How does Radiomics actually work? – Review
Wie geht Radiomics eigentlich? – Review

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ABSTRACT
Personalized precision medicine requires highly accurate diagnostics. While radiological research has focused on scanner and sequence technologies in recent decades, applications of artificial intelligence are increasingly attracting scientific interest as they could substantially expand the possibility of objective quantification and diagnostic or prognostic use of image information. In this context, the term “radiomics” describes the extraction of quantitative features from imaging data such as those obtained from computed tomography or magnetic resonance imaging examinations. These features are associated with predictive goals such as diagnosis or prognosis using machine learning models. It is believed that the integrative assessment of the feature patterns thus obtained, in combination with clinical, molecular and genetic data, can enable a more accurate characterization of the pathophysiology of diseases and more precise prediction of therapy response and outcome. This review describes the classical radiomics approach and discusses the existing very large variability of approaches. Finally, it outlines the research directions in which the interdisciplinary field of radiology and computer science is moving, characterized by increasingly close collaborations and the need for new educational concepts. The aim is to provide a basis for responsible and comprehensible handling of the data and analytical methods used.

Key points:
▪ Radiomics is playing an increasingly important role in imaging research.
▪ Radiomics has great potential to meet the requirements of precision medicine.
▪ Radiomics analysis is still subject to great variability.
▪ There is a need for quality-assured application of radiomics in medicine.

Citation Format

ZUSAMMENFASSUNG
Introduction

The demands of personalized precision medicine require highly accurate diagnostics. Although in recent decades radiological research has focused on the evaluation of scanner and sequence technologies for more accurate disease diagnosis, scientific interest is now focused on current implementations of artificial intelligence (AI) for optimized diagnostics. The implementation possibilities for AI techniques in radiology are manifold: automated lesion detection and characterization, creation of biobanks, dose optimization, structured reporting and radiomics [2, 3]. For the sake of completeness, it should not be forgotten that AI techniques are also used in the latest generation of scanners to optimize data acquisition itself.

The term “radiomics” describes the extraction of quantitative features from image data such as examinations using computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET) and correlation with clinical, genetic or molecular data using AI methods such as machine learning or deep learning. The concept appears promising: using AI methods, information can be extracted from image data that goes far beyond what the human eye can detect. It is assumed that the assessment of these characteristics and feature patterns obtained from the image data when combined with clinical, molecular and genetic data can enable a more precise characterization of the pathophysiology of diseases as well as a statement on therapy response and probable outcome. Some of the applied techniques have been known for decades, but have been developed substantially in recent years, opening up new approaches to the automated exploitation of image information. Publications on this topic go back to the end of the 1940s, and models such as neural networks were also intensively researched in the 1980s [4]. Optimized computing power together with methodological advances and increasing availability of large amounts of data to facilitate the training of models have led to a resumption of this work with impressive results [5], resulting in a more timely and efficient utilization of these techniques – a basis for subsequent potential clinical implementation. The scope of application in imaging diagnostics is diverse and ranges from oncological to cardiac and musculo-skeletal diagnostics.

Radiomics is playing an increasingly important role in imaging research due to its great potential to meet the requirements of precision medicine. Numerous studies provide an overview of the underlying concepts [6, 7]. However, it should be noted that every single step of radiomics analysis is subject to great variability. A responsible, comprehensible handling of the submitted data and applied analysis methods is therefore an indispensable basic requirement. Due to the novel way of dealing with image data, an even closer collaboration with medical imaging computing data scientists will be required in the future, as well as a restructuring of radiological training.

Radiomics, which describes a subset of AI implementation possibilities in radiology, follows an explicit scheme according to which image data is processed, segmented and analyzed. This overview article will present and explain this analysis.

Radiomics Hands-on

The 6 Phases of Radiomics Analysis

A radiomics analysis can essentially be divided into 6 steps: (i) data acquisition, (ii) definition of a region of interest (ROI), (iii) data (pre) processing, (iv) feature extraction, (v) selection of the features relevant to the problem and (vi) classification (Fig. 1) [8].

Data Acquisition

The way in which the data are acquired has a significant influence on the result of the radiomics analysis; therefore it is desirable to use imaging protocols that are standardized, reproducible and comparable [9]. For example, a study by Waugh et al. showed that a higher time-to-repetition (TR) enables better discrimination of texture features in breast MRI [10]. In their publication, Baessler et al. systematically tested the factors influencing the choice of sequence in MRI on feature robustness [11]. A high-resolution FLAIR sequence provided the highest feature robustness. On the other hand, the T2-weighted sequence with lower resolution acquired in comparison achieved the poorest feature stability. There were also differences in robustness among the various feature groups (matrices). The shape and GLZLM (GrayLevel Zone Length Matrix) groups achieved the highest robustness, while the histogram-based features were the least robust [11]. For this reason, Lambin et al. call for a stratified approach to data selection: detailed disclosure of imaging sequences, robust segmentation e.g. by multiple evaluators, phantom studies and imaging at different time points [9].

ROI Definition

Optimal ROI Size and Feature Maps

After data acquisition, the region of interest (ROI) is defined, which describes the area over which further analysis will occur. Most of the work related to radiomics deals with issues in oncology, and the ROI is typically set to identify the location of a lesion and apply the subsequent analysis accordingly. Here, too, there is great variability in the methodology of the ROI definition, which in turn has significant influence on the result. Three different ROI
Image Processing and Preprocessing

Image preprocessing precedes the actual feature extraction. Depending on the data set, this includes interpolation, signal normalization and gray value reduction.

Interpolation of the image data allows standardization of the spatial resolution in data. Studies have shown that higher resolution allows optimized feature extraction. In a study by Mayerhoefer et al., the best results were obtained with interpolation factors of 2–4 [1]. Comparability of the features obtained in the analysis is relevant for signal normalization. Three main approaches are described in the literature: min/max, the Z score and mean ± 3σ [18]. The “mean ± 3σ” method means that the intensities are normalized within μ ± 3σ, where μ describes the mean value of the gray values within the ROI, and σ the standard deviation. Consequently, gray values that are outside the range [μ - 3σ, μ + 3σ] are not considered for the analysis.

The reduction of gray values in the form of so-called “binning” during feature extraction results in an improvement in the signal-to-noise (SNR) ratio. It maps the gray value range occurring in the image as frequency distributions. Gray values used in the literature are 16, 32, 64, 128 and 256. In their study, Chen et al. recommend using 32 gray values [19], whereas Mahmoud-Ghonheim et al. use 128 [20].

Image preprocessing has a significant influence on feature robustness. Using a phantom, Wichmann et al. systematically investigated the influence of spatial resolution, gray value reduction and signal normalization on feature robustness [21]. They demonstrated that only 4 features, skewness (histogram), volume [ml] (shape), volume [vox] (shape) and run length non-uniformity [RLNU] (Gray Level Run Length Matrix, GLRLM), RLNU (GLRLM), remained robust over the variation of all parameters.

This clearly shows that specific recommendations for image processing are necessary.

Feature Extraction

Features that are typically used for radiomics analyses can be divided into 4 primary groups: First Order Statistics, Shape, and Texture Features, as well as Features obtained by wavelet transformation of relevant image sections [16]. The group of Texture Feature matrices include the matrices Gray Level Co-occurrence Matrix (GLCM), GLRLM, Gray Level Size Zone Matrix (GLSZM), Gray Level Dependence Matrix (GLDM) and Neighboring Grey Tone Difference Matrix (NGTDM). Multiple features are subsumed under each of these matrices. It should be noted that there is great variation in nomenclature, methodology and software implementation [22]. ▶ Table 1 provides a typical overview of the features of the individual matrices [23]. At the same time, efforts are being made towards the invariance of features with respect to protocols and corresponding standardization efforts [24]. The selection of feature extractors is based on the expectation of which characteristics are relevant for the analysis, and accordingly, extractors are often chosen or constructed that are invariant to, for example, global rotation or very low frequency gray value changes.

Baessler et al. impressively demonstrated the diagnostic value of texture features for the diagnosis of myocarditis using MRI.

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The definition and introduction of an RQS is an essential step to achieve independent assessment of different feature selection and classifier methods [28]. The separation between data used for the training or development of the prediction models and selection of features and those used as validation data is essential. This is necessary to ensure an overly optimistic assessment of the forecast accuracy. As a middle course, cross-validation can be used, in which the training and test data set are iteratively separated. It must be taken into account that the respective test data could be the basis for modeling decisions and therefore do not allow a completely independent assessment – a separate validation data set is required for this.

Parmar et al. have tested the stability and predictive performance of different feature selection and classifier methods [28]. Their results showed that among the different feature selection methods, the Wilcoxon test-based method (WLX) and mutual information maximization (MIM) achieved the highest stability. Among the classifiers, Bayesian achieved the best performance with an AUC value of 0.64 (SD± 0.05).

Due to the great variability of radiomics analysis, standardization of data collection, evaluation criteria and reporting is necessary. To this end Lambin et al. have defined a “Radiomics Quality Score” (RQS) [9], which describes a standardized analytical process starting with data selection, through imaging, feature extraction, analysis and modeling, as well as report generation. Each of these steps is divided into several sub-steps for which there are scoring points. The maximum achievable score (total RQS) is 36. The definition and introduction of an RQS is an essential step to...
wards a quality-assured application of radiomics in medicine, which aims to counter the variability problem of analysis – which already begins with the primary image data acquisition – by a dedicated reporting of the individual steps. The introduction of an RQS score seems particularly relevant in view of the expected future connection of clinical decision support systems with radiomic data [9].

Where does this lead?

In addition to standard radiomics approaches that use predefined features, recent development in the field of deep learning, the possibility to combine feature design and predictive model training and to implement them with effective model architectures, plays an increasingly important role in the use of complex image data [7, 29]. On the one hand, this enables the use of image information that is not covered by traditional features. On the other hand, there is the problem of interpreting deep learning models, the solution of which is increasingly the focus of research [30].

Summary

Radiomics is playing an increasingly important role in medical imaging due to its great potential to meet the requirements of precision medicine. However, it should be noted that every single step of radiomics analysis is subject to great variability. A responsible, comprehensible handling of the submitted data is therefore an indispensable basic requirement. In the future, radiomics will require an even closer collaboration with medical imaging computing data scientists, as well as a restructrering of radiological training.

Conflict of Interest

The authors declare that they have no conflict of interest.

References


