Radiomics in Oncology: A Practical Guide

Angel Alberich-Bayarri, PhD

Quibim, Valencia (ES)

Biomedical Imaging Research Group (GIBI230),

La Fe Health Research Institute, Valencia (ES)

European Society of Medical Imaging Informatics (EUSOMII)

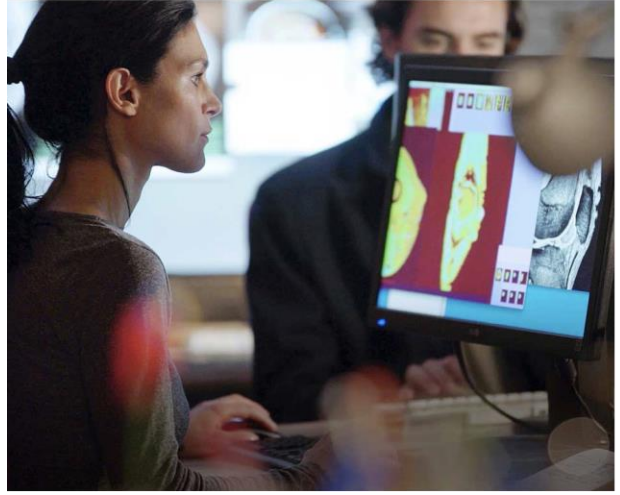
angel@quibim.com

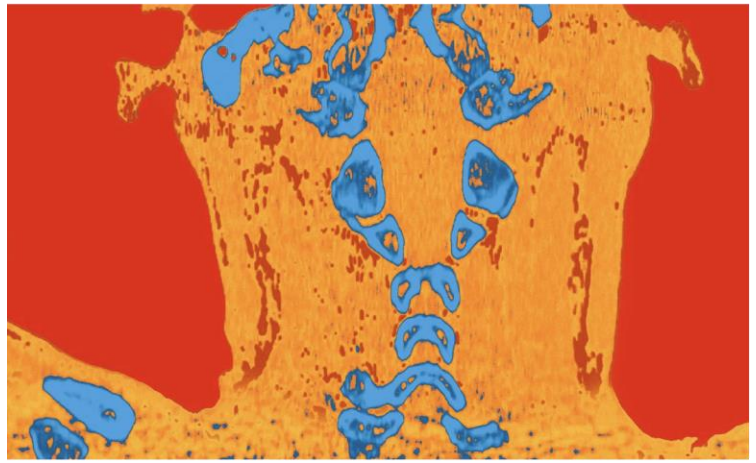
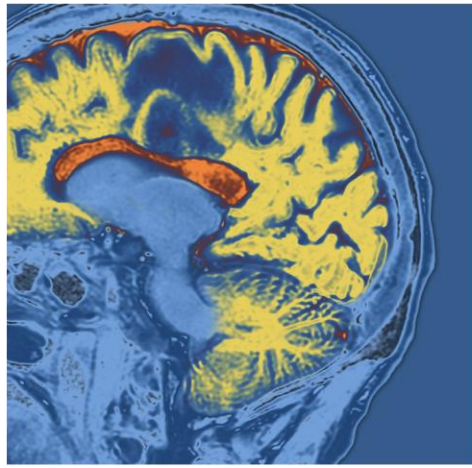
Conflicts of interest

- I am CEO, shareholder and President of BoD of Quibim

Outline

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



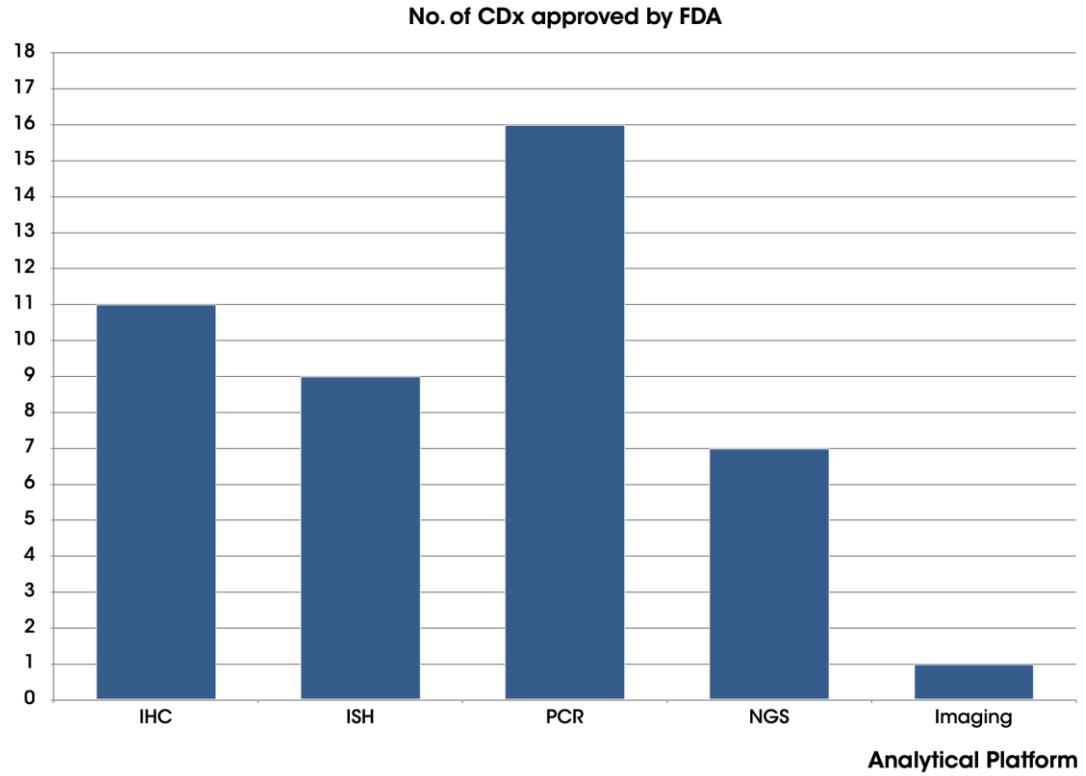



Introduction

- Utility of biomarkers in Precision Medicine (genomics, liquid biopsy, pathology, **imaging**).

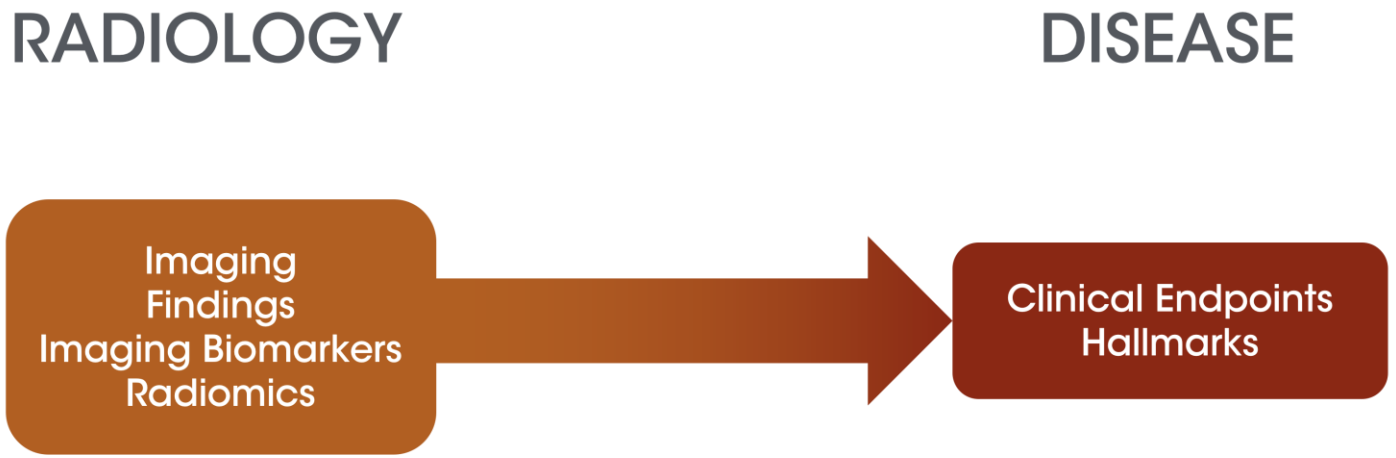
Introduction

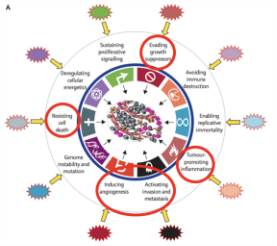
- Imaging biomarkers and radiomics are challenged to move from research into actionable solutions



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

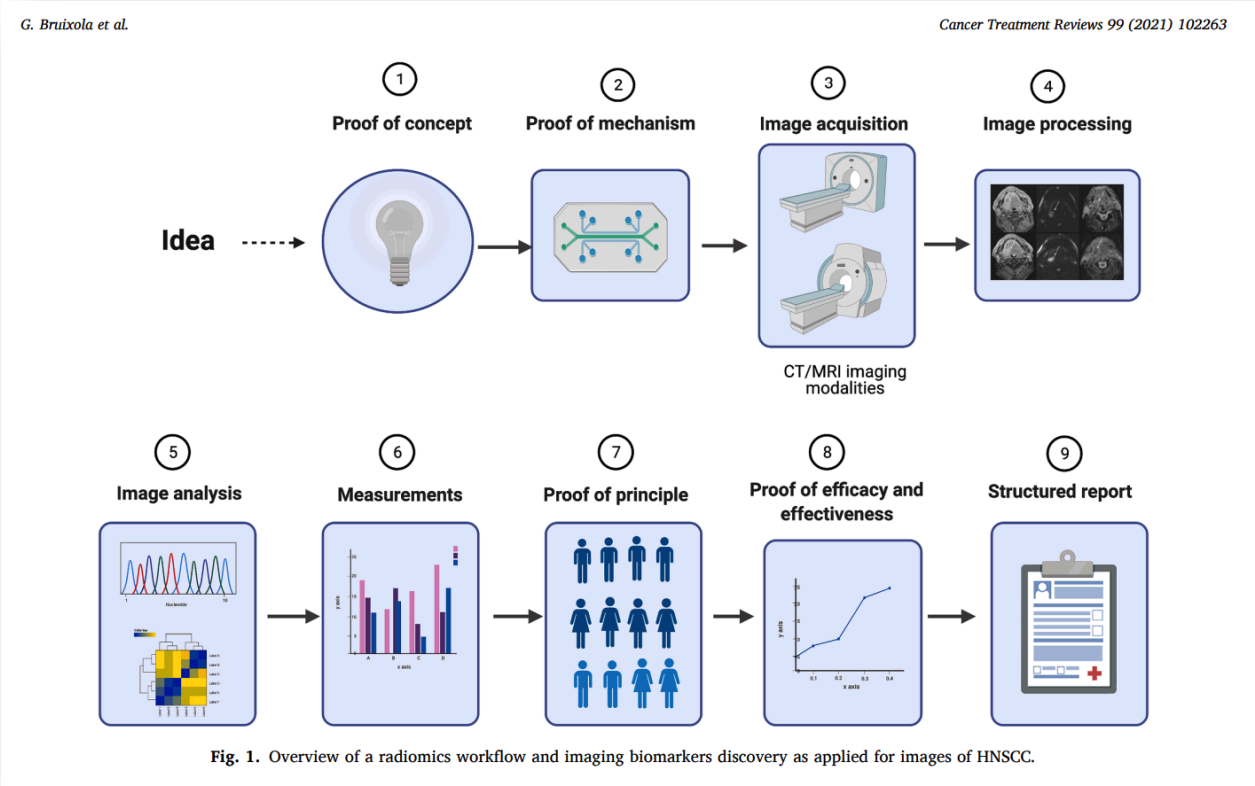
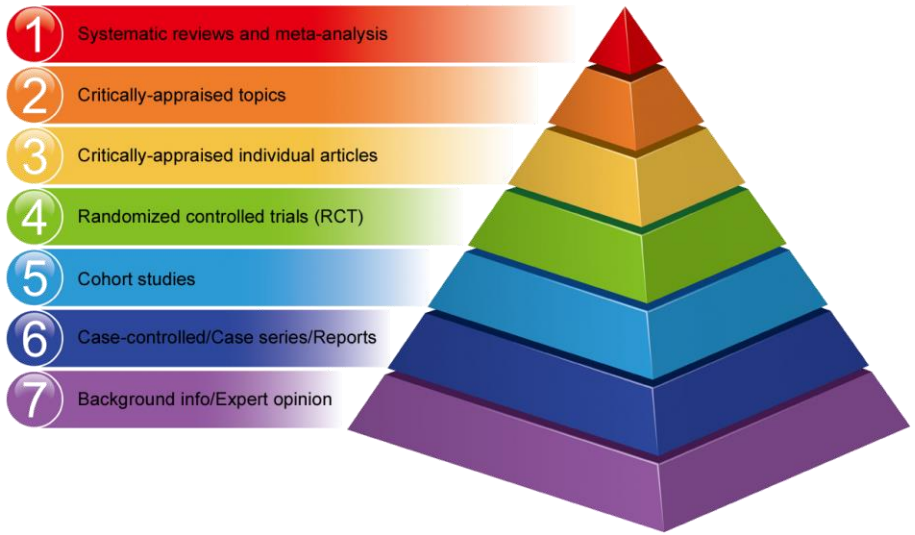


Fig. 1. Overview of a radiomics workflow and imaging biomarkers discovery as applied for images of HNSCC.

Bruixola G, Remacha E, Jiménez-Pastor A, Dualde D, Viala A, Montón JV, Ibarrola-Villava M, Alberich-Bayarri Á, Cervantes A. Radiomics and radiogenomics in head and neck squamous cell carcinoma: Potential contribution to patient management and challenges. Cancer Treat Rev. 2021 Sep;99:102263.

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

Radiomics

Clarifying other concepts:

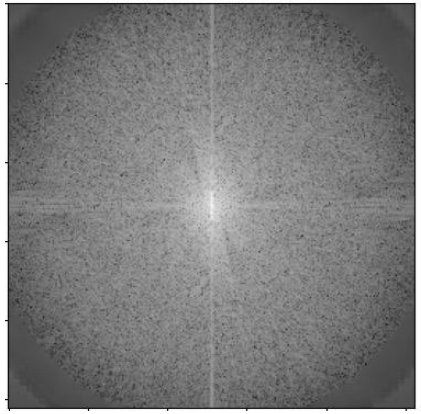
- Deep features: unlike Radiomics features, deep features are extracted without specific hand-crafted algorithms, by using deep convolutional neural networks
- End-to-end deep learning: use the image itself to classify the patients into groups

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:

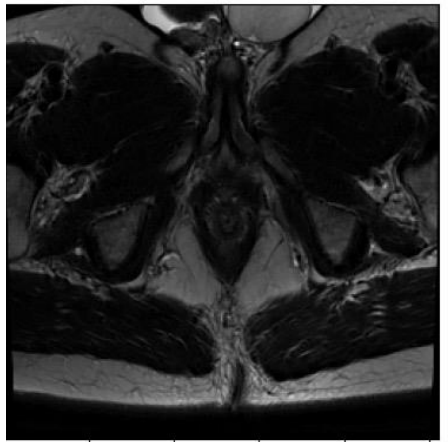
Low frequencies reconstruction



Purpose

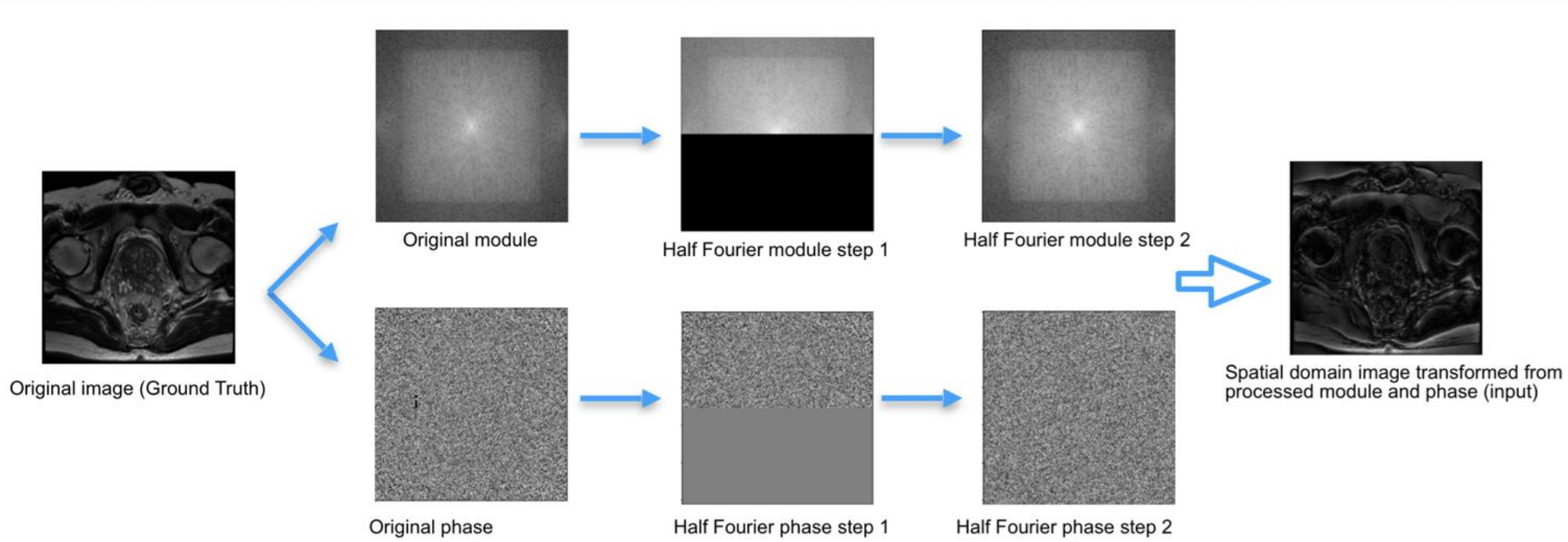
Learn frequency components from a dataset in order to generate homogenized shared features.

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:

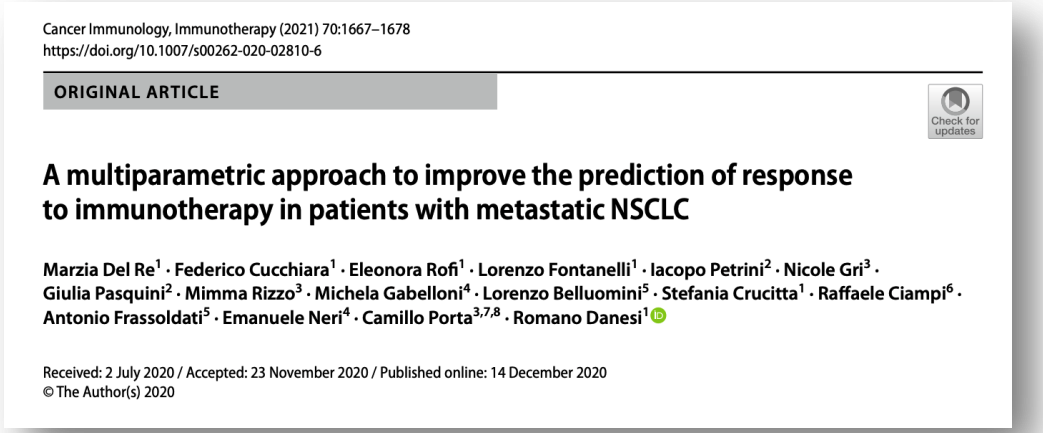
- 38 patients
- 25 Nivolumab as 2nd line or higher
- 13 Pembrolizumab as 1st line
- First radiological assessment:
  - 13 patients PR
  - 8 patients SD
  - 17 patients PD
- Overall response rate: 53% Pembro, 24% Nivo

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:

- 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 y c.*395G>C)
- NGS (Oncomine): Tumor mutational load (TML) in cfDNA
- Radiomic analysis: to identify imaging biomarkers of response to anti-PD-1



Cancer Immunology, Immunotherapy (2021) 70:1667–1678
https://doi.org/10.1007/s00262-020-02810-6

ORIGINAL ARTICLE

Check for updates

A multiparametric approach to improve the prediction of response to immunotherapy in patients with metastatic NSCLC

Marzia Del Re[1] · Federico Cucchiara[1] · Eleonora Rofi[1] · Lorenzo Fontanelli[1] · Iacopo Petrini[2] · Nicole Gri[3] · Giulia Pasquini[2] · Mimma Rizzo[3] · Michela Gabelloni[4] · Lorenzo Belluomini[5] · Stefania Crucitta[1] · Raffaele Ciampi[6] · Antonio Frassoldati[5] · Emanuele Neri[4] · Camillo Porta[3,7,8] · Romano Danesi[1]

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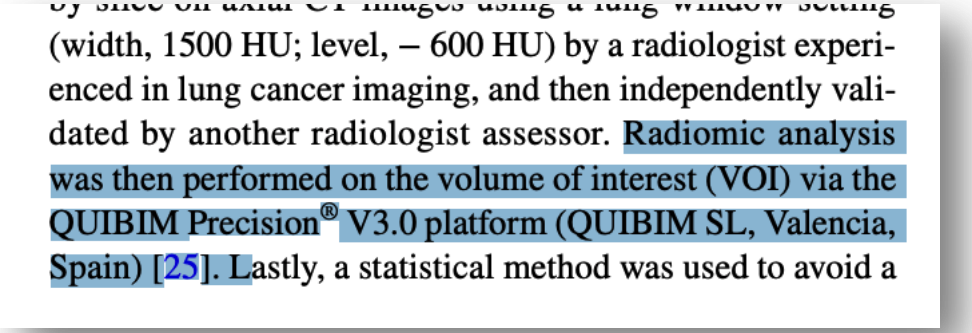


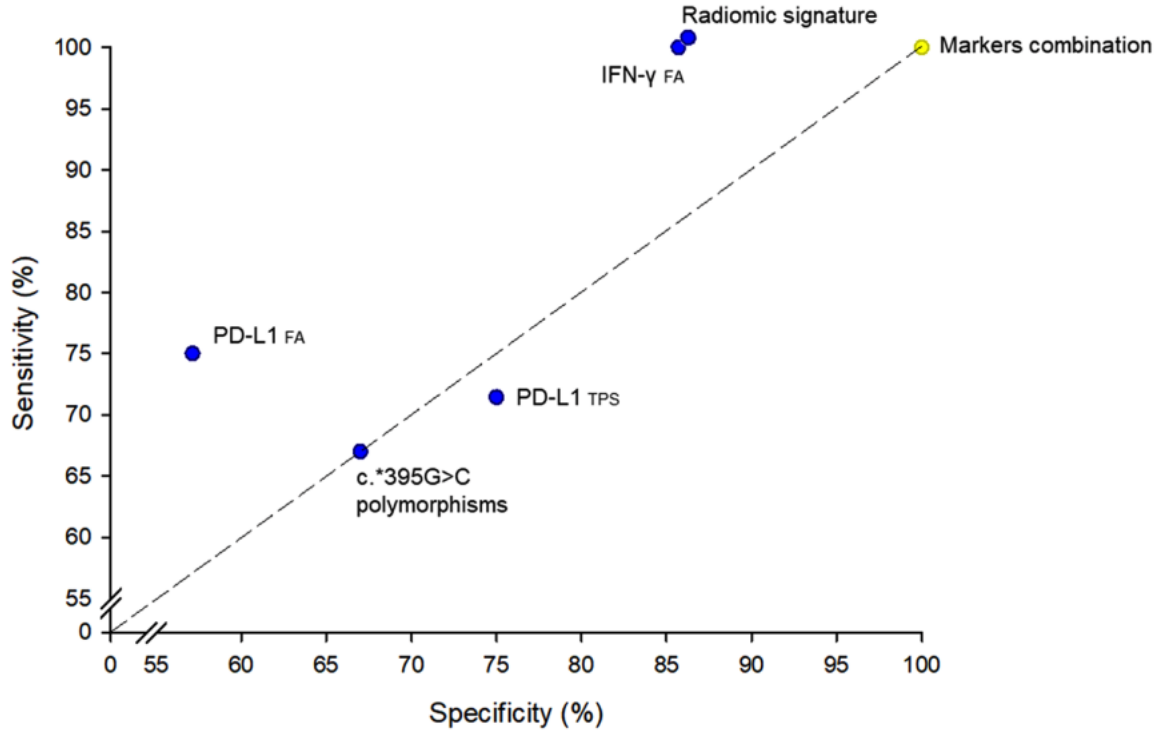
(width, 1500 HU; level, – 600 HU) by a radiologist experienced in lung cancer imaging, and then independently validated by another radiologist assessor. Radiomic analysis was then performed on the volume of interest (VOI) via the QUIBIM Precision® V3.0 platform (QUIBIM SL, Valencia, Spain) [25]. Lastly, a statistical method was used to avoid a

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

Response prediction (PD vs. PR / SD):

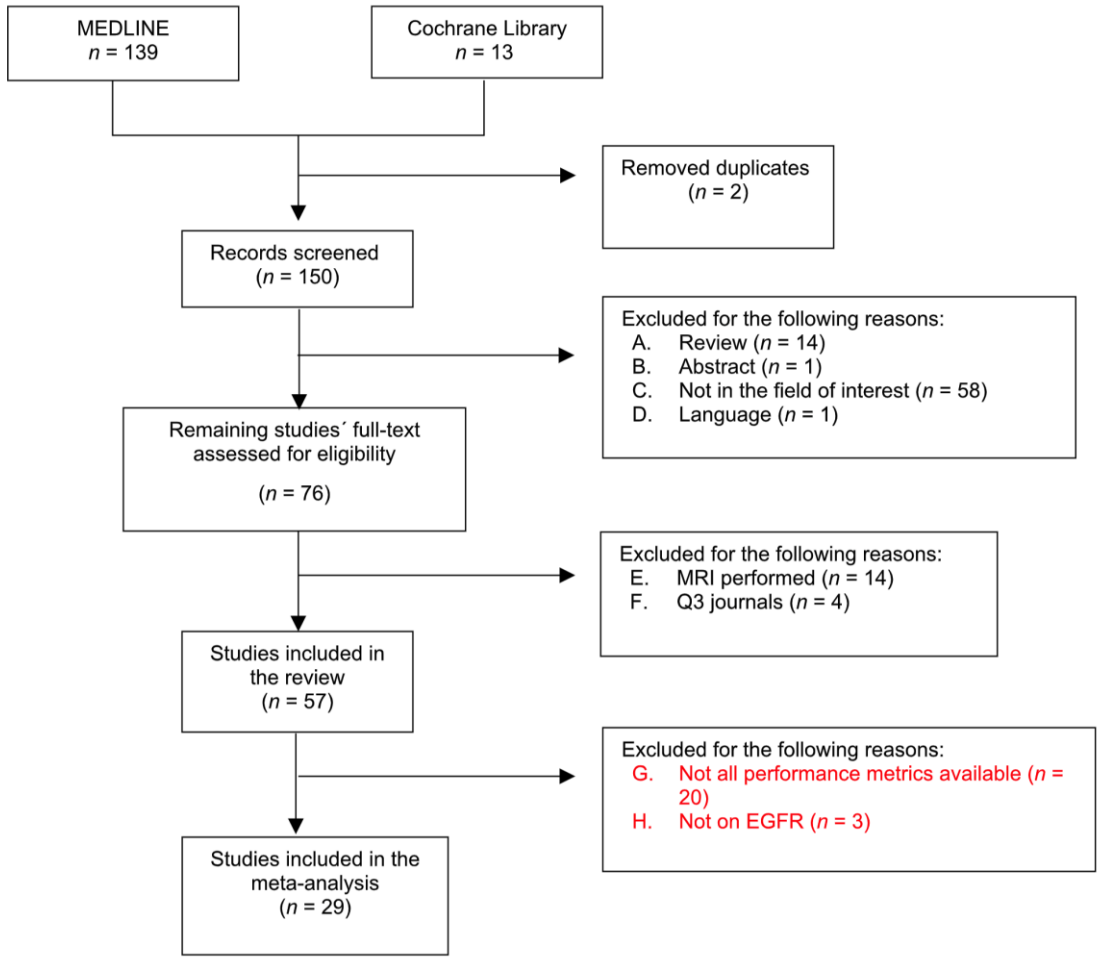
Fig. 4 Specificity and sensitivity of radiomic signature, PD-L1 and IFN-γ FA and c.*395G > C polymorphism



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.

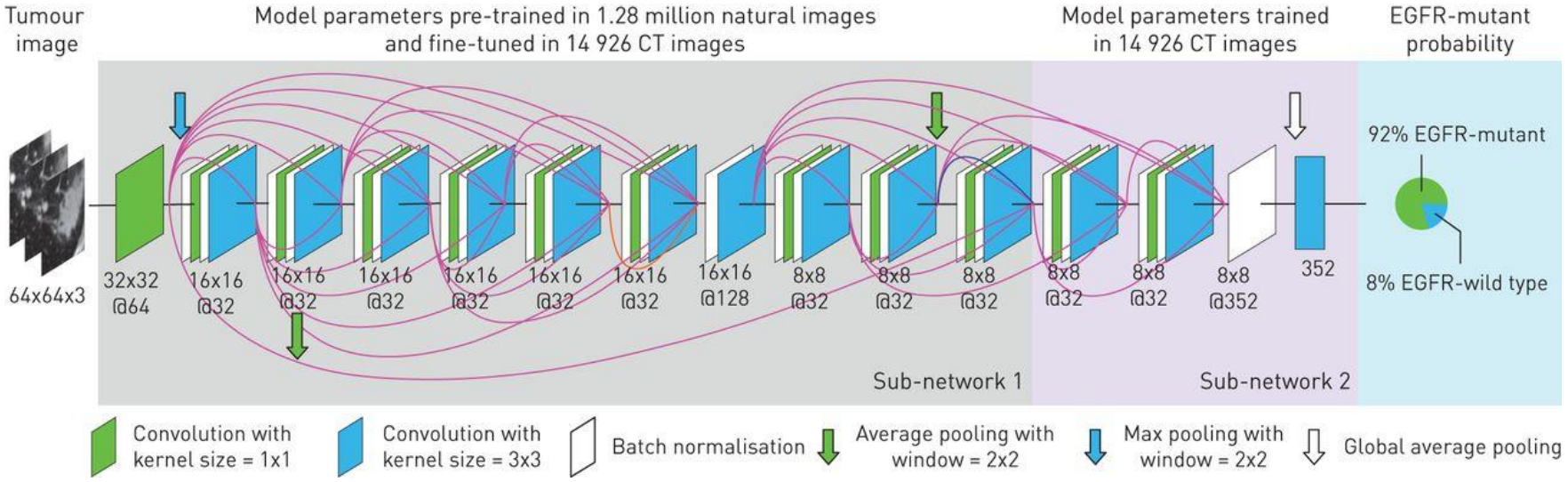
Use case: mutational status in Lung cancer

- 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

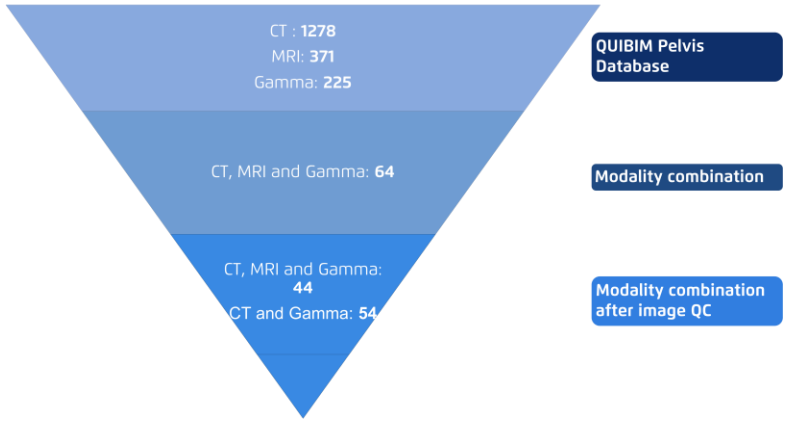
- Average AUC = 0.85 in differentiating EGFR-mutant and EGFR-wild type
- An example:

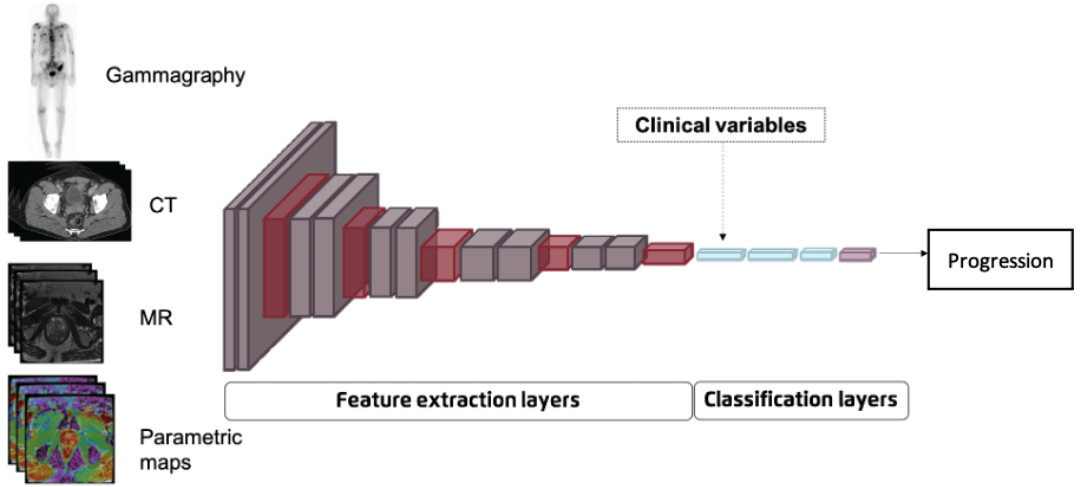


Wang S, et al. Predicting EGFR mutation status in lung adenocarcinoma on computed tomography image using deep learning. Eur Respir J. 2019 Mar 28;53(3):1800986.
Imyanitov EN, Iyevleva AG, Levchenko EV. Molecular testing and targeted therapy for non-small cell lung cancer: Current status and perspectives. Crit Rev Oncol Hematol. 2021 Jan;157:103194.

Use case: prediction of outcome in PCa

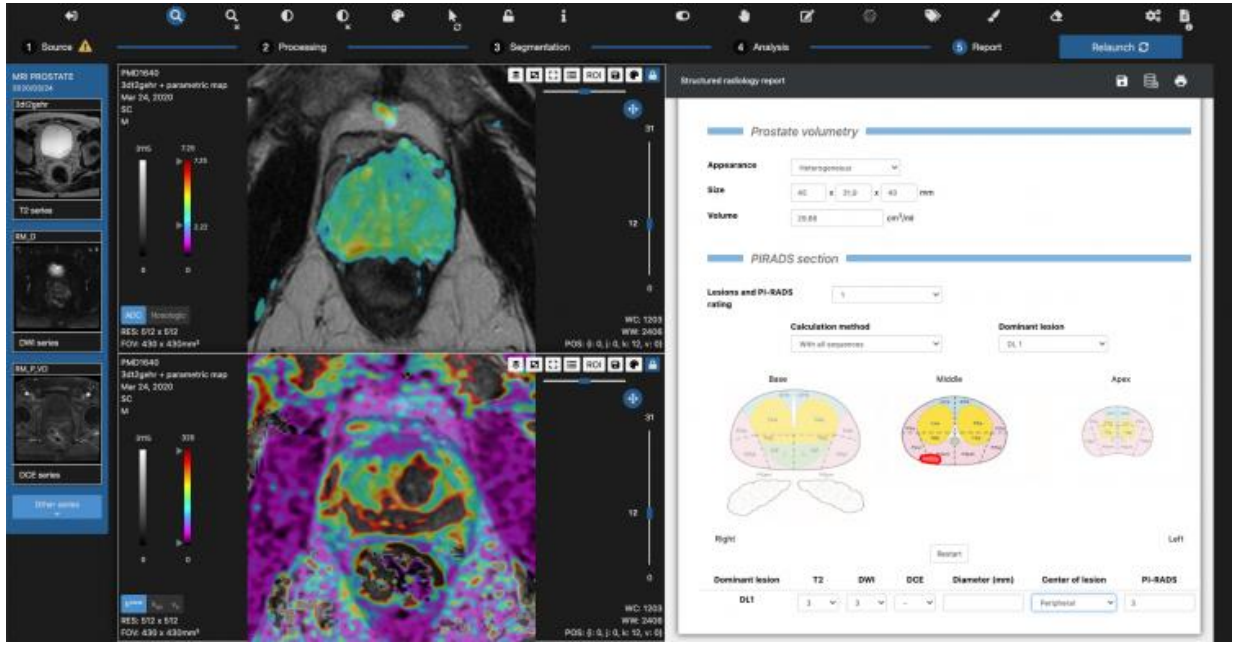
- Prostate cancer
- Prediction of biochemical relapse from baseline diagnostic exams
- To be used in the decision of earlier initiation of more intensive treatment scheme
- Top-tier pharma company (>1000 patients, multi-institution)

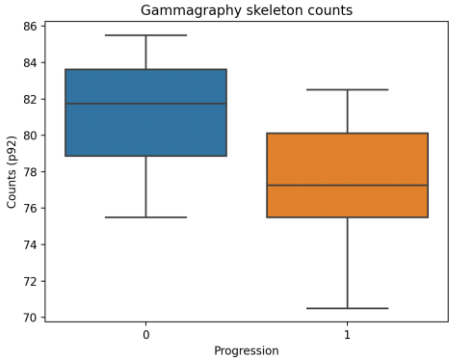


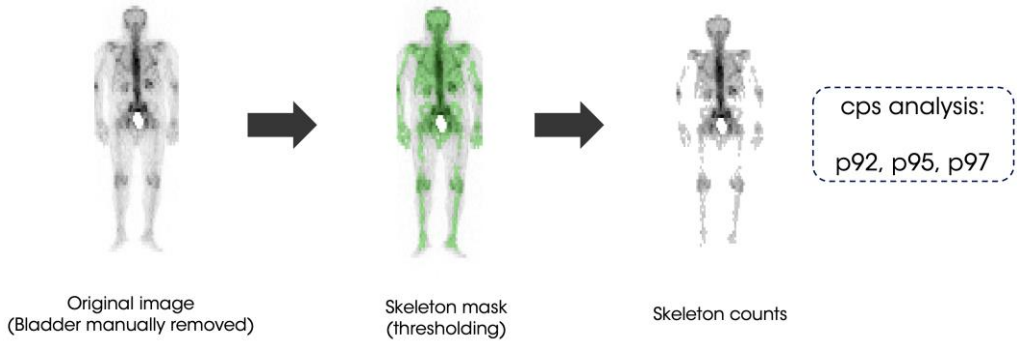


Use case: prediction of outcome in PCa

- Prostate cancer
- Prediction of biochemical relapse from baseline diagnostic exams

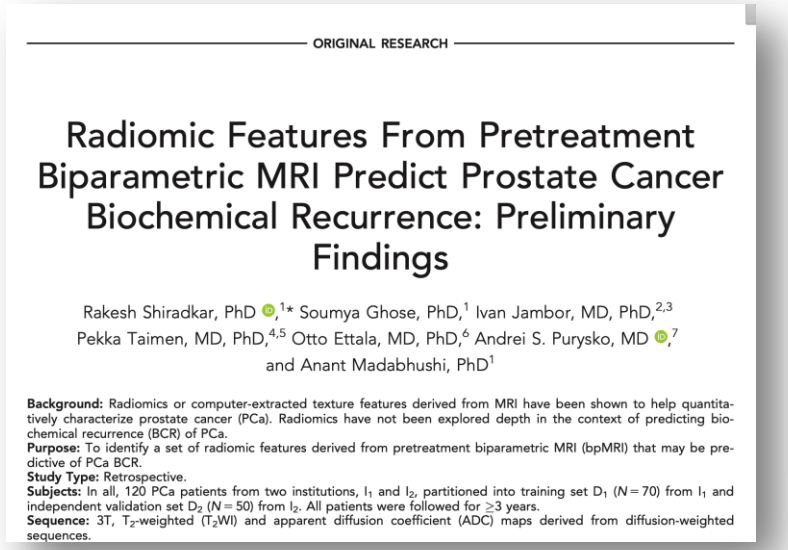






Use case: prediction of outcome in PCa

- 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

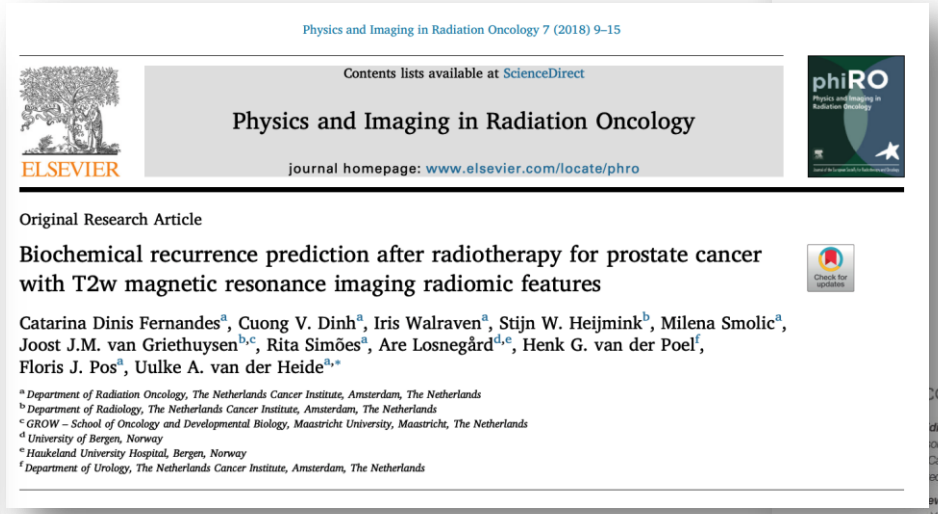


ORIGINAL RESEARCH

Radiomic Features From Pretreatment Biparametric MRI Predict Prostate Cancer Biochemical Recurrence: Preliminary Findings

Rakesh Shiradkar, PhD,[1]* Soumya Ghose, PhD,[1] Ivan Jambor, MD, PhD,[2,3] Pekka Taimen, MD, PhD,[4,5] Otto Ettala, MD, PhD,[6] Andrei S. Purysko, MD,[7] and Anant Madabhushi, PhD[1]

Background: Radiomics or computer-extracted texture features derived from MRI have been shown to help quantitatively characterize prostate cancer (PCa). Radiomics have not been explored depth in the context of predicting biochemical recurrence (BCR) of PCa.
Purpose: To identify a set of radiomic features derived from pretreatment biparametric MRI (bpMRI) that may be predictive of PCa BCR.
Study Type: Retrospective.
Subjects: In all, 120 PCa patients from two institutions, I_1 and I_2, partitioned into training set D_1 ($N = 70$) from I_1 and independent validation set D_2 ($N = 50$) from I_2. All patients were followed for ≥3 years.
Sequence: 3T, T_2-weighted (T_2WI) and apparent diffusion coefficient (ADC) maps derived from diffusion-weighted sequences.



Physics and Imaging in Radiation Oncology 7 (2018) 9–15

Contents lists available at ScienceDirect

Physics and Imaging in Radiation Oncology

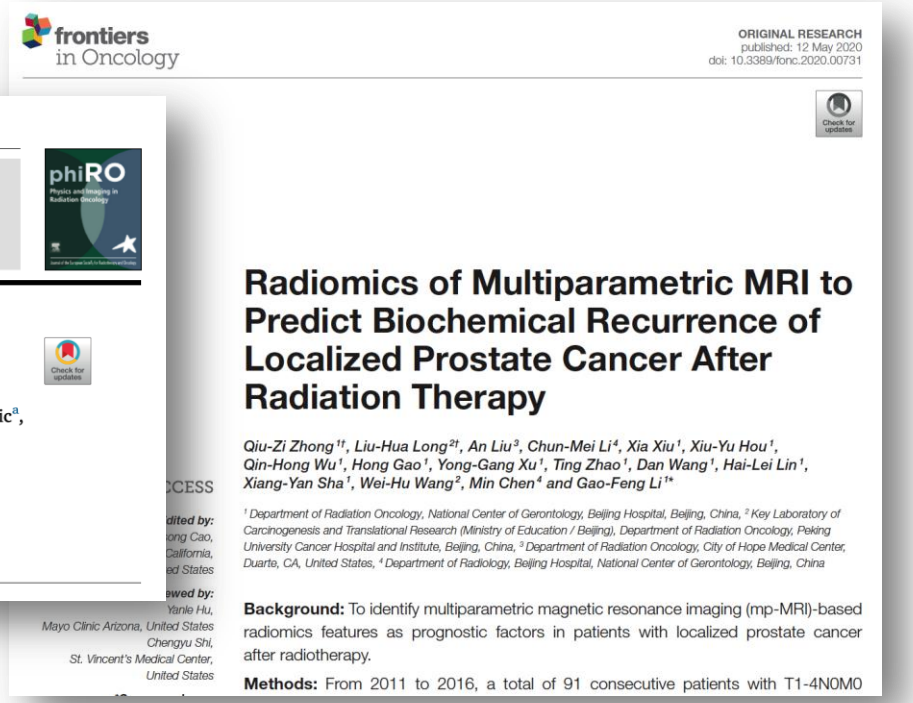
journal homepage: www.elsevier.com/locate/phro

Original Research Article

Biochemical recurrence prediction after radiotherapy for prostate cancer with T2w magnetic resonance imaging radiomic features

Catarina Dinis Fernandes[a], Cuong V. Dinh[a], Iris Walraven[a], Stijn W. Heijmink[b], Milena Smolic[a], Joost J.M. van Griethuysen[b,c], Rita Simões[a], Are Losnegård[d,e], Henk G. van der Poel[f], Floris J. Pos[a], Uulke A. van der Heide[a,*]

[a] Department of Radiation Oncology, The Netherlands Cancer Institute, Amsterdam, The Netherlands
[b] Department of Radiology, The Netherlands Cancer Institute, Amsterdam, The Netherlands
[c] GROW – School of Oncology and Developmental Biology, Maastricht University, Maastricht, The Netherlands
[d] University of Bergen, Norway
[e] Haukeland University Hospital, Bergen, Norway
[f] Department of Urology, The Netherlands Cancer Institute, Amsterdam, The Netherlands



frontiers in Oncology

ORIGINAL RESEARCH
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doi: 10.3389/fonc.2020.00731

Radiomics of Multiparametric MRI to Predict Biochemical Recurrence of Localized Prostate Cancer After Radiation Therapy

Qiu-Zi Zhong[1†], Liu-Hua Long[2†], An Liu[3], Chun-Mei Li[4], Xia Xiu[1], Xiu-Yu Hou[1], Qin-Hong Wu[1], Hong Gao[1], Yong-Gang Xu[1], Ting Zhao[1], Dan Wang[1], Hai-Lei Lin[1], Xiang-Yan Sha[1], Wei-Hu Wang[2], Min Chen[4] and Gao-Feng Li[1*]

[1] Department of Radiation Oncology, National Center of Gerontology, Beijing Hospital, Beijing, China, [2] Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education / Beijing), Department of Radiation Oncology, Peking University Cancer Hospital and Institute, Beijing, China, [3] Department of Radiation Oncology, City of Hope Medical Center, Duarte, CA, United States, [4] Department of Radiology, Beijing Hospital, National Center of Gerontology, Beijing, China

Background: To identify multiparametric magnetic resonance imaging (mp-MRI)-based radiomics features as prognostic factors in patients with localized prostate cancer after radiotherapy.

Methods: From 2011 to 2016, a total of 91 consecutive patients with T1-4N0M0

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