ANTICANCER RESEARCH *40*: 3605-3618 (2020)
doi:10.21873/anticanres.14350

*Review*

# Review of the Role of Radiomics in Tumour Risk Classification and Prognosis of Cancer

YEO LI WEN[1,2] and MICHELLE LEECH[1]

[1]*Applied Radiation Therapy Trinity, Discipline of Radiation Therapy, Trinity College, Dublin, Ireland;*
[2]*National University Cancer Institute, Singapore, Singapore*

**Abstract.** *Radiomics, an emerging field in radiation therapy, is hypothesized to improve classification of tumour risk and prognosis. Despite encouraging results, there are issues of practicality and interpretation of radiomic data. This study investigates the emerging role of radiomics in tumour risk classification and prognosis of breast and prostate cancer. A literature search was conducted using predefined terms to retrieve studies related to radiomics. Studies were evaluated and selected upon meeting the criteria defined. A total of 19 relevant publications were selected from 63 publications identified. Data from studies revealed significant area under the curve (AUC) values and high discriminative power. Significant AUC values for biochemical recurrence of disease and disease-free survival were reported for prognosis. Radiomics show promising potential in discriminating tumour risk and predicting prognosis of cancer using specified features. It is an alternative to conventional predictive tools and has the ability to improve with the use of existing tools.*

Breast cancer is the most common cancer in women worldwide (1), while prostate cancer (PCa) is the most common male malignancy in the US (2). The prediction of tumour risk classification and disease prognosis is crucial for quality management of these diseases and for the development of precision medicine. As commonly used for adjuvant therapy in breast and prostate cancer management, radiation therapy (RT) plays a major role in improving local control of the diseases and minimising biochemical failure and future metastasis or disease recurrence.



*Correspondence to:* Michelle Leech, Discipline of Radiation Therapy, School of Medicine, Trinity Centre for Health Sciences, St. James's Hospital Campus, Dublin, Ireland. Tel: +353 018963252, Fax: +353 018963246, e-mail: leechm@tcd.ie

*Key Words:* Radiomics, prediction, classification, tumour risk, prognosis, review.

## Breast Cancer

Breast cancer subtypes are assigned based on tumour histopathologic and molecular information. Despite earlier detection and diagnosis with more advanced imaging modalities, failure of radical treatment and cancer recurrence have contributed to significant mortality in breast cancer patients (3). Like PCa, tumour heterogeneity poses a challenge to prognosis prediction and suitability of treatment.

With complex gene expression in breast tumours, heterogeneity has been studied and analysed for its association with prognosis and risk of recurrence. As multiple driver mutations in breast cancer are dynamic and alter with time, there is an increasing need to assess heterogeneity for better prognosis prediction and treatment guidance (4). Current gene expression profiles are progressively going beyond features observed at conventional histopathologic examination to provide more information on tumour biology and distinguish between breast cancer tumour types, and ultimately improve prediction of recurrence and relevant clinical outcomes (4).

## Prostate Cancer

Poor risk stratification can greatly impede clinical outcomes in PCa. Overtreatment of indolent PCa and undertreatment of aggressive tumours are not uncommon. There is little evidence to differentiate patients proceeding with surgery or adjuvant RT against merely surveillance (5, 6). Reports have also shown that overtreatment in a large percentage of clinically indolent patients has led to significant toxicities (7). Conversely, undertreatment of aggressive radioresistant tumours could result in poor local control and higher morbidity risk (5). A US study has reported an associated 1.7-fold risk increase of non-organ confined disease after radical prostatectomy in patients with more than 12 months deferral of treatment (8). Similarly, despite

radical treatment, up to 40% of patients with clinically curable intermediate-risk disease will recur due to undertreatment (5). This highlights that current clinical models for risk classification could be improved.

## Radiomics

Radiomics is the process of converting digital medical images into mineable high-dimensional data by extracting high-throughput quantitative features (9). Exponential advancement in the field of medical image analysis has accelerated the growth and development of radiomics (10), and radiomics has been shown to be a promising tool in providing comprehensive characterisation of tumour biology (11, 12). When combined with statistical tools, biological models can be developed to potentially improve current prediction methods and accuracy of predicted clinical outcomes, far more than conventional analytical models (12).

Radiogenomics is concerned with the relationship between radiomic features extracted and the underlying molecular features at genomic level, which may improve identification of the underlying biological basis of imaging phenotypes (12). Its goal in RT is to improve stratification outcomes and provide better risk assessment, thereby allowing enhanced radiation therapy care (11). The two major approaches include correlating imaging features with specific genotype or molecular phenotype of tumours, and imaging phenotype with biological underpinnings (12). Genomic analyses can increase our understanding of the heterogeneity of tumours and potentially improve prediction of clinical outcomes.

Despite the potential for greater biological understanding of tumours with the introduction of radiomics, the use of radiomics-extracted quantitative data to provide insight on mechanisms at genetic and molecular levels is still debatable due to the limited evidence available and variables affecting the sensitivity of radiomics tools (13). The aim of this review is to identify if radiomics can improve the prediction of tumour risk classification and prognosis for prostate and breast cancer.

## Search Strategy for Identification of Studies

Using the preferred reporting items for systematic reviews and meta-analyses statement (PRISMA), a comprehensive radiomics literature search was conducted on PubMed, EMBASE, MEDLINE and Cochrane databases. Publication dates were limited to 10 years.

The following keywords were used in the search strategy: ("radiomics" OR "radiogenomics") AND ("prostate cancer OR "breast cancer") AND ("prognosis" OR "survival" OR "predict*" OR "accuracy" OR "tumour response" OR "tumour biology" OR "tumour type" OR "tumour characterisation" OR "classification" OR "stratification").

Full text studies were reviewed to identify studies fulfilling the predefined criteria. Eligible studies and their reference lists were screened and reviewed for other potential studies in the field. Review, comparative studies, clinical trials (both randomised controlled and non-randomised) of all phases were screened. The full texts of these studies were then reviewed to identify studies fulfilling the predefined inclusion and exclusion criteria.

Studies containing overlapping or insufficient data for extraction were excluded during screening. Reference lists and related studies/articles in each identified publication were also screened and reviewed to avoid missing relevant studies. Duplicates in the search results were removed.

## Outcome Measures

The outcome measures from the selected studies included predictability of the level of tumour risk classification, recurrence risk and disease-free survival (DFS).

## Statistical Analysis

Studies used receiver-operating characteristic curve analysis to determine the cut-off point of radiomics signature (Rad-score) for risk classification.

Univariate and multivariate Cox proportional hazards model and Kaplan-Meier curves were used to determine the association of radiomics imaging features with prognosis. Associations between radiomics and predictability of cancer prognosis were evaluated by reviewing the area under ROC curves (AUC).

## Quality Analysis

Quality analysis of selected papers was performed using Downs and Black's checklist (14) (Table I). This checklist was used to assess the quality of the studies and to elucidate evidence from quantitative studies for quality assessment. Studies were assessed based on their power calculation performance using 5 domains: 1) study quality, 2) external validity, 3) study bias, 4) confounding and selection bias and 5) power of study. The studies were evaluated and assigned a score (out of 28) corresponding to their level of quality: excellent [26-28]; good [20-25]; fair [15-19]; and poor [≤14].

The literature search yielded 63 relevant publications for inclusion, of which 19 were identified as suitable for further evaluation (Figure 1). No randomised control trials were found. The studies included were published between the years of 2010 and 2019. The sample sizes ranged from 49 to 381 participants.

## Prediction of Tumour Risk Classification

In assessing the accuracy of radiomics features in predicting tumour risk classification, 3 studies (15-17) showed

Table I. *Quality analysis scores using Downs and Black's checklist.*

| Question/ Included study | Li *et al.* (2016) | Monti *et al.* (2018) | Chaddad *et al.* (2018) | Algohary *et al.* (2018) | Chen *et al.* (2019) | Wang *et al.* (2017) | Bellolio *et al.* (2015) | Hamoen *et al.* (2015) | Zhang *et al.* (2017) | Crivelli *et al.* (2018) | Bonekamp *et al.* (2018) | Huang *et al.* (2018) | Li *et al.* (2016) | Sutton *et al.* (2015) | Park *et al.* (2018) | Gnep *et al.* (2017) | Wishart *et al.* (2010) | Candido *et al.* (2017) | Verma *et al.* (2014) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. Is the hypothesis/ aim/objective of the study clearly described? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 2. Are the main outcomes to be measured clearly described in the Introduction or Methods section? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 3. Are the characteristics of the patients included in the study clearly described? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 4. Are the interventions of interest clearly described? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 5. Are the distributions of principal confounders in each group of subjects to be compared clearly described? | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 6. Are the main findings of the study clearly described? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 7. Does the study provide estimates of the random variability in the data for the main outcomes? | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 |
| 8. Have all important adverse events that may be a consequence of the intervention been reported? | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| 9. Have the characteristics of patients lost to follow-up been described? | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 |

Table I. *Continued*

Table I. *Continued*

| Question/ Included study | Li *et al.* (2016) | Monti *et al.* (2018) | Chaddad *et al.* (2018) | Algohary *et al.* (2018) | Chen *et al.* (2019) | Wang *et al.* (2017) | Bellolio *et al.* (2015) | Hamoen *et al.* (2015) | Zhang *et al.* (2017) | Crivelli *et al.* (2018) | Bonekamp *et al.* (2018) | Huang *et al.* (2018) | Li *et al.* (2016) | Sutton *et al.* (2015) | Park *et al.* (2018) | Gnep *et al.* (2017) | Wishart *et al.* (2010) | Candido *et al.* (2017) | Verma *et al.* (2014) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 10. Have actual probability values been reported (*e.g.* 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001? | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| 11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited? | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 1 |
| 12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| 13. Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| 14. Was an attempt made to blind study subjects to the intervention they have received? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15. Was an attempt made to blind those measuring the main outcomes of the intervention? | 1 | 0 | 0 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| 16. If any of the results of the study were based on "data dredging", was this made clear? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

Table I. *Continued*

Table I. *Continued*

| Question/ Included study | Li *et al.* (2016) | Monti *et al.* (2018) | Chaddad *et al.* (2018) | Algohary *et al.* (2018) | Chen *et al.* (2019) | Wang *et al.* (2017) | Bellolio *et al.* (2015) | Hamoen *et al.* (2015) | Zhang *et al.* (2017) | Crivelli *et al.* (2018) | Bonekamp *et al.* (2018) | Huang *et al.* (2018) | Li *et al.* (2016) | Sutton *et al.* (2015) | Park *et al.* (2018) | Gnep *et al.* (2017) | Wishart *et al.* (2010) | Candido *et al.* (2017) | Verma *et al.* (2014) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 17. In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 |
| 18. Were the statistical tests used to assess the main outcomes appropriate? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 19. Was compliance with the intervention/s reliable? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 20. Were the main outcome measures used accurate (valid and reliable)? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 21. Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population? | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 |
| 22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time? | 1 | 0 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 |
| 23. Were study subjects randomised to intervention groups? | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |

Table I. *Continued*

Table I. *Continued*

| Question/ Included study | Li *et al.* (2016) | Monti *et al.* (2018) | Chaddad *et al.* (2018) | Algohary *et al.* (2018) | Chen *et al.* (2019) | Wang *et al.* (2017) | Bellolio *et al.* (2015) | Hamoen *et al.* (2015) | Zhang *et al.* (2017) | Crivelli *et al.* (2018) | Bonekamp *et al.* (2018) | Huang *et al.* (2018) | Li *et al.* (2016) | Sutton *et al.* (2015) | Park *et al.* (2018) | Gnep *et al.* (2017) | Wishart *et al.* (2010) | Candido *et al.* (2017) | Verma *et al.* (2014) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 24. Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 26. Were losses of patients to follow-up taken into account? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 27. Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total Score | 16 | 13 | 11 | 14 | 13 | 14 | 15 | 18 | 17 | 10 | 15 | 16 | 15 | 17 | 18 | 17 | 19 | 18 | 13 |

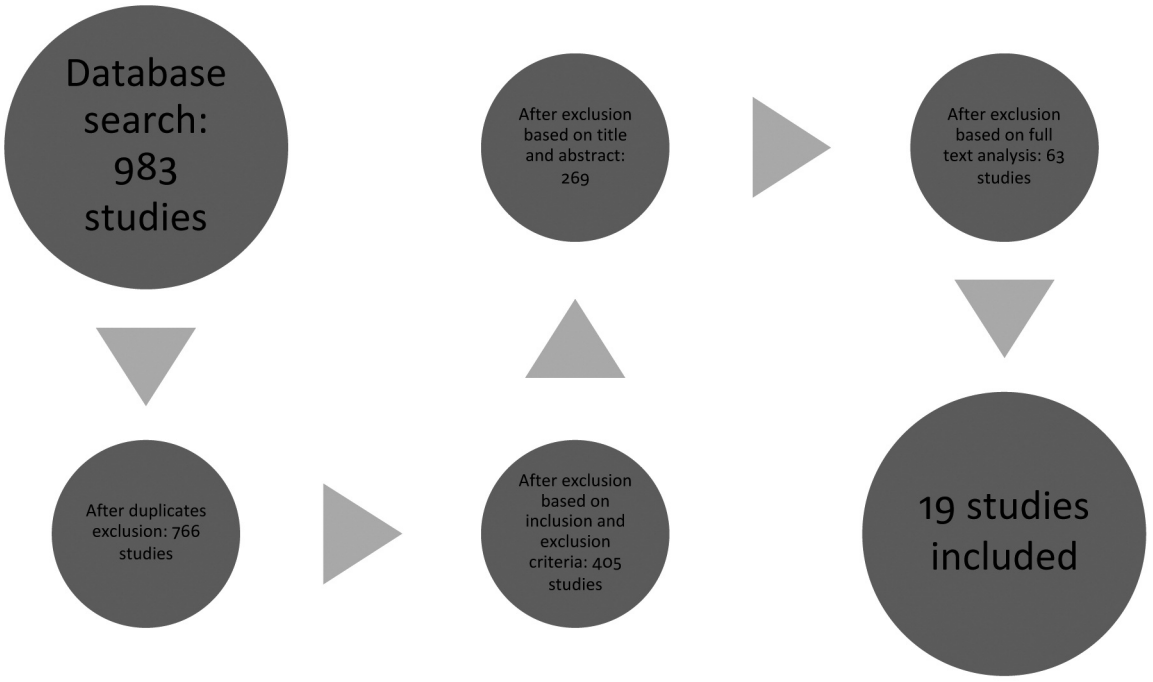


Figure 1. *Flow of search methodology.*

promising results. All 3 studies extracted radiomic features from MRI images.

Li *et al*. (16) and Monti *et al*. (17) demonstrated the correlation between image-based tumour phenotypes and molecular classification of breast tumours. Significant AUC values and high discriminative power in radiomic models were reported. Regarding the accuracy of radiomics in classifying prostate tumours and predicting Gleason score (GS), Chaddad *et al*. (15) reported the best performing AUC values with combined joint intensity matrix (JIM) and the grey level co-occurrence matrix (GLCM) radiomic features to predict for GS.

Comparing the performance of radiomic models to conventional classification methods, 3 studies (13, 18, 19) illustrated that radiomic models resulted in improved classification results by comparing the performance of MRI radiomics to Prostate Imaging Reporting and Data System (PI-RADS). All reported significant AUC values and an improvement in the overall accuracy of prediction with radiomic models. Chen *et al*. (18) reported a significantly higher AUC for differentiating high-grade from low-grade PCa for the radiomics-based model as compared to that of PI-RADS v2. Additionally, Wang *et al*. (19) added that a combination of MR radiomics and PI-RADS yielded higher AUC values than PI-RADS alone.

One of the major discussion points with respect to radiomics research is whether current tumour risk classification methods already yields satisfactory results, thereby making the requirement for radiomics research in this area redundant. In assessing the accuracy of radiomics in predicting tumour risk classification in this review, 3 studies (20-22) highlighted the satisfactory results in predicting risk classification achieved by existing available pathologic classifiers. Studies used Breast Imaging Reporting and Data System (BI-RADS) and PI-RADS as risk classifiers. Bellolio *et al*. (20) reported the presence of cancer on mammography in different BI-RADS categories and the positive and negative predictive values of BI-RADS classification, which were 55% and 92% respectively. Hamoen *et al*. (21) and Zhang *et al*. (22) both conducted a meta-analysis of PI-RADS for PCa and both reported high sensitivity and specificity of PCa detection with PI-RADS.

Crivelli (23) also reported the inadequacies present in current radiomic feature extraction and data sharing and the challenges faced by radiologists in this area.

Comparing the performance of radiomic models to conventional classification methods, Bonekamp *et al*. (24) argued that radiomics is not superior as the calculated AUC for the mean apparent diffusion coefficient (ADC) showed no significant difference in lesion characterisation performance when compared to radiomic machine learning.

Predictors of Breast and Prostate Cancer Prognosis

In assessing the use of radiomics to predict the prognosis of breast and prostate patients, 5 studies (4, 25-28) showed that promising results achieved by radiomic features. These studies focussed on the use of radiomics to predict the biochemical recurrence of disease and disease-free survival (DFS).

Three studies (4, 25-26) investigated the association between computer-extracted breast MRI phenotypes and the prognosis of breast cancer. Huang *et al*. (25) employed a combination of PET and MRI radiomics and reported a significant mean AUC in distinguishing recurrence-free survival. Similarly, Li *et al*. (4) also reported significant AUC in differentiating between good and poor prognosis. Sutton *et al*. (26) observed a statistically significant correlation of the overall model with Oncotype Dx RS and a significant Spearman's rank correlation coefficient, suggesting that image-based features are promising in predicting disease recurrence. Similarly, Park *et al*. (27) demonstrated the potential of radiomics in predicting DFS in invasive breast cancer patients. The radiomics nomogram achieved a higher C-index than the clinicopathological or Rad-score-only nomograms.

The prostate cancer study by Gnep *et al*. (28) on the association of radiomics and biochemical recurrence following RT also agreed that radiomics has potential in predicting disease prognosis. Haralick textural features were reported to have significant correlation with Gleason score and biochemical recurrence.

However, we must be cognisant that the need for radiomics to improve prediction of prognosis is challenged by existing prognostic tools that are already available. Wishart *et al*. (29) reported that the current prognostication model PREDICT for early breast cancer was discriminative and well-validated. The differences in overall actual and predicted mortality were low and not statistically significant. Significant AUC value for the model was observed. In an updated version of PREDICT, Candido *et al*. (30) demonstrated a further improved prognostication and treatment benefit model. PREDICT v1 and v2 were reported to have similar AUC for estrogen receptor (ER)-negative disease, but v2 had slightly higher AUC value than v1 for ER-positive disease.

In prostate cancer, Verma *et al*. (31) also challenged the need for radiomics as a prognostic tool by reporting that prostate specific antigen (PSA) density is itself a strong predictor and significant sensitivity and specificity can be achieved by these models.

## Prediction of Tumour Risk Classification

Overall, the results demonstrate that there is a growing body of literature supporting the potential of radiomics in improving risk classification for breast and prostate cancer (Table II).

The accuracy of radiomics models in predicting risk classification was supported by 3 studies (15-17). Li *et al*. (16) and Monti *et al*. (17) showed that image-based extracted phenotypes and radiomics features were promising in discriminating breast cancer subtypes and histological outcomes, respectively.

Li *et al*. (16) also found statistically significant associations between tumour phenotype and the respective receptor status. Aggressive tumours were observed to be larger, more irregular and more heterogeneous in contrast enhancement. Radiomics features, therefore, can characterise imaging phenotypes such as heterogeneity and contrast enhancement, which provide insights into tumour pathophysiologic characteristics. This could thus improve quantitative imaging assessment of tumours, broaden the potential for more accurate prognosis prediction and facilitate more personalised treatment management.

The use of radiomics to characterise intratumoural heterogeneity is supported by Monti *et al*. (17). Skewness and entropy were observed to be the most recurrent features in the radiomics predictive models employed in that study. This indicates randomness in tumour pathophysiological characteristics and highlights the importance of analysing tumour heterogeneity to differentiate between cancer subtypes.

Chaddad *et al*. (15) utilised joint intensity matrix (JIM) to translate image heterogeneity into texture predictors that were found to be associated with Gleason score (GS). The difference variance feature extracted from JIM was identified to have the greatest predictive power of GS, as variation between textures was clearly encoded. Such a radiomics approach shows promise in allowing greater understanding of the relationship between intensity values in multi-parametric images. Radiomics can account for cellular heterogeneity within the confirmed biopsy to give a more accurate GS score.

Comparing the performance of radiomic models to conventional classification methods, most studies supported that radiomics models have greater predictive value and could be combined with existing predictive models in some cases to further enhance that predictive power.

When comparing the performance of MR radiomics to PI-RADS in the case of tumour risk stratification, 3 studies (13, 18-19) reported better performance in radiomics models. PI-RADS standardises clinical reporting for consistent interpretation of multiparametric MRI (mp-MRI) in prostate cancer, however, inter-reader variation among radiologists limits the reproducibility of the results and the clinical applicability of PI-RADS as a reliable tool (32). In fact, Schimmöller *et al*. (33) reported a PI-RADS score of only moderate to good for inter-reader agreement when blinded. Therefore, there is a consensus among the studies that radiomics models outperformed PI-RADS because they can include tumour characteristics, which are imperceptible to the eye, hence, giving a higher efficacy in predictive performance.

Additionally, Wang *et al*. (19) reported that a combination of MR radiomics and PI-RADS improved the predictive performance of PI-RADS. This indicates an increased potential of radiomics in diagnosing better and stratifying clinically relevant PCa, therefore enabling clinicians to provide personalised clinical treatments for patients.

Table II. *Summary of included studies*.

| Author and year | Area of application | Data obtained | Findings |
|---|---|---|---|
| Li *et al*. (16) 2016 | Prediction of molecular classifications of breast cancer subtypes | AUC: 0.89, 0.69, 0.65, and 0.67 for distinguishing between ER+ *versus* ER–, PR+ *versus* PR–, HER2+ *versus* HER2–, and triple-negative *versus* others, respectively. | Computer-extracted image phenotypes have potential for high-throughput discrimination of breast cancer subtypes and may provide a quantitative predictive signature for advancing precision medicine. |
| Monti *et al*. (17) 2018 | Prediction of breast cancer histological outcomes | AUC: 0.826±0.006 for ER+/ER–, 0.875±0.009 for PR+/PR–, 0.838±0.006 for HER2+/HER2–, 0.876±0.007 for TN/NTN, 0.811±0.005 for ki67+/ki67–, and 0.895±0.006 for low grade/high grade. | DCE-MRI pharmacokinetic-based phenotyping has potential for accurate discrimination of the histological outcomes. |
| Chaddad *et al*. (15) 2018 | Predicting Gleason score of prostate cancer | Combined JIM and GLCM analysis gave the best performing AUC with values of 78.40% for GS≤6, 82.35% for GS=3+4, and 64.76% for GS≥4+3. | The new model based on JIM could better predict GS of PCa patients. JIM features could be complementary to GLCM techniques for the prediction of the GS in PCa patients. |
| Algohary *et al*. (13) 2018 | Risk categorization of prostate cancer patients on active surveillance | Three machine-learning classifiers, Quadratic Discriminant Analysis, Random Forests and Support Vector Machine yielded overall improved accuracy of 33, 60, 80% and 30, 40, 60% for patients in testing groups, as compared to PIRADS v2.0 alone. | Radiomic features shows promise in identifying the presence and absence of clinically significant disease in AS patients when PIRADS v2.0 assessment on MRI disagrees with pathology findings of MRI-TRUS prostate biopsies. |
| Chen *et al*. (18) 2019 | Prostate cancer differentiation and aggressiveness | When comparing PCa to non-PCa, the validation model had an AUC of 0.985, 0.982, and 0.999 with T2 WI, ADC, and T2 WI&ADC features, respectively. For low-grade *versus* high-grade PCa, the validation model had an AUC of 0.865, 0.888, and 0.93 with T2 WI, ADC, and T2 WI&ADC features, respectively. | The diagnostic performance of our T2WI or ADC radiomics-based models was high, and the comprehensive diagnostic efficacy was slightly increased. The efficacy of the radiomic model was better than that of PI-RADS scores. |
| Wang *et al*. (19) 2017 | Diagnostic performance of PI-RADS v2 in clinically relevant prostate cancer | Radiomics model had a significantly higher area under the ROC curve (Az) 0.955 (95%CI=0.923-0.976) than PI-RADS (Az: 0.878 (0.834-0.914), $p<0.001$) for PCa *versus* normal transitional zone (TZ). With the addition of radiomics, there was significant improvement of the performance of PI-RADS; for PCa *versus* peripheral zone (PZ) [Az: 0.983 (0.960-0.995)] and PCa *versus* TZ [Az: 0.968 (0.940-0.985)]. | For TZ cancer, radiomics showed more promising performance results than PI-RADS. The addition of MR radiomics significantly improved the overall performance of PI-RADS. |
| Bellolio *et al*. (20) 2015 | Predictive value of BI-RADS to detect cancer | The presence of cancer in mammographies classified as BI-RADS 0 was 4%. The prevalence of cancer for mammographies BI-RADS 1, 2, 3, 4 and 5 were 0, 3, 2.7, 17.7 and 72.4% respectively. The BI-RADS classification obtained positive and negative predictive values of 55% and 92% respectively. | BI-RADS classification 4 and 5 has a high positive predictive value for detecting cancer. |
| Hamoen *et al*. (21) 2015 | Use of the PI-RADS for PCa detection | PI-RADS has a sensitivity of 0.78 [95% confidence interval (CI)=0.70-0.84] and specificity of 0.79 (95%CI=0.68-0.86) for PCa detection, with negative predictive values ranging from 0.58 to 0.95. | PI-RADS has good diagnostic accuracy in PCa detection. |

Table II. *Continued*

Table II. *Continued*

| Author and year | Area of application | Data obtained | Findings |
|---|---|---|---|
| Zhang *et al*. (22) 2017 | A meta-analysis of the use of PI-RADS Version 2 | The meta-analysis of 13 studies and 2049 patients reported a pooled sensitivity and specificity of 0.85 (0.78-0.91) and 0.71 (0.60-0.80) respectively. Positive predictive values ranged from 0.54 to 0.97 and negative predictive values ranged from 0.26 to 0.92. | PI-RADS Version 2 demonstrated good diagnostic accuracy for PCa detection. |
| Crivelli *et al*. (23) 2018 | Challenge for radiologists in breast radiomics | The features together achieved the sensitivity of 84.44% and 85.56%, specificity of 91.11% and 91.67% with FPsI of 0.54 and 0.55 using k-NN and SVM classifiers, respectively, on local dataset. | The overall breast cancer detection performance of proposed scheme after combining geometric and textural features with both classifiers is improved in terms of sensitivity, specificity, and FPsI. |
| Bonekamp *et al*. (24) 2018 | Characterization of prostate lesions | Comparing the AUC for the mean ADC (AUCglobal=0.84; AUCzone-specific≤0.87) and the RML (AUCglobal=0.88, $p$=0.176; AUCzone-specific ≤0.89, $p$≥0.493) gives no significant difference in performance. | Radiomic model was comparable but did not perform better than mean ADC assessment. |
| Huang *et al*. (25) 2018 | Characterisation of breast cancer phenotype and prognosis | PET and MRI radiomics distinguished recurrence-free survival with a mean AUC value of 0.75 [95%CI=(0.62, 0.88) and 0.68 (95%CI=(0.58, 0.81)] for 1 and 2 years, respectively. | Radiomic features from PET and MRI images are promising in deciphering breast cancer phenotypes and are potential imaging biomarkers for prediction of breast cancer recurrence-free survival. |
| Li *et al*. (4) 2016 | Predicting risk of breast cancer recurrence | AUC of radiomics in distinguishing between good and poor prognosis: 0.88, 0.76, 0.68, and 0.55 for MammaPrint, Oncotype DX, PAM50 risk of relapse based on subtype, and PAM50 risk of relapse based on subtype and proliferation, respectively. | Quantitative breast MRI radiomics has potential for image-based phenotyping in assessing the risk of breast cancer recurrence. |
| Sutton *et al*. (26) 2015 | Prediction of results of genomic assay in breast cancer | Statistically significant correlation with Oncotype Dx RS (adjusted R-squared=0.20; $p$=0.0002) and a Spearman's rank correlation coefficient of 0.49 ($p$<0.0001) were observed. | Image-based features are promising in predicting the likelihood of disease recurrence. |
| Park *et al*. (27) 2018 | Prediction of disease-free survival (DFS) in invasive breast cancer patients | Radiomics nomogram estimated DFS [C-index, 0.76; 95% confidence interval (CI)=0.74-0.77] better than the clinicopathological (C-index, 0.72; 95%CI= 0.70-0.74) or Rad-score-only nomograms (C-index, 0.67; 95%CI=0.65-0.69). | Combining the radiomics nomogram improved individualised DFS estimation. |
| Gnep *et al*. (28) 2017 | Association of biochemical recurrence following RT for peripheral zone prostate cancer | 3 T2W and 1 ADC Haralick textural features had significant correlation with Gleason score ($p$<0.05). 28 T2W Haralick features and all 4 geometrical features had significant association with biochemical recurrence ($p$<0.05). | T2 -w Haralick features are suggested to be strongly associated with biochemical recurrence following prostate RT. |
| Wishart *et al*. (29) 2010 | PREDICT: predicts survival following surgery for invasive breast cancer | Differences in overall actual and predicted mortality were <1% at 8 years for the Eastern Cancer Registration and Information Centre dataset (18.9% *vs*. 19.0%) and West Midlands Cancer Intelligence Unit (WMCIU) (17.5% *vs*. 18.3%) with an AUC of 0.81 and 0.79. respectively. | Prognostication model PREDICT for early breast cancer was discriminative and well-validated. |

Table II. *Continued*

Table II. *Continued*

| Author and year | Area of application | Data obtained | Findings |
|---|---|---|---|
| Candido *et al*. (30) 2017 | An updated PREDICT breast cancer prognostication and treatment benefit prediction model | PREDICT v1 and v2 had similar AUC (0.724 and 0.726, $p$=0.67) for ER-negative disease, however, v1 had slightly smaller AUC than v2 for ER-positive disease (0.791 and 0.796, $p$=0.028).Verma *et al*. (31) | PREDICT v2 demonstrated improved prognostication and treatment benefit model as compared to the previous version. |
| 2014 | PSA density improves prediction of prostate cancer | The AUC for model A (PSA total, digital rectal exam, PSAf/t) was 0.59, ($p$<0.05) and was moderate but significant; only PSAf/t was a significant independent predictor of positive biopsy (OR=0.002, $p$<0.05). In model B (PSAf/t and PSA density; AUC=0.66, $p$<0.05), PSA density was the only strong predictor (OR=1067.93, $p$<0.05). | PSA density has potential discriminative predictive power for PCa. |

However, the findings of Algohary *et al*. (13) are limited in generalisability as the PI-RADS score of 3 cases were excluded from the study group intentionally. These cases had lesion characteristics that were not well-described and can give rise to potentially significant inter-observer variability (34). Therefore, the exclusion of the PI-RADS score of the 3 cases disregarded the major clinical challenge associated and was a limitation in the study.

For BI-RADS, Wanaporn and Ornsiri (35) reported wide variability in the interpretation of breast imaging. Radiologist experience and prior knowledge of BI-RADS guidelines accounted for the variability in agreement.

The accuracy of radiomic models in predicting risk classification is challenged by three studies (20-22), which argue that current methods of classifying tumours based on PI-RADS and BI-RADS have satisfactory sensitivity and specificity. Bellolio *et al*. (20) studied the predictive value of BI-RADS, which is employed to standardise breast image reporting, and drew a high positive predictive value for BI-RADS classification 4 and 5. However, on deeper analysis, this correlation from BI-RADS could be specific to the respective centre and cannot be generalised, since protocols, radiologist assessments and techniques utilised for biopsies differ. A similar protocol could be performed at various centres to validate this correlation of BI-RADS with tumour classification.

Both meta-analyses reported high sensitivity and specificity for the use of PI-RADS and demonstrated that PI-RADS is promising in accurately detecting PCa (21, 22). However, both studies also reported that significant heterogeneity is present in the calculation of the overall PI-RADS score. Hameon *et al*. (21) observed that studies with low concerns regarding the applicability of PI-RADS presented higher sensitivity and specificity, whereas those with high concerns presented lower sensitivity and specificity. This contrast proposes that more accurate use of PI-RADS could result in the improvement of the overall accuracy for PCa detection. Hence, there is value attached to PI-RADS and it can potentially predict PCa with high accuracy.

Considering radiologists' reviews on radiomics, Crivelli *et al*. (23) reported that the use of radiomics could be limited by the lack of an existing standardised system for radiomic feature extraction and data sharing. The lack of understanding of basic radiomics concepts among radiologists could also hinder the routine application of radiomics in the clinical setting. This coincides with the previous 2 meta-analyses which emphasised the importance of training radiologists in using radiomics and evaluate their respective learning curves (21, 22).

Comparing the performance of radiomic models to conventional classification methods, Bonekamp *et al*. (24) found that although radiomic machine learning performed better than radiologist assessment, it was only comparable and did not outperform mean ADC assessment. No added benefit of radiomics was observed compared to ADC. Hence, radiomics cannot be said to be superior in predicting tumour classification.

## Prediction of Cancer Prognosis

The potential of radiomic models in predicting biochemical recurrence of disease as well as disease-free survival is supported by 5 studies (4, 25-28). Huang *et al*. (25) and Li *et al*. (4) established the potential of radiomics features in the prediction of prognosis with statistically significant AUC reported in their studies. Huang *et al*. (25) demonstrated a

significant relationship between PET and MRI radiomics clusters and tumour grade. In fact, the potential prognostic value of breast cancer tumour grade for predicting disease survival rate was also reported and supported by Rakha *et al.* (36). This study focused on the histological grade of tumour and resulted in improved breast cancer classification and staging.

Huang *et al.* (25) also observed that PET and MRI radiomic features together have greater predictive potential then MRI radiomics alone. This could be valuable in deciphering breast cancer phenotypes and imaging biomarkers show promise in the prediction of disease prognosis. Similarly, in evaluating the risk of breast cancer recurrence, Li *et al.* (4) reported good differentiation between good and poor breast prognosis using quantitative MRI radiomics. Various gene-assay models were studied, and MRI phenotypes were selected from multiple linear regression analyses. The advances in gene expression profiling have brought about a greater understanding of the complexity within breast tumours and are useful in relating breast cancer expression profiles to prognosis and risk of disease recurrence (37).

The potential of radiomic models in predicting biochemical recurrence of disease is also reflected through the combination of imaging phenotypes with genomic data. Sutton *et al.* (26) correlated imaging phenotype with genomic information to improve the understanding of genetic variability and thus the ability to predict breast cancer prognosis across the different subtypes.

In predicting individualised DFS estimation in breast patients, Park *et al.* (27) reported that a combined radiomics-clinicopathological nomogram better predicted DFS outcome than the clinicopathological or Rad-score-only nomograms. This demonstrated the potential of radiomic nomograms in predicting individualised DFS estimation in breast patients. The development and validation of radiomics signature-based nomograms in the preoperative prediction of lymph node metastasis in colorectal cancer (38) and prediction of DFS in early-stage non-small cell lung cancer (39) have already been completed with promising study results. Furthermore, Park *et al.* (27) also demonstrated that a combined radiomics-clinicopathological nomogram gives better prognostic performance with a higher C-index and superior calibration. This is consistent with findings by Liu *et al.* (9) which suggest that better prognostic performance is attained when clinicopathological characteristics and radiomic features are used together to predict for sentinel lymph node metastasis. This further enhances the predictive power of radiomic nomograms in estimating disease prognosis.

In prostate cancer, Gnep *et al.* (28) demonstrated the potential of radiomics in predicting biochemical recurrence. Strong association of Haralick features with biochemical recurrence following prostate RT was observed, which is promising in aiding clinical managements when intensifying or de-intensifying treatments to achieve optimal care. In fact, the use of Haralick features for prediction of disease prognosis and progression in glioblastoma was conducted by Yang *et al.* (40), where Haralick features were found to be predictive of molecular subtypes and survival status in glioblastoma. This supports the feasibility of using tumour-derived imaging features to predict disease prognosis.

Similar to the use of radiomics in the classification of tumours, the actual need for a tool such as radiomics to improve prognosis prediction can be considered challenged by existing prognostic tools available for breast and prostate cancers. Wishart *et al.* (29) demonstrated the prediction capability of the current prognostication model PREDICT for early breast cancer. The PREDICT model is validated and highly discriminative and Candido *et al.* (30) reported encouraging results of the updated model along with improved overall calibration and discrimination.

In prostate cancer, Verma *et al.* (31) have discussed current prognostic tools. PSA density was reported to have strong discriminative power and is a potential predictor of different indices of aggressive prostate cancer. This could potentially reduce unnecessary biopsies and improve patient's care flow.

## Limitations and Challenges of Radiomics

There are several challenges and limitations of radiomics that must be addressed to establish its practicality in routine implementation. First, radiomics feature quantification is highly sensitive to acquisition modes and feature extraction methods. Variation across these models and methods can influence feature quantification and radiomic outcomes (41).

Second, inter-reader variability in some radiomic studies can influence accuracy of results. A number of feature extraction algorithms are user-dependent, and this could affect the reproducibility and stability of results obtained. A study by Saha *et al.* (42) showed that inter-reader variability in radiomics features has also contributed to the instability of these features and questioned the capability in improving tumour classification. It was reported that the average inter-reader stability for all radiomics features was 0.8474 (95%CI=0.8068-0.8858).

Third, as many of the current studies on radiomics involve a small cohort size, this may introduce bias to study results as a result of higher variability. More radiomic studies with larger sample sizes are needed to clearly define whether there is a clinical benefit in using radiomics.

Finally, the association between the imaged characteristics of tumours and actual tumour biology is indirect and complex. Although many relevant radiomic studies show promising results and statistical correlations between radiomic features and genetic phenotypes, the association cannot be directly inferred as causation.

## Conclusion

In conclusion, the role of radiomics in predicting risk classification and prognosis of disease in breast and prostate cancers is promising. Most studies in this review indicate the potential of radiomics in improving current prediction methods, however the added value must be considered in terms of the currently available prediction paradigms.

## Conflicts of Interest

The Authors have no conflicts of interest to declare in relation to this study.

## Authors' Contributions

Yeo Li Wen conducted the literature review and co-wrote the manuscript with Michelle Leech.

## References


1 Siegel RL, Miller KD and Jemal A: Cancer statistics, 2017. CA Cancer J Clin *67(1)*: 7-30, 2017. PMID: 28055103. DOI: 10.3322/caac.21387

2 Stoyanova R, Takhar M, Tschudi Y, Ford JC, Solorzano G, Erho N, Balagurunathan Y, Punnen S, Davicioni E, Gillies RJ and Pollack A: Prostate cancer radiomics and the promise of radiogenomics. Transl Cancer Res *5(4)*: 432-447, 2016. PMID: 29188191. DOI: 10.21037/tcr.2016.06.20

3 Ashraf AB, Daye D, Gavenonis S, Mies C, Feldman M, Rosen M and Kontos D: Identification of intrinsic imaging phenotypes for breast cancer tumors: preliminary associations with gene expression profiles. Radiology *272(2)*: 374-384, 2014. PMID: 24702725. DOI: 10.1148/radiol.14131375

4 Li H, Zhu Y, Burnside ES, Drukker K, Hoadley KA, Fan C, Conzen SD, Whitman GJ, Sutton EJ, Net JM, Ganott M, Huang E, Morris EA, Perou CM, Ji Y and Giger ML: Mr imaging radiomics signatures for predicting the risk of breast cancer recurrence as given by research versions of mammaprint, oncotype dx, and pam50 gene assays. Radiology *281(2)*: 382-391, 2016. PMID: 27144536. DOI: 10.1148/radiol.2016152110

5 Fraser M, Berlin A, Bristow RG and van der Kwast T: Genomic, pathological, and clinical heterogeneity as drivers of personalized medicine in prostate cancer. Urol Oncol *33(2)*: 85-94, 2015. PMID: 24768356. DOI: 10.1016/j.urolonc.2013.10.020

6 Spence W: Personalising prostate radiotherapy in the era of precision medicine: A review. J Med Imaging Radiat Sci *49(4)*: 376-382, 2018. PMID: 30514554. DOI: 10.1016/j.jmir.2018.01.002

7 Hudson TJ: Genome variation and personalized cancer medicine. J Intern Med *274(5)*: 440-450, 2013. PMID: 23751076. DOI: 10.1111/joim.12097

8 Weiner AB, Patel SG and Eggener SE: Pathologic outcomes for low-risk prostate cancer after delayed radical prostatectomy in the united states. Urol Oncol *33(4)*: 164.e111-167, 2015. PMID: 25624093. DOI: 10.1016/j.urolonc.2014.12.012

9 Liu C, Ding J, Spuhler K, Gao Y, Serrano Sosa M, Moriarty M, Hussain S, He X, Liang C and Huang C: Preoperative prediction of sentinel lymph node metastasis in breast cancer by radiomic signatures from dynamic contrast-enhanced mri. J Magn Reson Imaging *49(1)*: 131-140, 2019. PMID: 30171822. DOI: 10.1002/jmri.26224

10 Kumar V, Gu Y, Basu S, Berglund A, Eschrich SA, Schabath MB, Forster K, Aerts HJ, Dekker A, Fenstermacher D, Goldgof DB, Hall LO, Lambin P, Balagurunathan Y, Gatenby RA and Gillies RJ: Radiomics: The process and the challenges. Magn Reson Imaging *30(9)*: 1234-1248, 2012. PMID: 22898692. DOI: 10.1016/j.mri.2012.06.010

11 Pinker K, Chin J, Melsaether AN, Morris EA and Moy L: Precision medicine and radiogenomics in breast cancer: New approaches toward diagnosis and treatment. Radiology *287(3)*: 732-747, 2018. PMID: 29782246. DOI: 10.1148/radiol.2018172171

12 Wu J, Tha KK, Xing L and Li R: Radiomics and radiogenomics for precision radiotherapy. J Radiat Res *59(1)*: i25-i31, 2018. PMID: 29385618. DOI: 10.1093/jrr/rrx102

13 Algohary A, Viswanath S, Shiradkar R, Ghose S, Pahwa S, Moses D, Jambor I, Shnier R, Böhm M, Haynes A-M, Brenner P, Delprado W, Thompson J, Pulbrock M, Purysko AS, Verma S, Ponsky L, Stricker P and Madabhushi A: Radiomic features on mri enable risk categorization of prostate cancer patients on active surveillance: Preliminary findings. J Magn Reson Imaging *48(3)*: 818-828, 2018. PMID: 29469937. DOI: 10.1002/jmri.25983

14 Downs SH and Black N: The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health *52(6)*: 377-384, 1998. PMID: 9764259. DOI: 10.1136/jech.52.6.377

15 Chaddad A, Kucharczyk MJ and Niazi T: Multimodal radiomic features for the predicting gleason score of prostate cancer. Cancers (Basel) *10(8)*, 2018. PMID: 30060575. DOI: 10.3390/cancers10080249

16 Li H, Zhu Y, Burnside ES, Huang E, Drukker K, Hoadley KA, Fan C, Conzen SD, Zuley M, Net JM, Sutton E, Whitman GJ, Morris E, Perou CM, Ji Y and Giger ML: Quantitative MRI radiomics in the prediction of molecular classifications of breast cancer subtypes in the tcga/tcia data set. NPJ Breast Cancer *2(1)*: 16012, 2016. PMID: 27853751. DOI: 10.1038/npjbcancer.2016.12

17 Monti S, Aiello M, Incoronato M, Grimaldi AM, Moscarino M, Mirabelli P, Ferbo U, Cavaliere C and Salvatore M: DCE-MRI pharmacokinetic-based phenotyping of invasive ductal carcinoma: A radiomic study for prediction of histological outcomes. Contrast Media Mol Imaging *2018(5076269)*: 11, 2018. PMID: 29581709. DOI: 10.1155/2018/5076269

18 Chen T, Li M, Gu Y, Zhang Y, Yang S, Wei C, Wu J, Li X, Zhao W and Shen J: Prostate cancer differentiation and aggressiveness: Assessment with a radiomic-based model vs. Pi-rads v2. J Magn Reson Imaging *49(3)*: 875-884, 2019. PMID: 30230108. DOI: 10.1002/jmri.26243

19 Wang J, Wu CJ, Bao ML, Zhang J, Wang XN and Zhang YD: Machine learning-based analysis of mr radiomics can help to improve the diagnostic performance of pi-rads v2 in clinically relevant prostate cancer. Eur Radiol *27(10)*: 4082-4090, 2017. PMID: 28374077. DOI: 10.1007/s00330-017-4800-5

20 Bellolio E, Pineda V, Burgos ME, Iriarte MJ, Becker R, Araya JC, Villaseca M and Mardones N: [predictive value of breast imaging report and database system (birads) to detect cancer in a reference regional hospital]. Rev Med Chil *143(12)*: 1533-1538, 2015. PMID: 26928614. DOI: 10.4067/s0034-98872015001200005

21 Hamoen EHJ, de Rooij M, Witjes JA, Barentsz JO and Rovers MM: Use of the prostate imaging reporting and data system (pi-rads) for prostate cancer detection with multiparametric

magnetic resonance imaging: A diagnostic meta-analysis. Eur Urol *67(6)*: 1112-1121, 2015. PMID: 25466942. DOI: 10.1016/j.eururo.2014.10.033

22 Zhang L, Tang M, Chen S, Lei X, Zhang X and Huan Y: A meta-analysis of use of prostate imaging reporting and data system version 2 (pi-rads v2) with multiparametric MR imaging for the detection of prostate cancer. Eur Radiol *27(12)*: 5204-5214, 2017. PMID: 28656462. DOI: 10.1007/s00330-017-4843-7

23 Crivelli P, Ledda RE, Parascandolo N, Fara A, Soro D and Conti M: A new challenge for radiologists: Radiomics in breast cancer. Biomed Res Int *2018(6120703)*: 11, 2018. PMID: 30402486. DOI: 10.1155/2018/6120703

24 Bonekamp D, Kohl S, Wiesenfarth M, Schelb P, Radtke JP, Götz M, Kickingereder P, Yaqubi K, Hitthaler B, Gählert N, Kuder TA, Deister F, Freitag M, Hohenfellner M, Hadaschik BA, Schlemmer HP and Maier-Hein KH: Radiomic machine learning for characterization of prostate lesions with MRI: Comparison to adc values. Radiology *289(1)*: 128-137, 2018. PMID: 30063191. DOI: 10.1148/radiol.2018173064

25 Huang SY, Franc BL, Harnish RJ, Liu G, Mitra D, Copeland TP, Arasu VA, Kornak J, Jones EF, Behr SC, Hylton NM, Price ER, Esserman L and Seo Y: Exploration of PET and MRI radiomic features for decoding breast cancer phenotypes and prognosis. NPJ Breast Cancer *4(1)*: 24, 2018. PMID: 30131973. DOI: 10.1038/s41523-018-0078-2

26 Sutton EJ, Oh JH, Dashevsky BZ, Veeraraghavan H, Apte AP, Thakur SB, Deasy JO and Morris EA: Breast cancer subtype intertumor heterogeneity: MRI-based features predict results of a genomic assay. J Magn Reson Imaging *42(5)*: 1398-1406, 2015. PMID: 25850931. DOI: 10.1002/jmri.24890

27 Park H, Lim Y, Ko ES, Cho HH, Lee JE, Han BK, Ko EY, Choi JS and Park KW: Radiomics signature on magnetic resonance imaging: Association with disease-free survival in patients with invasive breast cancer. Clin Cancer Res *24(19)*: 4705-4714, 2018. PMID: 29914892. DOI: 10.1158/1078-0432.Ccr-17-3783

28 Gnep K, Fargeas A, Gutiérrez-Carvajal RE, Commandeur F, Mathieu R, Ospina JD, Rolland Y, Rohou T, Vincendeau S, Hatt M, Acosta O and de Crevoisier R: Haralick textural features on t(2) -weighted MRI are associated with biochemical recurrence following radiotherapy for peripheral zone prostate cancer. J Magn Reson Imaging *45(1)*: 103-117, 2017. PMID: 27345946. DOI: 10.1002/jmri.25335

29 Wishart GC, Azzato EM, Greenberg DC, Rashbass J, Kearins O, Lawrence G, Caldas C and Pharoah PD: Predict: A new UK prognostic model that predicts survival following surgery for invasive breast cancer. Breast Cancer Res *12(1)*: R1, 2010. PMID: 20053270. DOI: 10.1186/bcr2464

30 Candido Dos Reis FJ, Wishart GC, Dicks EM, Greenberg D, Rashbass J, Schmidt MK, van den Broek AJ, Ellis IO, Green A, Rakha E, Maishman T, Eccles DM and Pharoah PDP: An updated predict breast cancer prognostication and treatment benefit prediction model with independent validation. Breast Cancer Res *19(1)*: 58, 2017. PMID: 28532503. DOI: 10.1186/s13058-017-0852-3

31 Verma A, St Onge J, Dhillon K and Chorneyko A: PSA density improves prediction of prostate cancer. Can J Urol *21(3)*: 7312-7321, 2014. PMID: 24978363.

32 Rosenkrantz AB, Ginocchio LA, Cornfeld D, Froemming AT, Gupta RT, Turkbey B, Westphalen AC, Babb JS and Margolis DJ: Interobserver reproducibility of the pi-rads version 2 lexicon: A multicenter study of six experienced prostate radiologists. Radiology *280(3)*: 793-804, 2016. PMID: 27035179. DOI: 10.1148/radiol.2016152542

33 Schimmöller L, Quentin M, Arsov C, Lanzman RS, Hiester A, Rabenalt R, Antoch G, Albers P and Blondin D: Inter-reader agreement of the esur score for prostate MRI using in-bore MRI-guided biopsies as the reference standard. Eur Radiol *23(11)*: 3185-3190, 2013. PMID: 23756958. DOI: 10.1007/s00330-013-2922-y

34 Wanaporn B and Ornsiri A: Accuracy of subcategories A, B, C in BI-RADS 4 lesions by combined mammography and breast ultrasound findings. Afr J Med Med Sci *2(3)*: 728-733, 2011.

35 Liddell H, Jyoti R and Haxhimolla HZ: MP-MRI prostate characterised pirads 3 lesions are associated with a low risk of clinically significant prostate cancer - a retrospective review of 92 biopsied pirads 3 lesions. Curr Urol *8(2)*: 96-100, 2015. PMID: 26889125. DOI: 10.1159/000365697

36 Rakha EA, Reis-Filho JS, Baehner F, Dabbs DJ, Decker T, Eusebi V, Fox SB, Ichihara S, Jacquemier J, Lakhani SR, Palacios J, Richardson AL, Schnitt SJ, Schmitt FC, Tan PH, Tse GM, Badve S and Ellis IO: Breast cancer prognostic classification in the molecular era: The role of histological grade. Breast Cancer Res *12(4)*: 207, 2010. PMID: 20804570. DOI: 10.1186/bcr2607

37 Ohnstad HO, Borgen E, Falk RS, Lien TG, Aaserud M, Sveli MAT, Kyte JA, Kristensen VN, Geitvik GA, Schlichting E, Wist EA, Sørlie T, Russnes HG and Naume B: Prognostic value of pam50 and risk of recurrence score in patients with early-stage breast cancer with long-term follow-up. Breast Cancer Res *19(1)*: 120, 2017. PMID: 29137653. DOI: 10.1186/s13058-017-0911-9

38 Huang YQ, Liang CH, He L, Tian J, Liang CS, Chen X, Ma ZL and Liu ZY: Development and validation of a radiomics nomogram for preoperative prediction of lymph node metastasis in colorectal cancer. J Clin Oncol *34(18)*: 2157-2164, 2016. PMID: 27138577. DOI: 10.1200/jco.2015.65.9128

39 Huang Y, Liu Z, He L, Chen X, Pan D, Ma Z, Liang C, Tian J and Liang C: Radiomics signature: A potential biomarker for the prediction of disease-free survival in early-stage (I or II) non-small cell lung cancer. Radiology *281(3)*: 947-957, 2016. PMID: 27347764. DOI: 10.1148/radiol.2016152234

40 Yang D, Rao G, Martinez J, Veeraraghavan A and Rao A: Evaluation of tumor-derived mri-texture features for discrimination of molecular subtypes and prediction of 12-month survival status in glioblastoma. Med Phys *42(11)*: 6725-6735, 2015. PMID: 26520762. DOI: 10.1118/1.4934373

41 Yip SS and Aerts HJ: Applications and limitations of radiomics. Phys Med Biol *61(13)*: R150-166, 2016. PMID: 27269645. DOI: 10.1088/0031-9155/61/13/r150

42 Saha A, Harowicz MR and Mazurowski MA: Breast cancer mri radiomics: An overview of algorithmic features and impact of inter-reader variability in annotating tumors. Med Phys *45(7)*: 3076-3085, 2018. PMID: 29663411. DOI: 10.1002/mp.12925

*Received April 22, 2020*
*Revised May 18, 2020*
*Accepted May 23, 2020*