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Review paper

Beyond imaging: The promise of radiomics

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ABSTRACT

The domain of investigation of radiomics consists of large-scale radiological image analysis and association with biological or clinical endpoints. The purpose of the present study is to provide a recent update on the status of this rapidly emerging field by performing a systematic review of the literature on radiomics, with a primary focus on oncologic applications. The systematic literature search, performed in Pubmed using the keywords: "radiomics OR radiomic" provided 97 research papers. Based on the results of this search, we describe the methods used for building a model of prognostic value from quantitative analysis of patient images. Then, we provide an up-to-date overview of the results achieved in this field, and discuss the current challenges and future developments of radiomics for oncology.

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1. Historical background

With the term "feature" we mean a descriptor of an image (e.g. of tumor or normal tissue regions) such as parameters derived from image intensity, texture, shape, etc. Although, the notion of using imaging features for predicting actions traces its roots to the early days of computer vision in the 1960s, its systemic application in medicine of imaging quantitative analysis only started in the 1980s [1]. This application has been primarily focused on computer-aided detection or diagnosis (CAD) [2,3]. CAD uses a set of quantitative image features describing the geometrical structure, intensity distribution and texture of a region of interest (ROI) that are used by statistical or machine learning classifiers in order to identify abnormal tissues in a variety of organs including liver, prostate, colon, breast. The output of this analysis is used by radiologists as a second opinion in detecting lesions and making diagnostic decisions [1–5].

CAD is often categorized into two major groups, computer-aided detection (CADe) and computer-aided diagnosis (CADx), the first focusing on a detection, localization and segmentation of lesions in medical images, the second on diagnosis, for example, distinction between benign and malignant lesions [3,6]. In CADe for breast cancer, features of the breast mammogram are used for detection of masses, architectural distortions, and microcalcifications. These can be detected using basic image enhancement methods, descriptors of statistical distribution of intensity values, and decomposition of the image through wavelet transforms in order to investigate differences between areas and background [2]. CAD algorithms are composed of two stages, detection and classification of suspicious regions into cancer or normal tissue. In the first stage, texture features are extracted from ROIs, automatically or manually contoured. Because many features can be extracted, CAD systems frequently incorporate feature selection algorithms to select the features contributing the most to diagnostic accuracy [4]. In the second stage a binary decision tree classifier is trained to distinguish lesion from normal breast tissue [7]. In contrast to CAD application in diagnostic radiology, we will be focusing on the extension of these quantitative imaging techniques into therapeutic oncology for the purpose of predicting response to treatment.

1.1. Definition of radiomics

The application of this approach to biological markers and therapeutic endpoints only started in past decade, when the concept of personalized medicine arose following the increasing use of genomics. Some early examples include the investigation of correlations between specific hepatocellular carcinoma imaging phenotypes with doxorubicin drug response in 2007 [8], and, in 2009, between PET-based features and response to radiotherapy [9].

Since 2010, this field has been formalized with the term "radiomics" [10,11]. The term originates from the words "radio" which refers to radiology, the science of acquiring medical images through the use of radiation (e.g., X-rays, CT, MRI). The suffix "omics" was first used in the term genomics to indicate the mapping of human genome. Later, this was widely used in biology as in the study of RNA (transcriptomics), proteins (proteomics), and metabolites (metabolomics), to emphasize the holistic feature of the research encompassing the entire view of a system [12]. Because radiomics combines quantitative analysis of radiological images and machine learning methods, it has its roots in CAD, and is considered as a new application of established techniques [13]. Two aspects of radiomics, however, are novel: the number of image features involved, which in CAD is usually 8–20, whereas in radiomics it is increased to a few hundred or thousands. Second, the domain of investigation for radiomics consists of association of features extracted form large–scale radiological image analysis with biological or clinical endpoints, resulting in both prognostic and predictive models [14]. Radiomics is a general science which can be applied to many biomedical areas, but the focus of this review will be primarily on oncological applications and its role in advancing personalizing cancer treatment.

It is currently recognized that solid tumors do not consist of a homogeneous entity, but rather are composed of multiple clonal sub-populations of cancer cells, exhibiting considerable spatial and temporal variability that could potentially yield valuable information about tumor aggressiveness [15]. Quantitative image features, called also "radiomic features" could provide richer information about intensity, shape, size or volume, and texture of tumor phenotype that is distinct or complementary to that provided by clinical reports, laboratory test results, and genomic or proteomic assays. Tumor molecular biopsy-based assays, besides being invasive, provide limited tumor characterization as the extracted sample does not always represent the entire population of tumor cells. Radiomics circumvents this by assessing the comprehensive three-dimensional tumor bulk by means of imaging information [16].

Different imaging modalities (e.g., MRI, CT, PET, ultrasound) are used as the basis for extracting these features [17]. The complete set of imaging features obtained for a patient using the available images is called the "radiome" [18]. A collection of features which holds prognostic and or predictive value is often called "radiomic signature". The fundamental hypothesis of radiomics is that quantitative analysis of tumor through a large amount of radiomic features can provide valuable diagnostic, prognostic or predictive information [19,20]. For tumors, heterogeneity assessed through imaging could be the expression of genomic heterogeneity, which would indicate worse prognosis, as tumors with more genomic heterogeneity are more likely to develop a resistance to treatment and to metastasize [21]. The aim of radiomics is to explore and exploit these sources of information to develop diagnostic, predictive, or prognostic radiomic model (signatures) to support personalized clinical decisions and improve individualized treatment selection [14].

2. Purpose of the work

Radiomics is a rapidly evolving field, and the purpose of the present study is to provide an update on its status. For this purpose, a systematic review of the literature is performed, with a primary focus on oncologic applications. The results of the literature search are used to provide an overview of the techniques and the results obtained in radiomics studies. Then, the current challenges and future developments of radiomics are discussed. The present overview, however, covers only the recent advancements in this field and is far from being a comprehensive discussion of medical image analysis. For further information, we invite the readers to refer to textbooks and reviews cited in the following sections.

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