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Radiomics and its emerging role in lung cancer research, imaging biomarkers and clinical management: State of the art

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ABSTRACT

With the development of functional imaging modalities we now have the ability to study the microenvironment of lung cancer and its genomic instability. *Radiomics* is defined as the use of automated or semi-automated post-processing and analysis of large amounts of quantitative imaging features that can be derived from medical images. The automated generation of these analytical features helps to quantify a number of variables in the imaging assessment of lung malignancy. These imaging features include: tumor spatial complexity, elucidation of the tumor genomic heterogeneity and composition, subregional identification in terms of tumor viability or aggressiveness, and response to chemotherapy and/or radiation. Therefore, a radiomic approach can help to reveal unique information about tumor behavior. Currently available radiomic features can be divided into four major classes: (a) morphological, (b) statistical, (c) regional, and (d) model-based. Each category yields quantitative parameters that reflect specific aspects of a tumor. The major challenge is to integrate radiomic data with clinical, pathological, and genomic information to decode the different types of tissue biology. There are many currently available radiomic studies on lung cancer for which there is a need to summarize the current state of the art.

1. Introduction

Lung cancer is the leading cause of cancer death in the world. Up to recently, the only current cure has been surgical removal of early stage disease. The results of the National lung cancer screening trial (NLST) showed a clear survival benefit for low dose computed tomography in current and former smokers [1]. This result prompted the Center for Medicare and Medicaid Services (CMS) to cover lung cancer screening in the United States for those subjects meeting the screening criteria. Meanwhile, the five year survival for this disease has slightly improved over the last fifty years. One of the bright spots in lung cancer research has been the introduction of patient-centered chemotherapy based on that patient's specific tumor cell mutations in advanced stage [2].

Imaging such as computed tomography (CT), positron emission tomography (PET), or magnetic resonance imaging (MRI) is vital in the diagnosis, staging, treatment planning, postoperative surveillance, and response evaluation in the routine management of lung cancer. Although these conventional modalities provide important information on lung cancer phenotypes, yet a great deal of genetic and prognostic information remains unrevealed. Recently, several studies have shown that functional imaging methods, such

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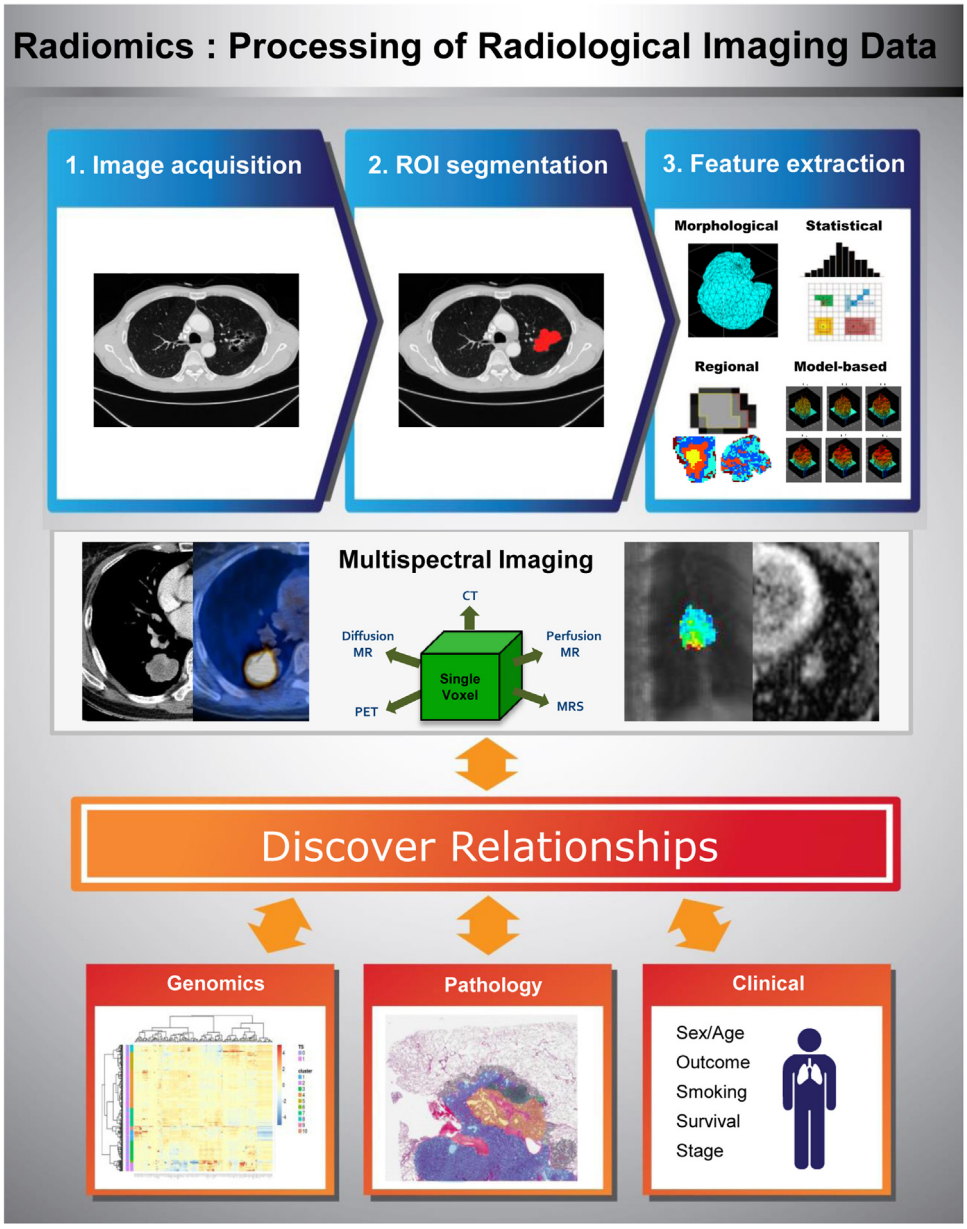

Fig. 1. Overview of radiomics, the processing of radiological imaging data.
Regions of interest are segmented for the whole tumor, and multiple quantitative features are extracted. Combining information from multiple imaging modalities provides a multispectral view of the tumor and allows improved tumor characterization. Discovering relationships among the radiomic features and genomic, pathology, and clinical data is a challenging but important step.

as diffusion-weighted MRI, perfusion techniques, PET and their combinations, allow the in-vivo depiction of physiologically and biologically important tumor processes and can even play a surrogate role in finding specific gene signatures by their characteristic imaging phenotypic expression pattern [3–9]. On the other hand, employing radiomics and radiogenomics have been found to be useful in quantifying overall tumor spatial complexity and identifying the tumor subregions that drive disease transformation, progression, and drug resistance [10–14]. These new methods will help drive further improvements in the personalization of gene-based lung cancer therapy. The purpose in this review is to consider the current state-of-the art in radiomics and radiogenomics and to offer concrete tools to implement these two approaches in thoracic oncology imaging.

1.1. What is radiomics

In the era of big data analytics, researchers have strived to discover the fundamental prognostic data embedded in medical and pathological images. Quantitative image features as well as traditional qualitative (semantic) features have shown some potential for precision medicine in oncology, and these features are continuously being refined and developed with evolving research [15–17]. With the recent availability of automated pipeline systems, quantitative computational features have gained attraction due to improved efficiency, reproducibility, and consistency [18,19]. *Radiomics* is a field of study in which high-throughput data is extracted and large amounts of advanced quantitative imaging features are analyzed from medical images (Fig. 1). The first step in radiomics requires the identification of the volumes of inter-