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Faiq A. Shaikh MD

Benjamin Franc MD, MS, MBA

Erastus Allen MBA

Evis Sala MD, PhD

Omer Awan MD, MPH

See next page for additional authors

Published In/Presented At

Shaikh, F., Franc, B., Allen, E., Sala, E., Awan, O., Hendrata, K., … Shrestha, R. (2018). Translational Radiomics: Defining the Strategy Pipeline and Considerations for Application-Part 1: From Methodology to Clinical Implementation. *Journal Of The American College Of Radiology: JACR*, *15*(3 Pt B), 538–542. https://doi.org/10.1016/j.jacr.2017.12.008

Authors
Faiq A. Shaikh MD; Benjamin Franc MD, MS, MBA; Erastus Allen MBA; Evis Sala MD, PhD; Omer Awan MD, MPH; Kenneth Hendrata MBA; Safwan Halabi MD; Sohaib A. Mohiuddin MD; Sana Malik DrPH; Dexter Hadley MD, PhD; and Rasu Shrestha MD, MBA

HHS Public Access
Author manuscript
J Am Coll Radiol. Author manuscript; available in PMC 2020 August 20.

Published in final edited form as:
J Am Coll Radiol. 2018 March ; 15(3 Pt B): 538–542. doi:10.1016/j.jacr.2017.12.008.

Translational Radiomics: Defining the Strategy Pipeline and Considerations for Application—Part 1: From Methodology to Clinical Implementation

Faiq Shaikh, MD[a], **Benjamin Franc, MD, MS, MBA**[b], **Erastus Allen, MBA**[c], **Evis Sala, MD, PhD**[d], **Omer Awan, MD, MPH**[e], **Kenneth Hendrata, MBA**[f], **Safwan Halabi, MD**[g], **Sohaib Mohiuddin, MD**[h], **Sana Malik, DrPH**[i], **Dexter Hadley, MD, PhD**[j], **Rasu Shrestha, MD, MBA**[k]

[a]Institute of Computational Health Sciences, UCSF, San Francisco, California.

[b]Department of Radiology and Biomedical Imaging, UCSF, San Francisco, California.

[c]UPMC Enterprises, Pittsburgh, Pennsylvania.

[d]Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, New York.

[e]Department of Radiology, Temple University, Philadelphia, Pennsylvania.

[f]Carnegie Mellon University, Pittsburgh, Pennsylvania.

[g]Department of Radiology, Stanford University, Palo Alto, California.

[h]Department of Radiology, Division of Nuclear Medicine, University of Miami, Miami, Florida.

[i]School of Social Welfare, Stony Brook University, New York, New York.

[j]Institute of Computational Health Sciences, UCSF, San Francisco, California.

[k]UPMC Enterprises, Pittsburgh, Pennsylvania.

Abstract

Enterprise imaging has channeled various technological innovations to the field of clinical radiology, ranging from advanced imaging equipment and postacquisition iterative reconstruction tools to image analysis and computer-aided detection tools. More recently, the advancements in the field of quantitative image analysis coupled with machine learning-based data analytics, classification, and integration have ushered us into the era of radiomics, which has tremendous potential in clinical decision support as well as drug discovery. There are important issues to consider to incorporate radiomics as a clinically applicable system and a commercially viable solution. In this two-part series, we offer insights into the development of the translational pipeline for radiomics from methodology to clinical implementation (Part 1) and from that to enterprise development (Part 2).

Corresponding author and reprints: Faiq Shaikh, MD, Institute of Computational Health Sciences, University of California San Francisco, San Francisco, CA, USA; faiq.shaikh@hotmail.com.

The authors have no conflicts of interest related to the material discussed in this article.

Keywords

Radiomics; enterprise; translational; precision; medicine; radiology

INTRODUCTION

Radiomics can be defined as the process of transferring the radiology interpretation knowledge from humans to machines by way of extracting large amounts of quantitative features from medical images using data characterization and quantification techniques to get insights into the structure, behavior, and therapy response profile of the disease entity being studied. Some of the better developed radiomic methodologies exist in the realm of lung cancer diagnosis and prognostication, as well as radiation therapy planning.

We define translational radiomics as a process of converting the basic radiomic methodologies into evidence-based clinically applicable models that then undergo the steps of platform standardization, algorithm integration, and applied business intelligence to create a commercialized product for mainstream use.

In this article (Part 1), we identify the steps involved in the process of translating the radiomics methodology into a clinical application, which include the four foundational components (clinical knowledge, radiomics technique, information architecture, and machine learning architecture), as well as the translational pipeline steps (systems thinking, data convergence, clinical workflow integration, and radiologist feedback and assessment; see Fig. 1).

INITIATING THE TRANSLATION—DEFINING ENTRY POINTS

Clinical Knowledge Transfer

Radiomics is a result of significant advancements made in clinical, computational, and applied physics within the realm of medical imaging. As the current imaging modalities become more sophisticated in deciphering more detailed anatomic and functional details, such as functional MRI, newer modalities and techniques, such as immuno-PET and bioluminescence, have made it possible to study the complex subcellular process involved in pathophysiology. As the clinical knowledge of interpreting and analyzing these new techniques expands, it is important to keep in mind their translatability to artificial intelligence–based methodologies such as radiomics and imaging genomics.

On one hand, any question posed as potentially addressed through a radiomics approach must have input from those most knowledgeable of the disease process and its natural evolution (eg, cardiologist, neurologist, or oncologist), those most familiar with its physical manifestations on pathology (eg, a pathologist with specialization in cardiovascular, neurologic, or oncologic processes), and those most cognizant of its manifestations on imaging, including subspecialty radiologists. On the other hand, radiomics is aligned with other “omic” techniques; it identifies features that are abstract and outside of the clinician’s everyday experience and relates those features to some clinically meaningful outcome or prediction. There is a need for these highly specialized approaches to reconcile with a deeper understanding of disease entities from a genotype-phenotype relationship point of view, which is being recognized as a model to associate clinical manifestation of disease with the molecular processes that are informed by the genomic signature (see Fig. 2). The final workflow infrastructure may well be too multispecialty to reside entirely within one department. Newer sections and divisions for computational medicine may best serve as hubs for these integrated systems driving precision medicine.

Radiomics Methodology Development

There is now an increasing level of understanding of the biologic and microstructural environment of the tumors (intratumor heterogeneity) and their relationship with the spectrum of tumor behaviors [1]. The concept of intertumor heterogeneity sheds light on the variation in the genetic and phenotypic profile between individuals with the same tumor type [2]. Based on these factors, it is becoming increasingly important to develop and validate algorithms that take into account both intraand intertumor heterogeneity. This is particularly important when evaluating treatment response in the setting of metastatic disease. It is necessary to use that knowledge to select the most relevant radiomic features that correlate best with the underlying tumor signature, and although some have argued that it may replace the need for biopsy in some cases (neural involvement), it will largely serve the purpose of significantly improving the specificity of imaging modalities and provide a deeper, richer, more nuanced, and incredibly useful understanding of the disease process and how to best treat it.

The core components of the radiomics technique include extracting raw image data sets, image segmentation, lesion detection, 3-D contouring, feature extraction and classification, statistical analysis using covariance matrices, and gleaning inferences for clinical decision support systems or drug discovery [3]. To increase the efficiency and fidelity of a radiomics technique, one has to understand which structural or metabolic imaging biomarkers are the best surrogate end points for the disease progression and outcomes. It is also imperative to perform robust comparative analyses between manual versus semi-automated versus automated tumor volu-metric segmentation to establish standardized protocols for radiomics application.

Information Architecture

PACS and vendor neutral archives mainly provide the architectural framework for a legal record and one-off reference and are designed to function for a clinical workflow. Current architectures are not conducive to research projects, and burgeoning image analysis techniques such as radiomics that deal with big data are creating an immense need for a formidable yet agile framework. Research also necessitates a consistent ontology for identifying disease cohorts by phenotype and for handling increasingly international collaborations. Given the large size of imaging data sets, it is more efficient to transport modeling and feature extraction code than to move exceedingly large data sets. Cloud computing, although enhancing scalability, requires moving large data sets that then still reside in one or more data centers. “Fog computing” refers to extending cloud computing to the edge of an enterprise’s network, to facilitate the operation of computing, storage, and networking services between end devices and cloud computing data centers, and it should be considered whereby petabytes of imaging data may stay on premises whereas feature extraction methods and results are shared among collaborating researchers [4]. Fog computing may also aid in meeting complex regulatory data compliance requirements in cross-jurisdictional commercial deployments and research collaborations [5].

Machine Learning Considerations

Beyond the development of novel feature extraction methods, success in the development and sharing of machine learning models in radiomics may be improved by incorporating the following practices: ontological agreement, standard software tool sets shared via containerization methods for reproducible research (which is a lightweight alternative to full machine virtualization that involves encapsulating an application in a container with its own operating environment), and, ideally, computational experiment reusability. The integration of independently developed data sets across disciplines and institutions is a significant challenge [6]. To address this challenge, standard ontologies are employed to avoid extensive translational work in the integration of data from disparate sources. Imaging ontologies include annotation models for labeling regions of interest [6] as well as standard naming and formats for macroscopic, microscopic, and molecular data elements [6]. Reproducibility is regarded as a fundamental requirement for the proper judgment of scientific claims. There is a spectrum of reproducibility ranging from publications without accompanying data or code to fully linked data and code for full replication. To meet the gold standard of full replication, a containerization method, such as Docker, can be valuable but does not necessarily share the composable parts of a machine learning pipeline. To enable other researchers to follow each step of the process clearly, the sharing of research objects, which in this case means radiomics algorithms developed for specific feature extraction from a specific modality, with stepwise workflow facilitates the reusability of component parts of the analysis and modeling [7].

THE TRANSLATION PIPELINE

Systems Thinking Considerations

Systems thinking involves studying a system by examining the linkages and interactions between the components that comprise its entirety [8]. It may be a novel but nevertheless important exercise to consider the principles of systems thinking as applied to radiomics, to organize, assess, and optimize its translation and prevent system failures. Factors in systemic failure may include confused goals, weak systemwide understanding, flawed design, inadequate feedback, poor cooperation, lack of accountability, and so on [8]. In terms of radiomics, examples for these include confused goals (poorly conceived clinical decision support systems application), weak systemwide understanding (underscoring the importance of a well-defined strategy for the translational process), flawed design (underestimated data convergence challenges), inadequate feedback (not adequately consulting with radiologists or referring physicians), or poor cooperation (lack of liaison between computational and medical experts).

Another important thing to ask is, what binds systems together rather than functional silo performance? Understanding and anticipating how the translational process for radiomics is intended to work, how it actually works, and how it may buckle under pressure can prevent system failure and ensure successful productization of radiomics solutions instead. Once identified, these systems checkpoints can be standardized across institutions and practices for streamlined data collection, quality assurance, and reproducibility. Currently, there are attempts to identify value-based metrics across various types of imaging suites to help establish systems thinking-based radiology performance assessment methods. Similar approaches in radiomics will help standardize it as a reliable methodology.

Convergence of Data From Other "Omics"

As diagnostic approaches get more sophisticated, they are able to generate large data sets that contain valuable information regarding underlying disease processes. This trend has been seen across various aspects of disease discovery and understanding, ranging from genomic determinants (genomics), transcribed ribonucleic acid (transcriptomics), protein expression (proteomics), metabolic processes (metabolomics), and structural or functional phenotypic manifestation (radiomics; see Fig. 2). As these data sets expand, development of tools for data mining and feature classification enable the important task of finding correlations between these datasets. Empowered by machine learning and advanced data mining tools, this process provides tremendous insights into otherwise cumbersome data sets. Currently, there is no platform that has the capability to incorporate large data sets being derived from advanced methodologies of radiomics and genomics and inferring trends and patterns within and correlations between them. Developing such a platform, which also has the capability of incorporating validated crowdsourced algorithms for radiogenomic assessment, will be the single most important facilitating factor for precision medicine.

Radiology Workflow Integration (Operational Checkpoints)

The clinical imaging workflow should be customized and optimized for each working environment. A key portion of the translation process involves delivering the machine learning algorithms to the point of care whereby there is seamless implementation throughout the Radiology Information System (RIS)/PACS. This seamless workflow can also be achieved by avoiding disruption of workflow, using separate workstations, and reducing the need for the radiologist to work in different locations. Tight integration with PACS is necessary to function as an effective clinical decision support tool, or radiologists will be less likely to use these tools.

Ideally, communication with vendors to integrate machine learning tools with adequate superuser training will allow these solutions to thrive in the long term, thereby increasing radiologist compliance. There needs to be a focus on identifying and decreasing pain points of the radiologist. Digital dashboard implementation may help radiologists become aware of the various unique tools and quantifiable data that will allow them to better understand the disease process and give a more nuanced report with greater confidence [9,10].

Some operational considerations include radiomics software integrated or interfaced with RIS/PACS, network bandwidth requirements, DICOM compliance and support, disaster recovery solutions, third-party vendor or Application Program Interface (API) interfaces, and length of training for superusers and users.

Radiologist Use Assessment and Feedback

To ensure user (imager) engagement, it is essential that a user-friendly pipeline is created that can be integrated into routine clinical practice. Furthermore, as radiomics outcomes become more validated, we need to focus on ways to make the results available to clinicians as part of standard clinical reports that are nuanced and in tune with the clinical scenario at hand so that they best guide clinical decision making.

A marketplace that acts as a radiomics hub should be established to allow for multi-institutional collaboration and feedback. This marketplace would allow users to share imaging and pathological data sets to augment the discovery of clinically viable radiomics tools. This platform would also allow collaborators to share data about diseases that are not prevalent at any one institution. This real-time collation and curation of imaging and pathological data could significantly catalyze radiomics discoveries.

CONCLUSION

There are several key steps in the translation of radiomics techniques to clinically impactful solutions, which we have outlined along with their considerations. Radiomics, if translated optimally, has the potential to drive imaging-based precision medicine. Further translation to enterprise is still a novel concept, and we will discuss in the Part 2 of this series a framework that identifies its unique challenges and attempts to provide a pathway to mainstream application that improves outcomes.

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TAKE-HOME POINTS

- Radiomics is an emerging methodology with significant potential in driving precision medicine.
- The strategy for the translation of radiomics includes identifying entry points of clinical knowledge, methodology and technique, information framework, and the machine learning component.
- The first phase of the translational process entails considerations for systems thinking, data integration and mining, workflow integration, and associated radiologist feedback.
- Developing a multi-omics platform that has the capability of incorporating validated crowdsourced algorithms for radiogenomic assessment is critical for advancement of precision medicine.
- A radiomics hub or marketplace is needed for multi-institutional collaboration and feedback to promote data sharing in data-intense radiomics discovery.

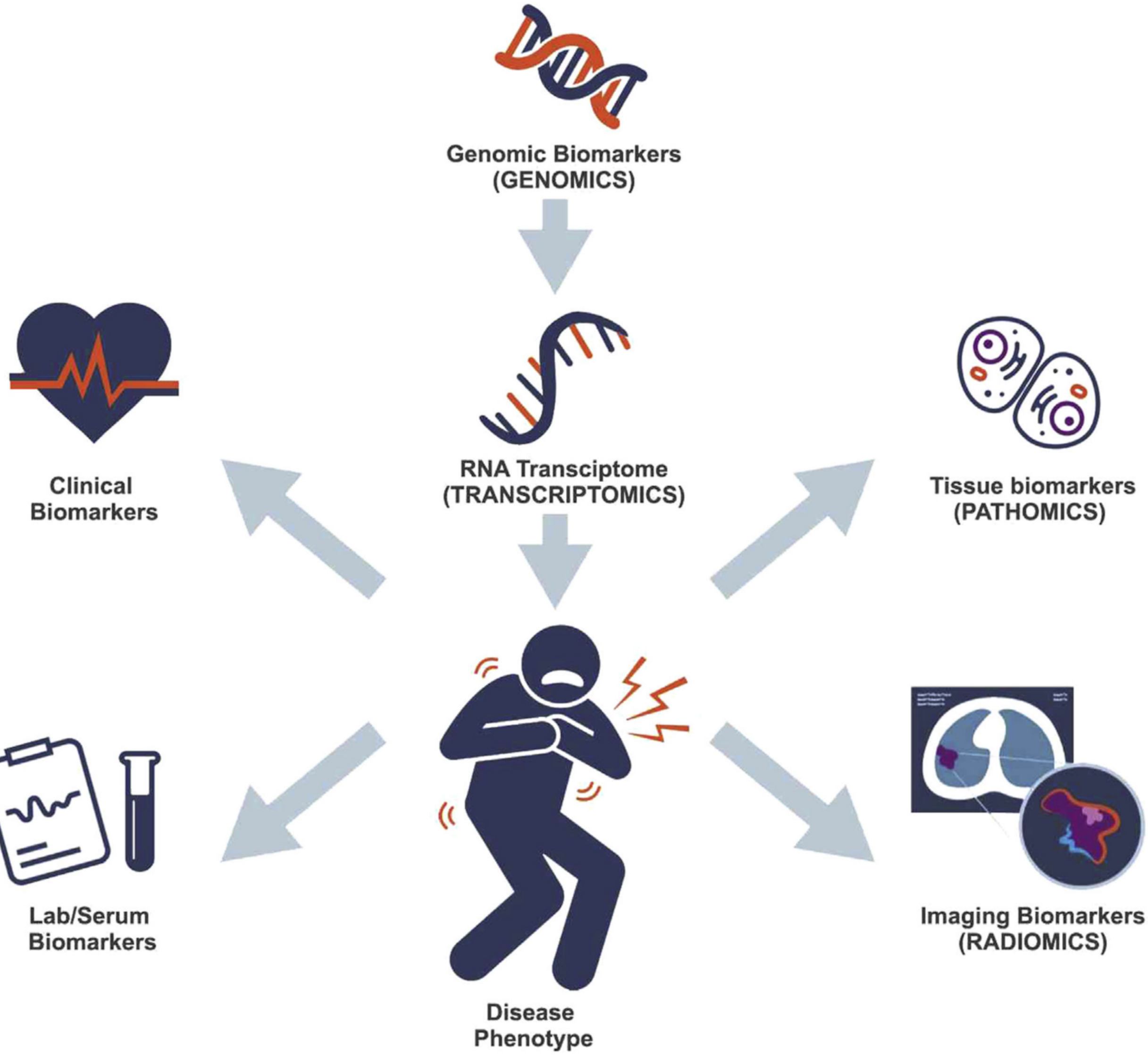

Fig 1.
The translational radiomics pipeline.

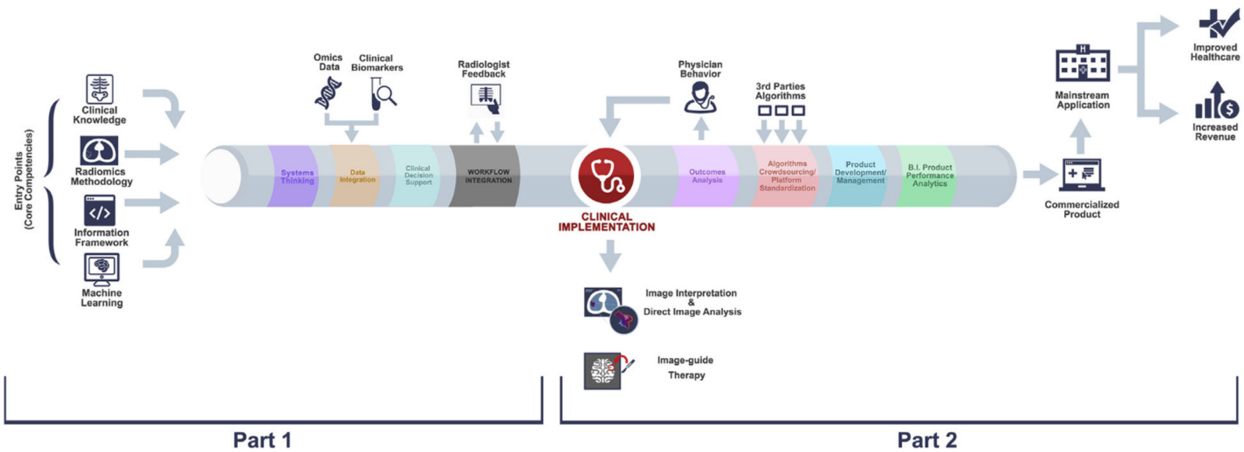

Fig 2.

The genotype-phenotype relationship and the “omics” involved.