

Cardiac Radiomics Analyses in Times of Photon-counting Computed Tomography for Personalized Risk Stratification in the Present and in the Future

Kardiale Radiomics Analysen in Zeiten von Photon-Counting Computertomographen zur personalisierten Risikostratifizierung in der Gegenwart und in der Zukunft

Authors

Isabelle Ayx, Rouven Bauer, Stefan O Schönberg, Alexander Hertel

Affiliations

Department of Radiology and Nuclear Medicine, Heidelberg University Medical Faculty Mannheim, Mannheim, Germany

Keywords

cardiac, cardiac risk stratification, myocardial texture analysis, radiomics, photon counting computed tomography

received 19.8.2024

accepted after revision 4.12.2024

Bibliography

Rofo

DOI 10.1055/a-2499-3122

ISSN 1438-9029


© 2025. Thieme. All rights reserved.

Georg Thieme Verlag KG, Oswald-Hesse-Straße 50, 70469 Stuttgart, Germany

Correspondence

Dr. Alexander Hertel

Department of Radiology and Nuclear Medicine, Heidelberg University Medical Faculty Mannheim, Theodor-Kutzer-Ufer 1–3, 68167 Mannheim, Germany
alexander.hertel@umm.de

 Deutsche Version unter: <https://doi.org/10.1055/a-2499-3122>.

ABSTRACT

Background The need for effective early detection and optimal therapy monitoring of cardiovascular diseases as the leading cause of death has led to an adaptation of the guidelines with a focus on cardiac computed tomography (CCTA) in patients with a low to intermediate risk of coronary heart disease (CHD). In particular, the introduction of photon-counting computed tomography (PCCT) in CT diagnostics promises significant advances through higher temporal and spatial resolution, and also enables advanced texture analysis, known as radiomics analysis. Originally developed in oncological imaging, radiomics analysis is increasingly being used in

cardiac imaging and research. The aim is to generate imaging biomarkers that improve the early detection of cardiovascular diseases and therapy monitoring.

Method The present study summarizes the current developments in cardiac CT texture analysis with a particular focus on evaluations of PCCT data sets in different regions, including the myocardium, coronary plaques, and pericoronary/epicardial fat tissue.

Conclusion These developments could revolutionize the diagnosis and treatment of cardiovascular diseases and significantly improve patient prognoses worldwide. The aim of this review article is to shed light on the current state of radiomics research in cardiovascular imaging and to identify opportunities for establishing it in clinical routine in the future.

Key Points

- Radiomics: Enables deeper, objective analysis of cardiovascular structures via feature quantification.
- PCCT: Provides a higher quality image, improving stability and reproducibility in cardiac CT.
- Early detection: PCCT and radiomics enhance cardiovascular disease detection and management.
- Challenges: Technical and standardization issues hinder widespread clinical application.
- Future: Advancing PCCT technologies could soon integrate radiomics in routine practice.

Citation Format

- Ayx I, Bauer R, Schönberg SO et al. Cardiac Radiomics Analyses in Times of Photon-counting Computed Tomography for Personalized Risk Stratification in the Present and in the Future. Rofo 2025; DOI 10.1055/a-2499-3122

ZUSAMMENFASSUNG

Hintergrund Die Notwendigkeit einer effektiven Früherkennung und eines optimalen Therapiemonitorings kardiovaskulärer Erkrankungen als häufigste Todesursache hat zu einer Anpassung der Leitlinien mit Fokussierung auf die kardiale Computertomografie (CCTA) bei Patienten mit einem niedrigen bis intermediären Risiko für eine koronare Herzkrankheit (KHK) geführt. Insbesondere die Einführung von Photon-

Counting-Computertomografen (PCCT) in der CT-Diagnostik verspricht erhebliche Fortschritte durch eine höhere zeitliche und räumliche Auflösung und ermöglicht auch fortgeschrittene Texturanalysen, bekannt als Radiomics-Analysen. Ursprünglich in der onkologischen Bildgebung entwickelt, finden Radiomics-Analysen zunehmend Anwendung in der kardialen Bildgebung und Forschung. Ziel ist es, sog. Imaging-Biomarker zu generieren, die die Früherkennung kardiovaskulärer Erkrankungen und das Therapiemonitoring verbessern.

Methode Die vorliegende Studie fasst die aktuellen Entwicklungen in der kardialen CT-Texturanalyse mit besonderer Fokussierung auf Auswertungen an PCCT-Datensätzen an unterschiedlichen Regionen, u. a. dem Myokard, koronarer Plaques und des perikoronaren/epikardialen Fettgewebes zusammen.

Schlussfolgerung Diese Entwicklungen könnten die Diagnostik und Behandlung von Herz-Kreislauf-Erkrankungen revolu-

tionieren und die Prognosen für Patienten weltweit erheblich verbessern. Ziel dieses Übersichtsartikels ist es, den aktuellen Stand der Radiomics-Forschung in der kardiovaskulären Bildgebung zu beleuchten und Möglichkeiten der Etablierung in der klinischen Routine in Zukunft aufzuzeigen.

Kernaussagen

- Radiomics: Ermöglicht tiefere, objektive Analyse kardiovaskulärer Strukturen durch Merkmalsextraktion.
- PCCT: Bietet höhere Bildqualität, verbessert Stabilität und Reproduzierbarkeit in der kardialen CT.
- Früherkennung: PCCT und Radiomics verbessern Erkennung und Management von Herz-Kreislauf-Erkrankungen.
- Herausforderungen: Technische und Standardisierungsprobleme erschweren die klinische Anwendung.
- Zukunft: Fortschritte bei PCCT-Technologien könnten Radiomics bald in die Routine integrieren.

Introduction

Cardiovascular diseases (CVD) are the leading causes of death worldwide [1], and their prevalence is increasing due, at least in part, to the demographic aging of the population [2]. Mortality has risen slightly again, mainly due to heart attacks and heart failure. Older people are affected, in particular, although regional differences in care are also discernible. However, new approaches in diagnostics and therapy, including state-of-the-art imaging and interventional procedures, are improving the prognoses of many heart patients [3]. This development makes it critical to understand more deeply the mechanisms leading to CVD, as well as measures for early detection and personalized risk stratification.

In this context, the further development of imaging diagnostics, especially through innovative technologies such as radiomics analysis, can open transformative new possibilities [4]. Radiomics refers to the advanced analysis of image features that have been extracted from standard imaging data, and it has the potential to provide deeper insight into subtle changes in cardiovascular structures. By quantifying image patterns that the human eye cannot capture, radiomics not only has the potential to enable more precise diagnosis and characterization of cardiovascular conditions but also to promote development of personalized therapeutic approaches [5].

Radiomics techniques applied in cardiac computed tomography (CCTA) can help analyze underlying discrete texture changes that are important for early detection and management of CVD [6]. Integration of radiomics in routine imaging could significantly improve early detection of heart disease and optimize the management of patients who are at increased risk for cardiovascular events. However, radiomics has not yet been integrated in clinical practice, as radiomics analyses suffer significantly from a lack of comparability and reproducibility [6].

The development of the photon-counting computed tomography (PCCT), which is known for its outstanding image quality

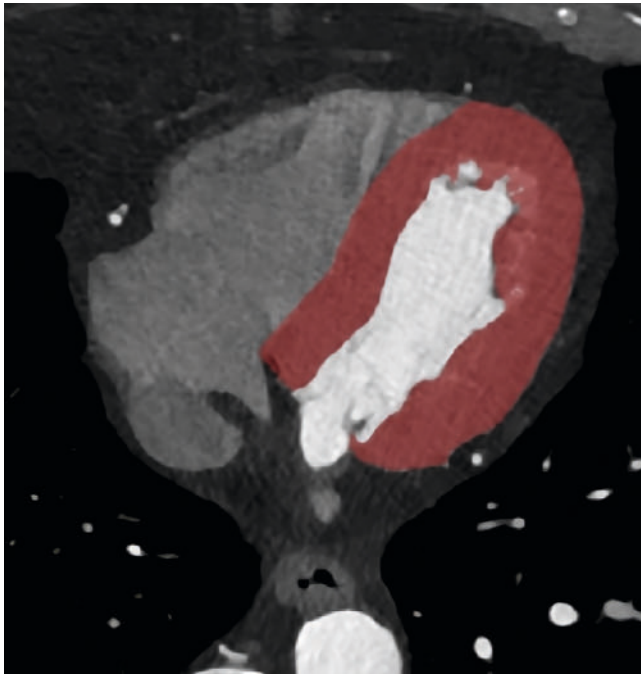
with high spatial and temporal resolution, improved signal-to-noise ratio, and reduced hardening artifacts, marks the start of a new era of radiomics imaging. Phantom studies have shown a high stability of radiomics parameters in test-retest settings in the past [7]. To ensure its integration in clinical routine, radiomics analyses have to demonstrate a stable and reliable reproducibility.

In addition, the number of cardiac CT examinations in Germany is expected to increase in the coming years. The updated ESC guidelines highlighted already in 2019 the benefits of CCTA in patients with intermediate risk for coronary heart disease [8]. The DISCHARGE study also highlighted the benefits of CCTA compared to invasive cardiac catheterization (ICA), as CCTA is associated with a lower periprocedural complication rate compared to ICA, without increasing the risk of developing over time a major adverse cardiovascular event (MACE) [9]. According to the latest Federal Joint Committee (GBA) resolution, this will now also be taken into account in Germany. As a result, CCTA is being introduced on 01/01/2025 as a health insurance benefit [10].

This review aims to highlight the role of radiomics analysis in cardiovascular imaging as well as its potential contributions to improving diagnostic accuracy and therapeutic strategies, particularly in light of PCCT's increasing availability worldwide. A deeper understanding of these advanced imaging techniques and their areas of application can provide a comprehensive overview of their importance in modern cardiovascular medicine and at the same time open new perspectives for future research.

Radiomics

Radiomics is an advanced method of image analysis that extracts highly detailed quantitative data from radiology images. This technique makes it possible, in the age of big data, to capture features that go far beyond what the human eye can detect, including texture, shape, intensity, and spatial patterns in the image [4]. In the context of cardiac imaging, radiomics focuses,



► **Fig. 1** Segmentation example of the left ventricular myocardium.

in particular, on the myocardium, plaques, and perivascular adipose tissue to detect subtle clues that can provide insight into medical conditions, their evolution and, in the future, potentially the response to treatments.

Radiomics functionality

The process of radiomics analysis involves several steps, starting with the precise acquisition of images under standardized conditions to ensure the comparability and reproducibility of the data. After image acquisition, a careful segmentation is performed in which the regions or volumes of interest (ROIs or VOIs – ► **Fig. 1**) are segmented [4].

This is particularly important in the cardiac field, where specific structures such as the myocardium, coronary plaques, or pericoronary adipose tissue have to be isolated precisely. The segmentation of the region to be examined can in principle be performed manually, semi-automatically, or automatically, whereby the focus has to be strictly on the region of interest while omitting the neighboring structures. In any case, the authors recommend that an experienced radiologist checks the segmentation.

Hundreds to thousands of radiomics features are then extracted from the areas specified. These features include first-order statistical information, shape-based features, texture-based features, and higher-dimensional features generated by advanced mathematical models. ► **Fig. 2** shows an overview of the different feature groups. The extracted data is further processed using various analytical and machine learning processes in order to provide diagnostic, prognostic, or predictive information. It is still possible to correlate the information obtained with clinical parameters in order to derive potential results [6, 11, 12, 13, 14]. ► **Fig. 3** shows the classic workflow of a radiomics analysis using the example of cardiac imaging on a PCCT.

Benefits of radiomics analyses

In the age of big data, radiomics is revolutionizing the way medical images are used in cardiac diagnostics by enabling objective and quantitative analysis of image features. This method stands in contrast to traditional CT imaging, whose interpretations are qualitative and strongly dependent on the experience of the radiologist [15]. Comprehensive data extraction makes it possible to detect subtle and early changes that are often present long before clinically noticeable symptoms appear. This offers the possibility of an earlier diagnosis and allows the start of preventive measures or early therapies, enabling a personalized treatment approach.

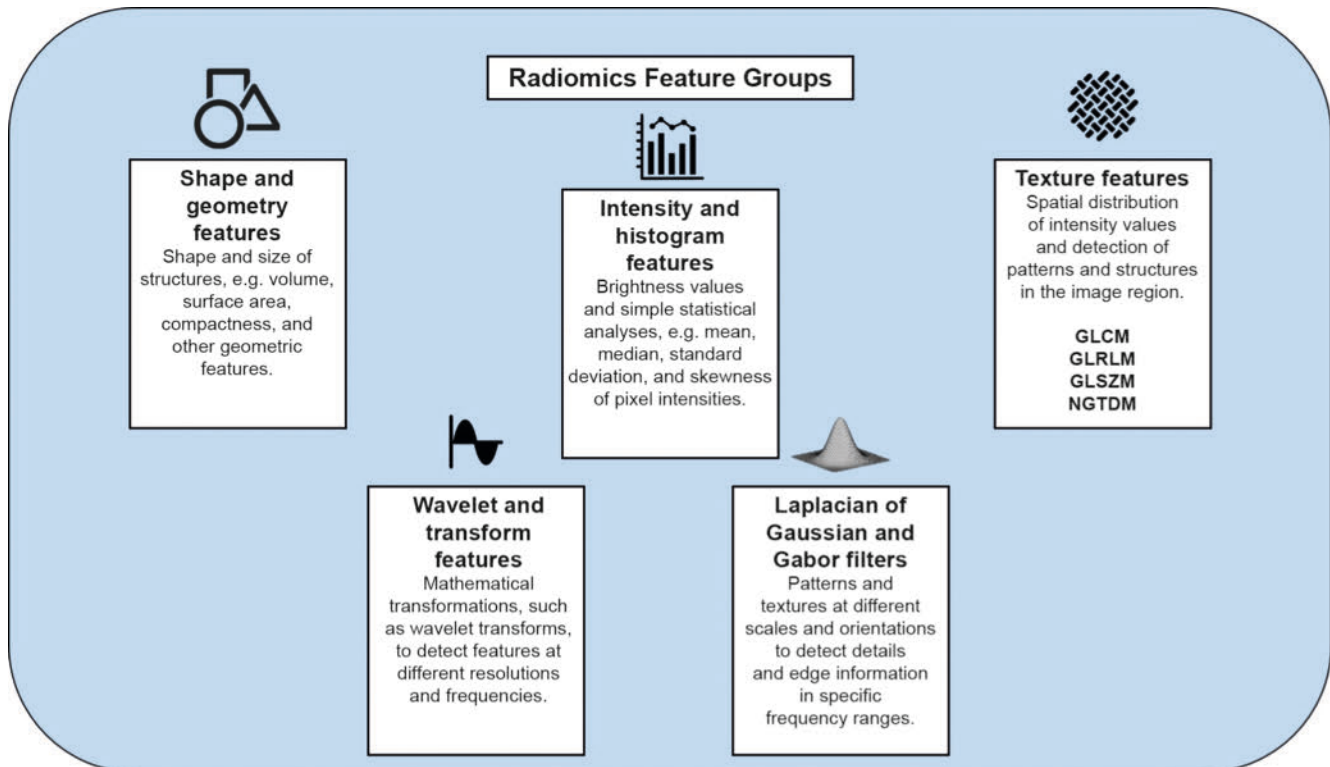
Current state of studies

Radiomics analyses of the left ventricular myocardium

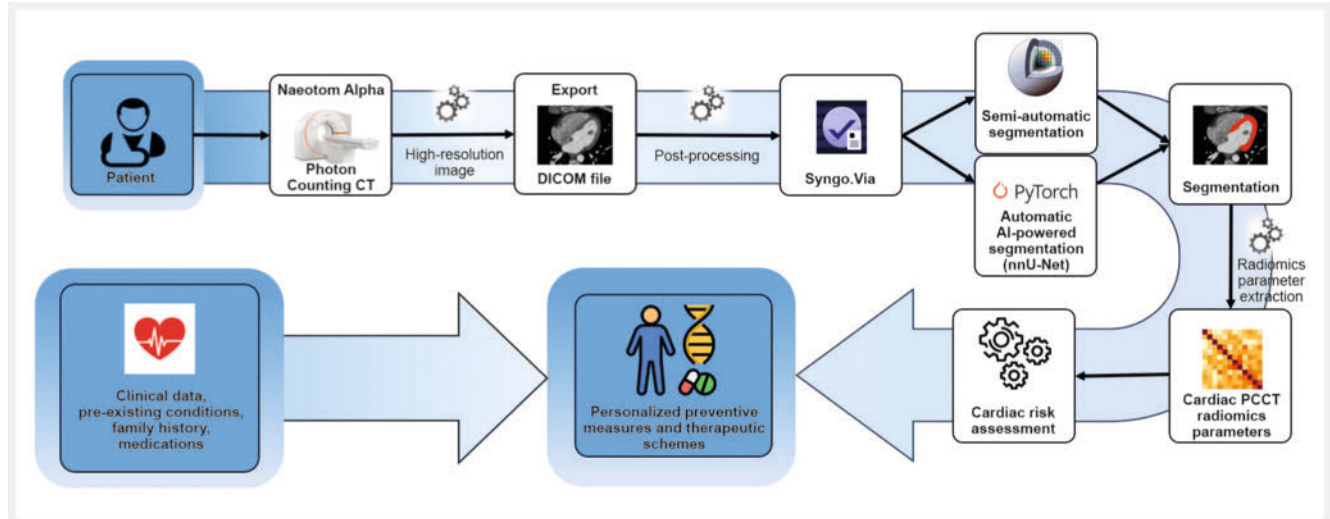
Although myocardial analysis is a domain of MRI imaging, several studies in the past have focused on visualizing texture changes in CT imaging, as well. Already in 2016, Antunes et al. demonstrated the potential of radiomics parameters to differentiate between patients with normal and scarred myocardial tissue after myocarditis in a small group of seven patients. The authors investigated first-order radiomics parameters for the left ventricular myocardium on normal and scarred myocardial tissue in differently contrasted CT scans of the heart, and they identified the “energy” parameter as the best parameter for distinguishing between normal and scarred tissue in all scans ($p < 0.001$) [16]. Building on these results, Hinzpeter et al. demonstrated in 2017 the feasibility of radiomics texture analysis for differentiating healthy and acutely infarcted myocardium in cardiac CT in 20 patients with acute myocardial infarction and in 20 matched controls. Three different radiomics features allowed a reliable distinction between both groups (kurtosis (AUC: 0.78, $p = 0.002$), correlation (AUC: 0.81, $p = 0.002$) and Short Run High Gray-Level Emphasis (SRHGLE) (AUC: 0.82, $p = 0.001$)) [17].

Mannil et al. went a step further and investigated the potential of texture analysis to detect myocardial fibroses that were not detectable visually using native cardiac CT images. For this purpose, their study included 27 patients with acute myocardial infarction, 30 patients with chronic myocardial infarction, and 20 patients without cardiac pathologies. It was not possible to differentiate visually between the groups. Texture analysis showed moderate accuracy in distinguishing between the three groups, but this was improved by combining the acute and chronic myocardial infarction group compared to the reference group (AUC 0.78, sensitivity 86%, specificity 81%) [18].

With the implementation of PCCT, there was also an increase in the number of cardiac radiomics analyses performed. A comparative study between the radiomics signature on the left ventricular myocardium in patients undergoing PCCT and energy-integrated CT (EICT) found comparability of first-order features, but higher-order features differed significantly between detector types. This suggests an influence of the detector technology on the radiomics signature, potentially due to the higher resolution of the PCCT [19]. Following this study, another study investigated the influence of



► Fig. 2 Illustration of the different radiomics feature groups.



► Fig. 3 Workflow of a radiomics analysis for CCTAs using a photon-counting computed tomograph.

virtual monoenergetic reconstructions with different kV levels on the radiomics stability at PCCT not only using a phantom model but also using the left ventricular myocardium. This study demonstrated that in the low kV range the stability of radiomics features on the myocardium is significantly reduced. As a result, the spectral reconstructions, both in vivo and in vitro, influence the radiomics signature [20]. To exploit the potential of the high resolution of PCCT, an in-house study investigated the influence of coronary

sclerosis on the left ventricular myocardium. The study was able to demonstrate an influence on the texture of the left ventricular myocardium depending on the severity of the Agatston score, potentially in terms of fibrosing due to chronic hypoperfusion. For this purpose, a radiomics signature was created by a random forest feature selected from four different texture features [21]. Esposito et al. investigated similarly discrete textural changes by correlating radiomics features of late-phase cardiac CT images from the visu-

► **Table 1** Overview of papers published on the topic of “Radiomics analyses of the left ventricular myocardium”.

Radiomics analyses of the left ventricular myocardium	EICT	
	Antunes et al. <i>Annu Int Conf IEEE Eng Med Biol Soc</i> 2016 [16]	Radiomics features could differentiate between patients with normal and scarred myocardial tissue after myocarditis.
	Hinzpeter et al. <i>PLoS ONE</i> 2017 [17]	Accuracy of differentiation between healthy and acutely infarcted myocardium by radiomics analysis.
	Mannil et al. <i>Investigative Radiology</i> 2018 [18]	Radiomics features for detecting myocardial fibrosis in native low dose CT imaging.
	Shu et al. <i>J. Nucl. Cardiol</i> 2022 [23]	Radiomics machine learning model for predicting chronic myocardial ischemia.
	Esposito et al. <i>Mol Imaging Biol</i> 2018 [22]	Radiomics analyses can distinguish different patterns of structural remodeling in patients with rVT.
	Kay et al. <i>Circ: Cardiovascular Imaging</i> 2020 [24]	Prediction of high-risk left ventricular hypertrophy phenotypes detected on MRI imaging on non-contrast cardiac CT by radiomics analysis.
	Cavallo et al. <i>Diagnostics</i> 2022 [25]	CCTA-based radiomics approach to identify left ventricular remodeling in patients with arterial hypertension.
	PCCT	
	Ayx et al. <i>Diagnostics</i> 2022 [21]	Possible detection of myocardial fibrosis using radiomics features depending on coronary artery sclerosis.
Wolf et al. <i>European Radiology Experimental</i> 2023 [20]	The stability of radiomics features in PCD-CT imaging decreases significantly below 90 keV, underscoring the need to standardize VMI values in order to ensure reproducibility in clinical applications.	

ally unscarred myocardium in patients with recurrent ventricular tachycardia with left ventricular function, left ventricular remodeling, and underlying cardiac disease. This study demonstrated an association of heterogeneous myocardium with systolic and diastolic function, as well as left ventricular dilatation. Using a radiomics signature, different patterns of left ventricular structural myocardial remodeling could be differentiated [22]. ► **Table 1** provides an overview of papers published on the topic of “Radiomics analyses of the left ventricular myocardium”.

Radiomics analyses of pericoronary or epicardial adipose tissue

In recent years, the focus of cardiovascular CT research has increasingly shifted to the role of perivascular adipose tissue. Vascular inflammation has been associated with structural changes and remodeling of perivascular adipose tissue. The recently outlined *perivascular fat attenuation index* (FAI) describes the inflammation-induced increase in Hounsfield Units (HU) and is considered a strong predictor of cardiovascular events. The texture analysis of perivascular adipose tissue is intended to go beyond the FAI and define potential *imaging biomarkers* that indicate the development of atherosclerosis at an early stage. In 2019, Oikonomou et al. investigated the radiomics profile of PVAT remodeling to improve cardiac risk prediction. Their first study took adipose tissue biopsies from 167 patients and correlated radiomics features with gene expressions representing inflammation, fibrosis, and angiogenesis. Tissue inflammation, as represented by TNFA expression, correlated best with the wave-transformed mean HU attenuation of adipose tissue. However, fibrosis and vascularization could be represented comparably or better by higher-grade textural fea-

tures than by mean HU attenuation. In addition, they analyzed radiomics features in 101 patients, who experienced MACE within 5 years after CCTA, and 101 matched controls. The fat radiomics profile (FRP) significantly improved MACE prediction compared to traditional risk factors such as coronary calcium score, coronary stenosis, and vulnerable plaque features ($p < 0.001$). In line with these results, FRP was significantly higher in patients with acute myocardial infarction compared to matched controls ($p < 0.001$) and displayed negative PVAT remodeling [26]. In a supplementary study, Lin et al. demonstrated that texture and geometry-based radiomics parameters of pericoronary adipose tissue were able to distinguish patients with myocardial infarction from patients with stable or no coronary heart disease [27].

Kahmann et al. investigated the influence of hypercholesterolemia on pericoronary adipose tissue using PCCT. Two texture characteristics were able to reliably distinguish between patients with and patients without the clinical risk factor of hypercholesterolemia in the test and validation set. Patients with hypercholesterolemia displayed a higher level of high density values in adipose tissue as a potential correlate of the inflammatory response, which was not evident visually [28]. However, not only the pericoronary adipose tissue, but also the epicardial adipose tissue has a physiological and pathophysiological influence on cardiac biology. In this context, a recently published study by Mundt et al. investigated the interaction between the radiomics signature of epicardial adipose tissue (EAT) and coronary calcifications. Based on 53 patients, who were divided into three different categories depending on the severity level of the Agatston score, a radiomics profile was created from four different texture features of the EAT, which correlates with the presence of calcified coronary plaques

► **Table 2** Overview of papers published on the topic of “Radiomics analyses of pericoronary and epicardial adipose tissue”.

Radiomics analyses of pericoronary and epicardial adipose tissue	EICT	
	Oikonomou et al. <i>European Heart Journal</i> 2019 [26]	Radiomics profile of the PVAT remodeling to improve cardiac risk predication.
	Lin et al. <i>JACC: Cardiovascular Imaging</i> 2020 [27]	Differentiation of patients with myocardial infarction and stable or non-existent coronary heart disease using radiomics parameters.
	Shang et al. <i>Eur Radiol</i> 2022 [31]	Predictive power of future acute coronary syndromes within 3 years by radiomics analyses.
	Agnese et al. <i>Heliyon</i> 2023 [30]	This study showed that texture analysis of epicardial fat (EF) and thoracic subcutaneous fat (TSF) by cardiac CT (CCT) revealed significant differences in radiomics parameters between patients with BMI ≤ 25 kg/m ² and BMI > 25 kg/m ² .
	Cundari et al. <i>La radiologia medica</i> 2024 [32]	CCTA is the standard for non-invasive diagnosis of CAD. New CT biomarkers such as coronary calcium score and texture analysis of adipose tissue improve risk stratification and personalized medicine.
	Szabo et al. <i>European Radiology</i> 2023 [33]	Radiomics analysis of pericardial adipose tissue enabled effective differentiation and prediction of cases of heart failure. Key features included increased size and texture heterogeneity of pericardial adipose tissue.
	Kim et al. <i>Bioengineering (Basel)</i> (2023) [34]	Pericoronary adipose tissue analysis (PCAT) by coronary CT angiography (CCTA) can identify both thin-cap fibroatheromas (TCFA) and micro-channels through radiomics features, which is consistent with intravascular optical coherence tomography findings and thus improves non-invasive risk stratification of at-risk plaques.
	PCCT	
	Tharmaseelan et al. <i>Int J Cardiovasc Imaging</i> 2022 [35]	Seven radiomics features of periaortic adipose tissue predicted the presence of local aortic calcification.
Mundt et al. <i>Diagnostics</i> 2024 [29]	In this study, four textural features of epicardial adipose tissue were identified that show significant differences between patients with and without coronary artery calcification. These features could serve as imaging biomarkers for detecting atherosclerosis.	
Mundt et al. <i>BMC Medical Imaging</i> 2023 [36]	Radiomics analysis of periaortic adipose tissue from 55 patients revealed features that correlate with coronary artery calcification. These features may serve as potential biomarkers for cardiovascular risk.	

and serves as a potential surrogate parameter for atherosclerosis in adipose tissue [29].

Furthermore, Agnese et al. (2023) investigated the influence of obesity on epicardial and thoracic subcutaneous adipose tissue. To do so, they divided the patient group into patients with a BMI of ≤ 25 kg/m² and patients with a BMI of > 25 kg/m². Although the volume of epicardial adipose tissue differed between the two patient populations ($p=0.014$), there was no relevant difference in the conventionally measured mean HU density ($p=0.28$). In contrast, however, a distinction between the two groups could be made based on five radiomics features, whereby a pronounced heterogeneity of gray levels deviating from the mean enabled a differentiation [30]. ► **Table 2** provides an overview of papers published on the topic of “Radiomics analyses of pericoronary and epicardial adipose tissue”.

Radiomics analyses of coronary plaques

In addition to the purely anatomical measurement of the degree of stenosis of a plaque, plaque characteristics have also become increasingly important and are taken into account as a supplementary feature in the new CADRADS 2.0 criteria. This currently

includes four different conventionally detectable plaque features: the napkin-ring sign, a low plaque density of less than 30 HU, punctate calcifications, and positive remodeling [9]. Even in non-obstructive stenoses, these parameters have an influence on patient outcomes [37, 38, 39]. In routine practice, however, risk stratification can be difficult, particularly with limited image quality and limited experience on the part of the radiologist [39]. For this reason, several studies have focused on radiomics analysis for coronary plaques. Already in 2017, Kolossvary et al. analyzed radiomics features to distinguish between plaques with and without the napkin-ring sign. Using eight conventional factors (plaque length and volume, mean plaque load, degree of stenosis, vascular wall remodeling, and mean, minimum, and maximum HU density), no reliable differentiation could be found between the two groups. By contrast, 20.6% of the radiomics parameters displayed a significant difference and allowed a reliable discrimination of the napkin-ring sign ($p<0.0012$) [40].

However, plaque analysis has also received a new boost through the implementation of PCCT. In 2023, Dunning et al. investigated the possibility of classifying coronary plaques into a low- or high-risk group using various virtual monoenergetic

► **Table 3** Overview of papers published on the topic of “Radiomics analyses of coronary plaques”.

Radiomics analyses of coronary plaques	EICT	
	Kolossvary et al. <i>Circ: Cardiovascular Imaging</i> 2017 [40]	Differentiation between plaques with and without napkin ring sign using radiomics features.
	Kolossvary et al. <i>European Heart Journal – Cardiovascular Imaging</i> 2019 [42]	Radiomics analysis outperformed conventional assessment of coronary plaque vulnerability.
	Li et al. <i>European Journal of Radiology</i> 2021 [43]	Radiomics analysis identifies hemodynamically significant coronary artery stenoses better than conventional parameters.
	Chen et al. <i>Radiology</i> 2023 [44]	A radiomics signature for vulnerable plaques developed using coronary CT angiography enables detection of plaques associated with an increased risk for future major cardiac events.
	PCCT	
	Dunning et al. <i>Proc SPIE Int Soc Opt Eng</i> 2023 [41]	A machine learning model based on radiomics and PCCT successfully differentiated between low and high-risk coronary plaques in 100 keV VMI and VNC images.
Kahmann et al. <i>Insights Imaging</i> 2024 [28]	A higher density of epicardial adipose tissue and a more heterogeneous plaque texture, analyzed by radiomics and PCCT, potentially contributes to identifying patients with increased cardiovascular risk.	

reconstructions (VMI) from the spectral dataset of the CCTA at the PCCT, as well as virtual native images (VNC) using a machine learning (ML) approach. A radiologist certified in cardiac imaging assigned the plaques to relevant groups based on conventional parameters. Semi-automatically segmented plaques could be classified automatically in the corresponding risk group in 100 keV VMI and VNC images using an ML model [41]. Another recently published study investigated the potential of radiomics-based plaque analysis in identifying high-risk plaques and obstructive plaques in relation to conventional parameters of the plaques themselves using 306 plaques and accompanying EAT. Patients at increased risk for cardiovascular events, defined by conventional parameters, were characterized by structural changes in plaque texture, particularly in terms of pronounced heterogeneity. Furthermore, it was possible to demonstrate an increased density of the EAT [28]. ► **Table 3** provides an overview of papers published on the topic of “Radiomics analyses of coronary plaques”.

Limitations and challenges of radiomics analysis in cardiac imaging

Despite the significant potential that radiomics offers for cardiac CT, the integration of this advanced analysis technique in clinical routines has so far been limited. The challenges that arise in the implementation of radiomics are varied, and they include technical, reproductive, and standardization-related aspects that can affect the reliability and stability of the features obtained [6].

Technical variabilities such as the choice of contrast agent, the image acquisition settings, different device manufacturers, as well as the tube voltage, the reconstruction kernel and the slice thickness have a significant influence on the consistency of the radiomics features [6]. These factors lead to a variability that limits the reproducibility of the data and thus the reliability of

the radiomics analysis. In addition, the methods used for segmentation and the software used to extract features can vary, which introduces further uncertainty to the data analysis.

Although innovative approaches such as the use of PCCT show promising improvements in terms of signal-to-noise ratio and spatial resolution, there are still differences in the radiomics characteristics between PCCT and conventional EICT [19]. These differences could be attributed to the special characteristics of the new technology, and could thus influence the development of cardiac radiomics analysis in the future. However, due to the limited number of studies at present, it is important to view with caution the potential of PCCT with regard to improved texture analysis. A recently published study reported a very good test-retest stability of 97.1% but a poor comparability between PCCT and conventional CT scanners [45]. Nevertheless, radiomics analyses using PCCT have the potential to enable increased use and become established in clinical routines once the widespread use of PCCT is feasible.

A major limitation of radiomics analysis is the high number of characteristics examined, which in combination with mostly small cohorts can lead to statistical problems. The high number of characteristics tested increases the probability that significances arise by chance (multiple testing problem), especially due to the often used 5% standard error rate [46]. In addition, radiomics studies often represent secondary analyses of existing cohorts that were originally designed to address other questions. This use leads to limitations in the statistical significance and reduces the generalizability of the results [47]. Future studies should therefore rely on larger cohorts and specific design strategies to minimize these limitations and strengthen the robustness of radiomics analyses.

Outlook

In an era of big data and rapid advances in detector technology, cardiac radiomics analyses are no longer a distant dream of the future. Additionally, the rapid development of artificial intelligence is opening new possibilities in texture analysis, for example, using neural networks and machine learning solutions. Integration of cardiac radiomics in clinical routines can soon be a reality thanks to the latest technology and advances in standardized segmentation options. These advances are putting the future within reach in terms of providing optimized patient care through personalized cardiovascular risk stratification and therapy monitoring based on imaging biomarkers.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

- [1] Sidelnikov E, Dornstauder E, Jacob C et al. Healthcare resource utilization and costs of cardiovascular events in patients with atherosclerotic cardiovascular disease in Germany – results of a claims database study. *Journal of Medical Economics* 2022; 25: 1199–1206. doi:10.1080/13696998.2022.2141964
- [2] Robert Koch-Institut. Welche Auswirkungen hat der demografische Wandel auf Gesundheit und Gesundheitsversorgung? 2015. doi:10.17886/RKIPUBL-2015-003-9
- [3] Deutsche Herzstiftung (Hg.)/Deutscher Herzbericht – Update 2024
- [4] Gillies RJ, Kinahan PE, Hricak H. Radiomics: Images Are More than Pictures, They Are Data. *Radiology* 2016; 278: 563–577. doi:10.1148/radiol.2015151169
- [5] Reimer RP, Reimer P, Mahnken AH. Assessment of Therapy Response to Transarterial Radioembolization for Liver Metastases by Means of Post-treatment MRI-Based Texture Analysis. *Cardiovasc Intervent Radiol* 2018; 41: 1545–1556. doi:10.1007/s00270-018-2004-2
- [6] Ayx I, Froelich MF, Baumann S et al. Radiomics in Cardiac Computed Tomography. *Diagnostics* 2023; 13: 307. doi:10.3390/diagnostics13020307
- [7] Hertel A, Tharmaseelan H, Rotkopf LT et al. Phantom-based radiomics feature test-retest stability analysis on photon-counting detector CT. *Eur Radiol* 2023; 33: 4905–4914. doi:10.1007/s00330-023-09460-z
- [8] Knuuti J, Wijns W, Saraste A et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *European Heart Journal* 2020; 41: 407–477. doi:10.1093/eurheartj/ehz425
- [9] Danzi GB, Piccolo R. CT or Invasive Coronary Angiography in Stable Chest Pain. *N Engl J Med* 2022; 387: 376–380. doi:10.1056/NEJMc2206973
- [10] Richtlinie Methoden vertragsärztliche Versorgung: Computertomographie-Koronarangiographie bei Verdacht auf eine chronische koronare Herzkrankheit, Gemeinsamer Bundesausschuss, BAnz AT 26.04.2024 B2
- [11] Zwanenburg A, Vallières M, Abdalah MA et al. The Image Biomarker Standardization Initiative: Standardized Quantitative Radiomics for High-Throughput Image-based Phenotyping. *Radiology* 2020; 295: 328–338. doi:10.1148/radiol.2020191145
- [12] Parekh V, Jacobs MA. Radiomics: a new application from established techniques. *Expert Review of Precision Medicine and Drug Development* 2016; 1: 207–226. doi:10.1080/23808993.2016.1164013
- [13] Mayerhoefer ME, Materka A, Langs G et al. Introduction to Radiomics. *J Nucl Med* 2020; 61: 488–495. doi:10.2967/jnumed.118.222893
- [14] Reuzé S, Schernberg A, Orlhac F et al. Radiomics in Nuclear Medicine Applied to Radiation Therapy: Methods, Pitfalls, and Challenges. *International Journal of Radiation Oncology*Biophysics* 2018; 102: 1117–1142. doi:10.1016/j.ijrobp.2018.05.022
- [15] Polidori T, De Santis D, Rucci C et al. Radiomics applications in cardiac imaging: a comprehensive review. *Radiol med* 2023; 128: 922–933. doi:10.1007/s11547-023-01658-x
- [16] Antunes S, Esposito A, Palmisanov A et al. Characterization of normal and scarred myocardium based on texture analysis of cardiac computed tomography images. In: 2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) Orlando: IEEE; 2016: 4161–4164
- [17] Hinzpeter R, Wagner MW, Wurnig MC et al. Texture analysis of acute myocardial infarction with CT: First experience study. *PLoS ONE* 2017; 12: e0186876. doi:10.1371/journal.pone.0186876
- [18] Mannil M, Von Spiczak J, Manka R et al. Texture Analysis and Machine Learning for Detecting Myocardial Infarction in Noncontrast Low-Dose Computed Tomography: Unveiling the Invisible. *Invest Radiol* 2018; 53: 338–343. doi:10.1097/RLI.0000000000000448
- [19] Ayx I, Tharmaseelan H, Hertel A et al. Comparison Study of Myocardial Radiomics Feature Properties on Energy-Integrating and Photon-Counting Detector CT. *Diagnostics (Basel)* 2022; 12. doi:10.3390/diagnostics12051294
- [20] Wolf EV, Müller L, Schoepf UJ et al. Photon-counting detector CT-based virtual monoenergetic reconstructions: repeatability and reproducibility of radiomics features of an organic phantom and human myocardium. *Eur Radiol Exp* 2023; 7: 59. doi:10.1186/s41747-023-00371-8
- [21] Ayx I, Tharmaseelan H, Hertel A et al. Myocardial Radiomics Texture Features Associated with Increased Coronary Calcium Score-First Results of a Photon-Counting CT. *Diagnostics (Basel)* 2022; 12. doi:10.3390/diagnostics12071663
- [22] Esposito A, Palmisano A, Antunes S et al. Assessment of Remote Myocardium Heterogeneity in Patients with Ventricular Tachycardia Using Texture Analysis of Late Iodine Enhancement (LIE) Cardiac Computed Tomography (cCT) Images. *Mol Imaging Biol* 2018; 20: 816–825. doi:10.1007/s11307-018-1175-1
- [23] Shu Z-Y, Cui S-J, Zhang Y-Q et al. Predicting Chronic Myocardial Ischemia Using CCTA-Based Radiomics Machine Learning Nomogram. *Journal of Nuclear Cardiology* 2022; 29: 262–274. doi:10.1007/s12350-020-02204-2
- [24] Kay FU, Abbara S, Joshi PH et al. Identification of High-Risk Left Ventricular Hypertrophy on Calcium Scoring Cardiac Computed Tomography Scans: Validation in the DHS. *Circ Cardiovascular Imaging* 2020; 13: e009678. doi:10.1161/CIRCIMAGING.119.009678
- [25] Cavallo AU, Troisi J, Muscogiuri E et al. Cardiac Computed Tomography Radiomics-Based Approach for the Detection of Left Ventricular Remodeling in Patients with Arterial Hypertension. *Diagnostics* 2022; 12: 322. doi:10.3390/diagnostics12020322
- [26] Oikonomou EK, Williams MC, Kotanidis CP et al. A novel machine learning-derived radiotranscriptomic signature of perivascular fat improves cardiac risk prediction using coronary CT angiography. *European Heart Journal* 2019; 40: 3529–3543. doi:10.1093/eurheartj/ehz592
- [27] Lin A, Kolossváry M, Yuvaraj J et al. Myocardial Infarction Associates With a Distinct Pericoronary Adipose Tissue Radiomic Phenotype. *JACC: Cardiovascular Imaging* 2020; 13: 2371–2383. doi:10.1016/j.jcmg.2020.06.033

- [28] Kahmann J, Nörenberg D, Papavassiliu T et al. Combined conventional factors and the radiomics signature of coronary plaque texture could improve cardiac risk prediction. *Insights Imaging* 2024; 15: 170. doi:10.1186/s13244-024-01759-9
- [29] Mundt P, Hertel A, Tharmaseelan H et al. Analysis of Epicardial Adipose Tissue Texture in Relation to Coronary Artery Calcification in PCCT: The EAT Signature! *Diagnostics* 2024; 14: 277. doi:10.3390/diagnostics14030277
- [30] Agnese M, Toia P, Sollami G et al. Epicardial and thoracic subcutaneous fat texture analysis in patients undergoing cardiac CT. *Heliyon* 2023; 9: e15984. doi:10.1016/j.heliyon.2023.e15984
- [31] Shang J, Ma S, Guo Y et al. Prediction of acute coronary syndrome within 3 years using radiomics signature of pericoronary adipose tissue based on coronary computed tomography angiography. *Eur Radiol* 2022; 32: 1256–1266. doi:10.1007/s00330-021-08109-z
- [32] Cundari G, Marchitelli L, Pambianchi G et al. Imaging biomarkers in cardiac CT: moving beyond simple coronary anatomical assessment. *Radiol med* 2024; 129: 380–400. doi:10.1007/s11547-024-01771-5
- [33] Szabo L, Salih A, Pujadas ER et al. Radiomics of pericardial fat: a new frontier in heart failure discrimination and prediction. *Eur Radiol* 2023; 34: 4113–4126. doi:10.1007/s00330-023-10311-0
- [34] Kim JN, Gomez-Perez L, Zimin VN et al. Pericoronary Adipose Tissue Radiomics from Coronary Computed Tomography Angiography Identifies Vulnerable Plaques. *Bioengineering* 2023; 10: 360. doi:10.3390/bioengineering10030360
- [35] Tharmaseelan H, Froelich MF, Nörenberg D et al. Influence of local aortic calcification on periaortic adipose tissue radiomics texture features – a primary analysis on PCCT. *Int J Cardiovasc Imaging* 2022; 38: 2459–2467. doi:10.1007/s10554-022-02656-2
- [36] Mundt P, Tharmaseelan H, Hertel A et al. Periaortic adipose radiomics texture features associated with increased coronary calcium score – first results on a photon-counting-CT. *BMC Med Imaging* 2023; 23: 97. doi:10.1186/s12880-023-01058-7
- [37] Williams MC, Moss AJ, Dweck M et al. Coronary Artery Plaque Characteristics Associated With Adverse Outcomes in the SCOT-HEART Study. *Journal of the American College of Cardiology* 2019; 73: 291–301. doi:10.1016/j.jacc.2018.10.066
- [38] Puchner SB, Liu T, Mayrhofer T et al. High-Risk Plaque Detected on Coronary CT Angiography Predicts Acute Coronary Syndromes Independent of Significant Stenosis in Acute Chest Pain. *Journal of the American College of Cardiology* 2014; 64: 684–692. doi:10.1016/j.jacc.2014.05.039
- [39] Yoon YE, Lim T-H. Current Roles and Future Applications of Cardiac CT: Risk Stratification of Coronary Artery Disease. *Korean J Radiol* 2014; 15: 4. doi:10.3348/kjr.2014.15.1.4
- [40] Kolossváry M, Karády J, Szilveszter B et al. Radiomic Features Are Superior to Conventional Quantitative Computed Tomographic Metrics to Identify Coronary Plaques With Napkin-Ring Sign. *Circ Cardiovascular Imaging* 2017; 10: e006843. doi:10.1161/CIRCIMAGING.117.006843
- [41] Dunning CA, Rajiah P, Hsieh S et al. Classification of high-risk coronary plaques using radiomic analysis of multi-energy photon-counting-detector computed tomography (PCD-CT) images. In: *Iftekharuddin KM, Chen W (eds) Medical Imaging 2023: Computer-Aided Diagnosis San Diego: SPIE; 2023: 102*
- [42] Kolossváry M, Park J, Bang J-I et al. Identification of invasive and radiopaque markers of coronary plaque vulnerability using radiomic analysis of coronary computed tomography angiography. *European Heart Journal – Cardiovascular Imaging* 2019; 20: 1250–1258. doi:10.1093/ehjci/jez033
- [43] Li L, Hu X, Tao X et al. Radiomic features of plaques derived from coronary CT angiography to identify hemodynamically significant coronary stenosis, using invasive FFR as the reference standard. *European Journal of Radiology* 2021; 140: 109769. doi:10.1016/j.ejrad.2021.109769
- [44] Chen Q, Pan T, Wang YN et al. A Coronary CT Angiography Radiomics Model to Identify Vulnerable Plaque and Predict Cardiovascular Events. *Radiology* 2023; 307: e221693. doi:10.1148/radiol.221693
- [45] Zhu L, Dong H, Sun J et al. Robustness of radiomics among photon-counting detector CT and dual-energy CT systems: a texture phantom study. *Eur Radiol* 2024. doi:10.1007/s00330-024-10976-1
- [46] Koçak B. Key concepts, common pitfalls, and best practices in artificial intelligence and machine learning: focus on radiomics. *Diagn Interv Radiol* 2022; 28: 450–462. doi:10.5152/dir.2022.211297
- [47] Park JE, Park SY, Kim HJ et al. Reproducibility and Generalizability in Radiomics Modeling: Possible Strategies in Radiologic and Statistical Perspectives. *Korean J Radiol* 2019; 20: 1124–1137. doi:10.3348/kjr.2018.0070
- [48] Otsuka K, Fukuda S, Tanaka A et al. Napkin-Ring Sign on Coronary CT Angiography for the Prediction of Acute Coronary Syndrome. *JACC: Cardiovascular Imaging* 2013; 6: 448–457. doi:10.1016/j.jcmg.2012.09.016