Nuclear Medicine and Molecular Imaging (2019) 53:164–166
https://doi.org/10.1007/s13139-019-00578-x

PERSPECTIVE

ISSN (print) 1869-3482
ISSN (online) 1869-3474

Perspectives in Radiomics for Personalized Medicine and Theranostics

Seunggyun Ha [1,2]

Received: 1 January 2019 / Revised: 11 January 2019 / Accepted: 13 January 2019 / Published online: 23 January 2019

Abstract

Radiomics handles imaging biomarker from high-throughput feature extraction through complex pattern recognition that is difficult for human to process. Recent medical paradigms are rapidly changing to personalized medicine, including molecular targeted therapy, immunotherapy, and theranostics, and the importance of biomarkers for these is growing day by day. Even though biopsy continues to gold standard for tumor assessment in personalized medicine, imaging is expected to complement biopsy because it allows whole tumor evaluation, whole body evaluation, and non-invasive and repetitive evaluation. Radiomics is known as a useful method to get imaging biomarkers related to intratumor heterogeneity in molecular targeted therapy as well as one-size-fits-all therapy. It is also expected to be useful in new paradigms such as immunotherapy and somatostatin receptor (SSTR) or prostate-specific membrane antigen (PSMA)-targeted theranostics. Radiomics research should move to multimodality (CT, MR, PET, etc.), multicenter, and prospective studies from current single modality, single institution, and retrospective studies. Image-quality harmonization, intertumor heterogeneity, and integrative analysis of information from different scales are thought to be important keywords in future radiomics research. It is clear that radiomics will play an important role in personalized medicine.

Keywords Radiomics · Personalized medicine · Theranostics · Oncology · PET

Radiomics is an emerging field, defined as the high-throughput extraction of quantitative features from medical images [1]. This approach provides high-dimensional data describing properties of shape and texture of tumors captured on imaging modality, and the radiomics features are believed to contain information that reflects underlying tumor pathophysiology [2]. One of the reasons why radiomics is important is that it allows evaluation of tumor heterogeneity [3, 4]. Genomic instability, one of the hallmarks of cancer, causes intratumor and intertumor heterogeneity through clonal evolution and is known to cause treatment failure [5, 6]. More accurate evaluation of these genomic landscapes requires multiple and serial tumor sampling, which is clinically impractical in terms of cost and invasiveness [7, 8]. Radiomics can complement the disadvantages of biopsy because of the availability of whole body and whole tumor evaluation as well as non-invasive and repetitive imaging [9]. The primary goal of radiomics is to build a clinically relevant predictive, descriptive, or prognostic model using radiomics features [10].

The recent paradigm of cancer management has been rapidly changed to personalized medicine. Unlike historic "one-size-fits-all" medicine, personalized medicine evaluates specific tumor markers to select for patients who may benefit from molecularly targeted therapy by maximizing therapeutic effect and minimizing toxicity [11]. Based on these strategies, molecular targeted drugs targeting cancer driver mutations such as EGFR and ALK mutations have been used in clinical practice [12–14]. Further, the development of immune checkpoint inhibitor drugs has led to a shift to a new era of personalized medicine, with many studies having been conducted to find immune checkpoint markers available in clinical practice [15–17]. Another major challenge to personalized medicine is theranostics, a new medical field of combining specified therapeutics and specified diagnostics. In fact, this concept has been practiced for decades through the use of radioactive iodine therapy and is very familiar with nuclear medicine physicians [18]. In recent years, somatostatin receptor (SSTR) has attracted much attention as a molecular target for theranostics

✉ Seunggyun Ha
seunggyun.ha@gmail.com

[1] Radiation Medicine Research Institute, Seoul National University College of Medicine, Seoul, South Korea

[2] Department of Nuclear Medicine, Seoul National University Hospital, Seoul, South Korea

for gastroenteropancreatic neuroendocrine tumors [19]. In addition, radiolabeled ligands targeting prostate-specific membrane antigen (PSMA) are expected to have good results in diagnosis and treatment in patients with hormone refractory prostate cancer [20].

The potential of usefulness of positron emission tomography (PET) radiomics for personalized medicine has been widely reported in various cancers, as it has been in the purpose of tumor marker evaluation, selection of patients expecting a better response, and development of prognostic markers [21–23]. The intratumor heterogeneity assessment through PET radiomics features has been shown to successfully predict the prognosis of EGFR tyrosine kinase inhibitors in non-small cell lung carcinoma [24, 25]. Meanwhile, there is a lack of radiomics studies on immune checkpoint inhibitors due to limited accumulated data. However, PET radiomics are expected to be useful in immunotherapy, since it has been reported that tumor metabolism is closely related to transcriptomic data of the immune landscape in the tumor microenvironment [26, 27].

There are several challenges with radiomics. In technical aspects, radiomics features are vulnerable to imaging and reconstruction settings [28]. This is an obstacle to multicenter trials which are essential for the transition to clinical implementation. Therefore, harmonization of images of different quality will be important for more accurate and more robust results from radiomics research. Up to now, radiomics studies have been mainly focused on single imaging modality including FDG PET. However, it is considered that a process of integrating image information of different scales from anatomical to molecular levels is necessary in the future. There is also a need to study the potential of radiomics for SSTR or PSMA-targeted imaging which is highlighted in theranostics. Furthermore, radiomics studies involving NGS-based bioinformatics are also needed. Finally, more research is needed on the evaluation of intertumor heterogeneity as well as intratumor heterogeneity. Despite those challenging issues, it is obvious that the potential of radiomics is promising in playing an important role in personalized medicine and theranostics.

Compliance with Ethical Standards

Conflict of Interest Seunggyun Ha declared that this work was supported by a grant from the Basic Science Research Program through the National Research Foundation of Korea (NRF) (no. 2018R1D1A1A02086383).

Ethical Approval This work does not contain any studies with human participants or animals performed by any of the authors. For this type of study formal consent is not required.

Informed Consent None.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Lambin P, Rios-Velazquez E, Leijenaar R, Carvalho S, van Stiphout RG, Granton P, et al. Radiomics: extracting more information from medical images using advanced feature analysis. Eur J Cancer. 2012;48:441–6.
2. Gillies RJ, Kinahan PE, Hricak H. Radiomics: images are more than pictures, they are data. Radiology. 2015;278:563–77.
3. Yip SS, Aerts HJ. Applications and limitations of radiomics. Phys Med Biol. 2016;61:R150.
4. Sala E, Mema E, Himoto Y, Veeraraghavan H, Brenton J, Snyder A, et al. Unravelling tumour heterogeneity using next-generation imaging: radiomics, radiogenomics, and habitat imaging. Clin Radiol. 2017;72:3–10.
5. Negrini S, Gorgoulis VG, Halazonetis TD. Genomic instability — an evolving hallmark of cancer. Nat Rev Mol Cell Biol. 2010;11:220.
6. Gerlinger M, Swanton C. How Darwinian models inform therapeutic failure initiated by clonal heterogeneity in cancer medicine. Br J Cancer. 2010;103:1139.
7. Gerlinger M, Rowan AJ, Horswell S, Larkin J, Endesfelder D, Gronroos E, et al. Intratumor heterogeneity and branched evolution revealed by multiregion sequencing. N Engl J Med. 2012;366:883–92.
8. Collins DC, Sundar R, Lim JS, Yap TA. Towards precision medicine in the clinic: from biomarker discovery to novel therapeutics. Trends Pharmacol Sci. 2017;38:25–40.
9. O'Connor JP, Rose CJ, Waterton JC, Carano RA, Parker GJ, Jackson A. Imaging intratumor heterogeneity: role in therapy response, resistance, and clinical outcome. Clin Cancer Res. 2015;21:249–57.
10. Hatt M, Tixier F, Visvikis D, Le Rest CC. Radiomics in PET/CT: more than meets the eye? J Nucl Med. 2017;58:365–6.
11. Kalia M. Personalized oncology: recent advances and future challenges. Metabolism. 2013;62:S11–S4.
12. Mok TS, Wu Y-L, Thongprasert S, Yang C-H, Chu D-T, Saijo N, et al. Gefitinib or carboplatin–paclitaxel in pulmonary adenocarcinoma. N Engl J Med. 2009;361:947–57.
13. Shaw AT, Kim D-W, Nakagawa K, Seto T, Crinó L, Ahn M-J, et al. Crizotinib versus chemotherapy in advanced ALK-positive lung cancer. N Engl J Med. 2013;368:2385–94.
14. Lee CK, Brown C, Gralla RJ, Hirsh V, Thongprasert S, Tsai C-M, et al. Impact of EGFR inhibitor in non-small cell lung cancer on progression-free and overall survival: a meta-analysis. J Natl Cancer Inst. 2013;105:595–605.
15. Topalian SL, Drake CG, Pardoll DM. Immune checkpoint blockade: a common denominator approach to cancer therapy. Cancer Cell. 2015;27:450–61.
16. Topalian SL, Hodi FS, Brahmer JR, Gettinger SN, Smith DC, McDermott DF, et al. Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. N Engl J Med. 2012;366:2443–54.
17. Yarchoan M, Hopkins A, Jaffee EM. Tumor mutational burden and response rate to PD-1 inhibition. N Engl J Med. 2017;377:2500–1.
18. Ahn B-C. Personalized medicine based on theranostic radioiodine molecular imaging for differentiated thyroid cancer. Biomed Res Int. 2016;2016:1680464.
19. Strosberg J, El-Haddad G, Wolin E, Hendifar A, Yao J, Chasen B, et al. Phase 3 trial of ^{177}Lu-Dotatate for midgut neuroendocrine tumors. N Engl J Med. 2017;376:125–35.
20. Lütje S, Heskamp S, Cornelissen AS, Poeppel TD, van den Broek SA, Rosenbaum-Krumme S, et al. PSMA ligands for radionuclide

imaging and therapy of prostate cancer: clinical status. Theranostics. 2015;5:1388.
21. Yip SS, Kim J, Coroller TP, Parmar C, Velazquez ER, Huynh E, et al. Associations between somatic mutations and metabolic imaging phenotypes in non-small cell lung cancer. J Nucl Med. 2017;58:569.
22. Bang J-I, Ha S, Kang S-B, Lee K-W, Lee H-S, Kim J-S, et al. Prediction of neoadjuvant radiation chemotherapy response and survival using pretreatment [^{18}F] FDG PET/CT scans in locally advanced rectal cancer. Eur J Nucl Med Mol Imaging. 2016;43:422–31.
23. Ha S, Park S, Bang J-I, Kim E-K, Lee H-Y. Metabolic radiomics for pretreatment ^{18}F-FDG PET/CT to characterize locally advanced breast cancer: histopathologic characteristics, response to neoadjuvant chemotherapy, and prognosis. Sci Rep. 2017;7:1556.
24. Park S, Ha S, Lee S-H, Paeng JC, Keam B, Kim TM, et al. Intratumoral heterogeneity characterized by pretreatment PET in non-small cell lung cancer patients predicts progression-free survival on EGFR tyrosine kinase inhibitor. PLoS One. 2018;13:e0189766.
25. Cook GJ, O'Brien ME, Siddique M, Chicklore S, Loi HY, Sharma B, et al. Non-small cell lung cancer treated with Erlotinib: heterogeneity of ^{18}F-FDG uptake at PET—association with treatment response and prognosis. Radiology. 2015;276:883–93.
26. Choi H, Na KJ. Integrative analysis of imaging and transcriptomic data of the immune landscape associated with tumor metabolism in lung adenocarcinoma: clinical and prognostic implications. Theranostics. 2018;8:1956.
27. Na KJ, Choi H. Tumor metabolic features identified by ^{18}F-FDG PET correlate with gene networks of immune cell microenvironment in head and neck cancer. J Nucl Med. 2018;59:31–7.
28. Galavis PE, Hollensen C, Jallow N, Paliwal B, Jeraj R. Variability of textural features in FDG PET images due to different acquisition modes and reconstruction parameters. Acta Oncol. 2010;49:1012–6.