Radiomics in Oncology: A Practical Guide

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Conflicts of interest

• I am CEO, shareholder and President of BoD of Quibim
Outline

1. Introduction
2. Radiomics
3. Use cases
4. Conclusions
Introduction

• Utility of biomarkers in Precision Medicine (genomics, liquid biopsy, pathology, imaging).
Introduction

• Imaging biomarkers and radiomics are challenged to move from research into actionable solutions
Introduction

• Challenge: bridge imaging with clinical endpoints and hallmarks of the disease

Hanahan. Redefining war on cancer.
Introduction

• The creation of AI models from radiomics features and imaging biomarkers must follow a rigorous procedure
Introduction

• A growing number of research publications show promising results of radiomics features and imaging biomarkers for prediction of clinical outcomes

• A high number of AI-models developed are based on single-center studies and therefore not externally validated

• There is a lack of large meta-analysis generating the evidence that is needed for an impact in clinical guidelines and redefinition of treatment response criteria
Radiomics

• Radiomics feature extraction is founded on the principles of texture analysis
Clarifying other concepts:

• **Deep features**: unlike Radiomics features, deep features are extracted without specific hand-crafted algorithms, by using deep convolutional neural networks

• **End-to-end deep learning**: use the image itself to classify the patients into groups

A recommendation is to follow always a multiple strategy approach, based on radiomics analysis, deep features extraction, and image-based end-to-end deep learning
Radiomics

Dealing with image quality harmonization across sites:

**Low frequencies reconstruction**

**Purpose**

Learn frequency components from a dataset in order to generate homogenized shared features.

Keep clinical features such as lesions or anatomical structures.
Radiomics

Dealing with image quality harmonization across sites: self-supervised learning approach
Use case: prediction of response in metastatic NSCLC

- Prediction of response to immunotherapy in metastatic lung cancer
- Anti-PD-1 therapies significantly improve the prognosis of a subgroup of patients with NSCLC
- There is still an absence of a key predictive biomarker of response to Immune Checkpoint Inhibitors
- Intratumoral heterogeneity assessed by IHC can also cause false negatives and some patients with low PD-L1 expression may benefit from Pembrolizumab
- Tumoral phenotype, including PD-L1 expression can change through time as a response to alterations of tumoral microenvironment and to clonal selection induced by treatments
- A large number of candidate biomarkers have been proposed

Del Re M, Cucchiara F, Rofi E, Fontanelli L, Petrini I, Gri N, Pasquini G, Rizzo M, Gabelloni M, Belluomini L, Crucitta S, Ciampi R, Frassoldati A, Neri E, Porta C, Danesi R. A multiparametric approach to improve the prediction of response to immunotherapy in patients with metastatic NSCLC. Cancer Immunol Immunother. 2021 Jun;70(6):1667-1678. doi: 10.1007/s00262-020-02810-6. Epub 2020 Dec 14. PMID: 33315149; PMCID: PMC8139911.
Use case: prediction of response in metastatic NSCLC

Study:

- 38 patients
- 25 Nivolumab as 2nd line or higher
- 13 Pembrolizumab as 1st line
- First radiological assessment:
  - 13 patients PR
  - 8 patients SD
  - 17 patients PD
- Overall response rate: 53% Pembro, 24% Nivo
Use case: prediction of response in metastatic NSCLC

Study:

- **ddPCR**: expression of PD-L1 and IFN-γ mRNA in plasma-derived exosomes
- **Real-time PCR**: Selected variants of PD-L1 gene (i.e. c.-14-368 T>G and c.*395G>C)
- **NGS** (Oncomine): Tumor mutational load (TML) in cfDNA
- **Radiomic analysis**: to identify imaging biomarkers of response to anti-PD-1
Use case: prediction of response in metastatic NSCLC

Response prediction (PD vs. PR / SD):

**Fig. 4** Specificity and sensitivity of radiomic signature, PD-L1 and IFN-γ FA and c.*395G>C polymorphism
Use case: mutational status in Lung cancer

- Accessibility to gene sequencing and liquid biopsy is limited as a standard-of-care globally
- Computed Tomography is standard-of-care for lung cancer detection and follow-up
- Having a non-invasive estimate of mutational status is key for early patient stratification
Use case: mutational status in Lung cancer

- Average AUC = 0.85 in differentiating EGFR-mutant and EGFR-wild type

- An example:

Wang S, et al. Predicting EGFR mutation status in lung adenocarcinoma on computed tomography image using deep learning. Eur Respir J. 2019 Mar 28;53(3):1800986.

Imyanitov EN, Iyevleva AG, Levchenko EV. Molecular testing and targeted therapy for non-small cell lung cancer: Current status and perspectives. Crit Rev Oncol Hematol. 2021 Jan;157:103194.
Use case: prediction of outcome in PCa

- Prostate cancer
- Prediction of biochemical relapse from baseline diagnostic exams
- To be used in the decision of earlier initiation of more intensive treatment scheme
- Top-tier pharma company (>1000 patients, multi-institution)
Use case: prediction of outcome in PCa

• Prostate cancer
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Use case: prediction of outcome in PCa

- Prostate cancer
- Prediction of biochemical relapse from baseline diagnostic exams.
- Current evidence based on single-center studies: 90-120 patients
- AUC 0.63 – 0.92
Other projects

• Prediction of low PFS in lung cancer patients treated with immunotherapy (candidate molecule vs. Pembrolizumab). Retrospective evaluation of Phase I – III trial data. Top-tier pharma company.

• Chaimeleon project. Accelerating lab to market transition of AI tools in cancer (pan-cancer: breast, prostate, lung, colo-rectal)
Conclusions

• Preliminary findings linking radiomics and AI models with clinical endpoints exist in current research.

• There is a severe lack of studies incorporating external validation across different institutions.

• Single-center studies for linking radiomics with clinical endpoints are not validating proofs.

• We are in ‘evidence generation mode’. Systematic reviews and meta-analysis are urgently needed.

• Radiomics contributes to better tumor and environment characterization, patient stratification, early detection of relapse after treatment and development of precision medicine.
Thank you