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DEVELOPS EARLY DETECTION AND CANCER MONITORING VIA RADIOMICS

Turgunov B. Sh
Ergashaliyev A. G.

Introduction

Early cancer detection is crucial for both medical and societal reasons, as it allows for the possibility of curative treatment when the cancer is still localized, as has been covered elsewhere in this special issue. Since the advent of symptoms is frequently linked to late-stage incurable disease, it is ideal to find early malignancies in asymptomatic individuals. But it's also very evident that before early detection paradigms can be totally successful, there are significant problems that need to be resolved, including false positives, overdetection, overdiagnosis, and overtreatment. Early detection paradigms are therefore inherently multistep procedures whose objective is to maximize various trade-offs between the diagnosis's sensitivity and specificity at each stage. Medical imaging has always been a vital part of pipelines for early cancer detection.

Table 1. Imaging modalities in early detection paradigms.

Cancer	Primary screen(s)	Secondary screen(s)
Lung	LDCT/DxCT	Endoscopy, PET, Bx
Breast	Mammography/digital	US, mpMRI, Bx
Pancreatic	Serum, pancreatic juice	CT radiomics, MRI, Bx
Skin	Optical	Bx
GI	Optical (OCT)	Bx
Liver/HCC	CT/MRI	US, MR elastography
Cervical	Optical	Bx

Abbreviations: Bx, biopsy; DxCT, diagnostic CT; GI, gastrointestinal; HCC, hepatocellular carcinoma; LDCT, low-dose CT; mpMRI, multiparametric MRI; OCT, optical coherence tomography; US, ultrasound.

In contrast to qualitative interpretations of the images, we will argue in this review that quantitative analysis of these images using "radiomics" offer higher clinical utility to maximize diagnosis and risk assessment. Moreover, based on the biology of the early lesion and whether the imaging test is a primary or secondary filter, the resulting predictive machine-learning models can be adjusted to maximize either sensitivity or specificity. The sensitivity of

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primary screens should be extremely high, and the specificity of subsequent (secondary) screens should increase.

Radiomics

The process of transforming images into organized, mineable data and then using that data for prognosis, diagnosis, prediction, and/or longitudinal monitoring is known as radiomics. The idea that "Images are Data" and that they represent the underlying pathobiology of the area of interest (ROI; ref. 3) is the foundation of the entire endeavor. In the last ten years of its existence, the field of radiomics has grown rapidly and has recently undergone extensive study elsewhere. As seen in **Fig. 1**, the traditional radiomic analysis process extracts image-based features from the lesion and/or adjacent tissues (i.e., ROIs). A skilled radiologists can score these aspects meaningfully.

The computed features are then frequently examined using traditional machine learning techniques to create models that predict the relevant dependent variable or variables (4). In machine learning, binary outcomes—such as cancer versus non-cancer, aggressive versus indolent, etc.—are the simplest to model and are frequently most pertinent to early detection paradigms. Though they typically call for far larger training sets, machine learning algorithms can also model more complicated continuous outcomes like progression-free survival and time to recurrence. The radiomic feature set must be whittled down to a manageable number in order to prevent overfitting. This is accomplished by first eliminating unstable and redundant features in order of priority, and then selecting the features that provide the most information about the desired outcome.

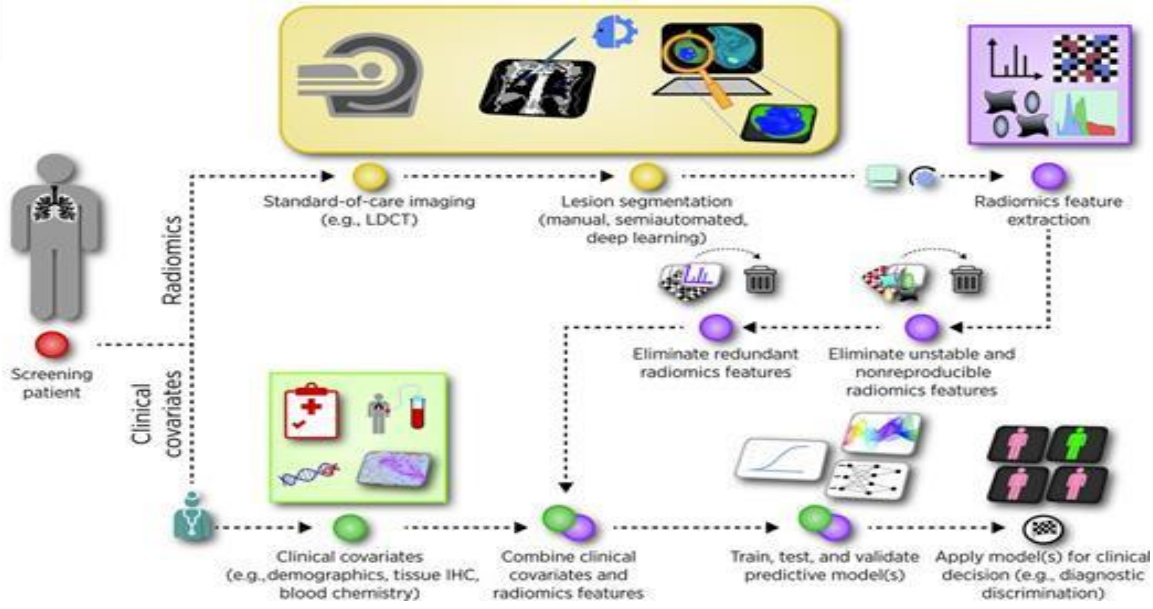

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Fig. 1. The pipeline for radiomics. Either prospectively or retrospectively, patient standard-of-care imaging and data (as available) are collected. The ROIs (such as pulmonary nodules) are identified by radiologists or imaging scientists, after which they are segmented manually, automatically, or using DL algorithms. Following ROI segmentation, radiomic features (purple) are extracted. Radiomic features that are correlated, unstable, and nonreproducible are removed. In order to create a predictive model that can be used for clinical decision-making, the remaining radiomics features are combined with pertinent clinical covariates (green). **Figure 1** is adapted from Tunali et al.

The biggest obstacle is getting access to large, high-quality datasets that are thoroughly annotated with regard to the relevant outcome(s), regardless of the radiomic approach and pipeline used. It is impossible to overstate the significance of this final requirement. Results such as recurrence, progression-free survival, or time to recurrence are among the many radiomic studies in the cancer care continuum that are rarely recorded in easily accessible structured formats. As a result, these endpoints must be manually recorded through chart review, which is time-consuming and demands specialized knowledge to correctly extract. However, the crucial outcome (cancer vs. noncancer; indolent vs. aggressive) is frequently, or can be, recorded in structured formats in an early detection paradigm, which lessens some of the restrictions related to data curation.

Imaging Techniques

US

US has the unquestionable benefits of being able to image deep body tissues in real time and being highly accessible, but its excessive operator dependence has been a problem for its early detection schema. A set of methods known as "elastography," which can quantitatively image tissue stiffness—which is known to increase with hyperplasia—is being used to aggressively solve this problem.

X-ray

Superior tissue penetration is exhibited by high-energy photons, which can be absorbed by electron-dense materials like calcium deposits or contrast agents. Densities of soft tissues also absorb these, making it possible to

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distinguish between different types of tissue, such as lung parenchyma, muscle, connective tissue, and adipose.

MRI

The benefit of MRI is that it provides superior soft tissue (and tumor) contrast without using ionizing radiation, in addition to having excellent tissue penetration. However, motion artifacts are a common result of long acquisition times in MRI, particularly in abdominal tissues. Advanced compressed sensing techniques, such as MR fingerprinting, are helping to mitigate this. Unlike the current minutes, these techniques have the potential to render MR images in seconds. The benefit of MRI is that it provides superior soft tissue (and tumor) contrast without using ionizing radiation, in addition to having excellent tissue penetration. However, motion artifacts are a common result of long acquisition times in MRI, particularly in abdominal tissues.

Conclusions

Images are information. Quantitative analyses of these data, as previously mentioned, can produce highly predictive models based on a sparse set of informative imaging features. Using supervised ROI identification and user-defined feature extraction, conventional radiomics creates machine learning models. Predictive models with extremely high accuracies are the outcome of these. Combining the radiomics model with orthogonal clinically derived data—such as demographics, histopathology, genomics, and serum markers—always improves accuracy. You can find other, more thorough reviews of DL and AI in imaging (3–6).

Both conventional and deeply learned radiomic training sets necessitate substantial amounts of carefully selected data. Finding clean results is necessary for curation, as they are subsequently applied to classifier tasks. This raises two issues: first, it is often necessary to manually define and curate outcome data in an organized manner; second, very large datasets are not easily accessible. Examples of these data include cancer versus noncancer and low grade versus high grade.

Adopting a large distributed learning network, in which organizations curate and store their own data and share algorithms to enhance training, testing, and validation, is a potential future solution to address the majority of these

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problems (11). A more straightforward version of this would be for journals to mandate the deposit of code, either uncompiled or compiled, in an easily accessible repository. This would allow for the testing and replication of promising models at various locations.

Notably, DL was used in two of the most well-known recent studies to detect breast cancer from mammography (49) and to predict lung nodule status from LDCT scans (36). With the justification that "code used for training the models has a large number of dependencies on internal tooling, infrastructure, and hardware, and its release is therefore not feasible," the authors declined to share the code in both cases. This is not acceptable, especially if public funds were used to create the training data.

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