Radiomics in RayPlus: a Web-Based Tool for Texture Analysis in Medical Images

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Published online: 22 October 2018
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Abstract

Radiomics has been shown to have considerable potential and value in quantifying the tumor phenotype and predicting the treatment response. In most scenarios, the commercial and open-source software programs are available for quantitative analysis in medical images to streamline radiomics research. However, at this stage, most of these programs are local applications and require users to have experience in programming and software engineering, which clinicians usually do not have. Therefore, in this article, a web-based tool was proposed to flexibly support radiomics research workflow tasks. Radiomics in RayPlus requires zero installation, is easy to maintain, and accessible anywhere via any PC or MAC with an Internet connection. The system provides functions including multimodality image import and viewing, ROI definition, feature extraction, and data sharing. As a web application, it appears an effective way to multi-institution and multi-department collaborative radiomics research and moreover, its transparency, flexibility, and portability can greatly accelerate the pace of clinical data analysis.

Keywords Medical image · Texture analysis · Radiomics · Software design · Web technology

Introduction

Multimodality imaging procedures play an indispensable role in clinical diagnosis and treatment in modern medicine. The typical medical images are computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET). Nowadays, clinicians acquire a fast-growing number of the medical images from patients, and the use of these images has greatly expanded from a diagnostic tool to a more central position in the context of individualized medicine [1–4].

At present, the effective utilization of this large amount of medical imaging data is still challenging. Recently, there is an important advancement in quantitative imaging analysis termed as “radiomics” [5]. Radiomics is the high-throughput extraction of advanced quantitative features from medical

images, usually using mathematical texture analysis. Previous work has shown that these features may provide great potential to both improve tumor diagnosis and act as proxies of genetics and tumor response [6–10]. It significantly improves our ability to stratify patients for personalized treatments.

The radiomics tools now available can provide necessary information to clinicians. MaZda is a tool for image texture analysis that is widely used for radiomics research [11]. The original article has been cited more than 200 times. It includes tools including contouring, feature reduction, and analysis but only runs on MS Windows operating system. Chang-Gung image texture analysis (CGITA) and computation environment for radiotherapy research (CERR) are both open-source MATLAB-based programs for texture analysis in medical images [12, 13]. CGITA is developed for the analysis of molecular images while CERR is widely used in radiotherapy research, and work is underway to add a radiomics toolbox to the platform [14, 15]. SlicerRadiomics is an extension for 3DSlicer that encapsulates pyradiomics library [16, 17]. 3DSlicer is an open-source software package for image analysis, includes many extensions, and has been used in various influential radiomics projects. However, because of their intended use, their functionality is limited. For example, modifying feature parameters and reviewing results seem impossible with these two tools. Imaging Biomarker Explorer (IBEX) is an open-source platform for radiomics image feature

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extraction, based on MATLAB and C++ programming languages [18]. It displays the processed images to determine the settings, and its flexibility allows the user to optimize the settings for an application. Importantly, IBEX is able to export entire feature sets, so users from other institutions can easily apply the same features. Although IBEX has many features, it can only run on Windows system, and a few of dependency files are needed (vc2005redist, vc2012redist), which make its accessibility limited.

Usually, the clinicians do not have experience in programming and software engineering. The lack of an easy-to-maintain and accessible tool has made previous radiomics research difficult to clinicians, let alone sharing the data and models to validate between departments and institutions. At least three problems may cause the difficulties to independent validation of published work. Firstly, the feature names are varied when implemented by different groups. Secondly, the parameters used for calculating sometimes are invisible to clinicians in several tools or software. And thirdly, because the region of interest (ROI) is usually segmented by different tools, it makes the reproducibility a tough task. As a result, the validation and application of radiomics research findings in clinical practices have been notably impeded.

We developed a web-based tool for texture analysis in medical images in RayPlus to flexibly support common radiomics workflow tasks such as multimodality image data import and review, development of feature extraction algorithms, ROI definition, and consistent data sharing among multiple institutions. It is a self-contained and ready-to-use software, with preimplemented typical data importers, image filters, and feature extraction algorithms. Because of its browser/server design, image data, ROIs, and feature algorithm-related data can be easily and consistently shared so that users from different institutions can reproduce the results of radiomics workflows. It requires zero installation and is easy-to-maintain. The system is also based on a well-known Web browser user interface, making it very user-friendly, and on multiplatform intranet technologies, allowing access with any existing device.

Methods

Module Design

Radiomics research regularly comprises four stages: patient cohort identification and image data import, region of interest (ROI) segmentation in the images, features extraction, and statistical analysis and modeling [19]. Radiomics in RayPlus follows this workflow.

Our previously related work, RayPlus, is a web-based platform for medical image processing [20]. Based on its model-view-controller (MVC) architecture, radiomics in RayPlus continues the consistency of design. The MVC view component represents the workspace of reviewing multimodality images

with delineated structures and is implemented on browser side. The MVC controller and model component represent image preprocessing, parameter, and calculation algorithms and are implemented on server side. Because of the unit testing implementation, users have the option of reviewing the corresponding result at each stage. Thanks to the MVC technique, a complete module can be exported or imported easily such as preprocessing algorithms, feature extraction algorithms, model formulas, and model parameters. This greatly helps maintain data consistency and result reproducibility when outside institutions attempt to validate feature extraction algorithms and response models.

Radiomics in RayPlus has four functional modules: delineation, segmentation, histogram analysis, and features extraction, as shown in Fig. 1. Image data import and viewer used RayPlus existed module. Image data is uploaded via the browser by hyper text transfer protocol secure (https) protocol, and medical images are rendered in HTML5 canvas element for review. To deal with ROI definition, browser-side delineation and server-side segmentation are developed with WebSocket connection to keep an effective interaction. Histogram analysis and feature extraction are fully calculated on server side. Hence, once a new version or upgrade of the system is installed on the host server, all users can access it straight away.

As a web-based system, RayPlus cannot connect to PACS and RIS/HIS at present so the images will need to be exported from the PACS and upload through the website. Since radiomics research usually needs a large number of image data, there is a local uploader for more executable. The current online system can import DICOM [21] and RAW data.

Image viewer is a basic module in RayPlus for navigation and visualization of multimodality medical images. Users can navigate to different images in axial, coronal, and sagittal orientations, quickly go to the corresponding anatomy using the intersection tool, measure the distance and angle, select the preset window/level setting or color map and manually set them. Although the viewer is a website, it could be used as usual local viewer, as shown in Fig. 2.

ROI Definition

Accurate ROI definition is an important step in the radiomics workflow. There is no universal segmentation algorithm that can work for all medical image applications. With proper parameter settings, there are many segmentation algorithms that could segment the region of interest automatically or semi-automatically. However, the result of each algorithm can be different even for the same algorithm performed multiple times with different initializations [22]. Hence, we supply users with WYSIWIG (“what you see is what you get”) ROI definition.

We implemented two segmentation methods of the ROI definition: 2D- and 3D-delineated contouring. 2D-delineated contouring is a manual segmentation, and users delineate the ROI slice by slice. Between two delineated slices, bilinear

Fig. 1 The functional modules of Radiomics in RayPlus and its workflow. The delineation is implemented on browser side while the other modules are implemented on server side

interpolation can be applied to get the final result. To regular shape ROIs, it will fulfill the requirement. But when it comes to irregular shape ROIs, even though it is a straightforward solution, it may bring problems such as time wasting and high inter-user variability. To minimize the inter-user variability and increase consistency in ROI, the 3D-delineation is a semi-automatic contouring tool. In 3D-delineation, users need to overlay the ROIs on three different orientations, as shown in Fig. 3. Based on the manual 3D-delineation, distance map (DM), OSTU, and morphological filtering algorithms were

used to segment the ROI automatically [23, 24]. Both methods can be modified by 2D-delineated contours to get an accurate ROI.

Histogram Analysis

Histogram analysis gives a graphical and intuitive description of the delineated ROI. In medical images, a particular range of the pixels usually represents a particular human tissue or component. In CT images, for instance, the pixels in an ROI of –

Fig. 2 The RayPlus viewer of MPR display. The three planes are shown: coronal (upper left), sagittal (bottom left), and axial (right). The green crosses show the position of the other two planes and can be moved using the mouse, causing the positions of the other two planes to change

Fig. 3 The 3D-delineation. User overlays the ROIs on three different orientations (a) and gets the segmentation (b)

100~30 HU may represent fat. The component of ROIs may indicate the diverse subtype of the lesion.

After ROI delineation, based on the histogram of ROI, it can be initially analyzed before feature extraction with quantitative statistics of the different value range in the ROI, including minimum, maximum, volume, mean, variance and radio, as shown in Fig. 4. More histogram-based but not so obvious features such like entropy, skewness, and kurtosis are calculated in the feature extraction.

Preprocessing and Feature Extraction

In this step, users specify the image preprocessing algorithms applied to the image and the feature categories and their parameters. Figure 5 is a screenshot of the graphical user interface (GUI). By clicking the “calculation” button in the workspace, users can review the intermediate results of feature extraction. Furthermore, the results can be stored and downloaded in .csv format file for statistical analysis in R or SPSS.

There are five filters to do the image preprocessing: logarithm, exponential, Laplacian of Gaussian (LoG), Wavelet, and Gabor, as shown in Table 1 [25–27]. Logarithm and exponential filters are used to rescale on the range of the initial original image. LoG filter is used to emphasize areas of gray level change, and the sigma defines how coarse the emphasized texture should be. Wavelet and Gabor filters are used to separate the image by frequency bands while it retains the spatial information in each band. Wavelet filter computes eight decompositions in each of the three dimensions with six kernel functions, and Gabor filter computes 13 orientations with five scales.

The feature categories currently available in radiomics in RayPlus are listed in Table 2, including histogram features, volumetric features, morphologic, and texture features including gray-level co-occurrence matrix (GLCM) features, gray-level size zone matrix (GLSZM) features, and gray-level run length matrix (GLRLM) features [28–33].

Three settable parameters are addressed on user interface. “Voxel Array Shift” ensures non-negative values in the image

Fig. 4 The histogram analysis of a tumor. The colorful bricks of the histogram represent corresponding component listed on the table. The minimum and maximum of a component can be set manually while the other statistics are calculated automatically

Fig. 5 The GUI of feature extraction. Users have the option of preprocessing, feature calculation, and parameters. The results are listed in table and can be downloaded

in feature energy and total energy. “Binwidth” determines the fixed width of each bin in histogram feature calculation whose default value is 25. “Distance” presents the distances between the center voxel and the neighbor in texture feature calculation. In some feature calculation, a very small number are added to prevent logarithm of zero.

Implementation and Results

We applied HTML5 and CSS3 to layout the user interaction facilities and JavaScript to accomplish the browser-side controlling and alter the content that is displayed. It has been designed to use the native HTML and JavaScript capabilities of browsers. Consequently, browser plugins are not necessary, and the hardware requirements of the client remain low. On the server side, the calculation was implemented by C++ language. The VTK [34] and the Eigen library [35] were used.

The results of feature extraction in radiomics in RayPlus were compared with IBEX and SlicerRadiomics using a ROI of $45 \times 40 \times 18$ voxels without any filtering. The errors of all features are less than one ten thousandth. The reason of errors is considered as the difference of precision between different programming languages.

After creating the first prototype, an evaluation was carried out with ten clinicians. The clinicians were from two different hospitals in Shenzhen and Wuhan, including six radiologists

and four oncologists. One radiologist was a professor from the Department of Radiology at the Peking University Shenzhen Hospital, one oncologist was an associate professor from the Department of Oncology at the Wuhan Union Hospital, and others are young doctors and medical students from these two departments. All of the clinicians had experience with other analysis tools in medical images. Their inputs were taken using a questionnaire and interviews.

The prevailing view was that the web-based tool was the best choice for the radiomics research. Some clinicians tried their projects by radiation therapy planning systems. Although most of the clinicians were very experienced in using these systems, however, the compatibility between different systems and tools left a lot of manual work to be done. Furthermore, a web-based tool gave them more convenience and flexibility. Security and privacy protection was another focus point. There were radiologists concerned about the privacy of the image data on the cloud. On the other hand, some of them suggested that we should try to connect with PACS/RIS in a future version to avoid the time-consuming uploading.

At the time of this writing, radiomics in RayPlus is being used for a project about non-small cell lung cancer (NSCLC) research that involves two institutes. It can be accessed at www.rayplus.net.

Discussion

Radiomics in RayPlus provides a promising approach to enable clinicians to perform radiomics research without any installation and device limitation. Meanwhile, the potential disadvantages of a web-based tool are obvious as well. The latency is limited by the network bandwidth, and the high concurrency will lead to degradation in performance. The RayPlus architecture runs on AliCloud (www.aliyun.com) currently, and it can be easily migrated to Amazon Web Service and Microsoft

Table 1 The preprocessing filters of radiomics in RayPlus

Filter	Comment
LoG	Emphasize areas of gray level change
Logarithm	Rescale on the range of the original image
Exponential	
Wavelet	Separate the image by frequency bands
Gabor	

Table 2 The image features of radiomics in RayPlus

Category	Comment	Features
Histogram	Histogram features describe the distribution of voxel intensities in the ROI.	Energy, entropy, minimum, percentiles, maximum, mean, median, range, mean absolute deviation, robust mean absolute deviation, root mean squared, skewness, kurtosis, variance, and uniformity
Volumetric	Volumetric features describe the shape of the ROI in 3D. These features are quantitative descriptors in a radiology report.	Volume, surface area, surface area to volume ratio, maximum 3D diameter, and maximum 2D diameter
Morphologic	Morphologic features describe the shape of the ROI in 3D. Usually, these features are semantic descriptors in a radiology report.	Sphericity, compactness, spherical disproportion, major axis, least axis, minor axis, elongation, and flatness
Texture	GLCM	Autocorrelation, joint average, sum average, joint entropy, sum entropy, joint energy, sum squares, cluster shade, cluster tendency, contrast, correlation, difference average, difference entropy, difference variance, homogeneity, maximum probability, inverse difference moment, inverse difference moment normalized, inverse difference, inverse difference normalized, informal measure of correlation, and maximum probability
	GLSZM	Small area emphasis, large area emphasis, gray level non-uniform, gray-level non-uniform normalized, size zone non-uniform, gray-level non-uniform normalized, zone percentage, gray-level variance, zone entropy, zone variance, low gray-level zone emphasis, high gray-level zone emphasis, small area low gray-level emphasis, small area high gray-level emphasis, large area low gray-level emphasis, and large area high gray-level emphasis
	GLRLM	Short-run emphasis, long-run emphasis, gray-level non-uniformity, gray-level non-uniformity normalized, run length non-uniformity, run length non-uniformity normalized, run percentage, gray-level variance, run variance, run entropy, low gray-level run emphasis, high gray-level run emphasis, short-run low gray-level emphasis, short-run high gray-level emphasis, long-run low gray-level emphasis, and long-run high gray-level emphasis

Azure. An important issue is the mechanism for security and privacy protection. When the image data is uploading, the patient information such as patient name and patient ID will be erased. Additionally, RayPlus uses role-based access control and secure sockets layer (SSL) to protect the system from vicious and illicit read/write of data. In the future, more work about the security is planned.

Modeling in quantitative imaging analysis is a crucial topic involving how to use the features in diagnosis or treatment. There are many approaches that can be used to modeling, such as logistic regression, principal component analysis, and random forest. The techniques can differ greatly depending on applications. At this point, establishing a universal workflow for model development is not easy to achieve, so the presently online version does not provide an environment for modeling.

Now, we have been working on the next version of radiomics in RayPlus, mainly focused on the efficiency and easy using of collaborative project. The adding functions include more data formats support (e.g., NIfTI format) and providing common algorithms for modeling.

Conclusion

Radiomics in RayPlus implemented the framework for radiomics and quantitative imaging analysis. It serves as a web application with zero installation and well-designed graphical user interface to accelerate collaborative work. The clinicians can focus on their applications and development of radiomics workflow without worrying about data consistency and review, algorithm reliability, and result reproducibility. It provides a web-based tool for quantitative imaging analysis and can be a convenient and powerful tool to streamline common radiomics workflow tasks. As a web application, it appears an effective way to multi-institution and multi-department collaborative research, which is very important to radiomics. Moreover, its transparency, flexibility, and portability can greatly accelerate the pace of clinical data analysis.

Acknowledgments We wish to express our gratitude to Dr. Ruiguang Zhang and Dr. Quan Chen from the Department of Radiology, Wuhan Union Hospital, Wuhan, China, for all the inspiring discussions. And thanks to Mrs. Feifei Liu for the user interface design.

Funding information Dr. Rong Yuan acknowledges financial support from SZSM201612071.

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