

Role of artificial intelligence in diagnostic oral pathology- A modern approach

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Abstract

Over the decades, new equipment was emerged in medical field, and we have witnessed the importance of medical imaging such as computed tomography, magnetic resonance imaging, ultrasound, mammography and X-ray and their contribution in successful diagnosis and treatment of various diseases. Now, we are in era of artificial intelligence (AI), where machines were modeled after human brain's ability to take inputs and produce outputs from given data. AI has a wide range of uses and applications in health services industry. Factors such as increase in workload, complexity of work and potential fatigue of doctors may compromise diagnostic ability and outcome. AI components in imaging machines would reduce this workload and drive greater efficiency. They also have access to a greater wealth of data than human counterparts and can detect cancer with more accuracy than humans. This study presented an overview of AI, its recent advances in pathology and future prospects.

Keywords: Artificial intelligence, image analysis, machine learning, oral cancer, pathology

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INTRODUCTION

Over the decades, new equipment was emerged in medical field, and we have witnessed the importance of medical imaging such as computed tomography, magnetic resonance imaging, ultrasound, mammography and X-ray and their contribution in successful diagnosis and treatment of various diseases.^[1] With substantial increase in workload and complexity of work, potential fatigue of doctors, human experts and researchers may compromise the outcome. Nowadays, pathologists have to go over a large number of slides to come to a complete diagnosis. At times, they may need additional immunohistochemical stains for the same.^[2] Even though newer advances are available in

medical field and large amounts of cancer data are available, it is still the accurate prediction of disease prediction remained an unanswered question for the physicians. Despite the use of radiation therapy for the treatment of head and neck cancers, the long-term survival of such patients is quite poor (5-year survival rate as low as 50%), due to the development of secondary metastasis.^[3,4] As it is critical to identify potential high-risk patients prior to treatment, it is important to develop a model using which better-informed decision could be made regarding patient risk stratification.^[5]

Machine learning (ML) has played a significant role over the years in nearly every aspect of the STEM, i.e., science,

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technology, engineering and medicine.^[6] ML is a branch of artificial intelligence (AI) that employs a variety of statistical, probabilistic and optimization techniques that allows computers to “learn” from past examples and to detect hard-to-discern patterns from large, noisy or complex data sets.^[7] In simple words, it is a system that takes in data, finds patterns, trains itself using the data and gives an output. ML, like statistics, is used to analyze and interpret data. ML methods have become popular tool for medical researchers and are able to predict outcomes of cancer type effectively. Evidence from literature suggested that the accuracy of cancer prediction outcome improved by 15%–20% over the years with the application of ML techniques.^[7] Recently, deep learning (DL), a subfield of ML, has risen to the forefront of AI community.^[8] DL technique is described as the application of multi-layered artificial neural networks to a wide range of problems, and they are very effective at analyzing images. Convolutional neural networks (CNNs), one of the most popular DL tools for pattern recognition tasks, very effective at analyzing images.

Pathologists and radiologists are fundamentally similar, as they both extract information from images. Some tasks once performed by pathologists such as cell counts, typing and screening of blood and Papanicolaou tests have been automated, leaving pathologists to handle complex tasks.^[9] Yu *et al.*, in their study, found that computers could predict the grade and stage of lung cancer better than pathologists.^[10] Despite the perceived threat of AI, it is possible that AI tools can be boon to pathologists by increasing their value, efficiency, accuracy and personal satisfaction.^[9] Owing to the success of AI in nonmedical applications, many researchers believed that AI and DL, in particular, are invaluable in digital pathology.^[11]

ORAL CANCER AND MACHINE LEARNING

The incidence of cancer and mortality is rapidly increasing worldwide. As per the estimates of the World Health Organization (WHO) in 2015, cancer is the first or second leading cause of death in nearly 91 of 172 countries.^[12] Oral and pharyngeal cancer grouped together, is the sixth-most common cancer in the world.^[13] Globally, lips, oral cavity and pharyngeal cancers constitute up to 3.8% of all cancer cases and 3.6% of cancer deaths.^[14] In high-risk countries such as India, Pakistan, Sri Lanka and Bangladesh, oral cancer is the most common cancer in men, may contribute up to 25% of all new cases.^[13] Given the rising incidence of oral cancers, there is an immense need for tailored approaches to prevention, screening and treatment interventions.

Many scholars believed that the treatment method is the common influential factor that influences the survival rate and posttreatment recurrence of oral cancer patients. They suggested for the need of a method that effectively uses pretreatment disease information to categorize similar patients suffering from oral cancer and improve their overall treatment rates, thereby enhancing overall quality care.^[15] Data mining technology and analysis facilitate medical expert’s decision-making in diagnosis, treatment and patient management. Decision tree is a data mining technique characterized by features such as classification and prediction and is considered a type of supervised learning. Tseng *et al.*, in their study adopted an integrated procedure that combines the clustering and classification features of data mining technology to determine the differences between symptoms shown in past cases where patients died from or have survived oral cancer.^[16]

APPLICATION OF ARTIFICIAL INTELLIGENCE IN PATHOLOGY

Microscopic morphology is considered as gold standard in diagnostic pathology.^[17] Pathology specimens undergo multiple processes that include formalin fixation, grossing, paraffin embedding, tissue sectioning and finally staining. In general, it is human pathologist that provides pathology diagnosis by observing stained specimen on the glass slide using a microscope. However, the main limitation associated with morphologic diagnosis is the variability among the pathologists. Therefore, for consistent and more accurate diagnosis, it is important to introduce AI in the pathology domain. Lately, numerous attempts were made in which the entire histopathological slide was scanned and then saved as a digital image (whole slide image).^[18]

In the USA, approximately one million biopsies were performed in the cancer of prostate (CaP), among them, only 20% are found to be positive for cancer. This implies that pathologists are spending huge amount of time looking at benign tissue, which in general can be easily distinguishable from cancer.^[19] This points out the need for computer-aided diagnosis that allows pathologists to focus more on difficult to diagnose cases rather than sieving through benign tissue.^[20]

Based on recent reporting on cancer, oral cancer is the most reported cancer affecting 4.5 million as per the WHO, and approximately 85% are responsible for death. Early detection will lead to reduction in death rate by 70%.^[21] The diagnosis and grading of oral epithelial dysplasia are mainly based on the combination of architectural changes and the appearance of specific histological features. Such features include loss

of polarity due to proliferation of immature cells, variations in size and shape of nuclei, increase in nuclear-cytoplasmic ratio, irregularly distributed nuclear chromatin, increased mitotic figures.^[22] For pathologists, this process, i.e., the effectiveness of cancer diagnosis, is time-consuming, subjective and inconsistent due to inter- and intra-observer variations.^[23] This further necessitates for the need of computer-aided image classification system with quantitative analysis of histological features for rapid, consistent and quantitative cancer diagnosis.^[24]

To overcome the limitations such as clinicopathological acumen, expertise of oral onco-pathologist and interobserver variations, automatic detection of cancer with the help of classifiers and better features have been studied over the years. In 2003, Landini and Othman introduced a novel method for labeling layers in histological sections of multi-layered or polystratified tissues. However, this approach was entirely two-dimensional (2D), may be useful as a formal descriptor of the spatial arrangements.^[25] In another study, the same authors measured statistical properties of the graph networks to characterize, geometrically, the architectural organization of normal, premalignant and malignant tissues in 2D sections. Their results indicated unbiased and reproducible quantification with discrimination rates of 67%, 100% and 80% for normal, premalignant and malignant cells, respectively.^[26] Krishnan *et al.* worked on improving the classification accuracy based on textural features by grading the histopathological tissue sections into normal, oral submucous fibrosis (OSF) without dysplasia and OSF with dysplasia. Combination of texture and higher-order spectra resulted in 95.7% accuracy, with sensitivity of 94.5% and specificity of 98.8%. Moreover, they also have proposed oral malignancy index to diagnose benign and malignant tissues just one number that helps clinicians in making a more objective detection of benign/malignant oral lesions.^[27] In 2015, Das *et al.* developed a computer-assisted quantitative microscopic method, i.e., an automated segmentation method for the identification of keratinization and keratin pearl from *in situ* oral histological images. This method achieved 95.08% segmentation accuracy in comparison with expert-based ground truths.^[28]

The architectural variations of epithelial layers and the presence of keratin pearls, which can be observed in microscopic images, are key visual features in oral cancer diagnosis. The computer aided tool doing the same identification task would certainly provide crucial aid to clinicians for evaluation of histological images during diagnosis. Das *et al.* proposed a two-stage approach for computing oral histology images, where 12-layered ($7 \times 7 \times$

3 channel patches) deep convolution neural network (CNN) is used for the segmentation of constituent layers; in the first stage and in the second stage, the keratin pearls are detected from the segmented keratin regions using texture-based feature (Gabor filter) trained random forests. Detection accuracy was found to be 96.88% for the detection of keratin pearls using texture-based random forest classifier.^[29]

In 2016, Lu *et al.* developed a computer-aided method for the diagnosis of tongue cancer in an animal model, in which cancer was chemically induced. The following histological processing of tongue tissue, representative areas of stained tissue were captured for classifying tumor and nontumor tissue. Texture feature describing epithelium structures was the most discriminating feature. They obtained an average sensitivity of 96.5% and a specificity of 99% for tongue cancer detection.^[24] In 2019, Jeyaraj and Samuel Nadar, developed a DL algorithm for automated, computer-aided oral cancer detecting system by investigating patient hyperspectral images. They have obtained a classification accuracy of 91.4% with sensitivity 0.94 and a specificity of 0.91 for 100 image datasets.^[30]

Any classification system has to be a self-learning and adjusting system that adjusts the rules to a given final outcome. Such a system will remain stable and expands its knowledge in the future, and it stays close to human performance of gathering ideas and knowledge.^[31]

ARTIFICIAL INTELLIGENCE AS ORAL CANCER PROGNOSTIC MODEL

ML is not new to cancer research. According to the PubMed statistics, majority of the papers published on ML and cancer were concerned with using of such learning methods to identify, classify, detect or distinguish tumors and other malignancies. It is always remained a challenge for the researchers to predict the cancer treatment outcome/prognosis. Over the past two decades, the body of literature in relation ML and cancer prognosis has increased. In majority of these studies, gene expression profiles, clinical variables and histological parameters are encompassed and fed as an input to the prognostic procedure.^[32] In cancer prognosis/prediction, one is concerned with three predictive tasks, i.e., (i) the prediction of cancer susceptibility (risk assessment); (ii) the prediction of cancer recurrence and (iii) the likelihood of redeveloping a type of cancer after complete or partial remission.^[7,32]

Macroscale information such as family history, age, diet, weight, high-risk habits and exposure to environmental

carcinogens could be used for prediction purposes. However, these parameters do not provide sufficient information to make robust decisions. With the advent of genomic, proteomic and imaging technologies, new kinds of molecular information using molecular biomarkers and cellular parameters have been proven as very informative indicators for cancer prediction.

It is evident from the literature that when both clinicopathologic and genomic data were used, the prognosis results for cancer are more accurate. Chang *et al.*, in their study, applied a hybrid of feature selection and ML methods in oral cancer prognosis. Their results revealed that the prognosis is superior with the presence of both clinicopathologic and genomic markers.^[33] In another study by Exarchos *et al.*, the authors aimed to identify the factors that dictate oral squamous cell carcinoma progression and subsequently predict potential relapses of the disease. They suggested a multiparametric decision support system and exploited heterogeneous sources of data such as clinical, imaging and genomic. This study illustrated in an explanatory way how the integration of heterogeneous sources of data, by means of ML classifiers, can produce accurate results regarding the prediction of cancer recurrence.^[34] It is evident that the integration of multidimensional heterogeneous data, combining with the application of different techniques, can provide promising tools for inference in the cancer domain.

MOBILE MOUTH SCREENING ANYWHERE

Researchers from Kingston University (U. K.) and University of Malay (Malaysia) working on a project, i.e., Mobile Mouth Screening Anywhere (MeMoSA) app, which is used to capture images of the oral cavity for remote interpretation by specialists. They will train a DL system that distinguishes between thousands of photos with and without signs of oral cancer, then integrate that system into the app.^[35] Professor Dr. Sok Ching Cheong of Cancer Research Malaysia believed that the “incorporation of AI within MeMoSA holds a lot of promise in ensuring that the efforts we make in early detection continue to break barriers across regions where the disease is most prevalent.”^[36]

CONCLUSION

Even though it is encouraging that the pathologic field in AI is expanding to disease severity assessment and prognosis prediction, still a large amount of data is needed to develop AI that covers the range of clinical situations. Although the image analysis methods for digital pathology are rapidly finding application in cancer diagnosis; one has

to remember that it is the pathologist who can provide the feedback on the system’s performance and his knowledge, advise and supervision become more important. Moreover, no pathologist should be afraid of losing his/her position due to these advancements in pathology. On the contrary, pathologist will be the best equipped to interpret the findings with the help of AI and DL, in turn, may lead to new research ideas.

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Conflicts of interest

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REFERENCES

- Shen D, Wu G, Suk HI. Deep learning in medical image analysis. *Annu Rev Biomed Eng* 2017;19:221-48.
- Litjens G, Sánchez CI, Timofeeva N, Hermsen M, Nagtegaal I, Kovacs I, *et al.* Deep learning as a tool for increased accuracy and efficiency of histopathological diagnosis. *Sci Rep* 2016;6:26286.
- Yeh SA. Radiotherapy for head and neck cancer. *Semin Plast Surg* 2010;24:127-36.
- Baxi SS, Pinheiro LC, Patil SM, Pfister DG, Oeffinger KC, Elkin EB. Causes of death in long-term survivors of head and neck cancer. *Cancer* 2014;120:1507-13.
- Diamant A, Chatterjee A, Vallières M, Shenouda G, Seuntjens J. Deep learning in head and neck cancer outcome prediction. *Sci Rep* 2019;9:2764.
- Jordan MI, Mitchell TM. Machine learning: Trends, perspectives, and prospects. *Science* 2015;349:255-60.
- Cruz JA, Wishart DS. Applications of machine learning in cancer prediction and prognosis. *Cancer Inform* 2007;2:59-77.
- Schmidhuber J. Deep learning in neural networks: An overview. *Neural Netw* 2015;61:85-117.
- Jha S, Topol EJ. Adapting to artificial intelligence: Radiologists and pathologists as information specialists. *JAMA* 2016;316:2353-4.
- Yu KH, Zhang C, Berry GJ, Altman RB, Ré C, Rubin DL, *et al.* Predicting non-small cell lung cancer prognosis by fully automated microscopic pathology image features. *Nat Commun* 2016;7:12474.
- Tizhoosh HR, Pantanowitz L. Artificial intelligence and digital pathology: Challenges and opportunities. *J Pathol Inform* 2018;9:38.
- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68:394-424.
- Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. *Oral Oncol* 2009;45:309-16.
- Shield KD, Ferlay J, Jemal A, Sankaranarayanan R, Chaturvedi AK, Bray F, *et al.* The global incidence of lip, oral cavity, and pharyngeal cancers by subsite in 2012. *CA Cancer J Clin* 2017;67:51-64.
- Taiwan Public Health Report 2009. Available from: http://www.mohw.gov.tw/MOHW_Upload/doc/98%E5%B9%B4%E4%B8%AD%E6%96%87%E7%89%88%E8%A1%9B%E7%94%9F%E5%B9%B4%E5%A0%B1_0042862000.pdf. [Last accessed on 2019 May 18].
- Tseng WT, Chiang WF, Liu SY, Roan J, Lin CN. The application of data mining techniques to oral cancer prognosis. *J Med Syst* 2015;39:59.
- Chang HY, Jung CK, Woo JI, Lee S, Cho J, Kim SW, *et al.* Artificial intelligence in pathology. *J Pathol Transl Med* 2019;53:1-2.
- Komura D, Ishikawa S. Machine learning methods for histopathological image analysis. *Comput Struct Biotechnol J* 2018;16:34-42.

19. Epstein JI, Allsbrook WC Jr., Amin MB, Egevad LL. Update on the Gleason grading system for prostate cancer: Results of an international consensus conference of urologic pathologists. *Adv Anat Pathol* 2006;13:57-9.
20. Gurcan MN, Boucheron LE, Can A, Madabhushi A, Rajpoot NM, Yener B. Histopathological image analysis: A review. *IEEE Rev Biomed Eng* 2009;2:147-71.
21. Erickson BJ, Korfiatis P, Kline TL, Akkus Z, Philbrick K, Weston AD. Deep learning in radiology: Does one size fit all? *J Am Coll Radiol* 2018;15:521-6.
22. Wenig BM. Squamous cell carcinoma of the upper aerodigestive tract: Precursors and problematic variants. *Mod Pathol* 2002;15:229-54.
23. Ismail SM, Colclough AB, Dinnen JS, Eakins D, Evans DM, Gradwell E, *et al.* Observer variation in histopathological diagnosis and grading of cervical intraepithelial neoplasia. *BMJ* 1989;298:707-10.
24. Lu G, Qin X, Wang D, Muller S, Zhang H, Chen A, *et al.* Quantitative diagnosis of tongue cancer from histological images in an animal model. *Proc SPIE Int Soc Opt Eng* 2016;9791. pii: 97910L.
25. Landini G, Othman IE. Estimation of tissue layer level by sequential morphological reconstruction. *J Microsc* 2003;209:118-25.
26. Landini G, Othman IE. Architectural analysis of oral cancer, dysplastic, and normal epithelia. *Cytometry A* 2004;61:45-55.
27. Krishnan MM, Venkatraghavan V, Acharya UR, Pal M, Paul RR, Min LC, *et al.* Automated oral cancer identification using histopathological images: A hybrid feature extraction paradigm. *Micron* 2012;43:352-64.
28. Das DK, Chakraborty C, Sawaimoon S, Maiti AK, Chatterjee S. Automated identification of keratinization and keratin pearl area from *in situ* oral histological images. *Tissue Cell* 2015;47:349-58.
29. Das DK, Bose S, Maiti AK, Mitra B, Mukherjee G, Dutta PK. Automatic identification of clinically relevant regions from oral tissue histological images for oral squamous cell carcinoma diagnosis. *Tissue Cell* 2018;53:111-9.
30. Jeyaraj PR, Samuel Nadar ER. Computer-assisted medical image classification for early diagnosis of oral cancer employing deep learning algorithm. *J Cancer Res Clin Oncol* 2019;145:829-37.
31. Kayser K, Hoshang SA, Metzke K, Goldmann T, Vollmer E, Radziszowski D, *et al.* Texture- and object-related automated information analysis in histological still images of various organs. *Anal Quant Cytol Histol* 2008;30:323-35.
32. Kourou K, Exarchos TP, Exarchos KP, Karamouzis MV, Fotiadis DI. Machine learning applications in cancer prognosis and prediction. *Comput Struct Biotechnol J* 2015;13:8-17.
33. Chang SW, Abdul-Kareem S, Merican AF, Zain RB. Oral cancer prognosis based on clinicopathologic and genomic markers using a hybrid of feature selection and machine learning methods. *BMC Bioinformatics* 2013;14:170.
34. Exarchos KP, Goletsis Y, Fotiadis DI. Multiparametric decision support system for the prediction of oral cancer recurrence. *IEEE Trans Inf Technol Biomed* 2012;16:1127-34.
35. Andrea Park. Researchers Training AI Mobile App to Detect Early Signs of Oral Cancer. Available from: <https://oralcancernews.org/wp/researchers-training-ai-mobile-app-to-detect-early-signs-of-oral-cancer/>. [Last accessed on 2019 Sep 30].
36. Can Artificial Intelligence Spot Warning Signs of Oral Cancer? Kingston University Experts Develop System for Mobile Phone App in New Study. Available from: <https://www.kingston.ac.uk/news/article/2201/04-jun-2019-can-artificial-intelligence-spotwarning-signs-of-oral-cancer-kingston-universityexperts-develop-system-for/>. [Last accessed on 2019 Sep 30].