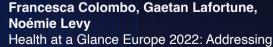
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Radiomics in Cardiovascular Imaging: Current Role and Future Perspectives

Radiomics may lead to personalised management and treatment of cardiovascular diseases, which could impact patients' prognosis.



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key points

- In recent years, multiple radiomics-based tools have been investigated in the field of cardiovascular imaging.
- Radiomics may predict outcomes of cardiac diseases without the need of invasive procedures.
- Cardiac CT radiomics may enhance the assessment of advanced atheromatous plaques, improving risk stratification and treatment in patients with CAD.
- Radiomics may improve cardiac MRI prognostic value and its well-known capability of myocardial characterization even without the use of contrast agents.

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Introduction

Radiomics represents a promising image analysis technique that aims to improve the diagnosis, the characterisation, and the prognosis of diseases by extracting objective quantitative features that may be missed by human eye (Sollini et al. 2019). While mainly developed through oncologic research to obtain information on the characteristics of tumours (Gillies et al. 2016), there is an increasing interest in the use of radiomics for cardiac purposes (Ashrafinia et al. 2021). As cardiovascular diseases represent the main cause of morbidity and mortality worldwide (Virani et al. 2020), there is an ever increasing clinical request for non-invasive diagnostic approaches (Selvanayagam 2016). Therefore, radiomics biomarkers detected by data extraction from cardiac computed tomography (CT) and cardiac magnetic resonance imaging (CMR) may be a valuable tool to assess several cardiac pathologies, such as atherosclerotic coronary artery disease (CAD), myocardial viability, and cardiomyopathies (Kumar et al.

2012; Raisi-Estabragh et al. 2020). Recently, machine learning (ML) and deep learning (DL) algorithms have provided even more options, allowing to better evaluate the characteristics of cardiac disease (Langs et al. 2018).

Radiomics in Cardiac CT

Cardiac CT angiography (CCTA) has gained a pivotal role in assessing CAD and plays a critical part in evaluating cardiac structures (Hoffmann et al. 2012). CCTA can noninvasively visualise coronary arteries and plaque morphology, representing an invaluable tool for risk stratification, and guide treatment plans in patients with CAD (Douglas et al. 2015).

Recently, some exploratory papers have evaluated the feasibility and diagnostic performance of cardiac CT radiomics analysis (Kolossváry et al. 2019; Mannil et al. 2019).

In the last few years, some authors developed a radiomics-based ML model that proved to be superior to conventional evaluation of CCTA in the assessment of advanced atheromatous plaques. In particular, the

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model performed better than radiologists in measuring low attenuation areas and average Hounsfield units of the plaque resulting in a more accurate evaluation of high-risk atherosclerotic lesions, facilitating risk stratification of patients (Kolossváry et al. 2019).

Peri-coronary adipose tissue inflammation is another critical element in the development of atherosclerotic plaque, progression, and rupture. Radiomics features extracted from cardiac CT images have demonstrated potential in evaluating the association between atherosclerotic plaques and perivascular adipose tissue risk for left ventricular hypertrophy (Esposito et al. 2018; Kay et al. 2020).

Cardiac CT is also essential for the differential diagnosis of cardiac masses in order to establish optimal treatment strategies. However, differentiation is challenging due to the nonspecific clinical and imaging appearances of many cardiac masses (Poterucha et al. 2019). Nam et al. explored the role of CT radiomic features to differentiate pannus from thrombus and vegetation, showing that the algorithms were superior to radiologists in identifying pannus from non-pannus

Cardiac CT radiomics may become the next tool to detect image biomarkers more precisely, facilitating improved identification of vulnerable patients

inflammation, fibrosis, and vascularity, more precisely than mean attenuation alone (Oikonomou et al. 2019). These results highlighted that the texture phenotype of adipose tissue might provide a non-invasive approach for identifying microvascular adipose tissue remodelling (Antonopoulos et al. 2017; Oikonomou et al. 2019). In some authors' opinion, this may represent a gamechanger to distinguish patients with acute myocardial infarction from those with stable CAD or to predict patients with a high risk of major adverse cardiac events (MACE) (Lin et al. 2020; Oikonomou et al. 2018).

Myocardial tissue characterisation has always been a prerogative of CMR, but with recent technological improvements, even CT scanners can play their part. With the introduction of texture analysis in 2016, CT imaging could discern between healthy and scarred myocardium (Antunes et al. 2016). Soon afterwards, the advent of radiomics analysis increased the capability of cardiac CT in differentiating healthy myocardial tissue from infarcted myocardium. Hinzpeter et al. found that cardiac CT texture analysis was helpful in determining healthy and infarcted myocardial tissue with good reproducibility and accuracy (Hinzpeter et al. 2017). Mannil et al. also demonstrated the capability of radiomics and ML in detecting myocardial infarction on non-contrast CT images acquired for calcium scoring (Mannil et al. 2018).

Ventricular arrhythmias (VA) represent an essential prognostic factor in patients with cardiovascular diseases. Researchers have also explored the capability of radiomic features to predict recurrent VA in patients with different remodelling patterns sustained by various cardiomyopathies, such as patients with high arrhythmic (Nam et al. 2019). Chun et al. compared the capability of radiomics and CT attenuation values in differentiating left atrial appendage thrombus from circulatory stasis and found that the addition of radiomics features represented an added value to help radiologists to identify thrombus in a single early-phase scan (Chun et al. 2021).

Despite these exciting applications, they represent only preliminary explorations.

These findings, do however, indicate that cardiac CT radiomics may become the next tool to detect image biomarkers more precisely, facilitating improved identification of vulnerable patients.

Radiomics in Cardiac MRI

CMR is pivotal in qualitatively and quantitively assessing cardiac structure and function. However, quantitative measures are limited by technical factors and poor discriminatory power due to the overlap of similar appearances of different pathologies. This sometimes makes it challenging to distinguish among similar morphological patterns, such as hypertensive heart disease, hypertrophic cardiomyopathy (HCM) or athletic cardiac remodelling, whose distinctions are critical to guide the clinical assessment, management, and therapy of these patients. Furthermore, CMR likely plays a fundamental role in predicting prognosis in many different clinical settings but its ability is still limited (Moss et al. 2002; Stecker et al. 2006). CMR-based radiomics is emerging as a valid option to help defining image phenotypes and improve diagnosis, prognosis and treatment selection.

Several papers have recently explored the feasibility

and potential clinical utility of radiomics and texture analysis with CMR.

Some authors have evaluated the ability of CMR radiomics analysis applied to non-contrast cine images to accurately differentiate between myocardial disease states and healthy, suggesting that radiomics features few studies have been recently published. In a study on patients with chronic myocardial infarction, Kotu et his group demonstrated that radiomics features extracted from LGE scar were superior to scar size and location in determining the risk of dangerous arrhythmias (Kotu et al. 2015). Similarly, Amano et al. showed that different

CMR radiomics has the potential to improve myocardial disease classification and prognosis

may be capable of highlighting myocardium alteration at a tissue level (Baessler et al. 2018). In particular, a recent study evaluated the ability of radiomics to identify distortions in myocardial architecture that are not detectable by the human eye. These signatures could discriminate accurately between the hearts of individuals with hypertension (morphologically normal at CMR) and those who are normotensive (Cetin et al. 2020).

Furthermore, Baessler et al. demonstrated that radiomic texture analysis applied to T1 and T2 maps was superior to mean T1, mean T2, and Lake Louise diagnostic criteria in discriminating infarct-like acute myocarditis (Baessler et al. 2019). The same group also demonstrated the possibility of accurately discerning patients with myocardial infarction from healthy controls through radiomics and texture analysis on CMR cine images without using an intravenous contrast agent, which could be a fundamental achievement for CMR imaging in terms of time-saving and safety (Baessler et al. 2018).

In addition, a recently published article stated that radiomics analysis of late gadolinium enhanced (LGE) CMR images is capable of distinguishing acute myocardial infarction from chronic myocardial infarction (Larroza et al. 2017).

It is important to remember that the assessment of myocardial infarction and myocardial viability are two of the most frequent requests for which clinicians refer to CMR, and these new radiomic tools could be invaluable in offering better clinical support.

As to prognosis and prediction of clinical outcomes, a

textural features extracted from LGE images could be useful to predict VA in HCM patients (Amano et al. 2018).

In summary then, CMR radiomics has the potential to improve myocardial disease classification and prognosis. However, the literature about CMR radiomics is still limited, and further efforts are needed to confirm these preliminary results and to facilitate the radiomics transition from academic to clinical settings.

Conclusion

Through specific, quantitative insights provided at a microstructural level, radiomics can favour a better understanding of the physiologic mechanisms of cardiac disease that can be of great value in developing tailored cardiovascular medicine therapy. And thus, in future, be gradually introduced into the clinical physicians' workflow.

However, even if most of the recently published papers have shown promising results applying radiomics to cardiac imaging, the current research is still far from supporting clinical decision-making. Radiomics-based cardiac imaging studies have been proved to show an overall insufficient methodological quality (Lambin et al. 2017; Ponsiglione et al. 2022). A more standardised methodology in the radiomics workflow is needed to cross the translational line between an exploratory investigation method and a standardised added value to precision medicine workflows.

Conflict of Interest

None.

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