

Radiomics

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Radiomics: a quantitative imaging biomarker in precision oncology

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Cancer treatment is heading towards precision medicine driven by genetic and biochemical markers. Various genetic and biochemical markers are utilized to render personalized treatment in cancer. In the last decade, noninvasive imaging biomarkers have also been developed to assist personalized decision support systems in oncology. The imaging biomarkers i.e., radiomics is being researched to develop specific digital phenotype of tumor in cancer. Radiomics is a process to extract high throughput data from medical images by using advanced mathematical and statistical algorithms. The radiomics process involves various steps i.e., image generation, segmentation of region of interest (e.g. a tumor), image preprocessing, radiomic feature extraction, feature analysis and selection and finally prediction model development. Radiomics process explores the heterogeneity, irregularity and size parameters of the tumor to calculate thousands of advanced features. Our study investigates the role of radiomics in precision oncology. Radiomics research has witnessed a rapid growth in the last decade with several studies published that show the potential of radiomics in diagnosis and treatment outcome prediction in oncology. Several radiomics based prediction models have been developed and reported in the literature to predict various prediction

endpoints i.e., overall survival, progression-free survival and recurrence in various cancer i.e., brain tumor, head and neck cancer, lung cancer and several other cancer types. Radiomics based digital phenotypes have shown promising results in diagnosis and treatment outcome prediction in oncology. In the coming years, radiomics is going to play a significant role in precision oncology. *Nucl Med Commun* 43: 483–493 Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

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Introduction

Cancer is caused by genetic mutations leading to uncontrolled growth of tissue and the cells can leave the tissue colony and metastasize in other parts of the body [1]. Conventionally, cancer is treated by surgery or chemotherapy or radiotherapy or combinations of these [2]. Often the selection of treatment depends upon the type of tumor, stage of the disease and general condition of the patient [2]. Although, clinicians consider these factors to decide the course of treatment, on several occasions these treatments fail [3]. This led to the evolution of personalized medicine in oncology [4]. Personalized oncology works on the principle of identification of subgroups of patients in particular disease types [4,5]. Many biomarkers and gene mutations have been investigated to identify the subgroups of the patients in various cancers

and targeted drugs for those subgroups [5,6]. For example, by sequencing and in situ hybridization techniques a patient subgroup with epidermal growth factor receptor mutation can be identified in non-small cell lung cancer patients. These high-risk patients do not respond well to conventional treatment options but show good response with targeted therapies like Erlotinib, Gefitinib, Afatinib and similar drugs [6–9]. Precision oncology has the potential to personalize the screening, risk stratifications, treatment selection and response assessment [4,5]. Although most approaches towards precision oncology are centered on biomarkers and genetic mutation assessments [7], artificial intelligence (AI) driven technologies are also being explored to improve the accuracy of precision oncology [10–12]. This technology-driven approach has also been tested in various fields in precision oncology, that is, screening, risk stratifications, treatment selection and response assessment [10,12]. AI-based precision oncology has achieved success as witnessed in published literature in the last few years. Various imaging biomarkers

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Radiomics

Radiomics as a word was first used by Lambin *et al.* in 2012 in order to describe the quantification of medical imaging data [17]. Radiomics is a process to extract high throughput data from medical images like CT, PET, MRI or SPECT by using advanced mathematical and statistical analysis of images [16,17]. The Radiomics process explores the heterogeneity, irregularity and size parameters of the tumor to calculate thousands of advanced features [16–18]. There are mainly two types of radiomics, i.e., handcrafted radiomics and deep learning-based radiomics. Here in this manuscript mainly we will discuss the first form of radiomics i.e. hand crafted radiomics and we will address these by the term radiomics itself [19].

Radiomics process

The Radiomics process involves various steps, i.e., image generation, segmentation of the region of interest (ROI) (e.g. a tumor), image preprocessing, radiomic feature extraction, feature analysis and selection and prediction model development [16–18]. The stepwise radiomic process is shown in Fig. 1.

Image generation

Medical equipment like CT, PET, MRI and SPECT are used to image the patient and three-dimensional images

are generated by sophisticated reconstruction techniques. These images are archived in image repository, that is, picture archiving communication system (PACS) for future utilization.

Segmentation

The images are transferred to the workstations and the ROI is delineated surrounding the tumor, to extract radiomic features from that part of the image. The ROI is generated by medical experts or physicists and typically stored as DICOM RT structure or Segmentation.

Preprocessing of image

Image preprocessing involves various steps performed on images and the ROI. As an example, the following steps are typically performed before radiomic extraction from the medical images [20].

Interpolation

Medical images are reconstructed and represented in three-dimensional matrices with one unit of the matrix called a voxel. Often voxels are not isotropic and to extract textural radiomic features, the voxels are often resampled or interpolated into isotropic voxels.

Resegmentation

The original ROI defined by expert or by automated segmentation is utilized to generate a morphological mask and intensity mask. The morphological mask is the original mask. The intensity mask is resegmented, which contains selected voxel inside or outside the morphological mask.

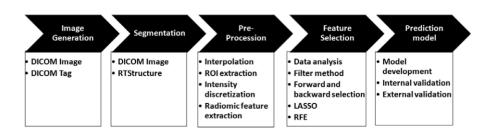
Region of interest extraction

Many features do not require voxels outside the ROI; hence the image volume is extracted for the image based on the ROI of intensity mask.

Intensity discretization

Medical images contain noise and often quantization of image intensities is performed to suppress the noise inside the ROI to calculate the texture features. Two

Fig. 1.



Radiomic process for radiomic feature extraction and feature selection.

approaches are used for intensity discretization, that is, (1) fixed number of bins and (2) fixed bin width.

Radiomic feature extraction

Automatic extraction of radiomic features is performed in this step. Thousands of radiomic features are generated in this step which is further processed in the radiomic analysis step.

Radiomic analysis and feature selection

While sometimes 1000+ features are extracted from medical images; these are not all useful for phenotyping a particular disease or for the development of an outcome prediction model. Many features are redundant and many have no association with the particular disease or outcome. Various statistical tests can be performed for feature reduction [21]. Hierarchical clustering, Spearman correlation, Pearson correlation paired t-test are performed to eliminate the redundancy of the feature; forward, backward feature selection, Least Absolute Shrinkage and Selection Operator or recursive feature elimination techniques are used to reduce the dimensionality of the features. Finally, the most appropriate features are selected for disease prognostication or prediction model development for various endpoints like overall survival, recurrence, treatment selection or prediction of treatment outcomes.

Prediction model development

Finally, the prediction model is developed and validated by using the selected features. These features may also be combined with clinical features to develop prediction models. Various machine algorithms have been used to develop a prediction model depending upon the need i.e., regression algorithms, Linear and Logistic regression, K-Nearest Neighbor, decision trees algorithms, i.e., Random Forest, Support Vector Machine, Bayesian Network, and deep learning algorithms, i.e., Convolutional Neural Networks, Recurrent Neural Networks and Artificial Neural Networks [22-24].

Radiomic features can be categorized into various groups [18]. Feature groups and the typical number of features extracted using Pyradiomics software [25] are shown in Table 1 (Supplementary material 1, Supplemental digital content 1, http://links.lww.com/NMC/A215).

Deep learning radiomics workflow

Recently, an alternative to handcrafted radiomic workflow, a deep learning-based radiomics workflow [26-28] has emerged. A deep learning-based radiomics workflow extracts features from medical images without predefined formulas. Images may be used with or without an ROI for this deep radiomic workflow. Usually, it is a twoor three-step process. Step (1) image data acquisition, (2) segmentation (may or may not be given), (3) development and validation of deep neural networks model. It is not possible in deep learning radiomics to describe features mathematically.

Radiomics and precision oncology

Radiomics has witnessed a rapid growth in the last decade with several studies published that show the potential of radiomics in diagnosis and treatment of cancer. Many radiomics based AI decision support systems have been developed in oncology and reported in literature. Figure 2 shows the process of precision oncology leveraging radiomic and artificial intelligence.

In the last few years a new aspect of radiomics, that is, Delta Radiomics is being researched [29]. Delta radiomics comprises extraction and comparison of quantitative features from sequential scans acquired over the course of treatment, which provides information on the efficacy of treatment.

Methodology

This study is approved by the Institutional Ethics Committee as a retrospective study. In this study, we have performed literature surveys to find the emerging trend of radiomics based publications in oncology. Our search criteria are optimized to search only those articles, which clearly mention radiomics or related terms like texture analysis in their title. We further extended our search and added year of publication as a criterion to find the total number of publications available on radiomics on PubMed and year-wise distribution of those publications. Furthermore, we added disease and segregated articles based on disease type. To understand the trend of imaging modality used for radiomic study we further included keywords like CT or PET or MRI along with search criteria in all fields. The details of search criteria adopted in this study are mentioned in Tables 2 and 3.

Results

We found in total 5243 articles published on radiomics since the year 2000 that satisfied our search criteria. Out of total articles published on radiomics, 624, 2234 and 2110 articles had mention of PET, CT and MRI, respectively (Table 4). The detailed distribution of the publications year wise in all categories are shown in Table 4. There were 123 studies published on radioiomic stability study. Maximum 549 articles were published on lung cancer alone followed by 533 articles on GI cancer (Fig. 3).

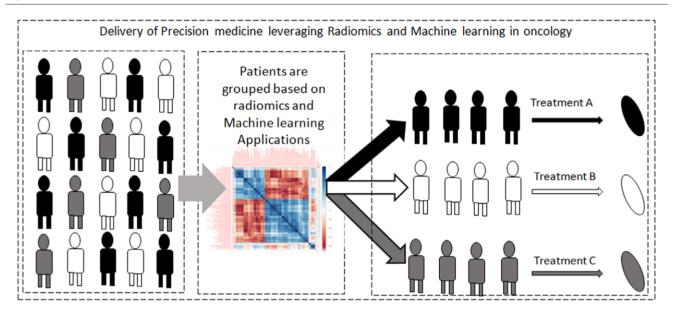
The percentage of radiomic articles published on CT and MRI are almost the same 45% and 42%, respectively (Fig. 3a). Radiomics articles published on lung and GI cancers contribute approximately 20% of total publications on radiomics (Fig. 3b).

Publication trend on radiomics has shown rapid growth in last decade (Fig. 4a). The trend shows that the yearly publications have increased many folds in the last 5 years (Fig. 4b). A similar growth trend has been

Table 1. Radiomic features can be extracted by using PyRadiomics software

Type of feature	Feature descriptions				
Shape-based features	Shape features are the descriptors of the three-dimensional size and shape of the ROI and independent from the gray level intensity distribution. These features are only calculated on the original image and mask.	13			
First-order statistics	First-order statistics describe the distribution of voxel intensities within the ROI region of the image.	17			
GLRLM	Gray Level Run Length Matrix (GLRLM) assesses the distribution of discretized gray levels in an image or in a stack of images assesses run lengths.	16			
GLCM	Gray Level Co-Occurrence Matrix (GLCM) expresses how combinations of discretized intensities of neighboring voxels in a 3D volume, are distributed along with one of the image directions.				
GLSZM	Gray Level Size Zone Matrix (GLSZM) counts the number of groups/zones of linked voxels with identical discretized gray level.	16			
NGTDM	Neighboring Gray Tone Difference Matrix (NGTDM) contains the sum of gray level differences of voxels with discretized gray level and the average discretized gray level of neighboring voxels within a Chebyshev distance δ.	5			
GLDM	Gray Level Dependence Matrix (GLCM) quantifies gray level dependencies in an image in terms of the number of connected voxels within distance δ that are dependent on the central voxel.	14			
LoG features	A Laplacian of Gaussian (LoG) filter is applied on the original image and one set of derived images is generated for each sigma value specified. Usually, 1-5 sigma values are used, we use 3 sigma values 1, 2, 3 and three sets of derived images are produced. Subsequently, radiomic features are extracted from these image sets.	270			
Wavelet features	Wavelet transformation of image is performed using the three-dimensional wavelet decomposition and 8 sets of images are generated from the original image set. Radiomic features are extracted for transformed image sets.	720			

Fig. 2.



Mechanism to deliver personalized medicine leveraging the machine learning and artificial intelligence to decode the digital signature of the individual patient.

witnessed in all imaging types (Fig. 4a and b) and all types of cancers (Fig. 5a and b). In our study, we found 85 articles which have utilized all three imaging modalities for radiomic study (Fig. 4c). Figure 4d shows the year wise publication of radiomic articles on stability of radiomic features.

Discussion

The utility of radiomic based prediction modeling has been tested widely in diagnosis and treatment of all varieties of solid tumors. Several studies have been performed to differentiate high-grade and low-grade gliomas and to develop various radiomic markers for treatment selection [26,27]. Several studies have shown

the association of radiomic features extracted from PET or MRI with survival in glioma [30–39]. Radiomics is widely used in diagnosis and treatment assessment of head and neck cancer [40]. A radiomic signature from PET, MRI and CT has been found to have a significant role in prediction of stage of tumor, HPV status, hypoxia status and gene expression in head and neck cancer [41–51]. Studies have shown the role of radiomics in characterization of sentinel lymph node metastasis in breast cancer noninvasively [52]. The role of radiomics has also been demonstrated by various researchers in breast cancer for response evaluation such as disease-free survival (DFS) [53–57]. The role of radiomics has been widely explored in lung cancer management [58]. Various

Table 2. The term and search criteria used to select study based on the above-mentioned criteria

Modality	Search Criteria					
Radiomics	"Texture Analysis" [Title] OR "Textural Analysis" [Title] OR "Imaging Biomarker" [Title] OR "Radiomic" [Title] OR "Radiomics" [Title] AND 2000/01/01: 2021/12/31 [do]					
Computed tomography	"Texture Analysis" [Title] OR "Textural Analysis" [Title] OR "Imaging Biomarker" [Title] OR "Radiomics" [Title] OR "Radiomic" [Title] AND ("CT" [ALL] OR "Computed Tomography" [ALL]) AND 2000/01/01: 2021/12/31 [dp]					
PET	"Texture Analysis" [Title] OR "Textural Analysis" [Title] OR "Imaging Biomarker" [Title] OR "Radiomics" [Title] OR "Radiomic" [Title] AND ("PET" [ALL] OR "Positron" [ALL]) AND 2000/01/01: 2021/12/31 [dp]					
MRI	"Texture Analysis" [Title] OR "Textural Analysis" [Title] OR "Imaging Biomarker" [Title] OR "Radiomics" [Title] OR "Radiomic" [Title] AND ("MRI" [ALL] OR "magnetic" [ALL]) AND 2000/01/01: 2021/12/31 [dp]					
PET and computed tomography	"Texture Analysis" [Title] OR "Textural Analysis" [Title] OR "Imaging Biomarker" [Title] OR "Radiomics" [Title] OR "Radiomic" [Title] AND ("PET" [ALL] OR "Positron" [ALL]) AND ("CT" [ALL] OR "Computed Tomography" [ALL]) AND 2000/01/01: 2021/12/31 [dp]					
PET and MRI	"Texture Analysis" [Title] OR "Textural Analysis" [Title] OR "Imaging Biomarker" [Title] OR "Radiomics" [Title] OR "Radiomics" [Title] AND ("MRI" [ALL] OR "magnetic" [ALL]) AND ("PET" [ALL] OR "Positron" [ALL]) AND 2000/01/01: 2021/12/31 [dp]					
MRI and computed tomog- raphy	"Texture Analysis" [Title] OR "Textural Analysis" [Title] OR "Imaging Biomarker" [Title] OR "Radiomics" [Title] OR "Radiomics" [Title] AND ("MRI" [ALL] OR "magnetic" [ALL]) AND ("CT" [ALL] OR "Computed Tomography" [ALL]) AND 2000/01/01: 2021/12/31 [dp]					
PET and computed tomogra- phy and MRI	("MRI" [ALL] OR "magnetic" [ALL]) AND ("PET" [ALL] OR "Positron" [ALL]) AND ("CT"[ALL] OR "Computed Tomography"[ALL])					
Radiomic stability	AND 2000/01/01: 2021/12/31[dp] "Texture Analysis" [Title] OR "Textural Analysis" [Title] OR "Imaging Biomarker" [Title] OR "Radiomic" [Title] OR "Radiomics" [Title] AND ("repeatability" [Title] OR "reproducibility" [Title] OR "stability" [Title]) AND 2000/01/01: 2021/12/31[dp]					

Table 3. The term and search criteria used to select radiomic studies published on various cancer types

Disease site	Search criteria				
Brain tumor	"Texture Analysis"[Title] OR "Textural Analysis"[Title] OR "Imaging Biomarker" [Title] OR "Radiomics" [Title] OR "Radiomic" [Title] AND ("Brain" [Title] OR "GBM" [Title] OR "glioblastoma" [Title] OR "glial" [Title]) AND 2000/01/01: 2021/12/31[dp]				
Head & neck cancer	"Texture analysis"[title] or "textural analysis"[title] or "imaging biomarker" [title] or "radiomics" [title] OR "Radiomic" [Title] and ("head- and-neck" [title] or "neck" [title] or "head" [title]) and 2000/01/01: 2021/12/31[dp]				
Lung cancer	"Texture Analysis" [Title] OR "Textural Analysis" [Title] OR "Imaging Biomarker" [Title] OR "Radiomics" [Title] OR "Radiomic" [Title] AND ("lung" [Title] OR "nsclc" [Title] OR "sclc" [Title]) AND 2000/01/01: 2021/12/31 [dp]				
Breast cancer	"Texture analysis"[title] or "textural analysis"[title] or "imaging biomarker" [title] or "radiomics" [title] OR "Radiomic" [Title] and "Breast" [title] and 2000/01/01: 2021/12/31[dp]				
Gastrointestinal cancer	"Texture Analysis" [Title] OR "Textural Analysis" [Title] OR "Imaging Biomarker" [Title] OR "Radiomics" [Title] OR "Radiomic" [Title] AND ("Gastrointestinal" [Title] OR "intestinal" [Title] OR "Liver" [Title] OR "HCC" [Title] OR "hepatocellular" [Title] OR "pancreatic" [Title] OR "pancreas" [Title] AND 2000/01/01: 2021/12/31 [dp]				
Cervical cancer	"Texture Analysis" [Title] OR "Textural Analysis" [Title] OR "Imaging Biomarker" [Title] OR "Radiomics" [Title] OR "Radiomic" [Title] AND ("Cervical" [Title] OR "Cervix" [Title]) AND 2000/01/01: 2021/12/31 [dp]				
Prostate cancer	"Texture Analysis" [Title] OR "Textural Analysis" [Title] OR "Imaging Biomarker" [Title] OR "Radiomics" [Title] OR "Radiomic" [Title] AND ("Prostate" [Title] OR "Prostatic" [Title]) AND 2000/01/01: 2021/12/31 [dp]				
Colorectal cancer	"Texture analysis" [title] or "textural analysis" [title] or "imaging biomarker" [title] or "radiomics" [title] OR "Radiomic" [Title] and ("Colorectal" [title] or "rectal" [title] or "Colon" [title]) and 2000/01/01: 2021/12/31 [dp]				

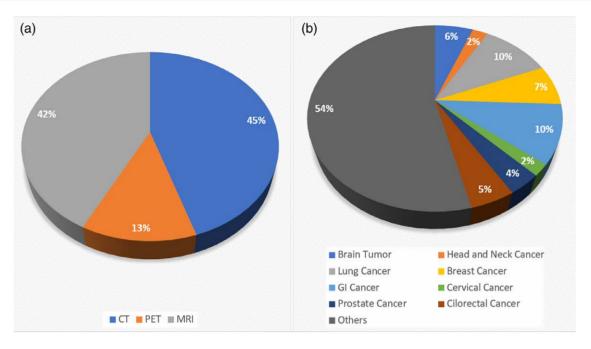
Table 4. The total and year wise publications on radiomics in oncology

Year	Publications on radiomics							
	2021	2020	2019	2018	2017	2016	2015	Total
Total	1549	1277	798	535	298	175	132	5243
CT	733	592	343	236	132	70	38	2234
PET	169	151	105	71	43	31	14	624
MRI	645	527	345	205	108	74	43	2110
CT-PET	142	118	82	46	33	26	5	475
PET-MR	42	33	21	17	9	6	2	135
CT-MRI	91	58	42	15	11	8	2	234
CT-MRI-PET	32	19	16	7	6	3	0	85
Stability	47	25	29	9	4	5	0	123
Brain tumor	80	74	45	36	24	14	8	307
Head & neck cancer	26	31	30	12	11	4	2	122
Lung cancer	155	157	78	71	39	20	10	549
Breast cancer	110	93	58	31	25	11	13	369
GI cancer	182	156	85	51	17	10	11	533
Cervical cancer	38	29	15	12	5	2	0	104
Prostate cancer	57	42	38	20	8	10	3	251
Colorectal cancer	82	69	39	22	10	11	9	187

studies have been performed to differentiate between benign and malignant tumor, pathology types (i.e. adenocarcinoma or squamous cell carcinoma), EGFR mutation

status and various TNM stages [59-65]. Literature published in the last one decade also suggests an increasing role of radiomic features in the prediction of OS, PFS,

Fig. 3.



Publications on radiomics: (a) Imaging modality wise distribution of articles; (b) disease wise distribution of articles.

Fig. 4.

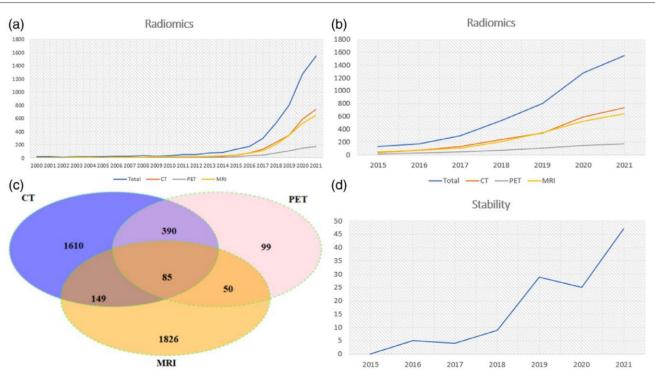


Figure shows (a) the trend of number of publications on PET, CT and MRI radiomics in oncology over the last two decades, (b) of number of publications on PET, CT and MRI radiomics in oncology since 2015. (c) Vann diagram shows the PET, CT and MRI imaging modality used for radiomic studies; (d) shows the trend of number of published radiomic stability issues since 2015.

Fig. 5.

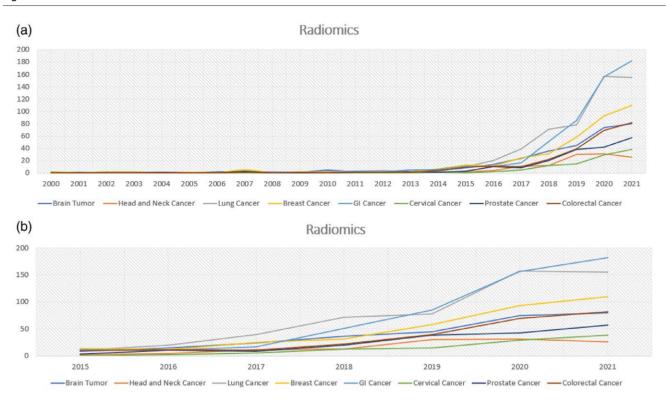


Figure shows (a) the trend of number of publications on radiomics in various cancer types over last two decades, (b) trend of number of publications on radiomics in various cancer types since 2015.

DFS, LRR, treatment response, toxicity and quality of life [66-72]. Radiomic features have been explored for the management of colorectal cancer. Various studies have demonstrated the role of radiomic features in the detection of lymph node metastasis, prediction of KRAS/NRAS/ BRAF mutation [73,74]. The role of radiomic features has also been investigated for treatment selection, treatment modification and DFS prediction [73,75-77]. Radiomics has been investigated in prostate cancer management and features extracted from MRI and PET have shown promising results. Several studies have shown the utility of radiomic features in the differentiation between benign and malignant tumor, aggressiveness of tumors and the Gleason Score [78-81]. Many researchers have also shown the utility of radiomic features extracted from MRI and PET to predict biochemical recurrence, PFS and OS [82-84], GI and liver cancer is another area where the role of radiomics has been investigated in disease management. The role of radiomics has been successfully demonstrated in microvascular invasion detection of liver cancer and differentiation in various kinds of GI malignancies, histology type and TNM staging in the GI cancer [85-91]. Various studies have demonstrated the role of radiomic features in detection of lymph node metastasis, OS, PSF and toxicity prediction in cervical cancer [92-95].

Our study shows an increasing trend of radiomics in oncology in the last decade. The last 5 years witnessed the tremendous growth of radiomic studies in oncology. In all major disease types growth of radiomic studies have been witnessed. Several articles have been published on radiomic stability problems that show the researchers have identified it as a major issue in radiomic implementation.

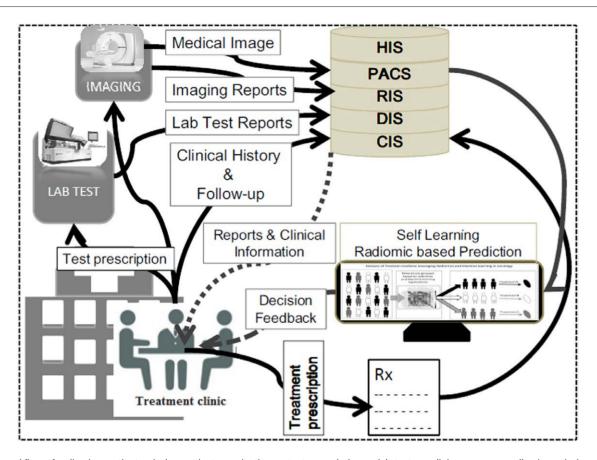
Implementation or radiomics based workflow in clinic

The future of radiomics lies in the clinical application of radiomics. A self-learning model may be developed and implemented in the clinic for participation in the decision support system. There will be requirements of a super-specialized model to address the specific clinical questions. As suggested by Lambin et al., the image archival system, that is, PACS has to be modified to picture archiving and radiomics knowledge systems to store radiomic signatures [16]. The future implementation of the radiomic process may look like Fig. 6.

Limitations of radiomic implementation

The main problem of radiomics is its limited repeatability and reproducibility which is thought to be mainly caused by the difference in scanners from different vendors, different acquisition protocols and intra scanner

Fig. 6



Clinical workflow of radiomics: patient arrival → patient examination → test prescription → lab test + radiology scan → radiomic analysis (self-learning prediction model) → decision support based on radiomic analysis → treatment prescription → follow-up data collection and entry.

variations. In our earlier repeatability and reproducibility study, we found that only 10% of CT radiomic features had a good repeatability and reproducibility in a clinical cohort and in phantoms [96]. Traverso et al. in a systematic literature review have also concluded that there are stability issues with majority of radiomic features [97]. In order to harmonize radiomic extraction tools, features and imaging standards, several initiatives are started by various agencies, like The Quantitative Imaging Network (QIN) [98], the Quantitative Imaging Biomarkers Alliance (QIBA) [99], and Quantitative Imaging in Cancer: Connecting Cellular Processes with Therapy (QuIC-ConCePT) [100]. These initiatives are working to standardize imaging and imaging biomarkers. The Image Biomarker Standardization Initiative (IBSI) is another consortium that works towards the harmonization of radiomic features across the globe by minimizing the deviation in imaging and standardizing the radiomic extraction process [101,102]. The radiomics quality score (RQS) is another such initiative proposed by Lambin et al. to address the issues related to radiomic study reporting [16]. Most of these initiatives will assist in advancing the standardization process of imaging biomarkers and are thus expected to address the repeatability and reproducibility challenges currently present in Radiomics.

Conclusion

This literature review is suggestive of the increasing role of radiomics in precision oncology. Publications on radiomics have increased many folds in the last 5 years. Initiatives like QIN, QIBA, QuIC-ConCePT, IBSI and RQS will be able to address repeatability and reproducibility of radiomic features. We envision that radiomics is going to play a pivotal role in phenotyping the cancer and guide cancer management to provide more precise treatments to patients in a true clinical environment soon.

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Consent for publication: All the authors consented to the publication.

Conflicts of interest

There are no conflicts of interest.

References

- Lodish H. Section 24.1, tumor cells and the onset of cancer. In: Lodish H, Berk A, Zipursky SL, et al. editors. Molecular cell biology. 4th ed. W. H. Freeman: 2000. Available from:https://www.ncbi.nlm.nih.gov/books/ NBK21590/
- Rai KR, Keating MJ. Treatment. In: Kufe DW, Pollock RE, Weichselbaum RR, et al., editors. Holland-Frei cancer medicine. 6th ed. BC Decker; 2003. Available from:https://www.ncbi.nlm.nih.gov/books/NBK12735/
- Maeda H, Khatami M. Analyses of repeated failures in cancer therapy for solid tumors: poor tumor-selective drug delivery, low therapeutic efficacy and unsustainable costs. Clin Transl Med. 2018; 7:11.
- Schwartzberg L. Kim ES. Liu D. Schrag D. Precision oncology: who. how, what, when, and when not? Am Soc Clin Oncol Educ Book 2017;
- Takeuchi S, Okuda S. Knowledge base toward understanding actionable alterations and realizing precision oncology. Int J Clin Oncol 2019;
- Goossens N, Nakagawa S, Sun X, Hoshida Y. Cancer biomarker discovery and validation. Transl Cancer Res 2015; 4:256-269.
- Biomarkers Definitions Working Group. Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. Clin Pharmacol Ther 2001; 69:89-95.
- Sasaki H, Endo K, Okuda K, Kawano O, Kitahara N, Tanaka H. Epidermal growth factor receptor gene amplification and gefitinib sensitivity in patients with recurrent lung cancer. J Cancer Res Clin Oncol 2008; 134:569-577.
- Bethune G, Bethune D, Ridgway N, Xu Z. Epidermal growth factor receptor (EGFR) in lung cancer: an overview and update. J Thorac Dis 2010; 2:48-51.
- Shimizu H, Nakayama KI. Artificial intelligence in oncology. Cancer Sci 2020: 111:1452-1460.
- 11 Deig CR, Kanwar A, Thompson RF. Artificial intelligence in radiation oncology. Hematol Oncol Clin North Am 2019; 33:1095-1104.
- Kann BH, Thompson R, Thomas CR Jr, Dicker A, Aneja S. Artificial intelligence in oncology: current applications and future directions. Oncology (Williston Park) 2019; 33:46-53.
- 13 O'Connor JP, Aboagye EO, Adams JE, Aerts HJ, Barrington SF, Beer AJ, et al. Imaging biomarker roadmap for cancer studies. Nat Rev Clin Oncol 2017: 14:169-186.
- Skwarski M, Higgins GS. A new roadmap to improve translation of imaging biomarkers. Br J Cancer 2016; 115:1443-1444.
- European Society of Radiology (ESR). ESR statement on the stepwise development of imaging biomarkers. Insights Imaging 2013; 4:147-152.
- Lambin P, Leijenaar RTH, Deist TM, Peerlings J, de Jong EEC, van Timmeren J, et al. Radiomics: the bridge between medical imaging and personalized medicine. Nat Rev Clin Oncol 2017; 14:749-762.
- 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; 48:441-446
- 18 Jha AK, Mithun S, Rangarajan V, Wee L, Dekker A. Emerging role of artificial intelligence in nuclear medicine. Nucl Med Commun 2021; 42:592-601.
- Afshar P, Mohammadi A, Plataniotis KN, Oikonomou A, Benali H. From handcrafted to deep-learning-based cancer radiomics: challenges and opportunities. IEEE Signal Process Mag 2019; 36:132-160.
- Image processing, https://ibsi.readthedocs.io/en/latest/02_Image_ processing.html. Last accessed on 15-05-2021
- 21 Bermingham ML, Pong-Wong R, Spiliopoulou A, et al. Application of highdimensional feature selection: evaluation for genomic prediction in man. Sci Rep 2015: 5:10312.
- Wang L, Alexander C. Machine learning in big data. Int J Math Eng Manag Sci. 2016; 1:52-61.
- 23 Goodfellow I, Bengio Y, Courville A. Deep learning. MIT Press; 2016. pp.
- Jordan MI, Mitchell TM. Machine learning: trends, perspectives, and prospects. Science 2015; 349:255-260.
- Radiomic Features. https://pyradiomics.readthedocs.io/en/latest/features. html. [Accessed 10 June 2021]

- 26 Li Z, Wang Y, Yu J, Guo Y, Cao W. Deep learning based radiomics (DLR) and its usage in noninvasive IDH1 prediction for low grade glioma. Sci Rep 2017: 7:1-11.
- Zhou L, Zhang Z, Chen YC, Zhao ZY, Yin XD, Jiang HB. A deep learningbased radiomics model for differentiating benign and malignant renal tumors. Transl Oncol 2019; 12:292-300.
- 28 Lao J, Chen Y, Li ZC, Li Q, Zhang J, Liu J, Zhai G. A deep learning-based radiomics model for prediction of survival in glioblastoma multiforme. Sci Rep 2017; 7:1-8.
- Fave X, Zhang L, Yang J, Mackin D, Balter P, Gomez D, et al. Deltaradiomics features for the prediction of patient outcomes in non-small cell lung cancer. Sci Rep 2017:7:588.
- Itakura H, Achrol AS, Mitchell LA, Loya JJ, Liu T, Westbroek EM, et al. Magnetic resonance image features identify glioblastoma phenotypic subtypes with distinct molecular pathway activities. Sci Transl Med 2015;
- 31 Bai Y, Lin Y, Tian J, Shi D, Cheng J, Haacke EM, et al. Grading of Gliomas by using monoexponential, biexponential, and stretched exponential diffusion-weighted MR imaging and diffusion kurtosis MR imaging. Radiology 2016: 278:496-504.
- 32 Chen W, Liu B, Peng S, Sun J, Qiao X. Computer-aided grading of Gliomas combining automatic segmentation and radiomics. Int J Biomed Imaging 2018: 2018:2512037.
- 33 Kickingereder P, Götz M, Muschelli J, Wick A, Neuberger U, Shinohara RT, et al. Large-scale radiomic profiling of recurrent glioblastoma identifies an imaging predictor for stratifying anti-angiogenic treatment response. Clin Cancer Res 2016; 22:5765-5771.
- Shim KY, Chung SW, Jeong JH, Hwang I, Park CK, Kim TM, et al. Radiomics-based neural network predicts recurrence patterns in glioblastoma using dynamic susceptibility contrast-enhanced MRI. Sci Rep 2021: 11:9974
- 35 Kim JY, Park JE, Jo Y, Shim WH, Nam SJ, Kim JH, et al. Incorporating diffusion- and perfusion-weighted MRI into a radiomics model improves diagnostic performance for pseudoprogression in glioblastoma patients. Neuro Oncol 2019; 21:404-414.
- 36 Grossmann P, Narayan V, Chang K, Rahman R, Abrey L, Reardon DA, et al. Quantitative imaging biomarkers for risk stratification of patients with recurrent glioblastoma treated with bevacizumab. Neuro Oncol 2017; 19:1688-1697.
- 37 Papp L, Pötsch N, Grahovac M, Schmidbauer V, Woehrer A, Preusser M, et al. Glioma survival prediction with combined analysis of In Vivo 11C-MET PET features, ex vivo features, and patient features by supervised machine learning. J Nucl Med 2018; 59:892-899.
- 38 Park JE, Kim HS, Jo Y, Yoo RE, Choi SH, Nam SJ, Kim JH. Radiomics prognostication model in glioblastoma using diffusion- and perfusionweighted MRI. Sci Rep 2020; 10:4250.
- Pérez-Beteta J, Molina-García D, Ortiz-Alhambra JA, Fernández-Romero A, Luque B, Arregui E, et al. Tumor surface regularity at MR imaging predicts survival and response to surgery in patients with glioblastoma. Radiology 2018; 288:218-225.
- 40 Jethanandani A, Lin TA, Volpe S, Elhalawani H, Mohamed ASR, Yang P, Fuller CD. Exploring applications of radiomics in magnetic resonance imaging of head and neck cancer: a systematic review. Front Oncol 2018; 8:131.
- 41 Ren J, Tian J, Yuan Y, Dong D, Li X, Shi Y, Tao X. Magnetic resonance imaging based radiomics signature for the preoperative discrimination of stage I-II and III-IV head and neck squamous cell carcinoma. Eur J Radiol 2018; 106:1-6.
- 42 Leijenaar RT, Bogowicz M, Jochems A, Hoebers FJ, Wesseling FW, Huang SH, et al. Development and validation of a radiomic signature to predict HPV (p16) status from standard CT imaging: a multicenter study. Br J Radiol 2018: 91:20170498.
- 43 Zhou Z, Chen L, Sher D, Zhang Q, Shah J, Pham NL, et al. Predicting Lymph Node metastasis in head and neck cancer by combining manyobjective radiomics and 3-dimensional convolutional neural network through evidential reasoning. Annu Int Conf IEEE Eng Med Biol Soc 2018; 2018:1-4.
- 44 Chen RY, Lin YC, Shen WC, Hsieh TC, Yen KY, Chen SW, Kao CH. Associations of tumor PD-1 ligands, immunohistochemical studies, and textural features in 18F-FDG PET in squamous cell carcinoma of the head and neck. Sci Rep 2018; 8:105.
- Chen L, Wang H, Zeng H, Zhang Y, Ma X. Evaluation of CT-based radiomics signature and nomogram as prognostic markers in patients with laryngeal squamous cell carcinoma. Cancer Imaging 2020; 20:28.
- 46 Crispin-Ortuzar M, Apte A, Grkovski M, Oh JH, Lee NY, Schöder H, et al. Predicting hypoxia status using a combination of contrast-enhanced

- computed tomography and [18F]-Fluorodeoxyglucose positron emission tomography radiomics features. Radiother Oncol 2018; 127:36-42.
- Zhang B, Tian J, Dong D, Gu D, Dong Y, Zhang L, et al. Radiomics features of multiparametric MRI as novel prognostic factors in advanced nasopharyngeal carcinoma. Clin Cancer Res 2017; 23:4259-4269.
- 48 Zhang B, He X, Ouyang F, Gu D, Dong Y, Zhang L, et al. Radiomic machine-learning classifiers for prognostic biomarkers of advanced nasopharyngeal carcinoma. Cancer Lett 2017; 403:21-27.
- van Rossum PS, Fried DV, Zhang L, Hofstetter WL, van Vulpen M, Meijer GJ, et al. The incremental value of subjective and quantitative assessment of 18F-FDG PET for the prediction of pathologic complete response to preoperative chemoradiotherapy in esophageal cancer. J Nucl Med 2016;
- 50 Wang G, He L, Yuan C, Huang Y, Liu Z, Liang C. Pretreatment MR imaging radiomics signatures for response prediction to induction chemotherapy in patients with nasopharyngeal carcinoma. Eur J Radiol 2018: 98:100-106.
- 51 Sanduleanu S, Jochems A, Upadhaya T, Even AJG, Leijenaar RTH, Dankers FJWM, et al. Non-invasive imaging prediction of tumor hypoxia: a novel developed and externally validated CT and FDG-PET-based radiomic signatures. Radiother Oncol 2020; 153:97-105.
- 52 Dong Y, Feng Q, Yang W, Lu Z, Deng C, Zhang L, et al. Preoperative prediction of sentinel lymph node metastasis in breast cancer based on radiomics of T2-weighted fat-suppression and diffusion-weighted MRI. Eur Radiol 2018; 28:582-591.
- 53 Chan H, Bhm VDV, Loo CE, Kga G. Eigentumors for prediction of treatment failure in patients with early-stage breast cancer using dynamic contrastenhanced MRI: a feasibility study. Phys Med Biol 2017; 62:62.
- 54 Braman NM, Etesami M, Prasanna P, Dubchuk C, Gilmore H, Tiwari P, et al. Intratumoral and peritumoral radiomics for the pretreatment prediction of pathological complete response to neoadjuvant chemotherapy based on breast DCE-MRI. Breast Cancer Res 2017; 19:57.
- 55 Partridge SC, Zhang Z, Newitt DC, Gibbs JE, Chenevert TL, Rosen MA, et al; ACRIN 6698 Trial Team and I-SPY 2 Trial Investigators. Diffusionweighted MRI Findings predict pathologic response in neoadjuvant treatment of breast cancer: the ACRIN 6698 multicenter trial. Radiology 2018: 289:618-627
- Tran WT, Gangeh MJ, Sannachi L, Chin L, Watkins E, Bruni SG, et al. Predicting breast cancer response to negadiuvant chemotherapy using pretreatment diffuse optical spectroscopic texture analysis. Br J Cancer 2017; 116:1329-1339.
- 57 Park H, Lim Y, Ko ES, Cho H-H, Lee JE, Han B-K. Radiomics signature on magnetic resonance imaging: association with disease-free survival in patients with invasive breast cancer. Clin Cancer Res 2018; 24:4705-4714.
- Avanzo M, Stancanello J, Pirrone G, Sartor G. Radiomics and deep learning in lung cancer. Strahlenther Onkol 2020; 196:879-887.
- Maldonado F, Boland JM, Raghunath S, Aubry MC, Bartholmai BJ, Deandrade M, et al. Non-invasive characterization of the histopathologic features of pulmonary nodules of the lung adenocarcinoma spectrum using computer aided nodule assessment and risk yield (CANARY) - a pilot study. J Thorac Oncol 2013; 8:452-460.
- 60 Liu Y, Balagurunathan Y, Atwater T, Antic S, Li Q, Walker RC, et al. Radiological image traits predictive of cancer status in pulmonary nodules. Clin Cancer Res 2017; 23:1442-1449.
- Zhang L, Chen B, Liu X, Song J, Fang M, Hu C, et al. Quantitative biomarkers for prediction of epidermal growth factor receptor mutation in non-small cell lung cancer. Transl Oncol 2018; 11:94-101.
- Wu W, Parmar C, Grossmann P, Quackenbush J, Lambin P, Bussink J, et al. Exploratory Study to Identify Radiomics Classifiers for Lung Cancer Histology. Front Oncol 2016; 6:71.
- Bashir U, Kawa B, Siddique M, Mak SM, Nair A, Mclean E, et al. Noninvasive classification of non-small cell lung cancer: a comparison between random forest models utilising radiomic and semantic features. Br J Radiol 2019: 92:20190159.
- 64 Zhu X, Dong D, Chen Z, et al. Radiomic signature as a diagnostic factor for histologic subtype classification of non-small cell lung cancer. Eur Radiol 2018: 28:2772-2778.
- 65 Fan L, Fang M, Li Z, et al. Radiomics signature: a biomarker for the preoperative discrimination of lung invasive adenocarcinoma manifesting as a ground-glass nodule. Eur Radiol 2019; 29:889-897.
- Cunliffe A, Armato SG 3rd, Castillo R, Pham N, Guerrero T, Al-Hallaq HA. Lung texture in serial thoracic computed tomography scans: correlation of radiomics-based features with radiation therapy dose and radiation pneumonitis development. Int J Radiat Oncol Biol Phys 2015; **91**:1048-1056.

- 67 Coroller TP, Grossmann P, Hou Y, Rios Velazquez E, Leijenaar RT, Hermann G, et al. CT-based radiomic signature predicts distant metastasis in lung adenocarcinoma. Radiother Oncol 2015: 114:345-350.
- Mattonen SA, Tetar S, Palma DA, Senan S, Ward AD. Automated texture analysis for prediction of recurrence after stereotactic ablative radiation therapy for lung cancer. Int J Radiat Oncol Biol Phys. 2015; 93:S5-S6.
- 69 Coroller TP, Agrawal V, Narayan V, Hou Y, Grossmann P, Lee SW, et al. Radiomic phenotype features predict pathological response in non-small cell lung cancer. Radiother Oncol 2016; 119:480-486.
- Aerts HJ, Grossmann P, Tan Y, Oxnard GR, Rizvi N, Schwartz LH, Zhao B. Defining a radiomic response phenotype: a pilot study using targeted therapy in NSCLC. Sci Rep 2016; 6:33860.
- 71 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; 276:883-893.
- 72 Huang Y, Liu Z, He L, Chen X, Pan D, Ma Z, et al. Radiomics signature: a potential biomarker for the prediction of disease-free survival in early-stage (I or II) non-small cell lung cancer. Radiology 2016; 281:947-957.
- 73 Huang YO, Liang CH, He L, Tian J, Liang CS, Chen X, et al. Development and validation of a radiomics nomogram for preoperative prediction of lymph node metastasis in colorectal cancer. J Clin Oncol 2016; 34:2157.
- Yang L, Dong D, Fang M, Zhu Y, Zang Y, Liu Z, et al. Can CT-based radiomics signature predict KRAS/NRAS/BRAF mutations in colorectal cancer? Eur Radiol 2018; 28:2058-2067.
- 75 Liu Z, Zhang XY, Shi YJ, Wang L, Zhu HT, Tang Z, et al. Radiomics analysis for evaluation of pathological complete response to neoadjuvant chemoradiotherapy in locally advanced rectal cancer. Clin Cancer Res 2017; 23:7253-7262.
- 76 Chang GJ, Rodriguezbigas MA, Skibber JM, Moyer VA. Lymph node evaluation and survival after curative resection of colon cancer; systematic review. J Natl Cancer Inst. 2004; 99:433-441.
- Toiyama Y, Inoue Y, Shimura T, Fujikawa H, Saigusa S, Hiro J, et al. Serum angiopoietin-like protein 2 improves preoperative detection of lymph node metastasis in colorectal cancer. Anticancer Res 2015; **35**:2849-2856.
- 78 Chen T, Li M, Gu Y, et al. Prostate Cancer Differentiation and Aggressiveness: Assessment With a Radiomic-Based Model vs. PI-RADS v2. J Magn Reson Imaging, 2019; 49:875-884.
- Wang J, Wu CJ, Bao ML, Zhang J, Wang XN, Zhang YD. Machine learningbased analysis of MR radiomics can help to improve the diagnostic performance of PI-RADS v2 in clinically relevant prostate cancer. Eur Radiol 2017: 27:4082-4090.
- 80 Algohary A, Viswanath S, Shiradkar R, Ghose S, Pahwa S, Moses D, et al. Radiomic features on MRI enable risk categorization of prostate cancer patients on active surveillance: preliminary findings. J Magn Reson Imaging 2018: **48**:818-828.
- 81 Chaddad A, Kucharczyk MJ, Niazi T. Multimodal radiomic features for the predicting Gleason score of prostate cancer. Cancers (Basel) 2018;
- 82 Lin YC, Lin G, Hong JH, Lin YP, Chen FH, Ng SH, Wang CC. Diffusion radiomics analysis of intratumoral heterogeneity in a murine prostate cancer model following radiotherapy: pixelwise correlation with histology. J Magn Reson Imaging 2017; 46:483-489.
- Shiradkar R, Ghose S, Jambor I, Taimen P, Ettala O, Purysko AS, Madabhushi A. Radiomic features from pretreatment biparametric MRI predict prostate cancer biochemical recurrence: preliminary findings. J Magn Reson Imaging 2018; **48**:1626-1636.
- Staal FCR, van der Reijd DJ, Taghavi M, Lambregts DMJ, Beets-Tan RGH, Maas M. Radiomics for the prediction of treatment outcome and survival in patients with colorectal cancer: a systematic review. Clin Colorectal Cancer 2021: 20:52-71.
- 85 Bakr S, Echegaray S, Shah R, Kamaya A, Louie J, Napel S, et al. Noninvasive radiomics signature based on quantitative analysis of computed tomography images as a surrogate for microvascular invasion in hepatocellular carcinoma: a pilot study. J Med Imaging (Bellingham) 2017; 4:041303.
- 86 Ma Z, Fang M, Huang Y, He L, Chen X, Liang C, et al. CT-based radiomics signature for differentiating Borrmann type IV gastric cancer from primary gastric lymphoma. Eur J Radiol 2017; 91:142-147.
- Ba-Ssalamah A, Muin D, Schernthaner R, Kulinna-Cosentini C, Bastati N, Stift J, et al. Texture-based classification of different gastric tumors at contrast-enhanced CT. Eur J Radiol 2013; 82:e537-e543.
- Liu S, Liu S, Ji C, Zheng H, Pan X, Zhang Y, et al. Application of CT texture analysis in predicting histopathological characteristics of gastric cancers. Eur Radiol 2017; 27:4951-4959.

- 89 Liu S, Zhang Y, Chen L, Guan W, Guan Y, Ge Y, et al. Whole-lesion apparent diffusion coefficient histogram analysis: significance in T and N staging of gastric cancers. BMC Cancer 2017; 17:665.
- 90 Liu S, Zhang Y, Xia J, Chen L, Guan W, Guan Y, et al. Predicting the nodal status in gastric cancers: the role of apparent diffusion coefficient histogram characteristic analysis. Magn Reson Imaging 2017;
- 91 Liu S, Zheng H, Zhang Y, Chen L, Guan W, Guan Y, et al. Whole-volume apparent diffusion coefficient-based entropy parameters for assessment of gastric cancer aggressiveness. J Magn Reson Imaging 2018; **47**:168-175
- 92 Lucia F, Visvikis D, Vallières M, Desseroit MC, Miranda O, Robin P, et al. External validation of a combined PET and MRI radiomics model for prediction of recurrence in cervical cancer patients treated with chemoradiotherapy. Eur J Nucl Med Mol Imaging 2019; 46:864-877.
- Sun C, Tian X, Liu Z, Li W, Li P, Chen J, et al. Radiomic analysis for pretreatment prediction of response to neoadjuvant chemotherapy in locally advanced cervical cancer: a multicentre study. EBioMedicine 2019;46:160-169.
- 94 Altazi BA, Fernandez DC, Zhang GG, Hawkins S, Naqvi SM, Kim Y, et al. Investigating multi-radiomic models for enhancing prediction power of cervical cancer treatment outcomes. Phys Med 2018;46:180-188.
- 95 Reuzé S, Orlhac F, Chargari C, Nioche C, Limkin E, Riet F, et al. Prediction of cervical cancer recurrence using textural features extracted from

- 18F-FDG PET images acquired with different scanners. Oncotarget 2017;
- 96 Jha AK, Mithun S, Jaiswar V, Sherkhane UB, Purandare NC, Prabhash K, et al. Repeatability and reproducibility study of radiomic features on a phantom and human cohort. Sci Rep 2021; 11:2055.
- 97 Traverso A, Wee L, Dekker A, Gillies R. Repeatability and reproducibility of radiomic features: a systematic review. Int J Radiat Oncol Biol Phys 2018; 102:1143-1158
- 98 National Cancer Institute, Division of Cancer Treatment & Diagnosis. Quantitative Imaging Network (QIN) [online], https://imaging.cancer.gov/ programs_resources/specialized_initiatives/qin.htm . last accessed on
- 99 Radiological Society of North America. Quantitative Imaging Biomarkers Alliance® (QIBA®). rsna.org/ttps://www.rsna.org/research/quantitativeimaging-biomarkers-alliance/. last accessed on 15-05-2021
- 100 QUantitative Imaging in Cancer: CONnecting CEllular Processes with Therapy, https://cordis.europa.eu/project/id/115151 last accessed on 15-05-2021
- 101 Zwanenburg A, Vallières M, Abdalah MA, Aerts HJWL, Andrearczyk V, Apte A, et al. The image biomarker standardization initiative: standardized quantitative radiomics for high-throughput image-based phenotyping. Radiology 2020; 295:328-338.
- 102 The image biomarker standardisation initiative, https://ibsi.readthedocs.io/ en/ latest/index.html, Last accessed on 15-05-2021.