

Developing Bayesian Networks based Prognostic Radiomics Model for Clear Cell Renal Cell Carcinoma Patients

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Abstract— Clear cell renal cell carcinoma (ccRCC) is one of the most aggressive histologic subtype of RCC. In this study, we developed and evaluated a Bayesian network as a prognostic model using computed tomography (CT) radiomic features and clinical information to predict the risk of death within 5 years for ccRCC patients. Seventy patients who had abdominal CT scans with delayed post-contrast phase and outcome data were enrolled. 3D volumes of interest (VOIs) covering the whole tumor on CT images were manually delineated. Image preprocessing techniques including, wavelet, Laplacian of Gaussian, and resampling of the intensity values to 32, 64 and 128 bin levels were applied on all VOIs. Different radiomic features, including shape, first-order, and texture features were extracted from the VOIs. For features selection, we first used the z-score method to normalize all image features, then the relevant features were selected based on mutual information (MI) criteria. The patients were divided into a low- and high-risk group based on survival or death at 5 years after surgery, respectively. Bayesian networks were used as a classifier for risk stratification. The model was evaluated using the area under the curve (AUC), sensitivity, specificity, and accuracy by 1000 bootstra resampling. The Bayesian model with Laplacian of Gaussian (LOG) filter showed the best predictive performance in this cohort with an AUC, sensitivity, specificity, and accuracy of 0.94, 85 %, 94%, and 89%, respectively. The results of the current study indicated that prognostic models based on radiomic features are very promising tools for risk stratification for ccRCC patients.

Index Terms— ccRCC, Radiomics, Bayesian Network, CT

I. INTRODUCTION

Renal cell carcinoma (RCC) with 403,000 new cases and 175,000 mortality annually forms 2-3% of all cancer diagnoses and death worldwide [1, 2]. Clear cell renal cell carcinoma (ccRCC) is one of the most aggressive histologic subtype of RCC [3-5]. For ccRCC patients, some clinical prognostic models by the International Union Against Cancer (UICC) and American Joint Committee on Cancer (AJCC) were proposed and developed [6]. Nevertheless, due to limited accuracy, their clinical application was not promising [7].

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Also, biopsy-based genes analysis to predict prognosis due to intra-tumor heterogeneity, invasive approaches and availability is limited [8]. Radiomics is a new concept in precision medicine to quantitative analysis of medical images enabling non-invasively to characterize tumor phenotype for diagnostic and prognostic models [9-16]. In this study, we developed and evaluated a Bayesian network as a prognostic model using computed tomography (CT) radiomic features and clinical information to predict the risk of death within 5 years for ccRCC patients.

II. MATERIALS AND METHODS

In this retrospective study, seventy patients who had abdominal CT with delayed post-contrast phase and outcome data from the cancer image archive (TCIA) [17] dataset were provided. The 3D region of interest (VOI) covering the whole tumor on CT images was manually segmented slice by slice by an experienced radiologist using the 3D slicer software package.

Image preprocessing techniques including, wavelet, Laplacian of Gaussian, and resampling of the intensity values to 32, 64 and 128 bin levels were applied on all VOIs. The radiomics features were extracted from each VOI on CT images using an open-source package PyRadiomics [18]. Extracted features included shape features (n=16), intensity first-order features (n=19), intensity histogram features (n=18), grey level co-occurrence matrix (GLCM) features (n=22), gray level run-length matrix (GLRLM) features (n=11), gray-level size zone matrix (GLSZM) features (n=13), and neighboring gray tone difference matrix (NGTDM) features (n=9) [18].

For features selection, first we used z-score method to normalize all image features, then relevant features are selected based on mutual information (MI) criteria. Patients divided into a low and high-risk group based on survival or death at 5 years after surgery, respectively. In this study, we used Bayesian network as a classifier for risk stratification. Model evaluated by area under the curve (AUC), sensitivity, specificity, and accuracy by 1000 bootstrapping resample.

III. RESULT

Table 1 summarizes the results of the all models for different data set. As shown, Bayesian model with Laplacian of Gaussian (LOG) filter showed the best predictive performance in the cohort, with an AUC, sensitivity,

specificity, and accuracy of 0.94, 85 %, 94%, and 89%, respectively.

Fig 1. compare the AUC of different preprocessing images

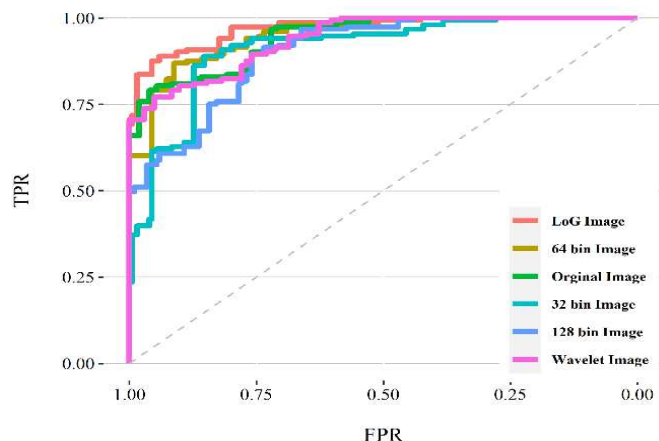


Fig. 1. AUC of different image data sets.

Radiomic models in this study was constructed using different image filter and various features including shape features, first-order feature, and texture features.

TABLE I. models performance for different image data set.

Original Images			
AUC	Sensitivity	Specificity	Accuracy
0.92	0.73	0.91	0.81
32 Bin Images			
AUC	Sensitivity	Specificity	Accuracy
0.91	0.77	0.90	0.80
64 Bin Images			
AUC	Sensitivity	Specificity	Accuracy
0.93	0.82	0.92	0.83
128 Bin Images			
AUC	Sensitivity	Specificity	Accuracy
0.9	0.71	0.88	0.79
Wavelet Images			
AUC	Sensitivity	Specificity	Accuracy
0.92	0.83	0.91	0.82
LoG Images			
AUC	Sensitivity	Specificity	Accuracy
0.94	0.85	0.94	0.89

IV. DISCUSSION AND CONCLUSION

Our study accompanied by previous research [6], demonstrated the prognostic power of CT image biomarker in risk stratification, despite intra- and inter-tumor heterogeneity most ccRCC tumors. However, future studies with larger sample sizes are needed to validate the finding of this study with reproducible and robust features [19, 20].

Prognostic models are the most important tools that can aid healthcare to guided therapy in cancer patients. The results of current study indicated that prognostic model based on

radiomics features are very promising tools for risk stratification for ccRCC patients.

REFERENCES

- [1] F. Bray, J. Ferlay, I. Soerjomataram, R. L. Siegel, L. A. Torre, and A. Jemal, "Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries," *CA: a cancer journal for clinicians*, vol. 68, no. 6, pp. 394-424, 2018.
- [2] S. A. Padala et al., "Epidemiology of Renal Cell Carcinoma," (in eng), *World J Oncol*, vol. 11, no. 3, pp. 79-87, Jun 2020, doi: 10.14740/wjon1279.
- [3] J. C. Cheville, C. M. Lohse, H. Zincke, A. L. Weaver, and M. L. Blute, "Comparisons of outcome and prognostic features among histologic subtypes of renal cell carcinoma," *The American journal of surgical pathology*, vol. 27, no. 5, pp. 612-624, 2003.
- [4] T. Gudbjartsson, S. Hardarson, V. Petursdottir, A. Thoroddsen, J. Magnusson, and G. V. Einarsson, "Histological subtyping and nuclear grading of renal cell carcinoma and their implications for survival: a retrospective nation-wide study of 629 patients," *European urology*, vol. 48, no. 4, pp. 593-600, 2005.
- [5] M. Nazari et al., "Noninvasive Fuhrman grading of clear cell renal cell carcinoma using computed tomography radiomic features and machine learning," (in eng), *Radiol Med*, vol. 125, no. 8, pp. 754-762, Aug 2020, doi: 10.1007/s11547-020-01169-z.
- [6] M. Nazari, I. Shiri, and H. Zaidi, "Radiomics-based machine learning model to predict risk of death within 5-years in clear cell renal cell carcinoma patients," (in eng), *Comput Biol Med*, vol. 129, p. 104135, Nov 23 2020, doi: 10.1016/j.compbiomed.2020.104135.
- [7] K.-H. Tsui, O. SHVARTS, R. B. SMITH, R. A. FIGLIN, J. B. deKERNION, and A. BELLDEGRUN, "Prognostic indicators for renal cell carcinoma: a multivariate analysis of 643 patients using the revised 1997 TNM staging criteria," *The Journal of urology*, vol. 163, no. 4, pp. 1090-1095, 2000.
- [8] T. Okegawa et al., "Intratumor heterogeneity in primary kidney cancer revealed by metabolic profiling of multiple spatially separated samples within tumors," *EBioMedicine*, vol. 19, pp. 31-38, 2017.
- [9] R. J. Gillies, P. E. Kinahan, and H. Hricak, "Radiomics: images are more than pictures, they are data," *Radiology*, vol. 278, no. 2, pp. 563-577, 2015.
- [10] G. Hajianfar et al., "Noninvasive O6 Methylguanine-DNA Methyltransferase Status Prediction in Glioblastoma Multiforme Cancer Using Magnetic Resonance Imaging Radiomics Features: Univariate and Multivariate Radiogenomics Analysis," *World Neurosurgery*, vol. 132, pp. e140-e161, 2019/12/01/ 2019, doi: https://doi.org/10.1016/j.wneu.2019.08.232.
- [11] S. Mostafaei et al., "CT imaging markers to improve radiation toxicity prediction in prostate cancer radiotherapy by stacking regression algorithm," (in eng), *Radiol Med*, vol. 125, no. 1, pp. 87-97, Jan 2020, doi: 10.1007/s11547-019-01082-0.
- [12] S. Rastegar et al., "Radiomics for classification of bone mineral loss: A machine learning study," (in eng), *Diagn Interv Imaging*, vol. 101, no. 9, pp. 599-610, Sep 2020, doi: 10.1016/j.diii.2020.01.008.
- [13] H. Abdollahi, I. Shiri, and M. Heydari, "Medical Imaging Technologists in Radiomics Era: An Alice in Wonderland Problem," (in eng), *Iran J Public Health*, vol. 48, no. 1, pp. 184-186, Jan 2019.
- [14] S. P. Shayesteh et al., "Treatment Response Prediction using MRI-based Pre-, Post- and Delta-Radiomic Features and Machine Learning Algorithms in Colorectal Cancer," (in eng), *Med Phys*, Apr 24 2021, doi: 10.1002/mp.14896.
- [15] H. Arabi, A. AkhavanAllaf, A. Sanaat, I. Shiri, and H. Zaidi, "The promise of artificial intelligence and deep learning in PET and SPECT imaging," (in eng), *Phys Med*, vol. 83, pp. 122-137, Mar 22 2021, doi: 10.1016/j.ejmp.2021.03.008.
- [16] I. Shiri et al., "Machine learning-based prognostic modeling using clinical data and quantitative radiomic features from chest CT images in COVID-19 patients," (in eng), *Comput Biol Med*, vol.

132, p. 104304, May 2021, doi: 10.1016/j.combiomed.2021.104304.

- [17] K. Clark et al., "The Cancer Imaging Archive (TCIA): maintaining and operating a public information repository," *Journal of digital imaging*, vol. 26, no. 6, pp. 1045-1057, 2013.
- [18] J. J. M. van Griethuysen et al., "Computational Radiomics System to Decode the Radiographic Phenotype," (in eng), *Cancer Res*, vol. 77, no. 21, pp. e104-e107, Nov 1 2017, doi: 10.1158/0008-5472.Can-17-0339.
- [19] I. Shiri et al., "Repeatability of radiomic features in magnetic resonance imaging of glioblastoma: Test-retest and image registration analyses," (in eng), *Med Phys*, vol. 47, no. 9, pp. 4265-4280, Sep 2020, doi: 10.1002/mp.14368.
- [20] M. Edalat-Javid et al., "Cardiac SPECT radiomic features repeatability and reproducibility: A multi-scanner phantom study," (in eng), *J Nucl Cardiol*, Apr 24 2020, doi: 10.1007/s12350-020-02109-0.