

## Radiomics: the process and the challenges

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### Abstract

“Radiomics” refers to the extraction and analysis of large amounts of advanced quantitative imaging features with high throughput from medical images obtained with computed tomography, positron emission tomography or magnetic resonance imaging. Importantly, these data are designed to be extracted from standard-of-care images, leading to a very large potential subject pool. Radiomics data are in a mineable form that can be used to build descriptive and predictive models relating image features to phenotypes or gene–protein signatures. The core hypothesis of radiomics is that these models, which can include biological or medical data, can provide valuable diagnostic, prognostic or predictive information. The radiomics enterprise can be divided into distinct processes, each with its own challenges that need to be overcome: (a) image acquisition and reconstruction, (b) image segmentation and rendering, (c) feature extraction and feature qualification and (d) databases and data sharing for eventual (e) ad hoc informatics analyses. Each of these individual processes poses unique challenges. For example, optimum protocols for image acquisition and reconstruction have to be identified and harmonized. Also, segmentations have to be robust and involve minimal operator input. Features have to be generated that robustly reflect the complexity of the individual volumes, but cannot be overly complex or redundant. Furthermore, informatics databases that allow incorporation of image features and image annotations, along with medical and genetic data, have to be generated. Finally, the statistical approaches to analyze these data have to be optimized, as radiomics is not a mature field of study. Each of these processes will be discussed in turn, as well as some of their unique challenges and proposed approaches to solve them. The focus of this article will be on images of non-small-cell lung cancer.

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### 1. Introduction

“Radiomics” involves the high-throughput extraction of quantitative imaging features with the intent of creating

mineable databases from radiological images [1]. It is proposed that such profound analyses and mining of image feature data will reveal quantitative predictive or prognostic associations between images and medical outcomes. In cancer, current radiological practice is generally qualitative, e.g., “a peripherally enhancing spiculated mass in the lower left lobe.” When quantitative, measurements are commonly limited to dimensional measurements of tumor size via one-dimensional (Response Evaluation Criteria In Solid Tumors

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[RECIST]) or two-dimensional (2D) (World Health Organization) long-axis measures [2]. These measures do not reflect the complexity of tumor morphology or behavior, nor, in many cases, are changes in these measures predictive of therapeutic benefit [3]. When additional quantitative measures are obtained, they generally average values over an entire region of interest (ROI).

There are efforts to develop a standardized lexicon for the description of such lesions [4,5] and to include these descriptors via annotated image markup into quantitative, mineable data [6,7]. However, such approaches do not completely cover the range of quantitative features that can be extracted from images, such as texture, shape or margin gradients. In focused studies, texture features have been shown to provide significantly higher prognostic power than ROI-based methods [8–11]. The modern rebirth of radiomics (or radiogenomics) was articulated in two papers by Kuo and colleagues. Following a complete manual extraction of numerous (>100) image features, a subset of 14 features was able to predict 80% of the gene expression pattern in hepatocellular carcinoma using computed tomographic (CT) images [12]. A similar extraction of features from contrast-enhanced magnetic resonance images (MRI) of glioblastoma was able to predict immunohistochemically identified protein expression patterns [13]. Although paradigm shifting, these analyses were performed manually, and the studies were consequently underpowered. In the current iteration of radiomics, image features have to be extracted automatically and with high throughput, putting a high premium on novel machine learning algorithm development.

The goal of radiomics is to convert images into mineable data, with high fidelity and high throughput. The radiomics enterprise can be divided into five processes with definable inputs and outputs, each with its own challenges that need to be overcome: (a) image acquisition and reconstruction, (b) image segmentation and rendering, (c) feature extraction and feature qualification, (d) databases and data sharing and (e) ad hoc informatics analyses. Each of these steps must be developed de novo and, as such, poses discrete challenges that have to be met (Fig. 1). For example, optimum protocols for image acquisition and reconstruction have to be identified and harmonized. Segmentations have to be robust and involve minimal operator input. Features have to be generated that robustly reflect the complexity of the individual volumes, but cannot be overly complex or redundant. Informatics databases that allow for incorporation of image features and image annotations, along with medical and genetic data, have to be generated. Finally, the statistical approaches to analyze these data have to be optimized, as radiomics is not a mature field of study. Variation in results may come from variations in any of these individual processes. Thus, after optimization, another level of challenge is to harmonize and standardize the entire process, while still allowing for improvement and process evolution.

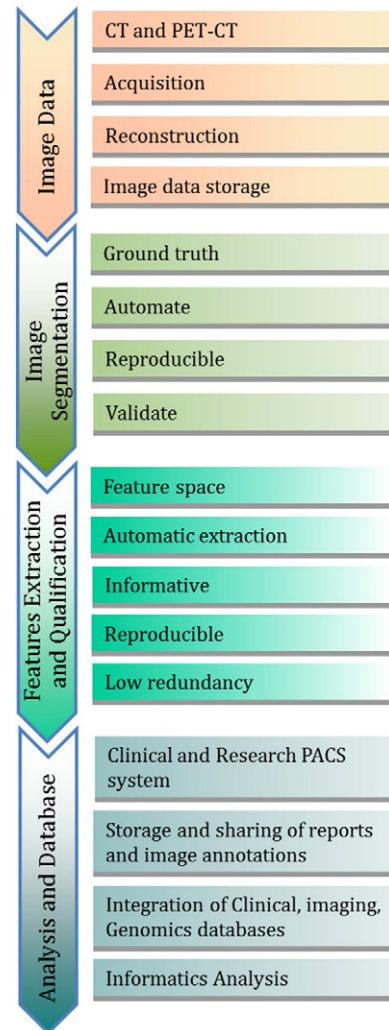


Fig. 1. The process and challenges in radiomics.

## 2. Image acquisition and reconstruction challenges

In routine clinical image acquisition, there is wide variation in imaging parameters such as image resolution (pixel size or matrix size and slice thickness), washout period in the case of positron emission tomography (PET) imaging, patient position, and the variations introduced by different reconstruction algorithms and slice thicknesses, which are different for each scanner vendor. Even this simple set of imaging issues can create difficulty in comparing results obtained across institutions with different scanners and patient populations. In addition, it is a challenge to identify and curate a large number of image data examples with similar clinical parameters such as disease stage.

### 2.1. Image acquisition and reconstruction

#### 2.1.1. CT

Of all the imaging modalities, CT appears to be the most straightforward and perhaps the easiest to compare across

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