European Radiology (2021) 31:3447–3467
https://doi.org/10.1007/s00330-020-07376-6

HEPATOBILIARY-PANCREAS

Pancreas image mining: a systematic review of radiomics

Bassam M. Abunahel[1] · Beau Pontre[2] · Haribalan Kumar[3] · Maxim S. Petrov[1]

Received: 20 May 2020 / Revised: 25 August 2020 / Accepted: 5 October 2020 / Published online: 5 November 2020

Abstract

Objectives To systematically review published studies on the use of radiomics of the pancreas.

Methods The search was conducted in the MEDLINE database. Human studies that investigated the applications of radiomics in diseases of the pancreas were included. The radiomics quality score was calculated for each included study.

Results A total of 72 studies encompassing 8863 participants were included. Of them, 66 investigated focal pancreatic lesions (pancreatic cancer, precancerous lesions, or benign lesions); 4, pancreatitis; and 2, diabetes mellitus. The principal applications of radiomics were differential diagnosis between various types of focal pancreatic lesions ($n = 19$), classification of pancreatic diseases ($n = 23$), and prediction of prognosis or treatment response ($n = 30$). Second-order texture features were most useful for the purpose of differential diagnosis of diseases of the pancreas (with 100% of studies investigating them found a statistically significant feature), whereas filtered image features were most useful for the purpose of classification of diseases of the pancreas and prediction of diseases of the pancreas (with 100% of studies investigating them found a statistically significant feature). The median radiomics quality score of the included studies was 28%, with the interquartile range of 22% to 36%. The radiomics quality score was significantly correlated with the number of extracted radiomics features ($r = 0.52$, $p < 0.001$) and the study sample size ($r = 0.34$, $p = 0.003$).

Conclusions Radiomics of the pancreas holds promise as a quantitative imaging biomarker of both focal pancreatic lesions and diffuse changes of the pancreas. The usefulness of radiomics features may vary depending on the purpose of their application. Standardisation of image acquisition protocols and image pre-processing is warranted prior to considering the use of radiomics of the pancreas in routine clinical practice.

Key Points

- *Methodologically sound studies on radiomics of the pancreas are characterised by a large sample size and a large number of extracted features.*
- *Optimisation of the radiomics pipeline will increase the clinical utility of mineable pancreas imaging data.*
- *Radiomics of the pancreas is a promising personalised medicine tool in diseases of the pancreas.*

Keywords Pancreas · Radiomics · Magnetic resonance imaging

Abbreviations

RQS Radiomics quality score

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00330-020-07376-6) contains supplementary material, which is available to authorized users.

Maxim S. Petrov
max.petrov@gmail.com

[1] School of Medicine, University of Auckland, Auckland, New Zealand

[2] School of Medical Sciences, University of Auckland, Auckland, New Zealand

[3] Auckland Bioengineering Institute, University of Auckland, Auckland, New Zealand

Introduction

Diseases of the pancreas are complex (with a wide array of genetic, environmental, and behavioural factors affecting them) and often lie on a continuum. Acute pancreatitis (AP) is the most common disease of the exocrine pancreas with the global incidence of 33.7 per 100,000 individuals per year [1]. One-fifth of individuals after first episode of AP develop recurrent acute pancreatitis (RAP), and 36% of those with RAP progress to chronic pancreatitis (CP) [2]. Pancreatic cancer is the most lethal disease of the pancreas with the global incidence and mortality of 8.1 and 6.9 per 100,000 general population per year, respectively [1]. Its common risk factors include familial pancreatic cancer kindred and deleterious germline mutations in pancreatic cancer susceptibility genes [3]. Also, several focal pancreatic lesions (pancreatic intraepithelial neoplasms-grade 3

(PanIN-3), intraductal papillary mucinous neoplasms, and mucinous cystic neoplasms) are considered precancerous [4]. Both pancreatitis and pancreatic cancer often lead to new-onset diabetes, termed 'diabetes of the exocrine pancreas'—the second most common type of new-onset diabetes in adults [5].

Imaging modalities (such as computed tomography (CT), magnetic resonance imaging (MRI), endoscopic ultrasonography, and positron emission tomography) are frequently used in management of diseases of the pancreas [6, 7]. Traditionally, their use predominantly includes subjective assessment of a handful of generic qualitative features that describe the underlying pathology of the pancreas. However, images of the pancreas contain an innumerable amount of objective data specific to each patient that could be harnessed to provide personalised management of patients [8, 9]. The field of quantitative image analysis has evolved in recent years and automatedly extracted features can now be analysed. The process of high-throughput extraction of image features from radiological images has been termed 'radiomics' [10]. Organ-specific radiomics promises to be a cornerstone of personalised medicine in the future. The use of radiomics in lung, liver, prostate, breast, kidney, rectum, and central nervous system diseases has been reviewed [11–17]. However, to date, there has been no systematic review on the use of radiomics in diseases of the pancreas.

The aim was to systematically benchmark published studies on radiomics of the pancreas and to determine their quality as well as the factors that are associated with it.

Methods

Search strategy

The search strategy was conducted in consultation with an experienced subject librarian to identify all relevant studies that reported on the use of radiomics of the pancreas in humans. A systematic literature search was conducted to identify all studies published from January 1, 2000 to April 15, 2020, using the MEDLINE database. No language restrictions were applied. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines were followed. The initial screening was done through the review of titles and abstracts. Full-text articles of potentially relevant studies were retrieved and assessed for eligibility. Relevant articles were also identified through reference lists of the retrieved full-text articles.

Eligibility criteria

Eligible studies had to investigate the applications of image analysis in pancreatic benign or precancerous lesions, pancreatic cancer, pancreatitis, or diabetes mellitus through extracting quantitative imaging features (i.e. radiomics). All imaging modalities were eligible. Studies were excluded if they were conducted not in humans; qualitative imaging features alone were reported; machine learning (e.g. convolutional neural network) was used to recognise image patterns without extracting quantitative features; they focused on technical (e.g. image pre-processing or image acquisition parameters) or patient-related parameters and their effect on the stability and reproducibility of extracted features; and they focused on a complication of pancreatic surgery (e.g. pancreatic fistula). Publications other than original articles (e.g. reviews, book chapters, editorials) were not considered.

Data extraction

The following data were extracted from the included studies, if available: authors, year of publication, country, cohort size, goal(s) of the study, type of imaging modality, parameters of imaging (e.g. slice thickness, imaging phase, MRI sequence), method of segmentation, type of feature extraction software, type of extracted features (i.e. quantitative radiomics only or semantic), type and number of extracted quantitative features, number of statistically significant quantitative features, and method of feature reduction and classification.

The included studies were grouped into three main categories based on the main goal of each study. The first category was differential diagnosis of diseases of the pancreas (e.g. differentiation between healthy pancreas and chronic pancreatitis or pancreatic cancer). The second category was classification of diseases of the pancreas, where more than two subtypes of the same disease of the pancreas were studied (e.g. classification of subtypes of pancreatitis or classification of histologic grades of pancreatic cancer). The third category was prediction of diseases of the pancreas (e.g. prediction of survival in patients with unresectable pancreatic cancer or prediction of patient response to a certain treatment). Within each category, all radiomics features were categorised into three main groups (at least one significant feature reported, no significant feature reported, and non-investigated feature) with the view to determining a clinically useful pattern.

Radiomics quality score

The radiomics quality score (RQS) was calculated for each individual study. In brief, the RQS assessed the quality of radiomics study in terms of robustness and reproducibility through assigning points based on 16 criteria [18]. The number of points depended on the importance of the respective criterion, with 36 points (100%) being the maximum number.

Statistical analysis

The associations of the RQS with number of extracted features and cohort size were investigated using Pearson correlation coefficient. The association between the RQS and the type of imaging modality was investigated using linear regression analysis (with CT set as the reference). Statistical analysis was performed using SPSS software (version 24). A p value of < 0.05 was considered statistically significant.

Results

Characteristics of the included studies

The total number of retrieved publications was 120 (Fig. 1). Seventy-two studies met the eligibility criteria and were included in the systematic literature review [19–90]. These studies encompassed a total of 8863 individuals. The sample size varied between 17 and 690 individuals, with a median of 100 individuals. Fifty-four studies (75.0%) employed CT [23, 24, 26–43, 45–49, 51, 52, 55–57, 59, 61–65, 68–71, 74–77, 80–83, 85–90]; nine studies (12.5%), MRI [44, 50, 53, 54, 58, 60, 66, 67, 78]; three studies (4.2%), endoscopic ultrasound [19–21]; and six studies (8.3%), positron emission tomography [22, 25, 72, 73, 79, 84]. Forty-four studies (61.1%) were conducted in Asia [19–21, 33, 35–38, 41–44, 48–52, 56–61, 63, 64, 66–74, 76, 77, 79, 80, 83, 84, 87–90], 20 studies (27.8%) in North America [22–32, 39, 40, 45, 55, 62, 65, 75, 82, 85], and eight studies (11.1%) in Europe [34, 46, 47, 53, 54, 78, 81, 86]. Other details are presented in Table 1.

Sixty-six (91.7%) studies applied manual segmentation of the pancreas, whereas six studies used semi-automated segmentation [24, 25, 29, 46, 56, 84]. Twenty-seven studies (37.5%) extracted only quantitative radiomics features, whereas 45 studies combined both radiomics and semantic features. The semantic features in the 45 studies were clinical features (e.g. age, gender, body mass index ($n = 45$), histopathological features (e.g. tumour grades, mitotic index) ($n = 15$), blood biomarkers (e.g. cancer antigen 19-9, carcinoembryonic antigen) ($n = 14$), and genetic signatures (e.g. HMGA2 and c-Myc genes, miRNA genomic classifier) ($n = 2$). Out of the 45 studies, 20 studies reported that the performance of combined model (i.e. significant radiomics features plus semantic features) is higher than the per-

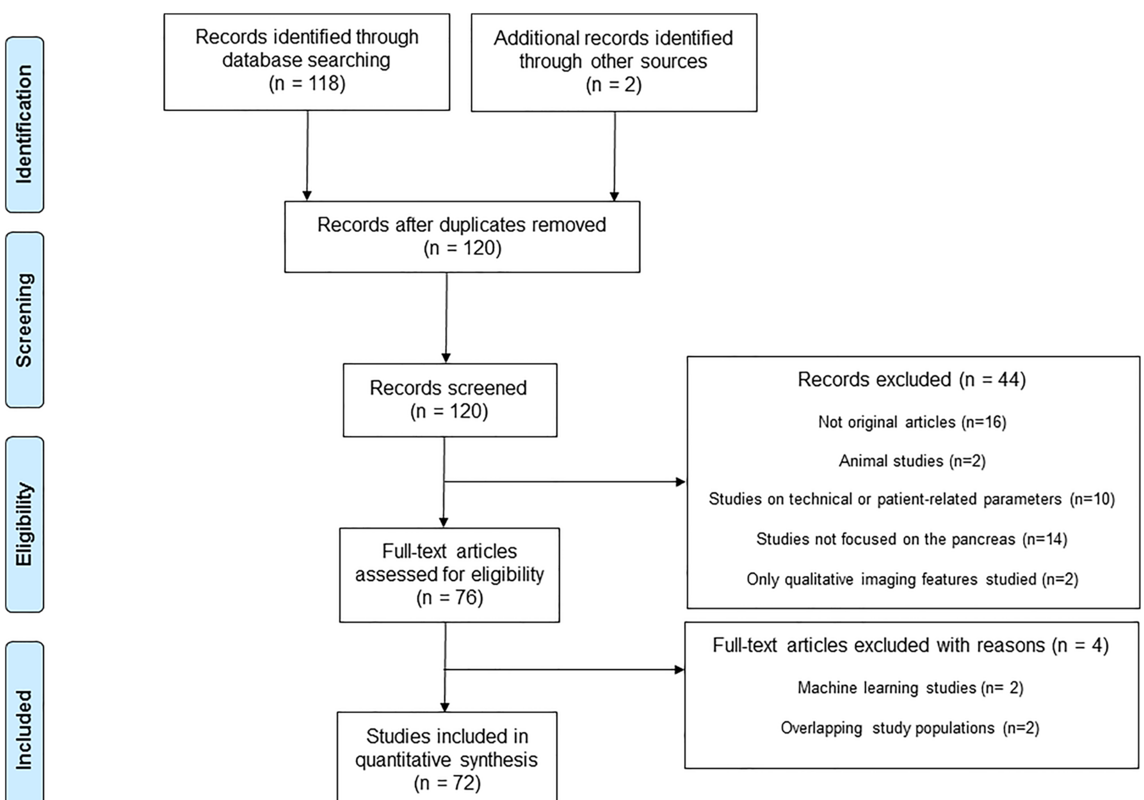

Fig. 1 Flowchart of the study selection process

Table 1 Characteristics of the included studies

Study ID	Year	Country	Sample size	Goal(s)	Imaging modality	Segmentation method	Feature type	Imaging phase (slice thickness)	Feature extraction software	% RQS (points)
Zhang et al [19]	2010	China	216	Differentiation of pancreatic cancer from healthy pancreas	EUS	Manual	Q only	–	MATLAB 7.1	19% (7)
Xu et al [20]	2013	China	25	Prediction of prognosis of unresectable pancreatic cancer[a]	EUS	Manual	Q only	–	C++ program	19% (7)
Zhu et al [21]	2013	China	388	Differentiation of pancreatic cancer from CP	EUS	Manual	Q only	–	MATLAB R2010a	22% (8)
Cui et al [22]	2016	USA	139	Prediction of prognosis of unresectable pancreatic cancer[b]	PET	Manual	Q only	–	In-house developed software	36% (13)
Hanania et al [23]	2016	USA	52	Classification of grades of IPMN	CECT	Manual	Q only	PAP	IBEX	31% (11)
Permuth et al [24]	2016	USA	38	Classification of grades of IPMN	CECT	Semi-automated	Q and S	PVP (3 mm)	In-house developed software	42% (15)
Yue et al [25]	2016	USA	25	Prediction of treatment response in PDAC[c]	PET	Semi-automated	Q and S	–	3D kernel-based approach	25% (9)
Canellas et al [26]	2017	USA	101	- Classification of grades of PNET - Prediction of prognosis of PNET[d]	CECT	Manual	Q and S	PVP (5 mm)	TexRAD	25% (9)
Cassinotto et al [27]	2017	Canada	99	Prediction of prognosis of resectable PDAC[e]	CECT	Manual	Q and S	PVP (2.5 mm)	TexRAD	14% (5)
Chen et al [28]	2017	USA	20	Prediction of treatment response in pancreatic cancer[f]	CT	Manual	Q only	– (3 mm)	In-house developed software	14% (5)
Dmitriev et al [29]	2017	USA	134	Classification of subtypes of pancreatic cyst	CECT	Semi-automated	Q and S	– (0.75 mm)	In-house developed software	14% (5)
Eilaghi et al [30]	2017	Canada	30	Prediction of prognosis of resectable PDAC[g]	CECT	Manual	Q only	PVP	In-house developed software	19% (7)
Attiyeh et al [31]	2018	USA	161	Prediction of prognosis of resectable PDAC[h]	CECT	Manual	Q and S	Multiphase (2.5 mm)	MATLAB R2015a	31% (11)
Chakraborty et al [32]	2018	USA	103	Prediction of risk of IPMN[i]	CECT	Manual	Q and S	PVP (2.5 mm)	MATLAB R2015a	33% (12)
Choi et al [33]	2018	South Korea	66	Classification of grades of PNET	CECT	Manual	Q and S	PAP and PVP (2.5–3.2 mm)	In-house developed software	17% (6)
Ciaravino et al [34]	2018	Italy	17	Prediction of treatment response in PDAC[j]	CECT	Manual	Q only	PAP (2 mm)	MaZda	17% (6)
Guo et al [35]	2018	China	42	Differentiation of PDAC from PNET[k]	CECT	Manual	Q and S	PAP and PVP (3 mm)	MATLAB R2014b	25% (9)
Li et al [36]	2018	China	127	Differentiation of PDAC from PNET[l]	CECT	Manual	Q and S	PVP (0.625 mm)	In-house developed software	17% (6)
Lin et al [37]	2018	China	34	Differentiation of PNET from IPAS[m]	CECT	Manual	Q and S	PAP and PVP (3–5 mm)	MATLAB R2014a	19% (7)
Yun et al [38]	2018	South Korea	88	Prediction of prognosis of resectable pancreatic cancer[n]	CECT	Manual	Q only	PAP (4 mm)	In-house developed software	28% (10)
Attiyeh et al [39]	2019	USA	103	Classification of grades of IPMN[o]	CECT	Manual	Q and S	PVP (2.5 mm)	In-house developed software	33% (12)
Attiyeh et al [40]	2019	USA	35	- Classification of mutation status in PDAC[p] - Classification of stromal content in PDAC	CECT	Manual	Q only	PVP (2.5 mm)	MATLAB R2015a	28% (10)
Bian et al [41]	2019	China	225	Prediction of risk of PDAC	CECT	Manual	Q only	PAP (0.5 mm)	Pyradiomics	28% (10)
Chen et al [42]	2019	China	389	Prediction of recurrence of AP	CECT	Manual	Q and S	PAP and PVP (5 mm)	IBEX	44% (16)
Cheng et al	2019	China	41	Prediction of prognosis of unresectable PDAC[q]	CECT	Manual	Q and S	PVP	TexRAD	19%

Table 1 (continued)

Study ID	Year	Country	Sample size	Goal(s)	Imaging modality	Segmentation method	Feature type	Imaging phase (slice thickness)	Feature extraction software	% RQS (points)
[43]								(5 mm)		(7)
Choi et al [44]	2019	South Korea	66	Prediction of prognosis of resectable PDAC[r]	MRI	Manual	Q and S	T2WI (6 mm)	TexRAD	19% (7)
Chu et al [45]	2019	USA	380	Differentiation of PDAC from healthy pancreas	CECT	Manual	Q only	PVP (0.75 mm)	In-house developed software	36% (13)
Cozzi et al [46]	2019	Italy	100	Prediction of prognosis of unresectable pancreatic cancer[s]	CT	Semi-automated	Q and S	–	LIFEx	28% (10)
D'Onofrio et al [47]	2019	Italy	100	Classification of grades of PNET	CECT	Manual	Q and S	PAP (5 mm)	MaZda	17% (6)
Gu et al [48]	2019	China	138	Classification of grades of PNET	CECT	Manual	Q and S	PAP and PVP (0.5–5 mm)	Pyradiomics	44% (16)
Guo et al [49]	2019	China	37	Classification of grades of PNET	CECT	Manual	Q and S	PAP (3 mm)	MATLAB R2014a	25% (9)
Guo et al [50]	2019	China	77	Classification of grades of PNET	MRI	Manual	Q and S	T2WI and DWI (5 mm)	Omni-Kinetics software	25% (9)
He et al [51]	2019	China	147	Differentiation of PDAC from PNET[t]	CECT	Manual	Q and S	PAP (5 mm)	Pyradiomics	42% (15)
Huang et al [52]	2019	China	45	Differentiation of PDAC from PL	CECT	Manual	Q and S	PAP and PVP (3 mm)	MaZda	28% (10)
Kaissis et al [53]	2019	Germany	132	- Classification of subtypes of PDAC - Prediction of prognosis of PDAC[u]	MRI	Manual	Q only	DWI and ADC map	Pyradiomics	36% (13)
Kaissis et al [54]	2019	Germany	55	- Classification of subtypes of PDAC - Prediction of treatment response in PDAC[v]	MRI	Manual	Q only	DWI and ADC map[w]	Pyradiomics	36% (13)
Khalvati et al [55]	2019	Canada	98	Prediction of prognosis of resectable PDAC[x]	CECT	Manual	Q and S	PVP (2–5 mm)	Pyradiomics	44% (16)
Kim et al [56]	2019	South Korea	116	Prediction of prognosis of resectable pancreatic cancer[y]	CECT	Semi-automated	Q only	PAP (3 mm)	In-house developed software	22% (8)
Li et al [57]	2019	China	111	- Classification of gene expression in PDAC - Prediction of prognosis of PDAC[z]	CECT	Manual	Q only	PVP (0.6 mm)	MATLAB R2016b	33% (12)
Li et al [58]	2019	China	119	Differentiation of PNET from SPN[aa]	MRI	Manual	Q and S	DCE-MRI[bb]	MaZda	28% (10)
Liang et al [59]	2019	China	137	Classification of grades of PNET	CECT	Manual	Q and S	PAP (3–5 mm)	MATLAB R2016a	44% (16)
Lin et al [60]	2019	China	259	Prediction of severity of AP	MRI	Manual	Q and S	DCE-MRI[cc]	IBEX	42% (15)
Lu et al [61]	2019	China	690	- Prediction of incidence of DM type 2 - Early diagnosis of DM type 2	CT	Manual	Q and S	– (4.93–4.98 mm)	In-house developed software	33% (12)
Nasief et al [62]	2019	USA	90	Prediction of treatment response in pancreatic cancer[dd]	CT	Manual	Q only	– (3 mm)	IBEX	33% (12)
Qiu et al [63]	2019	China	56	Classification of grades of PDAC	CECT	Manual	Q and S	PVP (2–6 mm)	In-house developed software	31% (11)
Ren et al [64]	2019	China	109	Differentiation of PDAC from MFP	CECT	Manual	Q and S	PAP and PVP (3 mm)	AnalysisKit	28% (10)
Sandrasegaran et al [65]	2019	USA	60	Prediction of prognosis of unresectable pancreatic cancer[ee]	CECT	Manual	Q only	PVP (4–5 mm)	TexRAD	28% (10)
Tang et al [66]	2019	China	303	Prediction of prognosis of resectable pancreatic cancer[ff]	MRI	Manual	Q and S	DCE-MRI[gg]	A.K. software	53% (19)
Wang et al	2019	China	50	Differentiation of PDAC from PNET	MRI	Manual	Q and S	DWI	Image J	19%

Table 1 (continued)

Study ID	Year	Country	Sample size	Goal(s)	Imaging modality	Segmentation method	Feature type	Imaging phase (slice thickness)	Feature extraction software	% RQS (points)
[67]								(6 mm)		(7)
Wei et al [68]	2019	China	87	Classification of gene expression in PCN[hh]	CECT	Manual	Q and S	PVP	MATLAB R2015b	33% (12)
Wei et al [69]	2019	China	260	Differentiation of SCN from non-SCN	CECT	Manual	Q and S	PVP (1–3 mm)	In-house developed software	36% (13)
Yang et al [70]	2019	China	78	Differentiation of SCN from MCN	CECT	Manual	Q only	PVP (2 or 5 mm)	LIFEx	33% (12)
Yu et al [71]	2019	China	120	Differentiation of PDAC from PNET[ii]	CECT	Manual	Q and S	PAP and PVP (1–7 mm)	A.K. software	25% (9)
Zhang et al [72]	2019	China	111	Differentiation of PDAC from AIP	PET/CT	Manual	Q only	0.98 mm	In-house developed software	36% (13)
Zhang et al [73]	2019	China	111	Differentiation of PDAC from AIP	PET/CT	Manual	Q and S	– (0.6 mm)	MATLAB R2017b	42% (15)
Zhou et al [74]	2019	China	106	- Prediction of prognosis of unresectable pancreatic cancer[jj] - Prediction of risk of unresectable pancreatic cancer	CECT	Manual	Q and S	PAP and PVP (5 mm)	MATLAB R2018a	42% (15)
Borhani et al [75]	2020	USA	39	Prediction of treatment response and prognosis of PDAC[kk]	CECT	Manual	Q and S	PAP (2.5 mm)	TexRAD	6% (2)
Chang et al [76]	2020	China	301	Classification of grades of PDAC	CECT	Manual	Q and S	PAP (1–3 mm)	IBEX	39% (14)
Fang et al [77]	2020	China	155	Prediction of metastasis of PDAC[ll]	CECT	Manual	Q only	PAP and PVP (1.25–5 mm)	MaZda	28% (10)
Frøkjær et al [78]	2020	Denmark	99	Differentiation of CP from healthy pancreas[mm]	MRI	Manual	Q only	DWI[nn] (2.6 mm)	Pyradiomics	22% (8)
Gao et al [79]	2020	China	17	Prediction of metastasis of PDAC[oo]	PET/MRI	Manual	Q and S	PET/ADC (4–6 mm)	LIFEx	33% (12)
Jang et al [80]	2020	South Korea	51	- Prediction of incidence of DM - Classification of subtypes of DM	CECT	Manual	Q only	PVP (2.5–5.0 mm)	In-house developed software	28% (10)
Kaissis et al [81]	2020	Germany	207	Classification of subtypes of PDAC[pp]	CECT	Manual	Q only	PVP	Pyradiomics	39% (14)
Kulkarni et al [82]	2020	Canada	131	Prediction of resection margin status of PDAC[qq]	CECT	Manual	Q only	PVP (2.5 mm)	LIFEx	17% (6)
Li et al [83]	2020	China	118	Prediction of metastasis of PDAC[rr]	CECT	Manual	Q and S	PVP (1 mm)	Pyradiomics	50% (18)
Lim et al [84]	2020	South Korea	48	Classification of mutation status in PDAC[ss]	PET	Semi-automated	Q only	–	CGITA	22% (8)
Mashayekhi et al [85]	2020	USA	56	Classification of subtypes of pancreatitis[tt]	CECT	Manual	Q only	PVP (3 mm)	In-house MATLAB program	28% (10)
Reinert et al [86]	2020	Germany	95	- Differentiation of PDAC from PNET - Classification of grades of PNET	CECT	Manual	Q and S	PVP (1 mm)	Pyradiomics	31% (11)
Shen et al [87]	2020	China	164	Classification of subtypes of PCN[uu]	CECT	Manual	Q and S	PAP (3–5 mm)	MATLAB R2017b	39% (14)
Xie et al [88]	2020	China	57	Differentiation of SCN from MCN	CECT	Manual	Q and S	PVP (3 mm)	MATLAB R2017a	28% (10)
Xie et al [89]	2020	China	220	Prediction of prognosis of resectable PDAC[vv]	CT	Manual	Q and S	– 3 mm	NM	53% (19)
Zhao et al [90]	2020	China	59	Classification of grades of PNET[ww]	CECT	Manual	Q and S	Non-enhanced and PVP (0.8 mm)	In-house developed software	44% (16)

Abbreviations: *A.K.*, artificial intelligence kit software; *ADC*, apparent diffusion coefficient; *AIP*, autoimmune pancreatitis; *AP*, acute pancreatitis; *CECT*, contrast-enhanced computed tomography; *CGITA*, Chang Gung Image Texture Analysis; *CP*, chronic pancreatitis; *CT*, computed tomography; *DCE*, dynamic contrast enhancement; *DM*, diabetes mellitus; *DWI*, diffusion-weighted image; *EUS*, endoscopic ultrasound; *IBEX*, imaging biomarker explorer; *IPAS*, intrapancreatic accessory spleen; *IPMN*, Intraductal papillary mucinous neoplasm; *LIFEx*, local image features extraction; *MCN*, mucinous cystic neoplasm; *MFP*, mass forming pancreatitis; *MRI*, magnetic resonance imaging; *NM*, not mentioned; *PAP*, pancreatic arterial phase; *PCN*, pancreatic cystic neoplasm; PDAC, pancreatic ductal adenocarcinoma; PET, positron emission tomography; *PL*, pancreatic lymphoma; *PNET*, pancreatic neuroendocrine tumour; *PVP*, portal venous phase; *Q*, quantitative; *RQS*, radiomics quality score; *S*, semantic; *SCN*, serous cystic neoplasm; *SPN*, solid-pseudopapillary neoplasm; *TexRAD*, texture radiology software

[a] Overall survival

[b] Locally advanced pancreatic cancer

[c] Radio-chemotherapy response

[d] Progression-free survival

[e] Disease-free survival in PDAC

[f] Radio-chemotherapy response

[g] Overall survival in pancreatic ductal adenocarcinoma

[h] Pre- and post-operative survival in PDAC

[i] Branch duct IPMN

[j] Radio-chemotherapy response

[k] PNEC grade 3

[l] Atypical PNET

[m] Hypervascular PNET

[n] Disease-free survival in pancreatic head cancer

[o] Branch duct IPMN

[p] SMAD4 mutation

[q] Overall survival and progression-free survival

[r] Recurrence free survival and overall survival

[s] Overall survival and local control for locally advanced pancreatic cancer

[t] Atypical non-functioning PNET

[u] Tumour subtypes and overall survival

[v] Molecular subtypes and chemotherapy response

[w] At b value = 600 s/mm^2 with EPI

[x] Overall survival

[y] Recurrence free survival

[z] c-Myc and HMGA2 genes as well as overall survival

[aa] Non-functioning PNET

[bb] DWI, ADC map, T2-weighted image fat saturated, and T1-weighted image fat saturated at different contrast enhancement phases

[cc] T1WI FS at different contrast enhancement phases

[dd] Radio-chemotherapy response

[ee] Overall survival

[ff] Early recurrence

[gg] T1-weighted image and T2-weighted image at different contrast enhancement phases

[hh] Ki67 index in IPMN and MCN
[ii] Non-hypervascular PNEN
[jj] Three months restenosis-free survival
[kk] Disease-free survival in resectable PDAC
[ll] Lymph node metastasis in resectable PDAC
[mm] Beside classification of CP based on two risk factors and two complications
[nn] At b value = 0 s/mm^2
[oo] Distant metastases
[pp] Quasi-mesenchymal and non-quasi-mesenchymal subtypes
[qq] Beside prediction of risk features including nodal status, tumour grades, lymphovascular invasion, and perineural invasion
[rr] Lymph node metastasis
[ss] KRAS, SMAD4, TP53, and CDKN2A mutations
[tt] Functional abdominal pain, recurrent AP, and CP
[uu] Including SCN, MCN, and IPMN
[vv] Disease-free survival and overall survival
[ww] Non-functional PNET

formance of radiomics model alone. The superiority of combined model was confirmed statistically in eight studies [22, 24, 31, 46, 48, 51, 59, 88].

Various approaches to dimensionality reduction were applied in the included studies in order to select the most useful radiomics feature and reduce the effect of overfitting. These approaches included univariate filter technique ($n = 17$), multivariate filter technique ($n = 20$), least absolute shrinkage and selection operator regression ($n = 18$), as well as principle component analysis ($n = 2$). The useful features were used as an input for training and validating classification model. Out of the 72 included studies, 36 studies applied supervised machine learning techniques (including random forest in nine studies); 14 studies, support vector machine; and 22 studies, logistic regression. The median RQS of the included studies was 28% (interquartile range 22–36%). The three most frequently observed RQS characteristics were discrimination statistics and applying resampling techniques, employing well-documented imaging protocol, and clinical usefulness of the model (Fig. 2). The three least frequently observed RQS characteristics were prospective study design, imaging at different time points, and comparing radiomics model with current gold standard method (Fig. 2). Fourteen studies (19.5%) analysed feature robustness through detecting inter-scanner differences and vendor-dependent features [33, 38, 42, 48, 55, 58, 61–63, 69, 71, 73, 82, 86].

Applications of radiomics of the pancreas

The median number of extracted radiomics features in the included studies was 166 (interquartile range 14–416). Eighteen studies (25%) used in-house developed software [22, 24, 28–30, 33, 36, 38, 39, 45, 56, 61, 63, 69, 72, 80, 85, 90], whereas the remaining studies used open source or commercial software. The types and number of extracted features in individual studies are presented in Table 2. The significant radiomics features in individual studies are presented in Tables 3, 4, and 5 (stratified by the primary goal of using radiomics). The main focus of radiomics in 56 studies (77.8%) was pancreatic cancer; four studies (5.6%), pancreatic precancerous lesions [23, 24, 32, 39]; six studies (8.4%), pancreatic benign lesions [29, 68–70, 87, 88]; four studies (5.6%), pancreatitis [42, 60, 78, 85]; and two studies (2.8%), diabetes mellitus [61, 80]. Nineteen studies (26.4%) primarily applied radiomics for differentiation between various diseases of the pancreas, 23 studies (32.0%) for classification of subtypes/histologic grades, and 30 studies (41.7%) for prediction of prognosis/treatment response (Fig. 3). Out of the 72 included studies, 28 studies extracted radiomics features and patterns with the use of different filters (including wavelet, square, square root, exponential, logarithm, gradient,

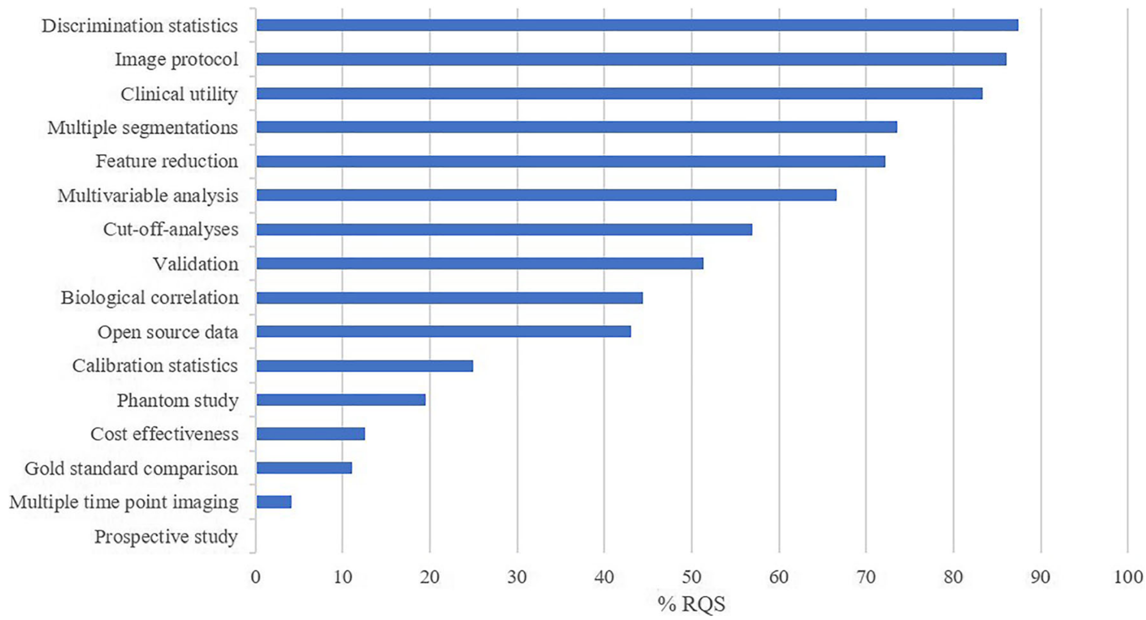

Fig. 2 Radiomics quality score of the included studies

Laws, local binary pattern, Laplacian of Gaussian, and fractal dimension filters).

Factors that affect radiomics quality score

Supplementary Table 1 details the RQS of individual studies. Overall, the RQS was significantly correlated with the number of extracted features ($r = 0.529$, $p < 0.001$) as well as with the cohort size ($r = 0.343$, $p = 0.003$). In its turn, the number of extracted features and the cohort size were significantly correlated with the number of statistically significant features ($r = 0.437$, $p < 0.001$; and $r = 0.437$, $p < 0.001$, correspondingly). Using CT as the reference, radiomics features extracted from MRI images resulted in an increase in the RQS by 1 point ($p = 0.732$); extracted from positron emission tomography images, in an increase in the RQS by 2 points ($p = 0.570$); extracted from endoscopic ultrasonography images, in a decrease in the RQS by 10 points ($p = 0.102$). Using CT as the reference, radiomics features extracted from MRI images resulted in 5 more statistically significant features ($p = 0.134$); extracted from endoscopic ultrasonography images, in 3 more statistically significant features ($p = 0.495$); extracted from positron emission tomography images, in 1 less statistically significant feature ($p = 0.680$).

Discussion

This is the first systematic review to investigate the use of radiomics of the pancreas and the factors that affect quantitative imaging features of the pancreas. A total of 72 studies that enrolled more than eight thousand participants were included, with the median sample size of 100 participants. The median number of investigated radiomics features in the included studies was 166, ranging from 4 to 2041 features. These features could be grouped into five main categories: shape features, first-order texture features, second-order texture features, filtered image features, and customised features [91]. Filtered image features appeared to be the most frequently observed significant radiomics features in the studies that employed them for classification (Table 4) and prediction (Table 5) of diseases of the pancreas. However, only 39% of studies (28 out of 72) used these features and more research is needed to confirm their usefulness in diseases of the pancreas. Future research also needs to determine the optimal filters as the included studies used a total of 10 different filters (including wavelet, square, square root, exponential, logarithm, gradient, Laws, local binary pattern, Laplacian of Gaussian, and fractal dimension filters). Second-order texture features were used in 94% of studies (68 out of 72) and they appeared to be the most frequently observed significant radiomics features in the studies focused on differential diagnosis of diseases of the pancreas (Table 3). The superiority of this group of features is likely explained by the fact that they capture the spatial arrangement and distribution of intensities within the pancreas using different types of matrices (e.g. grey level co-occurrence matrix, grey level run length matrix). Making use of large number of matrices may be required as the pancreas is a complex glandular organ

Table 2 Radiomics features investigated in the included studies

Study ID	Type of extracted features	Number of extracted features	Number of statistically significant features	Feature reduction and classification method
Zhang et al [19]	First-order texture features Second-order texture features Filtered image features	67	20	Leave one out, Bayes, and SFS algorithms for selection; SVM for classification
Xu et al [20]	First-order texture features Second-order texture features	22	22[xx]	SFS and fuzzy classification algorithms
Zhu et al [21]	First-order texture features Second-order texture features Filtered image features	105	16	Distance between class and SFS algorithms for selection; SVM for classification
Cui et al [22]	Shape features First-order texture features Second-order texture features Filtered image features	173	7	Elastic net and ICC > 0.8 for selection; Cox regression model for classification
Hanania et al [23]	Shape features First-order texture features Second-order texture features	360	10	ROC and FDR for selection; Logistic regression for classification
Permuth et al [24]	Shape features First-order texture features Second-order texture features Filtered image features	112	14	Pearson correlation for selection; PCA and logistic regression for classification
Yue et al [25]	Second-order texture features	12	3	Elastic net and LASSO regression for selection; Multivariate Cox regression model for classification
Canellas et al [26]	First-order texture features Second-order texture features Filtered image features	36	1	Independent sample *t* test for selection; Binary logistic regression for classification
Cassinotto et al [27]	Filtered image features	7[yy]	1	Univariate and multivariate Cox regression model
Chen et al [28]	First-order texture features	8	4	Generalised estimating equation model
Dmitriev et al [29]	Shape features First-order texture features	14	0[zz]	RF and convolution neural network
Eilaghi et al [30]	Second-order texture features	5	2	Cox regression model
Attiyeh et al [31]	First-order texture features Second-order texture features	255	0[aaa]	Univariate and multivariate Cox regression model
Chakraborty et al [32]	Second-order texture features Customised features[bbb]	135	17	Univariate and multivariate logistic regression model, Wilcoxon rank sum test, and ensemble model for selection; SVM and RF for classification
Choi et al [33]	Shape features First-order texture features	16	7[ccc]	Multivariate logistic regression analysis
Ciaravino et al [34]	First-order texture features	5	1	Wilcoxon correlation test
Guo et al [35]	First-order texture features Filtered image features	4	2	NA
Li et al [36]	First-order texture features	10	2	NA

Table 2 (continued)

Study ID	Type of extracted features	Number of extracted features	Number of statistically significant features	Feature reduction and classification method
Lin et al [37]	Filtered image features	4	2	NA
Yun et al [38]	First-order texture features Second-order texture features Filtered image features	8	4	Multivariate Cox regression model
Attiyeh et al [39]	First-order texture features Second-order texture features Customised features[ddd]	255	0	Univariate analysis and RF
Attiyeh et al [40]	First-order texture features Second-order texture features	255	28[eee]	Univariate analysis and fuzzy MRMR for selection; MDS and linear regression model for classification
Bian et al [41]	Shape features First-order texture features Second-order texture features Filtered image features	1029	12	Spearman correlation, variance, and LASSO regression for selection; Multivariate logistic regression for classification
Chen et al [42]	Shape features First-order texture features Second-order texture features	412	10	Independent sample *t* test, LASSO regression, and Spearman correlation for selection; Multivariate logistic regression and SVM for classification
Cheng et al [43]	First-order texture features Filtered image features	6[fff]	1[ggg]	Multivariate Cox regression model
Choi et al [44]	First-order texture features Filtered image features	36[hhh]	1[iii]	Multivariate Cox regression model
Chu et al [45]	Shape features First-order texture features Second-order texture features Filtered image features	478	40	MRMR and RF
Cozzi et al [46]	Shape features First-order texture features Second-order texture features	41	12[jjj]	Pearson correlation and elastic net regression for selection; Multivariate Cox regression model for classification
D'Onofrio et al [47]	First-order texture features	5	2	Mann-Whitney correlation test
Gu et al [48]	Shape features First-order texture features Second-order texture features Filtered image features	853	25	MRMR and RF
Guo et al [49]	Filtered image features	5	2	Multivariate logistic regression
Guo et al [50]	First-order texture features Second-order texture features	68	9[kkk]	Logistic regression analysis
He et al [51]	Shape features First-order texture features Second-order texture features Filtered image features	637	7	LASSO, SVM, and RF
Huang et al [52]	First-order texture features Second-order texture features Filtered image features	279	1	LASSO and multivariate logistic regression model
Kaissis et al	Shape features	1688	8	ICC and RF

Table 2 (continued)

Study ID	Type of extracted features	Number of extracted features	Number of statistically significant features	Feature reduction and classification method
[53]	First-order texture features Second-order texture features Filtered image features			
Kaissis et al [54]	Shape features First-order texture features Second-order texture features Filtered image features	1606	13	Spearman correlation and ICC for selection; Decision tree and regression models for classification
Khalvati et al [55]	Shape features First-order texture features Second-order texture features Filtered image features	410	2	ICC, LASSO, and Cox regression models
Kim et al [56]	Second-order texture features	4	1[lll]	Cox proportional hazards regression method
Li et al [57]	Filtered image features Customised features[mmm]	326	6	K-folds cross-validation and SVM
Li et al [58]	First-order texture features Second-order texture features Filtered image features	300	30	RDA, LDA, NDA, and PCA
Liang et al [59]	First-order texture features Second-order texture features Filtered image features	467	8	Mann-Whitney *U* test and LASSO regression model for selection; Multivariate logistic regression model for classification
Lin et al [60]	Shape features First-order texture features Second-order texture features	353	11	Independent sample *t* test and Boruta algorithm for selection; SVM for classification
Lu et al [61]	First-order texture features Second-order texture features Filtered image features	160	5	LASSO and multivariate logistic regression models
Nasief et al [62]	Shape features First-order texture features Second-order texture features Customised features[nnn]	1300	13	Spearman correlation, *t* test, linear regression, and mixed effect models for selection; Bayesian-regularisation-neural-network for classification
Qiu et al [63]	First-order texture features Second-order texture features	29	18	Logistic regression analysis for selection; SVM for classification
Ren et al [64]	Shape features First-order texture features Second-order texture features	396	9[ooo]	MRMR for selection; Multivariate logistic regression analysis for classification
Sandrasegaran et al [65]	First-order texture features Filtered image features	4[ppp]	1[qqq]	Multivariate Cox regression model
Tang et al [66]	Shape features First-order texture features Second-order texture features	1312	10	LASSO regression for selection; Multivariate logistic analysis for classification
Wang et al [67]	Second-order texture features	5	5	Binary logistic regression analysis
Wei et al [68]	Shape features Second-order texture features Filtered image features	409	20	LASSO regression for selection; SVM for classification

Table 2 (continued)

Study ID	Type of extracted features	Number of extracted features	Number of statistically significant features	Feature reduction and classification method
Wei et al [69]	First-order texture features Second-order texture features Filtered image features	409	22	LASSO regression and SVM
Yang et al [70]	Shape features First-order texture features Second-order texture features	28	9	LASSO regression and RF
Yu et al [71]	Second-order texture features	385	5	Multivariate logistic regression
Zhang et al [72]	First-order texture features Second-order texture features Filtered image features	418	8	Fisher's criterion > 0.01 and SFS for selection; SVM for classification
Zhang et al [73]	Shape features First-order texture features Second-order texture features	251	10	Spearman correlation, MRMR, and SVM for selection[rrr]; RF, adaptive boosting, and SVM for classification[sss]
Zhou et al [74]	Shape features First-order texture features Second-order texture features Filtered image features	620	14	Pearson correlation, LASSO regression and ICC analysis for selection; Cox regression model for classification
Borhani et al [75]	First-order texture features Filtered image features	6[ttt]	4	Mann-Whitney test, chi-square analysis, and multivariate logistic regression; Kaplan-Meier survival analysis and Cox model
Chang et al [76]	Shape features First-order texture features Second-order texture features	1452	10	SVM-RFE for selection; LASSO regression for classification
Fang et al [77]	First-order texture features Second-order texture features Filtered image features	300	17	Fisher's coefficient, POE with ACC, and MI for selection; Spearman's correlation coefficients for classification
Frøkjær et al [78]	Shape features First-order texture features Second-order texture features Filtered image features	851	5[uuu]	Tenfold cross-validation forward selection procedure, Naive Bayes classifier
Gao et al [79]	First-order texture features Second-order texture features	37	4[vvv]	Logistic regression analysis
Jang et al [80]	Shape features First-order texture features Second-order texture features	17	4[www]	Multivariate logistic regression
Kaissis et al [81]	Shape features First-order texture features Second-order texture features Filtered image features	1474	20	Gini impurity for feature selection; RF for classification
Kulkarni et al [82]	First-order texture features Second-order texture features	9	2[xxx]	Logistic regression analysis
Li et al [83]	Shape features First-order texture features Second-order texture features Filtered image features	2041	15	LASSO for selection; multivariable logistic regression for classification

Table 2 (continued)

Study ID	Type of extracted features	Number of extracted features	Number of statistically significant features	Feature reduction and classification method
Lim et al [84]	Shape features First-order texture features Second-order texture features	35	9[yyy]	Based on the Mann-Whitney *U* test
Mashayekhi et al [85]	Shape features First-order texture features Second-order texture features	54	11	Wilcoxon rank-sum for selection; Isomap and SVM for classification
Reinert et al [86]	First-order texture features Second-order texture features	92	8[zzz]	Binary logistic regression analysis
Shen et al [87]	First-order texture features Second-order texture features Filtered image features	547	5	ICC > 0.75, Pearson's correlation coefficient > 0.75, and Boruta method for selection; SVM, RF, and ANN for classification
Xie et al [88]	First-order texture features Second-order texture features	1942	18	Multivariable logistic regression analysis
Xie et al [89]	First-order texture features Second-order texture features Filtered image features	300	5	ICC > 0.75 and LASSO regression for selection; Multivariate Cox regression model for classification
Zhao et al [90]	First-order texture features Second-order texture features Filtered image features	585	6	MRMR for selection. SVM-RBF for classification

Abbreviations: *ACC*, average correlation coefficients; *ANN*, artificial neural network; *FDR*, false discovery rate; *ICC*, interclass correlation coefficient; *LASSO*, least absolute shrinkage and selection operator; *LDA*, linear discriminate analysis; *MDS*, multidimensional scaling; *MI*, mutual information; *MRMR*, minimum redundancy maximum relevant; *NA*, not applicable; *NDA*, non-linear discriminate analysis; *PCA*, principle component analysis; *POE*, classification error probability; *RDA*, raw data analysis; *RF*, random forest; *ROC*, receiver operating characteristic curve; *SFS*, sequential forward selection; *SVM*, support vector machine; *SVM-RBF*, support vector machine-radial basis function; *SVM-RFE*, support vector machine-recursive feature elimination

[xx] Based on fuzzy classification score

[yy] At different filtration scales

[zz] All the 14 extracted radiomics features were used to build classification model

[aaa] All the 255 extracted radiomics features were used to build predictive model

[bbb] Novel radiological features

[ccc] Three at arterial phase and four at venous phase

[ddd] The ratio of the area of the largest connected enhanced region and the area of the cyst region

[eee] For the main goal of the study (i.e. classification of mutation status)

[fff] At different filtration scales

[ggg] At different filtration scales

[hhh] At six different spatial filtration scales

[iii] Entropy at medium spatial filtration scale

[jjj] Four features for local control and eight features for overall survival analysis

[kkk] Four features from T2 weighted image and five from diffusion weighted image

[lll] Grey-level non-uniformity at angle of 135°

[mmm] Deep learning features

[mmm] Normalised entropy to standard deviation feature
[ooo] Five from arterial phase and four from portal phase
[ppp] At different filtration scales
[qqq] At medium scaling filter
[rrr] SVM with recursive feature elimination
[sss] SVM with both Gaussian radial basis function and linear kernel function
[ttt] At different spatial band filtration scales
[uuu] For differentiation between healthy pancreas and chronic pancreatitis
[vvv] One feature from positron emission tomography and three from apparent diffusion coefficient map
[www] In subgroup analysis, only surface area was significant predictor for type 2 diabetes mellitus
[xxx] Only for predicting the resection margin status of pancreatic head adenocarcinoma
[yyy] Based on gradient-based edge segmentation method
[zzz] For the main goal of the study

of a relatively small size, located deeply in the retroperitoneal space, and composed of different types of cells (i.e. acinar, ductal, endocrine)—each with different functions [92]. The exocrine part constitutes around 95% of the pancreas with two main types of cells being acinar cells and ductal cells. The endocrine part (i.e. islets of Langerhans) constitutes less than 5% of the pancreas, with five major types of cells being alpha cells, beta cells, delta cells, epsilon cells, and pancreatic polypeptide cells. Besides, the size of the pancreas may change during consumption of food [93–95]. These physical and physiological characteristics of the pancreas make radiomics investigation of the pancreas quite challenging and justify the extraction of large number of radiomics features that could describe the pancreas comprehensively. Further, extracting large number of features likely captures variabilities in genetic, environmental, and behavioural factors that cause diseases of the pancreas, hence enabling characterisation of each patient individually and ultimately resulting in personalised management [1]. In the future, the performance of radiomics models may, in principle, be enhanced by considering certain semantic features (e.g. demographics, blood biomarkers, genomics). However, it is a long way to go as, out of the 45 studies that reported on combined models, only 8 studies (18%) demonstrated a statistically significant superiority of combining radiomics and semantic features.

The other notable finding of the present systematic review was that the RQS had a significant positive correlation with the number of extracted features and the cohort size. However, the RQS in all the included studies altogether was rather low, with a median of 28%. The top three most consistently reported criteria were reporting discrimination statistics, applying well-documented imaging protocol, and studying the clinical utility of the extracted biomarker. By contrast, the three least frequently reported criteria were prospective study design, applying the delta radiomics (i.e. extracting features at different imaging time points), and comparing the results with gold standard. Worryingly, none of the included studies were prospective. Therefore, future radiomics studies of the pancreas should be conducted in a prospective fashion. The second least frequently observed criterion was the use of delta radiomics, where multiple images were obtained at different time points in order to test the reproducibility and stability of extracted radiomics features over a specific period of time. Out of the 72 included studies, only three studies met this criterion. Therefore, future studies on radiomics of the pancreas should extract and test radiomics features at multiple time points. The third common omission was the lack of comparison of radiomics findings with gold

Table 3 Radiomics features in the studies focused on differential diagnosis of diseases of the pancreas

Colour key		
Investigated features	At least one significant feature reported	Green
	No significant feature reported	Red
Non-investigated features		Grey

Diseases of the pancreas		Study ID	Customised features	Second-order texture features	Shape features	First-order texture features	Filtered image features
Chronic pancreatitis from	Healthy pancreas	Frøkjær et al. (78)	Grey	Green	Red	Green	Green
	Pancreatic cancer	Zhu et al. (21)	Grey	Green	Grey	Green	Green
SCN from	Non-SCN	Wei et al. (69)	Grey	Green	Grey	Green	Green
	MCN	Yang et al. (70)	Grey	Green	Red	Red	Grey
		Xie et al. (88)	Grey	Green	Grey	Red	Grey
PDAC from	PL	Huang et al. (52)	Grey	Green	Grey	Red	Red
	AIP	Zhang et al. (72)	Grey	Green	Grey	Red	Red
		Zhang et al. (73)	Grey	Green	Green	Green	Grey
	MFP	Ren et al. (64)	Grey	Green	Green	Green	Grey
	Healthy pancreas	Chu et al. (45)	Grey	Green	Green	Green	Green
		Zhang et al. (19)	Grey	Green	Grey	Red	Red
	PNET	He et al. (51)	Grey	Green	Green	Green	Red
		Wang et al. (67)	Grey	Green	Grey	Grey	Grey
		Yu et al. (71)	Grey	Green	Grey	Grey	Grey
		Reinert et al. (86)	Grey	Green	Grey	Green	Grey
		Guo et al. (35)	Grey	Grey	Grey	Green	Red
		Li et al. (36)	Grey	Grey	Grey	Green	Grey
PNET from	IPAS	Lin et al. (37)	Grey	Grey	Grey	Grey	Green
	SPN	Li et al. (58)	Grey	Green	Grey	Green	Red

standard. For example, results of many studies on the use of radiomics of the pancreas to determine prognosis of patients with pancreatic cancer were not compared with the well-established gold standards (tumour node

Table 4 Radiomics features in the studies focused on classification of diseases of the pancreas

Colour key		
Investigated features	At least one significant feature reported	Green
	No significant feature reported	Red
Non-investigated features		Grey

Subtypes	Pancreatic cyst	Dmitriev et al. (29)	Grey	Grey	Green	Green	Grey
		Shen et al. (87)	Grey	Red	Green	Grey	Green
	Pancreatitis	Mashayekhi et al. (85)	Grey	Green	Red	Red	Grey
	PDAC	Kaissis et al. (53)	Grey	Green	Red	Red	Green
		Kaissis et al. (81)	Grey	Green	Red	Red	Green
		Kaissis et al. (54)	Grey	Green	Green	Green	Green
Mutation status	PDAC	Attiyeh et al. (40)	Grey	Green	Green	Grey	Grey
		Lim et al. (84)	Grey	Green	Green	Red	Grey
Histologic grades	PDAC	Chang et al. (76)	Grey	Green	Green	Red	Grey
		Qiu et al. (63)	Grey	Green	Green	Grey	Grey
		Guo et al. (50)	Grey	Green	Green	Grey	Grey
		Gu et al. (48)	Grey	Green	Green	Green	Green
		Permuth et al. (24)	Grey	Green	Green	Green	Grey
		Choi et al. (33)	Grey	Grey	Green	Green	Grey
	PNET	D'Onofrio et al. (47)	Grey	Grey	Green	Grey	Grey
		Zhao et al. (90)	Grey	Green	Green	Grey	Green
		Guo et al. (49)	Grey	Grey	Grey	Grey	Green
		Liang et al. (59)	Grey	Green	Red	Grey	Green
		Hanania et al. (23)	Grey	Green	Red	Red	Grey
		Canellas et al. (26)	Grey	Red	Red	Grey	Green
		Attiyeh et al. (39)	Green	Red	Red	Grey	Grey
Gene expression	PCN	Wei et al. (68)	Green	Green	Grey	Green	Grey
	PDAC	Li et al. (57)	Green	Grey	Grey	Grey	Green

Table 5 Radiomics features in the studies focused on prediction of diseases of the pancreas

Colour key		
Investigated features	At least one significant feature reported	Green
	No significant feature reported	Red
Non-investigated features		Grey

Diseases of the pancreas			Study ID	Customised features	Filtered image features	Second-order texture features	First-order texture features	Shape features
Resection margin		PDAC	Kulkarni et al. (82)	Grey	Grey	Green	Green	Grey
Recurrence		Acute pancreatitis	Chen et al. (42)	Grey	Grey	Green	Green	Green
Prognosis	Resectable and unresectable	Pancreatic cancer	Tang et al. (66)	Grey	Grey	Green	Green	Green
			Cozzi et al. (46)	Grey	Grey	Green	Green	Green
			Attiyeh et al. (31)	Grey	Grey	Green	Green	Grey
			Xu et al. (20)	Grey	Grey	Green	Green	Grey
			Xie et al. (89)	Grey	Green	Green	Green	Grey
			Yun et al. (38)	Grey	Green	Green	Green	Grey
			Eilaghi et al. (30)	Grey	Grey	Green	Grey	Grey
			Kim et al. (56)	Grey	Grey	Green	Grey	Grey
			Cassinotto et al. (27)	Grey	Green	Grey	Grey	Grey
			Choi et al. (44)	Grey	Green	Grey	Red	Grey
			Khalvati et al. (55)	Grey	Green	Green	Red	Red
			Zhou et al. (74)	Grey	Green	Green	Red	Red
			Sandrasegaran et al. (65)	Grey	Green	Grey	Red	Grey
			Cheng et al. (43)	Grey	Green	Grey	Red	Grey
			Cui et al. (22)	Grey	Green	Red	Red	Green
Severity		Acute pancreatitis	Lin et al. (60)	Grey	Grey	Green	Red	Green
Metastasis		PDAC	Fang et al. (77)	Grey	Green	Green	Red	Grey
			Gao et al. (79)	Grey	Grey	Green	Red	Grey
			Li et al. (83)	Grey	Green	Red	Green	Red
Incidence		Diabetes mellitus	Lu et al. (61)	Grey	Green	Red	Green	Grey
			Jang et al. (80)	Grey	Grey	Green	Green	Green
Risk		PDAC	Bian et al. (41)	Grey	Green	Red	Red	Red
		IPMN	Chakraborty et al. (32)	Green	Grey	Green	Grey	Grey
Treatment response		Pancreatic cancer	Nasief et al. (62)	Green	Grey	Green	Green	Grey
			Borhani et al. (75)	Grey	Green	Grey	Green	Grey
			Chen et al. (28)	Grey	Grey	Grey	Green	Grey
			Ciaravino et al. (34)	Grey	Grey	Grey	Green	Grey
			Yue et al. (25)	Grey	Grey	Green	Grey	Grey

metastasis (TNM) staging system and MD-Anderson pre-treatment classification) [96]. It is also worth noting that, while histology is the gold standard for diagnosing focal pancreatic lesions, only 15 included studies used it (although it may not be ethical to use it in patients with benign lesions). Further, all the 6 radiomics studies on pancreatic benign lesions (such as serous cystadenoma) used CT only, which is considered suboptimal as accurate diagnosing of these benign lesions is quite challenging without the use of MRI (especially if lesions are of small size). Careful selection of gold standard in future studies on radiomics of the pancreas is encouraged.

There are several limitations that need to be acknowledged when interpreting the findings of the present review. First, there was a heterogeneity between the included studies in terms of image acquisition protocols. For example, different phases of CT and MRI sequences were employed in the primary studies. This brings to the fore the need to standardise image acquisition protocols in future radiomics studies of the pancreas. Second, the included studies used a range of software packages that not infrequently offer different algorithms for defining the same radiomics features. This highlights the need to standardise the definitions of imaging features. The Image Biomarker Standardisation Initiative aspires to standardise the extraction of imaging biomarkers from acquired imaging for the purpose of high-throughput quantitative image analysis [97]. This initiative needs to be taken into account in radiomics of the pancreas research. Third, the included studies disproportionately focused on focal pancreatic lesions. Only six studies investigated benign diseases that are characterised by diffuse changes of the pancreas (i.e. pancreatitis and diabetes mellitus) and high-quality radiomics studies in these diseases are now warranted [98]. Fourth, we designed the present systematic review to include only studies that applied handcrafted radiomics as the main method for extracting quantitative imaging features from radiological images. However, it is also possible to use machine learning to extract some features. For example, one study extracted 256 deep

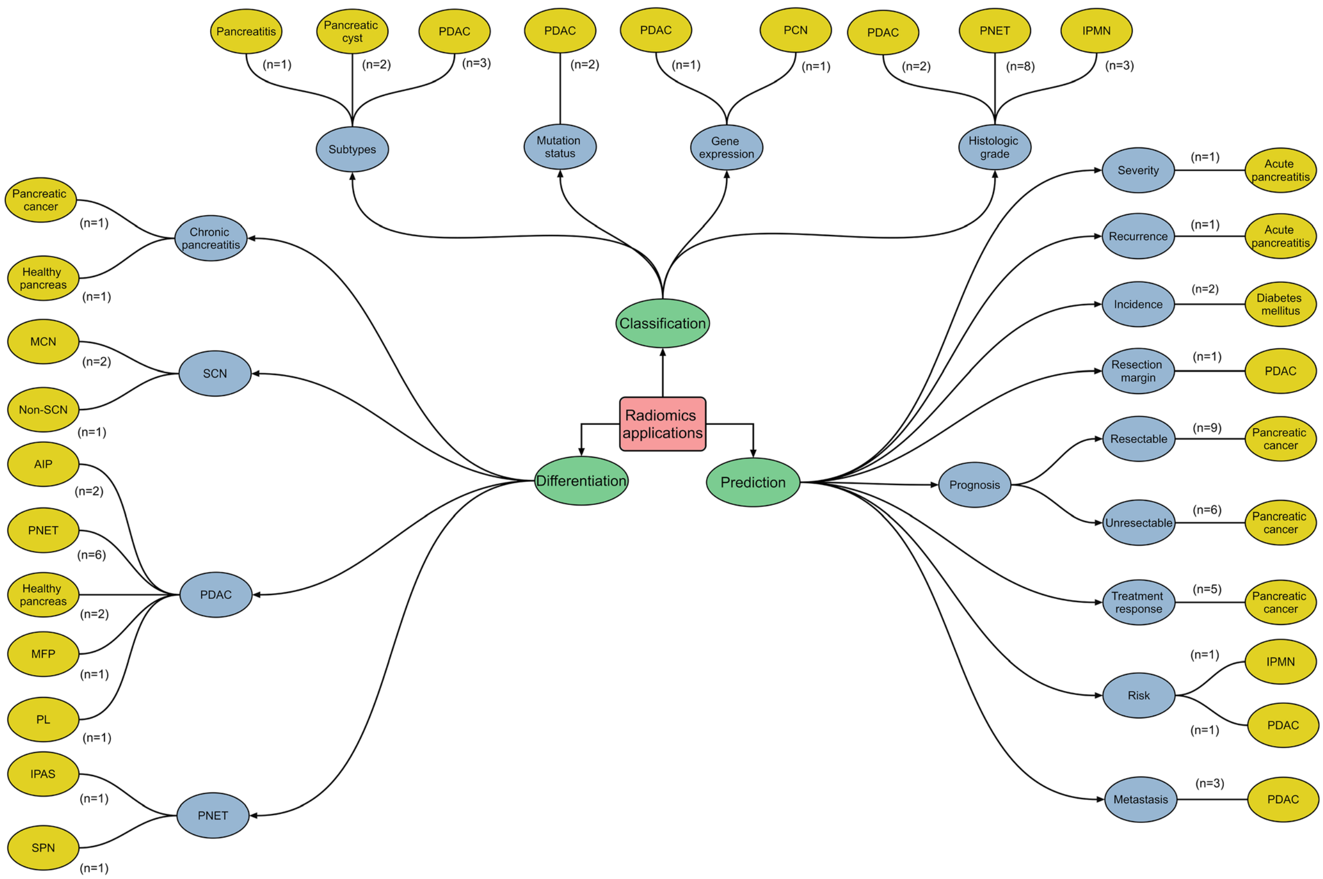

Fig. 3 Applications of radiomics of the pancreas. Only primary goals of individual studies are depicted. The complete list of goals of the individual studies is presented in Table 1. *Abbreviations*: *AIP*, autoimmune pancreatitis; *IPAS*, intrapancreatic accessory spleen; *IPMN*, intraductal papillary mucinous neoplasm; *MCN*, mucinous cystic neoplasm; *MFP*, mass forming pancreatitis; *PCN*, pancreatic cystic neoplasm; *PDAC*, pancreatic ductal adenocarcinoma; *PL*, pancreatic lymphoma; *PNET*, pancreatic neuroendocrine tumour; *SCN*, serous cystic neoplasm; *SPN*, solid pseudopapillary neoplasm

learning features from the first three layers of convolutional neural network model, in addition to the radiomics features [57]. Last, building predictive model is one of the promising applications of radiomics in diseases of the pancreas. Thirty studies applied radiomics for building predictive models; however, none of them appeared to follow the TRIPOD (Transparent Reporting of multivariable prediction model for Individual Prognosis or Diagnosis) guidelines [99].

In conclusion, the present systematic review demonstrated that radiomics of the pancreas emerges as a promising tool that could be used for personalised management of patients with diseases of the pancreas. To maximise the benefits of radiomics of the pancreas, future studies are best to have a large sample size (more than 100 participants), use standardised software packages that offer a large number of radiomics features (especially second-order texture features and filtered image features), investigate radiomics in prospective fashion, compare radiomics results with an appropriate gold standard, and apply delta radiomics.

Acknowledgements This study was part of the COSMOS program.

Funding COSMOS is supported, in part, by the Royal Society of New Zealand (Rutherford Discovery Fellowship to Associate Professor Max Petrov).

Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Associate Professor Max Petrov, MD, MPH, PhD.

Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Institutional Review Board approval was not required because the study was a secondary analysis of the literature.

Ethical approval Written informed consent was not required for this study because it was a secondary analysis of the literature.

Methodology
• retrospective
• diagnostic or prognostic study
• performed at one institution

References

1. Xiao AY, Tan MLY, Wu LM et al (2016) Global incidence and mortality of pancreatic diseases: a systematic review, meta-analysis, and meta-regression of population-based cohort studies. Lancet Gastroenterol Hepatol 1:45–55
2. Sankaran SJ, Xiao AY, Wu LM, Windsor JA, Forsmark CE, Petrov MS (2015) Frequency of progression from acute to chronic pancreatitis and risk factors: a meta-analysis. Gastroenterology 149:1490–1500
3. Becker AE, Hernandez YG, Frucht H, Lucas AL (2014) Pancreatic ductal adenocarcinoma: risk factors, screening, and early detection. World J Gastroenterol 20:11182–11198
4. Hruban RH, Takaori K, Klimstra DS et al (2004) An illustrated consensus on the classification of pancreatic intraepithelial neoplasia and intraductal papillary mucinous neoplasms. Am J Surg Pathol 28:977–987
5. Petrov MS (2017) Diabetes of the exocrine pancreas: American Diabetes Association-compliant lexicon. Pancreatology 17:523–526
6. Kumar H, DeSouza SV, Petrov MS (2019) Automated pancreas segmentation from computed tomography and magnetic resonance images: a systematic review. Comput Methods Programs Biomed 178:319–328
7. DeSouza SV, Priya S, Cho J, Singh RG, Petrov MS (2019) Pancreas shrinkage following recurrent acute pancreatitis: an MRI study. Eur Radiol 29:3746–3756
8. Gillies RJ, Kinahan PE, Hricak H (2016) Radiomics: images are more than pictures, they are data. Radiology 278:563–577
9. Petrov MS (2018) Harnessing analytic morphomics for early detection of pancreatic cancer. Pancreas 47:1051–1054
10. Kumar V, Gu Y, Basu S et al (2012) Radiomics: the process and the challenges. Magn Reson Imaging 30:1234–1248
11. Thawani R, McLane M, Beig N et al (2018) Radiomics and radiogenomics in lung cancer: a review for the clinician. Lung Cancer 115:34–41
12. Fan Y, Feng M, Wang R (2019) Application of radiomics in central nervous system diseases: a systematic literature review. Clin Neurol Neurosurg 187:105565
13. Wakabayashi T, Ouhmich F, Gonzalez-Cabrera C et al (2019) Radiomics in hepatocellular carcinoma: a quantitative review. Hepatol Int 13:546–559
14. Sun Y, Reynolds HM, Parameswaran B et al (2019) Multiparametric MRI and radiomics in prostate cancer: a review. Australas Phys Eng Sci Med 42:3–25
15. Valdora F, Houssami N, Rossi F, Calabrese M, Tagliafico AS (2018) Rapid review: radiomics and breast cancer. Breast Cancer Res Treat 169:217–229
16. Chen J, Remulla D, Nguyen JH et al (2019) Current status of artificial intelligence applications in urology and their potential to influence clinical practice. BJU Int 124:567–577
17. Horvat N, Bates DD, Petkovska I (2019) Novel imaging techniques of rectal cancer: what do radiomics and radiogenomics have to offer? A literature review. Abdom Radiol (NY) 44:3764–3774
18. Lambin P, Leijenaar RT, Deist TM et al (2017) Radiomics: the bridge between medical imaging and personalized medicine. Nat Rev Clin Oncol 14:749–762
19. Zhang M-M, Yang H, Jin Z-D, Yu J-G, Cai Z-Y, Li Z-S (2010) Differential diagnosis of pancreatic cancer from normal tissue with digital imaging processing and pattern recognition based on a support vector machine of EUS images. Gastrointest Endosc 72:978–985
20. Xu W, Liu Y, Lu Z et al (2013) A new endoscopic ultrasonography image processing method to evaluate the prognosis for pancreatic cancer treated with interstitial brachytherapy. World J Gastroenterol 19:6479–6484
21. Zhu M, Xu C, Yu J et al (2013) Differentiation of pancreatic cancer and chronic pancreatitis using computer-aided diagnosis of endoscopic ultrasound (EUS) images: a diagnostic test. PLoS One 8: e63820
22. Cui Y, Song J, Pollom E et al (2016) Quantitative analysis of (18)F-fluorodeoxyglucose positron emission tomography identifies novel prognostic imaging biomarkers in locally advanced pancreatic cancer patients treated with stereotactic body radiation therapy. Int J Radiat Oncol Biol Phys 96:102–109
23. Hanania AN, Bantis LE, Feng Z et al (2016) Quantitative imaging to evaluate malignant potential of IPMNs. Oncotarget 7:85776–85784
24. Permuth JB, Choi J, Balarunathan Y et al (2016) Combining radiomic features with a miRNA classifier may improve prediction of malignant pathology for pancreatic intraductal papillary mucinous neoplasms. Oncotarget 7:85785–85797
25. Yue Y, Osipov A, Fraass B et al (2016) Identifying prognostic intratumor heterogeneity using pre- and post-radiotherapy 18F-FDG PET images for pancreatic cancer patients. J Gastrointest Oncol 8:127–138
26. Canellas R, Burk KS, Parakh A, Sahani DV (2017) Prediction of pancreatic neuroendocrine tumor grade based on CT features and texture analysis. AJR Am J Roentgenol 210:341–346
27. Cassinotto C, Chong J, Zogopoulos G et al (2017) Resectable pancreatic adenocarcinoma: role of CT quantitative imaging biomarkers for predicting pathology and patient outcomes. Eur J Radiol 90:152–158
28. Chen X, Oshima K, Schott D et al (2017) Assessment of treatment response during chemoradiation therapy for pancreatic cancer based on quantitative radiomic analysis of daily CTs: an exploratory study. PLoS One 12:e0178961
29. Dmitriev K, Kaufman AE, Javed AA et al (2017) Classification of pancreatic cysts in computed tomography images using a random forest and convolutional neural network ensemble. Med Image Comput Comput Assist Interv 10435:150–158
30. Eilaghi A, Baig S, Zhang Y et al (2017) CT texture features are associated with overall survival in pancreatic ductal adenocarcinoma – a quantitative analysis. BMC Med Imaging 17:38
31. Attiyeh MA, Chakraborty J, Doussot A et al (2018) Survival prediction in pancreatic ductal adenocarcinoma by quantitative computed tomography image analysis. Ann Surg Oncol 25:1034–1042
32. Chakraborty J, Midya A, Gazit L et al (2018) CT radiomics to predict high-risk intraductal papillary mucinous neoplasms of the pancreas. Med Phys 45:5019–5029
33. Choi TW, Kim JH, Yu MH, Park SJ, Han JK (2018) Pancreatic neuroendocrine tumor: prediction of the tumor grade using CT findings and computerized texture analysis. Acta Radiol 59:383–392
34. Ciaravino V, Cardobi N, de Robertis R et al (2018) CT texture analysis of ductal adenocarcinoma downstaged after chemotherapy. Anticancer Res 38:4889–4895
35. Guo C, Zhuge X, Wang Q et al (2018) The differentiation of pancreatic neuroendocrine carcinoma from pancreatic ductal adenocarcinoma: the values of CT imaging features and texture analysis. Cancer Imaging 18:37
36. Li J, Lu J, Liang P et al (2018) Differentiation of atypical pancreatic neuroendocrine tumors from pancreatic ductal adenocarcinomas: using whole-tumor CT texture analysis as quantitative biomarkers. Cancer Med 7:4924–4931

37. Lin X, Xu L, Wu A, Guo C, Chen X, Wang Z (2018) Differentiation of intrapancreatic accessory spleen from small hypervascular neuroendocrine tumor of the pancreas: textural analysis on contrast-enhanced computed tomography. Acta Radiol 60: 553–560
38. Yun G, Kim YH, Lee YJ, Kim B, Hwang J-H, Choi DJ (2018) Tumor heterogeneity of pancreas head cancer assessed by CT texture analysis: association with survival outcomes after curative resection. Sci Rep 8:7226
39. Attiyeh MA, Chakraborty J, Gazit L et al (2019) Preoperative risk prediction for intraductal papillary mucinous neoplasms by quantitative CT image analysis. HPB (Oxford) 21:212–218
40. Attiyeh MA, Chakraborty J, McIntyre CA et al (2019) CT radiomics associations with genotype and stromal content in pancreatic ductal adenocarcinoma. Abdom Radiol (NY) 44:3148–3157
41. Bian Y, Guo S, Jiang H et al (2019) Relationship between radiomics and risk of lymph node metastasis in pancreatic ductal adenocarcinoma. Pancreas 48:1195–1203
42. Chen Y, T-w C, Wu C-q et al (2019) Radiomics model of contrast-enhanced computed tomography for predicting the recurrence of acute pancreatitis. Eur Radiol 29:4408–4417
43. Cheng S-H, Cheng Y-J, Jin Z-Y, Xue H-D (2019) Unresectable pancreatic ductal adenocarcinoma: role of CT quantitative imaging biomarkers for predicting outcomes of patients treated with chemotherapy. Eur J Radiol 113:188–197
44. Choi MH, Lee YJ, Yoon SB, Choi J-I, Jung SE, Rha SE (2019) MRI of pancreatic ductal adenocarcinoma: texture analysis of T2-weighted images for predicting long-term outcome. Abdom Radiol (NY) 44:122–130
45. Chu LC, Park S, Kawamoto S et al (2019) Utility of CT radiomics features in differentiation of pancreatic ductal adenocarcinoma from normal pancreatic tissue. AJR Am J Roentgenol 213:349–357
46. Cozzi L, Comito T, Fogliata A et al (2019) Computed tomography based radiomic signature as predictive of survival and local control after stereotactic body radiation therapy in pancreatic carcinoma. PLoS One 14:e0210758
47. D'Onofrio M, Ciaravino V, Cardobi N et al (2019) CT enhancement and 3D texture analysis of pancreatic neuroendocrine neoplasms. Sci Rep 9:2176
48. Gu D, Hu Y, Ding H et al (2019) CT radiomics may predict the grade of pancreatic neuroendocrine tumors: a multicenter study. Eur Radiol 29:6880–6890
49. Guo C, Zhuge X, Wang Z et al (2019) Textural analysis on contrast-enhanced CT in pancreatic neuroendocrine neoplasms: association with WHO grade. Abdom Radiol (NY) 44:576–585
50. Guo C-g, Ren S, Chen X et al (2019) Pancreatic neuroendocrine tumor: prediction of the tumor grade using magnetic resonance imaging findings and texture analysis with 3-T magnetic resonance. Cancer Manag Res 11:1933–1944
51. He M, Liu Z, Lin Y et al (2019) Differentiation of atypical non-functional pancreatic neuroendocrine tumor and pancreatic ductal adenocarcinoma using CT based radiomics. Eur J Radiol 117:102–111
52. Huang Z, Li M, He D et al (2019) Two-dimensional texture analysis based on CT images to differentiate pancreatic lymphoma and pancreatic adenocarcinoma: a preliminary study. Acad Radiol 26: e189–e195
53. Kaissis G, Ziegelmayer S, Lohöfer F et al (2019) A machine learning model for the prediction of survival and tumor subtype in pancreatic ductal adenocarcinoma from preoperative diffusion-weighted imaging. Eur Radiol Exp 3:41
54. Kaissis G, Ziegelmayer S, Lohöfer F et al (2019) A machine learning algorithm predicts molecular subtypes in pancreatic ductal adenocarcinoma with differential response to gemcitabine-based versus FOLFIRINOX chemotherapy. PLoS One 14:e0218642
55. Khalvati F, Zhang Y, Baig S et al (2019) Prognostic value of CT radiomic features in resectable pancreatic ductal adenocarcinoma. Sci Rep 9:5449
56. Kim HS, Kim YJ, Kim KG, Park JS (2019) Preoperative CT texture features predict prognosis after curative resection in pancreatic cancer. Sci Rep 9:17389
57. Li K, Xiao J, Yang J et al (2019) Association of radiomic imaging features and gene expression profile as prognostic factors in pancreatic ductal adenocarcinoma. Am J Transl Res 11:4491–4499
58. Li X, Zhu H, Qian X, Chen N, Lin X (2020) MRI texture analysis for differentiating nonfunctional pancreatic neuroendocrine neoplasms from solid pseudopapillary neoplasms of the pancreas. Acad Radiol 27:815–823
59. Liang W, Yang P, Huang R et al (2019) A combined nomogram model to preoperatively predict histologic grade in pancreatic neuroendocrine tumors. Clin Cancer Res 25:584–594
60. Lin Q, Y-f JI, Chen Y et al (2019) Radiomics model of contrast-enhanced MRI for early prediction of acute pancreatitis severity. J Magn Reson Imaging 51:397–406
61. Lu C-Q, Wang Y-C, Meng X-P et al (2019) Diabetes risk assessment with imaging: a radiomics study of abdominal CT. Eur Radiol 29:2233–2242
62. Nasief H, Zheng C, Schott D et al (2019) A machine learning based delta-radiomics process for early prediction of treatment response of pancreatic cancer. NPJ Precis Oncol 3:25
63. Qiu W, Duan N, Chen X et al (2019) Pancreatic ductal adenocarcinoma: machine learning–based quantitative computed tomography texture analysis for prediction of histopathological grade. Cancer Manag Res 11:9253–9264
64. Ren S, Zhang J, Chen J et al (2019) Evaluation of texture analysis for the differential diagnosis of mass-forming pancreatitis from pancreatic ductal adenocarcinoma on contrast-enhanced CT images. Front Oncol 9:1171
65. Sandrasegaran K, Lin Y, Asare-Sawiri M, Taiyini T, Tann M (2019) CT texture analysis of pancreatic cancer. Eur Radiol 29: 1067–1073
66. Tang TY, Li X, Zhang Q et al (2020) Development of a novel multiparametric MRI radiomic nomogram for preoperative evaluation of early recurrence in resectable pancreatic cancer. J Magn Reson Imaging 52:231–245
67. Wang YW, Zhang XH, Wang BT et al (2019) Value of texture analysis of intravoxel incoherent motion parameters in differential diagnosis of pancreatic neuroendocrine tumor and pancreatic adenocarcinoma. Chin Med Sci J 34:1–9
68. Wei R, Lin K, Guo Y, Li J, Wang Y (2019) Feasibility analysis of predicting expression of Ki67 in pancreatic cystic neoplasm based on radiomics. J Biomed Eng 36:1–6
69. Wei R, Lin K, Yan W et al (2019) Computer-aided diagnosis of pancreas serous cystic neoplasms: a radiomics method on preoperative MDCT images. Technol Cancer Res Treat 18: 1533033818824339
70. Yang J, Guo X, Ou X, Zhang W, Ma X (2019) Discrimination of pancreatic serous cystadenomas from mucinous cystadenomas with CT textural features: based on machine learning. Front Oncol 9:494
71. Yu H, Huang Z, Li M et al (2019) Differential diagnosis of nonhypervascular pancreatic neuroendocrine neoplasms from pancreatic ductal adenocarcinomas, based on computed tomography radiological features and texture analysis. Acad Radiol 3:332–341
72. Zhang Y, Cheng C, Liu Z et al (2019) Differentiation of autoimmune pancreatitis and pancreatic ductal adenocarcinoma based on multi-modality texture features in 18F-FDG PET/CT. Sheng Wu Yi Xue Gong Cheng Xue Za Zhi 36:755–762
73. Zhang Y, Cheng C, Liu Z et al (2019) Radiomics analysis for the differentiation of autoimmune pancreatitis and pancreatic ductal adenocarcinoma in 18F-FDG PET/CT. Med Phys 46:4520–4530

74. Zhou HF, Han YQ, Lu J et al (2019) Radiomics facilitates candidate selection for irradiation stents among patients with unresectable pancreatic cancer. Front Oncol 9:973
75. Borhani AA, Dewan R, Furlan A et al (2020) Assessment of response to neoadjuvant therapy using CT texture analysis in patients with resectable and borderline resectable pancreatic ductal adenocarcinoma. AJR Am J Roentgenol 214:362–369
76. Chang N, Cui L, Luo Y, Chang Z, Yu B, Liu Z (2020) Development and multicenter validation of a CT-based radiomics signature for discriminating histological grades of pancreatic ductal adenocarcinoma. Quant Imaging Med Surg 10:692–702
77. Fang WH, Li XD, Zhu H et al (2020) Resectable pancreatic ductal adenocarcinoma: association between preoperative CT texture features and metastatic nodal involvement. Cancer Imaging 20:17
78. Frøkjær JB, Lisitskaya MV, Jørgensen AS et al (2020) Pancreatic magnetic resonance imaging texture analysis in chronic pancreatitis: a feasibility and validation study. Abdom Radiol (NY) 5:1497–1506
79. Gao J, Huang X, Meng H et al (2020) Performance of multiparametric functional imaging and texture analysis in predicting synchronous metastatic disease in pancreatic ductal adenocarcinoma patients by hybrid PET/MR: initial experience. Front Oncol 10:198
80. Jang S, Kim JH, Choi S-Y, Park SJ, Han JK (2020) Application of computerized 3D-CT texture analysis of pancreas for the assessment of patients with diabetes. PLoS One 15:e0227492
81. Kaissis GA, Ziegelmayer S, Lohöfer FK et al (2020) Image-based molecular phenotyping of pancreatic ductal adenocarcinoma. J Clin Med 9:724
82. Kulkarni A, Carrion-Martinez I, Jiang NN et al (2020) Hypovascular pancreas head adenocarcinoma: CT texture analysis for assessment of resection margin status and high-risk features. Eur Radiol 30:2853–2860
83. Li K, Yao Q, Xiao J et al (2020) Contrast-enhanced CT radiomics for predicting lymph node metastasis in pancreatic ductal adenocarcinoma: a pilot study. Cancer Imaging 20:12
84. Lim CH, Cho YS, Choi JY et al (2020) Imaging phenotype using 18 F-fluorodeoxyglucose positron emission tomography–based radiomics and genetic alterations of pancreatic ductal adenocarcinoma. Eur J Nucl Med Mol Imaging 47:2113–2122
85. Mashayekhi R, Parekh VS, Faghih M, Singh VK, Jacobs MA, Zaheer A (2020) Radiomic features of the pancreas on CT imaging accurately differentiate functional abdominal pain, recurrent acute pancreatitis, and chronic pancreatitis. Eur J Radiol 123:108778
86. Reinert CP, Baumgartner K, Hepp T, Bitzer M, Horger M (2020) Complementary role of computed tomography texture analysis for differentiation of pancreatic ductal adenocarcinoma from pancreatic neuroendocrine tumors in the portal-venous enhancement phase. Abdom Radiol (NY) 45:750–758
87. Shen X, Yang F, Yang P et al (2020) A contrast-enhanced computed tomography based radiomics approach for preoperative differentiation of pancreatic cystic neoplasm subtypes: a feasibility study. Front Oncol 10:248
88. Xie T, Wang X, Li M, Tong T, Yu X, Zhou Z (2020) Pancreatic ductal adenocarcinoma: a radiomics nomogram outperforms clinical model and TNM staging for survival estimation after curative resection. Eur Radiol 30:2513–2524
89. Xie T, Wang X, Li M, Tong T, Yu X, Zhou Z (2020) Pancreatic ductal adenocarcinoma: a radiomics nomogram outperforms clinical model and TNM staging for survival estimation after curative resection. Eur Radiol 30:2513–2524
90. Zhao Z, Bian Y, Jiang H et al (2020) CT-radiomic approach to predict G1/2 nonfunctional pancreatic neuroendocrine tumor. Acad Radiol. https://doi.org/10.1016/j.acra.2020.01.002
91. Larue RT, Defraene G, De Ruysscher D, Lambin P, Van Elmpt W (2017) Quantitative radiomics studies for tissue characterization: a review of technology and methodological procedures. Br J Radiol 90:20160665
92. Das SL, Kennedy JI, Murphy R, Phillips AR, Windsor JA, Petrov MS (2014) Relationship between the exocrine and endocrine pancreas after acute pancreatitis. World J Gastroenterol 45:17196–17205
93. Pendharkar SA, Asrani VM, Xiao AY et al (2016) Relationship between pancreatic hormones and glucose metabolism: a cross-sectional study in patients after acute pancreatitis. Am J Physiol Gastrointest Liver Physiol 311:G50–58
94. Desouza SV, Yoon HD, Singh RG, Petrov MS (2018) Quantitative determination of pancreas size using anatomical landmarks and its clinical relevance: a systematic literature review. Clin Anat 31:913–926
95. DeSouza SV, Singh RG, Yoon HD, Murphy R, Plank LD, Petrov MS (2018) Pancreas volume in health and disease: a systematic review and meta-analysis. Expert Rev Gastroenterol Hepatol 12:757–766
96. Edge SB, Compton CC (2010) The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol 17:1471–1474
97. Zwanenburg A, Vallières M, Abdalah MA et al (2020) The image biomarker standardization initiative: standardized quantitative radiomics for high-throughput image-based phenotyping. Radiology 295:328–338
98. Pendharkar SA, Mathew J, Petrov MS (2017) Age- and sex-specific prevalence of diabetes associated with diseases of the exocrine pancreas: a population-based study. Dig Liver Dis 49:540–544
99. Collins GS, Reitsma JB, Altman DG, Moons KGM (2015) Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD): the TRIPOD statement. Ann Intern Med 162:55–63