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Perspectives of radiomics analysis in differential diagnosis of jaw neoplasms

Anna V. Lysenko [1], Andrey I. Yaremenko [2], Aleksandr I. Lyubimov [3], Vladimir M. Ivanov [4], Roman U. Shipov [4], Elizaveta A. Ivanova [1]

[1] Department of Maxillofacial Surgery, Research Institute of Dentistry and Maxillofacial Surgery, St. Petersburg, Russia
[2] Department of Maxillofacial Surgery, Pavlov University, St. Petersburg, Russia
[3] 1st Department for Surgeons' Advanced Training, Kirov's Military Medical Academy, St. Petersburg, Russia
[4] Peter the Great St. Petersburg Polytechnic University, St. Petersburg, Russia

Dr. Anna V. Lysenko, Department of Maxillofacial Surgery, Research Institute of Dentistry and Maxillofacial Surgery, Pavlov University, 44 Petrogradskaya Emb., 197101, St. Petersburg, Russia

Phone: +7 (812) 429-03-33
E-mail: lysenko.anna@mail.ru

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Summary

Radiomics extracts information from biomedical images using specific data characterization algorithms. This information – radiomic features – is traditionally unmeasured in conventional radiological images. After converting them into mathematical models, one can combine them with clinical and histological data to build prediction models simplifying diagnosis and treatment selection. Our study describes this approach and its opportunities in jaws neoplasm diagnostics. The prognostic and predictive potential of radiomics, combined with clinical data, could help the decision-making process and could lead to individualized surgical approach for jaw neoplasm. This method has the potential of more accurately assessing, classifying, risk stratifying, and guiding the management of jaw neoplasm. Radiomics has been gaining popularity due to potential applications in disease quantification, predictive modeling, treatment planning, and response assessment – paving way for the advancement of personalized medicine.

Keywords

Radiomics, jaw neoplasms, CT scan, predictive biomarker, prognostic indicator.

Introduction

Jaws host to a wide variety of cysts and neoplasms due to multiple tissues involved in tooth formation [1]. Numerous benign jaw tumors and several cysts of both odontogenic and nonodontogenic origin can exhibit a biologically aggressive course being incredibly challenging diagnostically [1, 2]. Clinical and radiographic findings of jaw lesions are often misleading and usually only the histologic examination can clarify the diagnosis [3]. Some jaw neoplasms have identic radiographic features and, conversely, some cysts can appear histologically identical and cannot be defined without radiographic findings[3]. The diagnosis of odontogenic lesions requires knowledge of a clinical and, especially, an associated radiographic features [3, 4]. But often it is necessary to have an idea about the nature of the formation already at the stage of X-ray study to have an opportunity to determine surgical tactics [5, 6].

Radiomics – "radi-" deriving from the science of radiology and "-omics" to indicate mapping of the human genome – is a rapidly evolving field providing non-invasive way to characterize tissues and organs using features extracted from standard-of-care medical imaging [7]. Radiomics is a quantitative imaging[7]. It implies the extraction of many features from medical images and its conversion to high-dimensional data [7, 8]. The main principle of radiomics is that pixels of an image and their relationships, contain information on phenotype, pathophysiology, and biology of a tissue [8]. In addition, we can extract hidden data from the medical image by using a quantitative analysis, thereby making the description of the radiograph more objective and entire. This idea is based on the theory that the signs obtained with the help of radiomics reflect the mechanisms that occur in formation at the genetic and molecular levels [9]. The goal of radiomics is to create a mathematical model and algorithm helping to analyze X-ray data and to characterize the pathophysiological features of the displayed tissues [9, 10].

Table 1. Summary of the most frequently used radiomic features

Category	Characteristic	Features
Form features	Characterize the geometric features of the study area	Size Shape Location of a lesion, etc.
First-order texture features	Describe the distribution of voxel intensities within the image region defined by the mask through commonly used and basic metrics	Mean gray-level intensity Energy Entropy Standard deviation, etc.
Higher-order texture features	Describe the statistical features of images obtained from the original ones by applying various mathematical operations	Gray Level Co-occurrence Matrix (GLCM) Features Gray Level Size Zone Matrix (GLSZM) Features Gray Level Run Length Matrix (GLRLM) Features Autoregressive model, etc.

To create such a model, one need to go through several stages [10]:

1. **Clinical task definition** – what information should we get from the image? (e.g. to determine a nature of the neoplasm).

2. **Database creation**. It is necessary to collect a database of medical images suitable for the clinical task (e. g. CBCT of patients with jaw neoplasms).

3. **Working with images:**
   a. **region of the interest (ROI) selection** – it is necessary to select an area for radiomic features collection in all images, usually the area of the neoplasm.
   b. **radiomic features extraction** – for each selected area in every image one should calculate its radiomic features (key features one can see in the Table 1).

4. **Choosing of the most informative features** from the full set of calculated.

5. **Creating of the mathematical model** based on the obtained signs. This model will predict the necessary sign – the type of tumor, the probability of malignancy, etc.

The field of radiomics has the significant potential for noninvasive differentiate of neoplasms [8, 10].

The aim of our study is to evaluate the possibility of using radiomic analysis in jaw neoplasms diagnostics.

Materials and methods

Patients' selection and examination

The study was performed in the Research Institute of Dentistry and Maxillofacial Surgery of the First Pavlov State Medical University in Saint Petersburg, Russia. We enrolled patients (N=23) showing the most common surgically assessed benign odontogenic jaw lesions. The basic requirement for enrollment was the presence of a radiologically visible osteolytic lesion of either uni- or multilocular configuration with or without an irregular outline. All patients underwent full clinical, radiological and pathological examination. An average median age of the patients was years, 12 of them were males and 11 were females. The diagnosis in all cases was confirmed by histologic examination, performed after surgical procedure. Morphological data are shown in the Table 2.

Table 2. Histological characteristics of studied tumors

№	Histological conclusion	Number of patients
1.	Jaw cysts	8
2.	Ameloblastoma	5
3.	Fibrous dysplasia	5
4.	Cementing fibroma	1
5.	Osteoid osteoma	1
6.	Odontogenic fibroma	1
7.	Myxoma	1
8.	Odontogenic calcifying epithelial tumor	1

CBCT scans were taken with the Planmeca Romexis (Finland). Secondary reconstruction yielded multiplanar data sets allowing visualization of the pathologic process in axial, coronal and sagittal plane. DICOM (Digital Imaging and Communications in Medicine) data sets were exported and saved for each individual to provide data for image segmentation.

Region of the interest (ROI) selection

Image segmentation is a process of ROI definition from the background or neighboring structures. We used the open-source software 3D Slicer for jaw lesions segmentation, performing it in a semi-automatic way. Afterward, we accomplished manual segmentation to control and ensure correct segmentation. Jaw neoplasm segmentation on CT images was based on detecting differences in density – main group. For control measurements, a segmentation of a similar zone on the healthy side of the jaw was performed – control group.

Radiomic features extraction and selection

We used the comprehensive open-source platform PyRadiomics built into 3D Slicer for radiomic analysis. The interface of the software is designed for medical images analyzing and managing the radiological data. The software processes and extracts radiomic characteristics from medical images using a large panel of hard-coded function algorithms.

We computed, extracted, and analyzed 104 radiomic features of the studied areas. These features were divided into 6 main types: 11 non-texture, 18 first-order statistics, 24 gray-level co-occurrence matrix (GLCM), 14 gray level dependence matrix (GLDM), 16 gray-level run-length matrix (GLRLM), 16 gray-level size zone matrix, and 5 neighborhood gray tone difference matrix.

Specificity of their calculation imply cross-correlation of many of them. This can lead to interpretation errors due to multicollinearity. We used the forward stepwise selection method, adding and removing according to their significance, determined by a statistical test. We also excluded non-textural ones from the comparative analysis since the shape and size of the allocated control area were determined by the operator.

Statistical analyses

We preformed statistical analyses using the IBM SPSS 22.0 (SPSS Inc., Chicago, IL) statistical software. Having the matched sample with plenty of features with non-normally distributed differences we used Wilcoxon signed-rank test for a primary comparison of groups locations. We also calculated Pearson correlation coefficient as a measure of correlation between radiomic features and groups. P values < 0.05 were regarded as indicating statistical significance.

Results

After feature extraction and selection, we obtained a subset containing 9 texture features (Tab. 3). These ones showed the least cross-correlation having statistically significant relationship with the presence of the jaw lesion.

The significantly higher correlation of the median gray level intensity within the ROI definitely attracts attention (Fig. 1). Moreover, 54 out of 92 studied texture features have strong (R >0.7) or medium (0.5 < R < 0.7) correlation with "median". It is not surprising that stepwise logistic regression with forward selection gives us model with this only variable. This fact confirms known idea that X-ray jaw neoplasm diagnosis bases on density differences detecting.

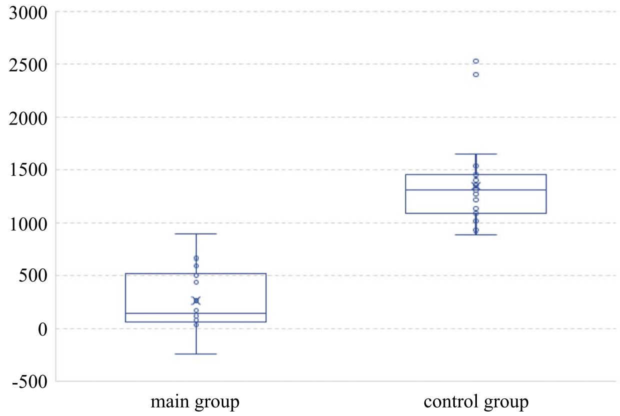

Figure 1. Median gray level intensity within region of interest in the studied groups

Statistically significant differences other most informative features displayed in the Figure 2.

Discussion

Preoperative x-ray analysis showed differences between jaw neoplasms, which can help in the differential diagnosis of jaw formations. After analysis, we found 9 texture features with significant differences between jaw lesions: median, uniformity, cluster shade, long run high gray level

Table 3. Radiomic feature subset

Feature	Feature type	Median value, quartiles		Wilcoxon statistics	Pearson, R
		main group	control group		
Median	First-order	137 [61; 513]	1313 [1111; 1429]	T = 0.0 p < 0.001	– 0.847
Uniformity	First-order	0.04 [0.03; 0.06]	0.02 [0.0; 4.2]	T = 0.0 p < 0.001	0.471
Cluster Shade	GLCM	4852 [185; 12546]	31715 [7444; 92685]	T = 16.0 p < 0.001	– 0.408
Long Run High Gray Level Emphasis	GMRLM	1273 [699; 2157]	6329 [4391; 12659]	T = 9.0 p < 0.001	– 0.466
Size Zone Non Uniformity	GLSZM	4213 [1923; 26871]	40854 [10831; 49983]	T = 0.0 p < 0.001	– 0.404
Zone Entropy	GLSZM	7.6 [7.2; 7.9]	7.8 [7.8; 8.4]	T = 12.0 p < 0.001	– 0.471
Zone Percentage	GLSZM	0.17 [0.12; 0.30]	0.44 [0.32; 0.60]	T = 1.0 p < 0.001	– 0.582
Busyness	NGTDM	2.72 [1.1; 5.6]	0.95 [0.4; 1.2]	T = 6.0 p < 0.001	0.328
Contrast	NGTDM	0.04 [0.03; 0.08]	0.15 [0.11; 0.22]	T = 0.0 p < 0.001	– 0.438

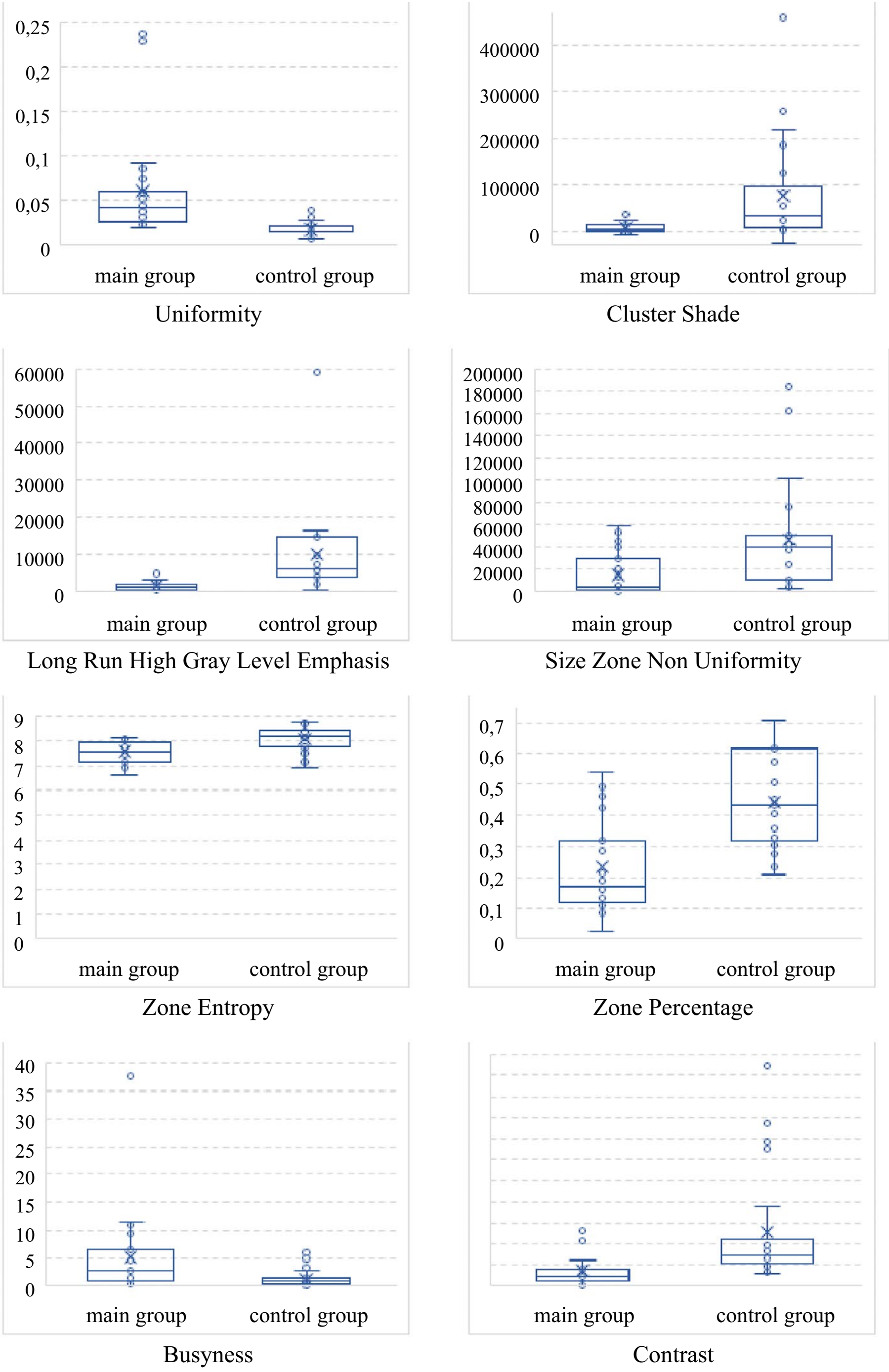

Figure 2. Informative subset of radiomic features in the studied groups

emphasis, size zone non uniformity, zone entropy, zone percentage, busyness and contrast.

Texture analysis has a potential application in the complex diagnosis of jaw neoplasms. Cystic lesions of the jaw are readily apparent on radiographs or CT, however subtle differences in internal components within the lesions are often difficult to assess quantitatively.

Texture analysis can complement histological findings and speed up treatment. Biopsy can often be uninformative because the inflammatory changes can be so extensive that it is difficult to distinguish them histologically from other cystic lesions without extensive additional tissue sampling to make a diagnosis. Non-invasive tissue analysis with texture analysis can provide more information and prevent additional invasive procedures. Texture analysis can extract mineable high-dimensional data from digital medical images and may aid in the identification and differentiation of various jaw lesions.

Conclusion

This pilot study demonstrates that differences in texture analysis features may help non-invasively differentiate several lesions of the jaw. This study adds to the limited previously published data and suggests a potentially novel image-based assessment of odontogenic cystic and lesions of the jaws, which can be considered as an adjunct to the diagnosis.

Radiomics is becoming increasingly more important in medical imaging. The progress of medical imaging data creates an environment ideal for machine-learning and data-based science.

Radiomics-based decision-support systems for precision diagnosis and treatment can be a powerful tool in modern medicine. Hence, the radiomic image analysis may effectively contribute to clinical decision-making and treatment management.

Conflict of interests

None reported.

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Перспективы использования радиомического анализа для дифференциальной диагностики новообразований челюстей

Анна В. Лысенко [1], Андрей И. Яременко [2], Александр И. Любимов [3], Владимир М. Иванов [4], Роман Ю. Шипов [4], Елизавета А. Иванова [1]

[1] Отдел челюстно-лицевой хирургии НИИ стоматологии и челюстно-лицевой хирургии, Санкт-Петербург, Россия
[2] Кафедра челюстно-лицевой хирургии, Первый Санкт-Петербургский государственный медицинский университет им. акад. И. П. Павлова, Санкт-Петербург, Россия
[3] 1-е отделение усовершенствования хирургов, Военно-медицинская академия им. С.М. Кирова, Санкт-Петербург, Россия
[4] Санкт-Петербургский политехнический университет Петра Великого, Санкт-Петербург, Россия

Резюме

Радиомика извлекает информацию из биомедицинских изображений, используя специальные алгоритмы характеристики данных. Эта информация – радиомические признаки – традиционно не измеряется в обычных радиологических изображениях. После преобразования их в математические модели их можно комбинировать с клиническими и гистологическими данными для построения прогностических моделей, упрощающих диагностику и выбор лечения. В нашем исследовании описан данный подход и его возможности в диагностике новообразований челюстей. Прогностический и прогностический потенциал радиомики в сочетании с клиническими данными может помочь в процессе принятия решений и может привести к индивидуальному хирургическому подходу при лечении новообразований челюстей. Этот метод имеет потенциал для более точной оценки, классификации, стратификации риска и управления лечением новообразований челюсти. Радиомика набирает популярность благодаря потенциальным приложениям для количественной оценки заболеваний, прогностического моделирования, планирования лечения и оценки ответа, что способствует развитию персонализированной медицины.

Ключевые слова

Радиомика, новообразования челюстей, компьютерная томография, прогностический биомаркер, прогностический индикатор.