were used in this study. The imaging protocol is described in [3]. Two DTI parameter maps (the Fractional anisotropy (FA), and average diffusivity (D)), and three DCE parameter maps (the volume transfer constant  $k^{\text{trans}}$ , fractional volume of extra-vascular extra-cellular space  $v_e$ , and fractional plasma volume  $v_p$ ) were calculated per pixel. Each ROI, constructed based on a biopsy core, was represented by the five-dimensional feature vector  $\langle \text{FA}, D, k^{\text{trans}}, v_e, v_p \rangle$ . These were the mean values of the corresponding parameters in all pixels within the ROI. The dataset included 240 normal, and 29 cancerous ROIs.

*KNN imputation for handling missing data*: First, we used one SVM classifier for mpMRI classification, and estimated the values of the missing data using k-nearest-neighborhood (KNN) approach. The KNN method finds the  $k$  nearest training samples, based on Euclidean distance, to the test data and estimates its missing DCE features with a weighted mean. This approach practically “fills in” the missing values to enable using the same classifier on cases with missing DCE features.

*Likelihood ratio for handling missing data*: The second method fused two different SVM classifiers, the first classifier (DTI-SVM) built using DTI MRI features (FA, D) and the second classifier (DCE-SVM) using DCE MRI features ( $k^{\text{trans}}, v_e, v_p$ ). Leave-one-patient-out cross-validation was performed for setting the parameters of each classifier. Those two classifiers were fused using the likelihood ratio-based fusion technique [6]. This technique is based on estimating each SVM’s posterior probability density for cancer and normal tissue using Gaussian mixture models. Then Bayesian decision rule and the product of the two-likelihood ratios were used to detect PCa. This method can handle missing data by assigning a value of one to the likelihood ratio related to the missing SVM classifier, which is DCE-SVM in this work, with no required changes to the decision rule.

*Removing DCE features*: In our data, all five parameters were available from all cases. We studied the effect of missing DCE components of the feature vector by removing them from an increasing number ( $m$ ) of cases ( $m = 1, \dots, 29$ ). In each step,  $m$  patient cases were randomly chosen and their corresponding DCE features were removed from the validation set of the leave-one-patient-out cross validation scheme. The cross validation was repeated 50 times for each value  $m$ , with missing DCE features to get a robust estimate of the effect of missing DCE features on the classification outcome.

**Results** – The cross-validation yielded a mean AUC of 0.95 using KNN imputation with SVM when DCE features of one patient were removed, showing almost no decline compared to the situation without missing data. It was noted that using  $k = 8$  neighbors provided the best results based on the AUC. In a similar cross-validation, the likelihood ratio fusion method resulted in a mean AUC of 0.93 when DCE features of one patient were removed. As shown in Fig.1, as the number ( $m$ ) of cases with missing DCE features was increased, the fused classifiers performed consistently better than the DTI-SVM (AUC=0.91), for up to  $m=22$  in case of KNN imputation and  $m=13$  for the likelihood ratio method. For all value of  $m$ , the standard deviation of AUC for the KNN method was smaller than the likelihood ratio technique, showing the robustness of the KNN method.

**Conclusions** – In this work, we reported two methods that successfully handle missing DCE features in computer-aided diagnosis using mpMRI. We showed that as an increasing number of cases with missing DCE features are presented to the classifiers, KNN imputation of missing features outperforms the fusion of two classifiers using Bayesian likelihood ratio in terms of AUC.

**Acknowledgments**: CIHR Operating grant, NSERC Discovery. **References**: [1] Canadian Cancer Statistics 2013. [2] J. O. Barentsz, et al., Eur Radiol. 2012, 22(4): 746-757. [3] Moradi, M., et al., JMRI 2012; 35(6): 1403-1413. [4] Abujudeh, H.H., et al., American Journal of Roentgenology 2010; 194(2): 430-434. [5] Kirchin, M.A., et al., Journal of Magnetic Resonance Imaging 2001; 14(3): 281-294. [6] Nandakumar, K., et al., Advances in Biometrics 2009: 743-752.

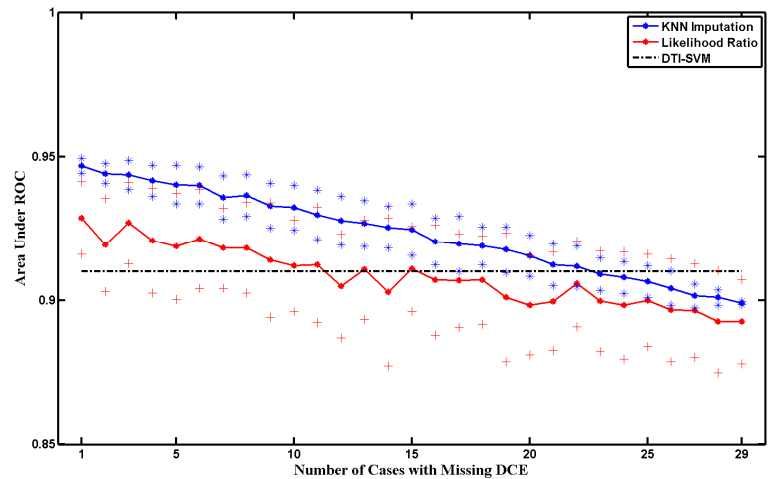


Fig. 1. AUC reduction as the number ( $m$ ) of missing DCE cases increases for the two proposed methods: KNN (Blue) and Likelihood Ratio fusion (Red). The black line marks the AUC of the DTI-SVM without missing data. \* and + mark  $\pm$  std for the two methods.