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Editorial

EDITORIAL

# The Evolving Status of Radiomics

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Lambin et al. introduced the term *radiomics* in 2012 (1) to describe the extraction of biologically relevant quantitative features from radiological images. They suggested that radiomic features (RFs), the invisible tissue infrastructural components of the objects being imaged, might be a valuable way to study cancer using computed tomography (CT) and other modalities. Such imaging studies are easily repeated and provide in vivo visualization and quantitative analysis of RFs throughout an imaged mass. Thus, they could support a personalized precision medicine approach to cancer diagnosis and serial assessment and prediction of response to treatment. Even so, radiomics has not evolved into a widely used, reliable component of cancer evaluation. The complicated nature of radiomics and its validation have raised questions, as have the reproducibility and generalizability of texture analysis and other fundamental components of the radiomics signature (2). In this issue of the Journal, Dercle et al. (3) demonstrated progress in several aspects of cancer analysis by radiomics and provided insights into future validation work.

In oncology, radiomics analysis involves the calculation of RFs from the images of the cancers. A wide variety of such features can be calculated. Examples include lesion size and shape, spatial histograms, and descriptors of the spatial arrangement of pixel intensities (texture) such as gray-scale co-occurrence matrices. These calculations are enabled by using several available software packages (3), but did not include pyradiomics (4). For example, in the Dercle study, the authors reported considering 1757 RFs and a nearly equal number of deep learning features. From these, the authors selected the four features most closely correlated with their image findings for analysis and validation. In 13 radiomics cancer studies summarized by Lambin et al. in 2017 (5), the features that proved useful varied, even in the same type of cancer. The development of a standard group of features and criteria for evaluating those features would be useful, although the biological variations of cancer may make this difficult. Standardization clearly will not be achieved unless the components of the radiomic analysis itself are more standard. To support this, Lambin et al. (5) have recommended a rigorous 16-component radiomics quality score (RQS) and transparent reporting of clinical radiomics study methods. This RQS was used and reported by Dercle et al. (3).

Dercle et al. (3) reported data involving 667 patients with metastatic colon cancer. These patients were part of a prospective blinded clinical trial comparing first-line treatment response of patients who received chemotherapy alone or in combination with an epidermal growth factor receptor (EGFR) inhibitor. Repeat CT scans at baseline and after 8 weeks of therapy were used to monitor change in the size and RFs of hepatic metastases. The CT scans were acquired at several different institutions following the same CT protocols, but the scan quality varied. Experienced radiologists blinded to outcomes were later asked to rank all CT images as high quality or standard in quality. In patients who received EGFR inhibitors, RFs derived from both high- and standard-quality CTs provided statistically significantly better prediction of treatment response and overall survival than change in tumor size or the baseline KRAS mutational status. Because these RFs were acquired from multiple CT scanners of varying quality in several institutions, the authors concluded that their radiomics signatures were resilient to CT technological variations and likely generalizable.

Dercle et al. (3) reported in Supplementary Materials that their RQS analysis yielded a conformity score of 78% (28 of 36 points) with the 16 components of the RQS. Reporting such compliance with the RQS is a positive step and should be a requirement of future radiomics research. CT texture phantoms, which could have helped document and possibly compensate for CT inconsistencies, are part of the RQS but were not available in the Dercle study. Such phantoms for CT radiomics have been developed (6) and validated (7) and should be part of future radiomics studies whenever possible.

Although Dercle reported results from 667 patients with metastatic colon cancer, there were only 100 patients in the validation group receiving anti-EGFR therapy. Samples of this size can be problematic in studies that employ deep learning approaches that are prone to overfitting. Dercle applied proper approaches to minimize overfitting, but whether overfitting was controlled remains uncertain. Validation of their RFs by prospective analysis of larger independent datasets of patients with metastatic colon cancer is warranted. In addition, retrospective validation of RFs from Dercle or other radiomic studies

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against large datasets with known tissue diagnoses—such as datasets that might be available from the National Institutes of Health, the American College of Radiology Imaging Network (8), or other sources—also could provide opportunities for radiomic validation.

The Dercle study shows many aspects of the rigor and attention to scan quality needed to allow radiomics to make consistent contributions to personalized cancer imaging. It also shows the complexity of radiomics analysis. Is radiomics too complex to become generally established in the radiological community? The work of Lambin et al. (1,5), that of the Image Biomarker Standardization Initiative (9), and others suggests that standardization and rigorous quality control are needed for radiomics to succeed. Will this be sufficient, or will the complexities of radiomics lead to it being available only in specialized imaging centers that serve as analysis referral sites? Further work is warranted to determine if the potential shown by the Dercle study and other radiomics work can be broadly validated and to establish the proper approach to radiomics in cancer evaluation.

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## Notes

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