REVIEW ARTICLE

ROLE OF RADIOMICS IN IMAGING OF HEAD AND NECK TUMORS- A REVIEW

Dr. Debopriyo Chatterjee*, Dr. Kaushik Dutta**, Dr. Divya Pandya***
Dr. Anwesha Banerjee****, Dr. Rekha Puttanavar***
Dr. Anwesha Biswas****

ABSTRACT

Developments in artificial intelligence and machine learning technologies of late have made it possible to evaluate radiological images automatically. Quantifiable biomarkers for diagnosis and prognosis have been developed as a result. In this article, we address radiomics applications for the head and neck area. Treatment prescription, prognosis, classification, and molecular characterisation are given particular attention. We provide an overview of the basic technical concepts, the general concept and standard procedure of radiomic analysis, as well as the apparent current and future difficulties in routine medicine. Cancers of the head and neck pose special diagnostic and treatment difficulties. The complex structure and diversity of the region being studied are the causes of these difficulties. These obstacles may be overcome by radiomics. The characterization and differentiation of various tumours and cysts of the head and neck region is also facilitated by the incorporation of radiomics. The study of specific oncologic functions and outcomes must be the focus of future multidisciplinary research, which requires multi-institutional collaboration and external evaluation.

KEY WORDS

Head and neck tumors, Imaging, modeling, Radiomics

ABOUT THE AUTHORS

*Post Graduate Trainee, **Professor and Head
***Associate Professor, ****Assistant Professor
Department of Oral Medicine and Radiology
Guru Nanak Institute of Dental Sciences and Research
Kolkata, India

CORRESPONDING AUTHOR

Dr. Debopriyo Chatterjee
Post Graduate Trainee (2nd Year)
Department Of Oral Medicine And Radiology
Guru Nanak Institute Of Dental Sciences And Research
157/F, Nilgunj Rd, Sahid Colony, Panihati, Kolkata, West Bengal
700114 e-mail : dchatterji67@gmail.com

INTRODUCTION

Due to their sometimes subtle and asymptomatic nature, which frequently leads to a delayed diagnosis at more advanced stages, head and neck tumors are linked to a high death rate. There are many distinct types of tumors and tumor-like diseases that can develop from various tissues in the head and neck region. These tissues include of the surrounding soft tissues and bones, as well as the paranasal sinuses, pharynx, oral cavity, larynx, thyroid, and lymph nodes. Squamous cell carcinoma (SCC), which makes about 90% of all head and neck tumors, is the most prevalent histological form of these tumors. Over 830,000 cases of head and neck tumors are recorded worldwide each year[1]. In India, more than 200,000 cases of head and neck cancers are reported annually[2].

Medical image analysis has grown rapidly over the last ten years, mostly as a result of the development of pattern recognition technologies and the growth of dataset sizes. As a result of these developments, methods for high-throughput quantitative feature extraction from images have been developed, turning them into data that can be mined. Then, using a technique called radiomics, this data may be analyzed to support decisions[3]. The quantitative mapping, or extraction, analysis, and modeling of numerous medical image aspects in connection to prediction targets, like clinical endpoints and genomic features, is known as "radiomics." The foundation of radiomics is decades of work in computer-aided diagnosis, prognosis, and treatment[4]. Finding a variety of quantitative characteristics in digital photos, storing the information in federated databases, and then mining the data to extract and apply knowledge are all steps in the process[4]. Radiomics contributes to and advances precision medicine for head and neck tumors in multiple ways: (I) it provides a quick, affordable, and repeatable method for longitudinal monitoring; (II) it produces prognostic and predictive biomarker values derived from standard imaging data; and (III) it non-invasively characterizes the tumor as a whole, accounting for its heterogeneity[5].

Our goal in this review is to give a general overview of radiomics while pointing out the several

fields of study where these methods can be used to treat head and neck tumors. Lesion segmentation, grading, differential diagnosis, prognosis prediction, therapy response assessment, and overall result prediction are a few of these.

RADIOMICS WORKFLOW

The process of radiomics consists of multiple discrete processes, such as:

(a) Obtaining the images

(b) Determining the volumes of interest, or those that might have prognostic significance

(c) Segmenting the volumes

(d) Processing the images

(e) Extracting and qualifying descriptive features from the volume

(f) Using these features to populate a searchable database

(g) Mining this data to develop classifier models that predict outcomes, either alone or in combination with other information such as demographic, clinical, comorbidity, or genomic data.

1.) Image Acquisition

Choosing an imaging protocol is the first step in radiomic studies. Non standardized imaging techniques are frequently employed, despite the fact that standardized imaging protocols are crucial for minimizing needless variability. Therefore, complete disclosure of the imaging procedures utilized is the only way to guarantee the repeatability and comparability of radiomic research[3].

2.) Identifying Volumes of Interest - those containing prognostic value

In any radiomics technique, defining the region of interest (ROI) in two-dimensional (2D) studies or the volume of interest (VOI) in three-dimensional (3D) research is an essential first step. Radiomic characteristics are computed using areas defined by ROIs and VOIs [6]. Cancer may have been discovered at one tumor site or at several locations at the time of diagnosis. Metastatic cancer patients usually have several lesions. Identifying both suspected and confirmed tumors as areas of interest is crucial in any scenario[3].

The idea of identifying physiologically different regions inside lesions using imaging data is not new. Using this method, regions with particular combinations of quantitative image data can be obtained by combining images with different acquisition settings, such as fluid attenuation sequences, diffusion-weighted imaging, and contrast-enhanced T1-weighted MR imaging. Because they represent physiologically unique volumes, each of which is distinguished by a particular combination of blood flow, cell density, necrosis, and oedema, these areas are known as habitats. Each of these habitats can yield additional radiomic properties that can be used to describe cancer lesions in depth[3].

3.) Segmentation

Segmentation is the process of grouping areas of an image that are part of the same class of objects[1].

Types of Segmentation:-

a) Manual Segmentation

b) Semi-Automatic Segmentation

c) Fully Automatic Segmentation

A) Manual Segmentation

When skilled radiologists work with small datasets, manual segmentation can produce accurate definitions of Regions of Interest (ROIs) and Volumes of Interest (VOIs). Nevertheless, this method takes a lot of time and can show a lot of variation among observers, which could skew the outcomes of radiomic analyses[1].

B) Semi-Automatic Segmentation

Applying algorithms that make use of several picture delineation tactics, such as region-growing, level set, graph cut, and active contour procedures, is part of the semi-automatic segmentation process. The stability of radiomic models can still be impacted by subjective bias, even if this method lessens manual labor and improves the resilience of radiomic characteristics, especially when substantial user corrections are involved[1].

Therefore, the repeatability of the obtained radiomic characteristics should be evaluated in investigations that employ manual or semi-automated picture segmentation with manual adjustments. This entails assessing variability between and between observers as well as eliminating any non-reproducible features from additional analysis[6].

C) Fully Automatic Segmentation-

Many methods for segmenting different organs in medical images have been created, and deep learning-based image segmentation is quickly gaining popularity. By successfully minimizing potential disparities between observers, these techniques have shown exceptional effectiveness in recognizing and segmenting lesions. The substantial quantity of data needed to train these models and their generalizability across various circumstances is a major disadvantage, though[6].

On the one hand, these methods can improve reproducibility and reduce workload in radiomic

research. However, for classification tasks, they do not necessarily need picture segmentation. Tumour segmentation is a crucial difficulty for guaranteeing the robustness of radiomic characteristics, especially in manual and semi-automated procedures, since the absence of defined segmentation methodologies can result in inconsistently repeatable models[1].

4.) Image Processing

Between feature extraction and picture segmentation, image processing is a crucial stage. With an emphasis on elements like pixel spacing, grey-level intensities, and the bins of the grey-level histogram, its main objective is to standardize the images from which radiomic information will be retrieved[6].

The following steps are involved in the picture processing process:

a) Isotropic Voxel Spacing Interpolation - This step improves reproducibility across datasets and guarantees that the majority of texture feature sets are rotationally invariant[6].

b)Intensity Outlier Filtering and Range Re-segmentation (Normalization) - Pixels or voxels that fall outside of a predetermined range of grey levels are removed from the segmented region using these procedures. Range re-segmentation is not relevant to data with arbitrary intensity units, like MRI, but it is usually required for CT and PET data. Intensity outlier filtering is used instead for MRI data[6].

b)Discretization - Discretization, which is conceptually comparable to making a histogram, entails dividing the original data into distinct range intervals (or bins). To make feature calculation manageable, this step is crucial[6].

5.) Extraction of Features

High-throughput quantitative image feature extraction is used in radiomics to describe volumes of interest (VOIs)[4]. Since there are several ways to calculate these traits, it is advised to follow the rules established by the Image Biomarker Standardization Initiative (IBSI). For all radiomic feature matrices, these rules offer a consensus on standardized computations[6]. In general, radiomic characteristics can be divided into four categories: shape-based features, model-based features, transform-based features, and statistical features, which include measurements based on histograms and textures. Furthermore, it is possible to extract these features from three-dimensional (3D) volumes of interest as well as two-dimensional (2D) regions of interest (ROIs)[7].

6.) Feature Selection and Dimension Reduction-

Following radiomic image analysis, it is critical to determine which pertinent features-such as the ability to differentiate between benign and malignant lesions-will be utilized in the statistical model to solve the clinical issue. Even though hundreds of radiomic feature candidates are usually identified, the number of model parameters needed would expand exponentially if all of them were used in the prediction model. As a result, many of these feature possibilities must be eliminated or changed. Dimensionality reduction is the name given to this technique.

High correlations are frequently seen in radiomic characteristics, indicating data redundancy. Therefore, using techniques like principal component analysis or linear discriminant analysis, some features may be eliminated while others may be pooled and swapped out for a representative feature. The relevant features that exhibit the highest level of interpatient variability, or natural biological variability, should be chosen from these representative traits[7]. Test-retest data, if available, can be very useful because it helps rank features according to their repeatability[3].

Finding the variables that are most pertinent to the particular task is the second phase in the feature selection process. For this first pick, a variety of methods can be employed, frequently based on machine learning techniques. These consist of random forest algorithms, recursive feature removal techniques, and knock-off filters. Nevertheless, the next logical step-often called the third step-in the dimension reduction workflow is to generate correlation clusters because many of these algorithms fail to take into account collinearities and correlations in the data[3].

Because few machine learning approaches effectively address correlations within the data, this third step may occasionally be integrated with the second stage. One sample characteristic can be chosen from each cluster thanks to correlation clusters, which aid in visualizing collections of highly associated features. Data visualization strategies, traditional statistical methodologies, or machine learning algorithms may serve as the foundation for this decision process[7].

The variable with the most biological and clinical variability in the dataset should generally be selected since it is more likely to accurately reflect the variances in the particular patient cohort. Furthermore, even once the data's dimensionality is reduced, data visualization is still essential[6].

7.) Building a Database

The efficacy of the predictive classifier model in radiomics and other domains depends on having sufficient data. In a binary classifier-based model, each feature usually requires 10 samples (patients)[3].

Furthermore, because the strongest models are those that can account for additional clinical or genetic characteristics, there is a greater need for large, high-quality data sets.

8.) Classifier Modelling and Data Sharing

Data mining is the process of finding patterns in huge data sets, and it may be used to massive, well-curated, high-quality data sets once they are available. Statistical methods, machine learning, or artificial intelligence may be used in this procedure. These range from supervised to unsupervised machine learning techniques, including Bayesian networks, support vector machines, and neural networks. These methods are agnostic in that they do not assume anything about the significance of the individual features, even when they employ training sets to obtain a priori knowledge. As a result, when learning begins, every feature is given equal weight. Hypothesis-driven methods that group features based on predetermined information content are at the other end of the data-mining spectrum. Although each of these strategies has advantages, the most effective models are those that are customized for a particular medical setting and, as a result, begin with a clearly defined endpoint[3].

In the event that a model's function approximation is not sufficiently balanced, overfitting or, to a lesser extent, underfitting may occur. When a model has too many degrees of freedom or too many input parameters, it can recall data and incorporate not only pertinent, disease-specific information but also variables that represent random fluctuations and picture noise. This is known as overfitting. When given data points during training, such a model produces accurate classification results; but, when given data points outside of the training dataset, the model's answer is incorrect-it lacks the ability to generalize knowledge. Regularization must be used to smooth the model function in order to prevent overfitting, or fewer input features must be used, which lowers the number of model parameters needed. Validation with a different dataset aids in identifying overfitting; training should be halted if the error in the training dataset starts to rise while it reduces in the validation dataset[7].

However, when a model is too simple, it can fail to accurately categorize data in both the training and validation datasets, a phenomenon known as underfitting. In this case, it could be essential to switch to a different model or provide more input data[7].

ROLE OF RADIOMICS IN HEAD AND NECK TUMOR IMAGING

1.) CHARACTERIZATION

The association between bioimaging characteristics (human papillomavirus (HPV) status, somatic mutations, methylation, subtypes of gene expression, and PD-L1 protein expression levels) and Head and neck squamous cell carcinoma (HNSCC) has been shown by recent radiomics studies. Of these, HPV status is the one that has attracted the greatest attention. The presence of the virus is linked to a superior response to radiation therapy, a younger patient age at presentation, and distinct tumour shape (smaller initial tumours, substantial cervical adenopathy). Radiomics-based biomarkers may be employed in the future as a feasible substitute to confirm HPV status following positive p16 immunohistochemistry testing, provided that they are backed by adequate data. Several studies have used texture analysis to define HPV status in HNSCC[1].

2.) STAGING

Pre-treatment staging is a crucial aspect of diagnostic and therapy planning, and it has a direct bearing on the prognosis of tumours. Although surgery is the primary treatment, other possibilities include immunotherapy, targeted therapy, concurrent chemoradiotherapy, and induction chemotherapy. According to studies, the lymph node status and T-stage of head and neck cancers have a significant impact on the treatment option and, consequently, the prognosis of cancer patients. A trustworthy radiomics assessment of the tumour's stage before therapy can help guide treatment choices, reducing the chance of side effects and recurrence. A T-staging model of locally advanced laryngeal carcinoma might be effectively established using radiomics[1]. Specifically, it was demonstrated that the MRI radiomic signature was an additional preoperative staging tool that distinguished between stage III–IV and stage I–II squamous cell carcinoma[1].

3.) TREATMENT

Pre and Intra Treatment Imaging :

Oncologists can improve therapy outcomes and patients' tolerance to therapy by creating customized treatment programs and putting preventative measures in place. Many studies on tumour response to total dose, fractionation, and fraction dosage may be made possible by the potential for cone beam CT (CBCT) devices to perform delta radiomics for image guided radiation. It has been shown that reproducible CBCT features are just as good as CT features for predicting patients' overall survival[1].

By extracting quantitative features from picture sets obtained during therapy, delta-radiomics adds a temporal component and offers insights into the evolution of feature values. Improved diagnosis, prognosis, prediction, monitoring, image-based intervention, or evaluation of therapeutic response are all potential benefits of delta-radiomics[4].

Short term outcome:

Predicting results in nearby non-cancerous tissues, like glandular tissues (parotid and large salivary glands), may also be helpful. The research has noted a general decline in the complexity and variety of parotid tissue. A correlation between the dosage schedule and the estimated structural change following radiation was suggested by the finding that the change in mean volume and intensity was connected with pre-treatment dosimetric parameters[1].

Long term outcome:

These consist of xerostomia, trismus, and hearing loss. One prevalent side effect that presents a problem for long-term patient management is radiation xerostomia. In this context, several studies with diverse goals have been conducted. For example, Sheikh et al. forecasted a binary outcome of xerostomia three months following radiation treatment[8].

4.) METASTASIS AND RECURRANCE

An unfavourable prognostic characteristic associated with an increased likelihood of recurrent illness is extra nodal extension (ENE) of cervical lymph node metastases. This lends credence to the use of adjuvant radiation in conjunction with chemotherapy. The identification of ENE may help guide treatment choices, reduce morbidity, and avoid surgery in patients who are likely to require adjuvant chemoradiation. Kann et al. developed and validated quantitative imaging techniques to detect ENE before surgery[9].

5.) SURVIVAL

Many patients are already at an advanced stage of their illness when they receive their initial diagnosis. The prognosis remains poor, with 5-year survival rates ranging from 80% for nasopharyngeal cancer (NPC) to 25% for hypopharyngeal carcinoma (HPC). More accurate patient survival rate prediction is required to develop even more effective treatment plans.

The most common radiomic models used in research studies on the application of radiomics in HNC are those that predict survival. The goal of Shen et al. was to investigate the radiomic model's prediction value using MRI characteristics[10]. Five models were established from 327 patients. Harrell's concordance index (C-index) was used to assess these models' prognostic efficacy. The model that combined DNA in non-metastatic tumours, global health stage, and radiomics was determined to be the most effective.

LIMITATIONS OF RADIOMICS

Due to the retrospective, monocentric nature of most current radiomics research, care should be taken when interpreting the results that are published. Specifically, the small sample size that often characterizes these works may result in bias in patient selection, making them inaccurately representative of the population as a whole. Additionally, there aren't many device makers, and data collection methods are frequently used, which may lead to arbitrary patterns that introduce biases into the models. Unfortunately, without access to larger and more diverse datasets, these are hard to find. Generally speaking, these problems could result in models that are unable to replicate their success in fresh studies[1].

Another problem that is partially connected to the latter is the lack of standardization in radiological imaging methods, which may potentially affect the models' generalizability and, ultimately, their clinical application[3].

The very common absence of external validation is another issue that could lead to overfitting of the prediction model[4].

Significant variation in the segmentation, feature extraction, and selection processes, along with the modelling techniques used, continue to be disadvantages[1].

CONCLUSION

The use of Radiomics in head and neck tumour imaging has been the subject of numerous studies. Gomes JPP et al. studied the texture analysis of magnetic resonance imaging (MRI) to distinguish between ameloblastoma and odontogenic keratocyst and came to the conclusion that MRI texture analysis could be used as a non-invasive technique to distinguish between the two conditions[11]. In a study on the use of magnetic resonance imaging biomarkers to enhance the differentiation of benign and malignant parotid tumours through diagnostic model analysis, Liu et al. came to the conclusion that MRI-based texture analysis is a useful technique for distinguishing between benign and malignant parotid tumours, and that the chosen biomarkers improved preoperative diagnosis when compared to the reference model[12]. According to a study by Lysenko et al. on the use of radiomics in the differential diagnosis of ameloblastomas and dentigerous cysts, radiomics is a novel method for the non-invasive differential diagnosis of tumours of the jaw that is based on texture features taken from CT data[13].

Thus because of their complicated regional anatomy, small size, diversity in oncologic pathology, and post-treatment anatomical site alterations, Head and Neck Tumours provide significant hurdles for radiologists and physicians[14].Future efforts must focus on strong external validation within multi-

institutional collaborative efforts to standardize, improve, and finally implement radiomics and machine learning software in clinical practice, even though these techniques have the potential to overcome the current limitations of imaging in the head and neck area.

REFERENCES

1.) Tortora M, Gemini L, Scaravilli A, Ugga L, Ponsiglione A, Stanzione A et.al. Radiomics Applications in Head and Neck Tumor Imaging- A Narrative Review.Cancers. 2023;15:1174-1199.

2.) Kulkarni MR. Head and Neck Cancer Burden in India.IJHNS. 2013;4(1):29-35.

3.) Gillies RJ, Kinahan PE, Hedvig H. Radiomics: Images Are More Than Pictures, They Are Data.Radiol. 2016;278(2):563-577.

4.) Lambin P, Leijenaar RTH, Deist TM, Peerlings J, de Jong EEC, van Timmeren J et.al. Radiomics: the bridge between medical imaging and personalized medicine. Nat.Rev. 2017;14:749-762.

5.) Wong AJ, Kanwar A, Mohamed AS, Fuller CD. Radiomics in head and neck cancer: from exploration to application. Transl Cancer Res 2016;5(4):371-382.

6.) van Timmeren JE, Cester D, Tanadini-Lang S, Alkadhi H, Baessler B. Insights into Imaging. 2020;1-16.

7.) Mayerhoefer ME, Materka A, Langs G, Haggstrom I, Szczypinski P, Gibbs P et.al. Introduction to Radiomics. J Nucl Med 2020; 61:488–495.

8.) SheikhK, Lee S.H, Cheng.Z , LakshminarayananP, Peng.L, HanP et.al. Predictingacuteradiation induced xerostomia in head and neck Cancer using MR and CT Radiomics of parotid and submandibular glands. Radiat. Oncol. 2019;14(131).

9.) Kann BH, Aneja S, Loganadane GV, Kelly JR, Smith SM, Decker RH et.al. Pretreatment Identification of Head and Neck Cancer Nodal Metastasis and Extranodal Extension using Deep Learning Neural Networks. Sci.Rep. 2018;8.

10.) Shen H, WangY, Liu D, LvR, Huang Y, Peng C et.al. Predicting Progression-Free Survival Using MRI-Based Radiomics for Patients with Nonmetastatic Nasopharyngeal Carcinoma. Front. Oncol. 2020;10.

11.) Gomes JPP, Ogawa CM, Silveira RV, Castellano G, De Rosa CS, Yasuda CL et.al. Magnetic resonance imaging texture analysis to differentiate ameloblastoma from odontogenic keratocyst. Nature. 2022;12.

12.) Liu Y, Zheng J, Zhao J, Yu L, Lu X, Zhu Z et.al. Magnetic resonance image biomarkers improve differentiation of benign and malignant parotid tumors through diagnostic model analysis. Oral Radiol. 2021.

13.) Lysenko AV, Yaremenko AI, Zubareva AA, Shirshin AV, Lyubinov AI, Ivanova EA. Application of radiomics in the differential diagnosis in ameloblastomas and dentigerous cysts. Part 2. Cell Ther Transplant.2022; 11(3-4): 93-98.

14.) van Dijk LV, Fuller CD. Artificial Intelligence and Radiomics in Head and Neck Cancer Care: Opportunities, Mechanics, and Challenges. ASCO Educ Book. 2021;225-235.