The Impact of Non-invasive Cardiac MRI for Evaluating Coronary arteries & Myocardial Deformation

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Dr. Kishi is a specialist in cardiology as well as an expert in diagnostic imaging. He has therefore been playing an active role as a supervising physician in the field of cardiovascular diagnostic imaging. For a three-year period from 2011, he was engaged in research focusing mainly on the MESA* study as a research supervising physician at the Johns Hopkins University in the United States. In addition, at the annual meeting of the American College of Cardiology in 2013, his study on myocardial strain was named the "Best Poster Award Winner at ACC 13". In this report, Dr. Kishi discusses cardiac diseases, lifestyle diseases, and new methods for evaluating myocardial function.

Abstract

When evaluating the coronary arteries, it is important to have a clear understanding of the particular characteristics of each imaging modality and to establish a diagnosis based on a variety of images acquired using different modalities. In particular, MR coronary angiography (MRCA) is useful for examining patients in whom CT is difficult or impossible (e.g., patients with severe calcification or patients in whom the use of contrast medium is contraindicated). Another advantage of MRCA is that it can be used to visualize the coronary artery lumen in order to evaluate next-generation stents known as bioresorbable vascular scaffold (BVS) stents.[1]
The evaluation of myocardial motion based on images has long been a challenge, but myocardial strain analysis using cine MRI is currently attracting attention. With the use of MR-Wall Motion Tracking (MR-WMT), a software application introduced by Canon Medical, quantitative assessment of cardiac functional impairment can be performed easily, making this application extremely useful in routine clinical practice.

My basic philosophy in medical practice is to provide optimal care for patients with atherosclerosis by employing a variety of diagnostic and therapeutic methods in combination. For imaging of the coronary arteries, in addition to echocardiography, coronary angiography (CAG), and single-photon emission computed tomography (SPECT), new techniques such as CT coronary angiography (CTCA) and MR coronary angiography (MRCA) are now available. CTCA has quickly gained widespread clinical acceptance in recent years, and the clinical usefulness of MRCA is also attracting attention. These techniques provide images with different characteristics, and it is therefore important to consider how these different types of images should be used in combination.

In this lecture, I would like to discuss the clinical usefulness of MRCA, mainly as compared to CTCA, as well as the clinical usefulness of myocardial strain analysis using cine MRI.

Usefulness of MRCA

1. Indications for MRCA and the diagnostic capabilities

We have been employing MRCA since the installation of a Vantage Titan™ 1.5T system (Canon Medical Systems) at Mitsui Memorial Hospital since 2015. At our hospital, MRCA is performed for patients with severe calcification to rule out coronary artery disease, patients of reproductive age, patients whom use of contrast medium is contraindicated due to allergy or impaired renal function,

* MESA: Multi-Ethnic Study of Atherosclerosis

and patients with morphological abnormalities such as coronary artery malformations or coronary artery aneurysms.

Figure 1 shows images of a 66-year-old woman with severe calcification. The calcification scores were 281.5 in the LAD and 168.6 in the LCX, with severe calcification observed in the proximal LAD and LCX #13. Because it was difficult to evaluate the coronary arteries using CTCA, MRCA was performed. In the MRCA images, the coronary arteries were clearly depicted, and it was obvious that the severe calcification in the proximal LAD observed in CTCA images was not associated with stenosis (Figure 1a). On the other hand, significant stenosis was observed in LCX #13 (Figure 1b), and invasive coronary angiography was therefore performed.

Due to the aging population, the number of patients with renal failure is increasing, and about 100 patients start dialysis treatment at our facility every year. One limitation of CTCA is that it involves the use of contrast medium and is therefore contraindicated in patients with renal failure. However, with the introduction of MRCA, which does not employ contrast medium, significant progress has been made in the evaluation of the coronary arteries in such patients.

Figure 2 shows images of a 65-year-old man with end-stage renal failure who was receiving peritoneal dialysis treatment. The calcification score was extremely high (total score of 6447), making it difficult to evaluate the coronary artery lumens with CTCA, and MRCA was therefore performed. In the MRCA images, total occlusion was observed in the proximal RCA, but the distal portion of the RCA was visualized, suggesting the presence of collateral vessels (Figure 2a). In the LAD, significant stenosis was observed at three locations (Figure 2b).

In SPECT images, perfusion defects in the RCA segments were observed, suggesting ischemia of the inferior wall at the apex (Figure 3). In invasive coronary angiography performed subsequently, total occlusion was seen in the proximal RCA, and its distal branches were not visualized. As previously observed in the MRCA images, stenosis was found in the LAD with calcification, and jeopardized collateral vessels running toward the RCA were also visualized.

A multicenter study has been conducted to evaluate the diagnostic capabilities of MRCA.[2] In this study, the area under the curve (AUC) was 0.91 for all subjects (n = 127), 0.91 for all vessels evaluated (n = 630), and 0.87 for all segments evaluated (n = 1461). These results indicate that MRCA can provide reliable diagnostic information. The diagnostic capabilities of MRCA and the image quality scores were also assessed in subjects with a heart rate of 70 bpm or higher and subjects with a heart rate of less than 70 bpm. Although the results showed differences between these two groups in the visualization of RCA #1 and #2, the diagnostic capabilities were found to be equivalent for other vessels. For subjects with a BMI of 25 or higher, no differences were found in diagnostic capabilities, although motion of the diaphragm sometimes affected the image quality. In a study that evaluated the diagnostic capabilities of MRCA in 19 patients with severe coronary artery calcification (with an Agatston score of 600 or higher), in whom invasive coronary angiography is considered the gold standard, the results showed that MRCA was able to achieve higher specificity and diagnostic accuracy than CTCA.[3] Based on the results of this study, it can be said that MRCA can serve as a useful complement to CTCA.

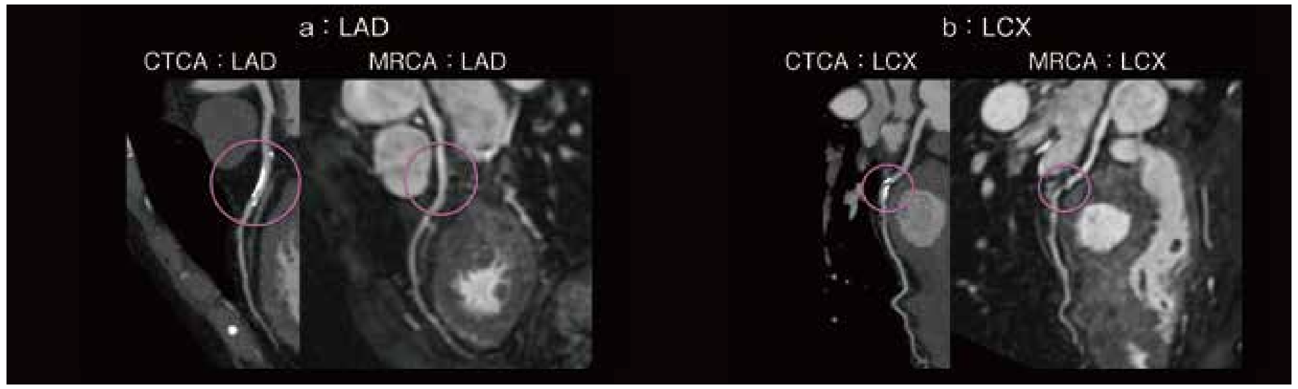


Figure 1 Usefulness of MRCA in a patient with severe calcification.

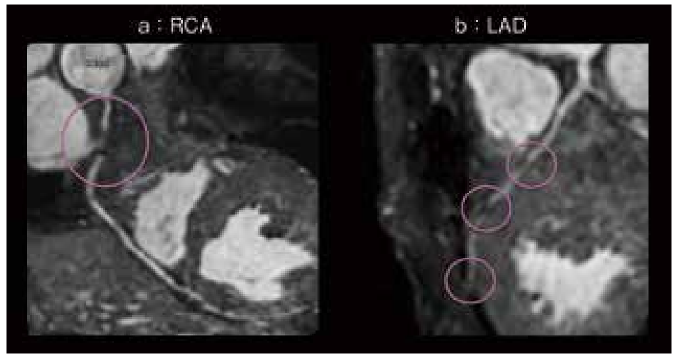


Figure 2 Usefulness of MRCA in a patient with end-stage renal failure.

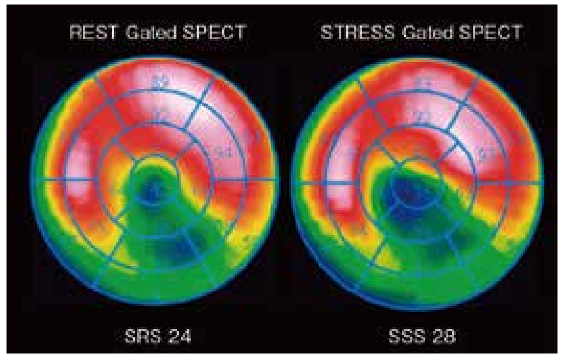


Figure 3 SPECT images of the same patient as in Figure 2.

2. MRCA for patients with next-generation bioresorbable vascular scaffold (BVS) stents

One of the challenges that is often encountered in the clinical use of MRCA is that it is difficult to assess areas inside a bare-metal stent (BMS) or a drug-eluting stent (DES). However, in December 2016, a BVS stent manufactured by Abbott was introduced for sale in Japan. The BVS stent (which is also referred to as a "dissolvable stent") is composed of lactic acid polymers. It breaks down and dissolves 2 or 3 years after placement in the vessel, leaving only platinum markers at both ends. Because these platinum markers can cause artifacts in CT images, there has been increasing interest in employing MRCA for follow-up examinations. In MR images acquired using 3D TSE and 3D FLASH, the scaffold composed of lactic acid polymers could be clearly visualized, and MRCA images comparable to CAG images were obtained.[4]

Figure 4 shows images of a typical patient at our hospital, where a clinical trial to evaluate BVS stents is currently being conducted.[1] This patient was a 48-year-old man with a myocardial infarction. He had a past medical history and a family history of diabetes, hyperlipidemia, and hypertension, and visited our hospital in 2010. In this patient, a BMS was placed in the infarcted region, and a BVS stent was then placed in the stenotic region of LCX #13 with a luminal stenosis of 90%. About 18 months after the procedure, the patient complained of chest pain, and ECG abnormalities were noted. CTCA was performed, but it was not possible to evaluate the region where the BVS stent was placed. MRCA was therefore performed. In Figure 4, images a and b were obtained using invasive coronary angiography: image a shows the stenotic region in LCX #13, and image b shows the same region after placement of the BVS stent (3.0 mm × 18 mm). In images c and d acquired using CTCA, blooming artifacts are observed at the locations of the platinum markers, interfering with accurate evaluation. On the other hand, image e and f acquired using MRCA are unaffected by the presence of the platinum markers of the BVS stent, making it possible to confirm that restenosis has not developed.

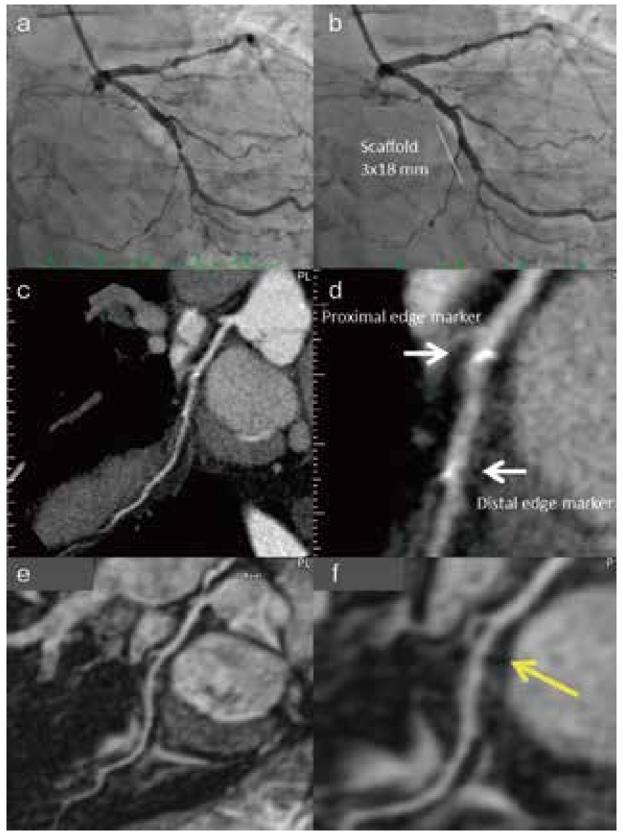


Figure 4 Comparison of visualization of the coronary artery lumen after placement of a BVS stent.

a, b: Images obtained using invasive coronary angiography.
c, d: CTCA images. e, f: MRCA images.
MRCA allows the coronary artery lumen to be evaluated in the segment where the BVS stent has been placed.

As discussed above, MRCA can be used to evaluate patients in whom CTCA is difficult or impossible to perform, such as patients with severe calcification, renal failure, or other contraindications to the use of contrast medium. MRCA is unaffected by the patient's heart rate or body habitus, and it is comparable to CTCA in terms of its diagnostic capabilities. In addition, new findings suggest that MRCA can be used for follow-up examinations after placement of a BVS stent. These features of MRCA clearly demonstrate its usefulness for evaluating the coronary arteries.

Clinical Usefulness of Myocardial Strain analysis with Cine imaging

1. Myocardial Strain analysis in echocardiographic images

The myocardium consists of three layers, and the movements of each of these layers is responsible for the complex movements of the heart. Each myocardial fiber moves in a different direction, such as the longitudinal direction (longitudinal strain), the circumferential direction (circumferential strain), or the radial direction (radial strain), in such a manner that the entire heart contracts toward its center (Figure 5). Visualizing these complex movements in order to evaluate the myocardium has long been a challenge. We therefore performed myocardial strain analysis.

In the myocardial strain analysis algorithm, myocardial function can be evaluated based on the amount of strain of the myocardial fibers. The concept is based on a method employed in echocardiography.
In echocardiography, the endocardium and epicardium are traced to extract the myocardium. The system then analyzes the movements of the myocardium during the cardiac cycle and calculates the movement distance using the following formula:

$$Strain\,(\varepsilon) = \frac{\Delta L}{L0} \times 100\%$$

In echocardiographic images, the amount of strain can be measured using a method known as speckle tracking echocardiography (STE). In particular, longitudinal strain is the most important factor. In patients with angina, longitudinal strain gradually decreases due to functional impairment of the endocardium, which is followed by reductions in circumferential strain and radial strain. In 2D echo imaging, strain analysis can be performed as shown in Figure 6. A lower negative peak in the strain curve indicates better myocardial function in the corresponding segment. In patients with cardiac diseases such as ischemic heart disease, the strain curve of an affected segment becomes shallow and bimodal.

When I was studying in the United States, I was involved in a clinical study on myocardial strain analysis based on the data obtained in the CARDIA study.[5] The CARDIA study is a cohort study which was initiated in 1985 and followed various cardiovascular risk factors such as blood pressure in healthy young adults 18 to 30 years of age until they reached 43 to 55 years of age. The objective of my research was to investigate the effects of the cumulative blood pressure on the myocardium.[6] In 2015, the results of my study were reported by 66 media outlets, including *The New York Times*. In this study, blood pressure values were measured regularly in about 3500 subjects 18 to 30 years of age, and the correlation between the cumulative blood pressure and systolic dysfunction (defined as a left ventricular ejection fraction [LVEF] of 50% or less) and the correlation between the cumulative blood pressure and diastolic dysfunction were evaluated by calculating the AUC. The results did not show a correlation between the cumulative blood pressure and systolic dysfunction, but they did show a correlation between the cumulative blood pressure and impaired diastolic function. Myocardial strain analysis was then performed to evaluate both systolic and diastolic function. The subjects were divided into 10 groups based on their cumulative blood pressure. Compared to the reference group (the group with the lowest cumulative blood pressure, in which the systolic blood pressure was 85 to 99 mmHg), the group with the highest cumulative blood pressure showed no statistically significant difference in the LVEF (Figure 7). However, the results of myocardial strain analysis showed that myocardial function began to decline at a normal or high-normal cumulative blood pressure, with a significant decrease observed in longitudinal strain. Similar findings were obtained for the diastolic phase: a lower cumulative blood pressure was associated with better myocardial function, and a normal or higher cumulative blood pressure was associated with poor myocardial function. Since around 2008, there have been many reports concerning a variety of parameters obtained by myocardial strain analysis and their relationships with cardiac function. In a report on the usefulness of myocardial strain analysis as compared to LVEF measurement in patients with heart failure,[7] the AUC values were 0.62 for LVEF, 0.69 for global circumferential strain (GCS), and 0.64 for global longitudinal strain (GLS), and it was concluded that myocardial strain analysis is more useful than LVEF measurement. This report further suggested that myocardial strain analysis may prove to be useful for predicting cardiac events in patients with impaired systolic function.

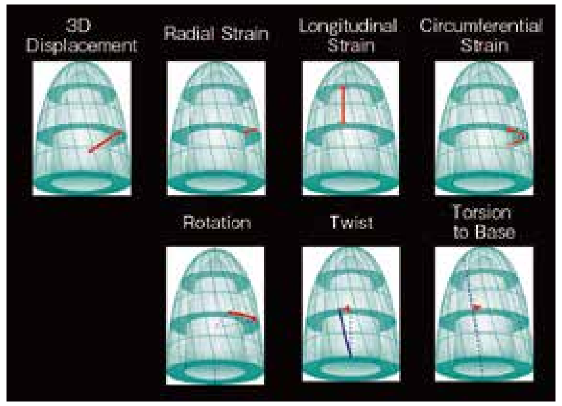


Figure 5 Myocardial deformation (movement of the myocardium).

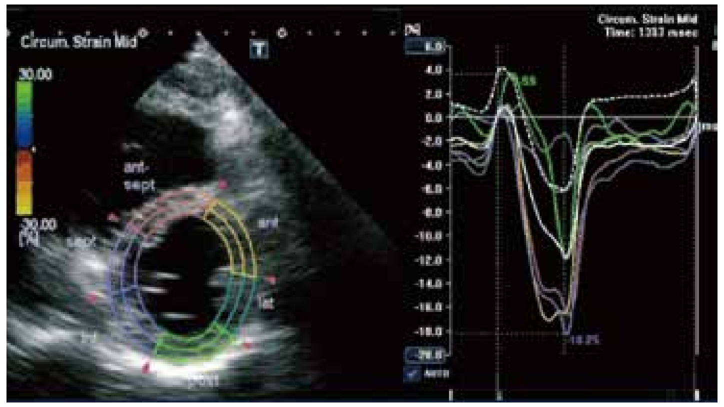


Figure 6 Longitudinal strain analysis in 2D echo imaging.

2. Development of MR-Wall Motion Tracking (MR-WMT) and the clinical usefulness

The Johns Hopkins University has reported the findings of a study on the usefulness of myocardial strain analysis using MRI in clinical patients, including patients who later developed heart failure.[8] Univariate analysis showed a significant difference in outcome for patients with a lower LVEF, suggesting that the LVEF could serve as an index for predicting the onset of heart failure. However, multivariate analysis showed no significant difference for patients with a lower LVEF. On the other hand, multivariate analysis of myocardial strain analysis using MRI showed that strain is an independent prognostic factor for the development of heart failure. When the group with a strain value above the median value was compared with the group with a strain value below the median value, a significant difference in the hazard ratio was observed between the two groups.

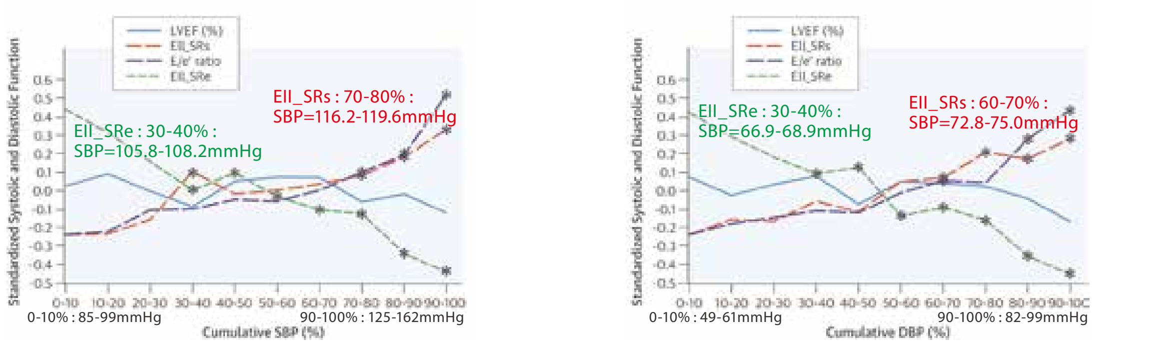
Why is the LVEF less useful than myocardial strain as an index for predicting the onset of heart failure? One hypothesis is that compensatory changes occur during myocardial contraction. Yoneyama et al. performed myocardial strain analysis using tagging MRI to investigate this hypothesis.[9] The results of their study showed that the torsional strain that occurs during contraction helps to compensate for the poor circumferential strain, thus maintaining acceptable radial strain and LVEF. This means that cardiomyopathy can be detected in its early stages by performing myocardial strain analysis rather than by measuring the LVEF.

It should be noted that tagging MRI requires a longer processing time because it involves a number of sequential procedures, including HARP for tag line analysis, DENSE for analysis of pixel displacement, and SENC for analysis of strain in the direction perpendicular to the scan plane.

Dr. Lima and other researchers at the Johns Hopkins University worked together with Canon Medical Systems to develop software known as "MR-WMT" for performing myocardial strain analysis using cine MRI. This software was introduced asa new application for Vitrea™, a medical image processing workstation manufactured by Canon Medical Systems (Figure 8).

In MR-WMT, the inner and outer surfaces of the myocardial wall are traced on the cine MRI image in the same manner as in echocardiography, and the specified

The subjects were divided into 10 groups based on their cumulative blood pressure over a period of 25 years, and each group was compared against the reference group (0-10%).



*: p<0.05 vs. the 0-10% group. Ell = Longitudinal strain

The degree of myocardial injury is reflected earlier in the strain values than in the LVEF or E/e' ratio.

Figure 7 Myocardial strain analysis for evaluation of systolic and diastolic function (excerpted from Reference 5).

myocardium is automatically tracked to allow its motion to be observed (Figure 9). Helle-Valle et al. compared tagging MRI images against cine MRI images processed using MR-WMT and found that smoother strain curves could be obtained from the images processed by MR-WMT.[10]

In strain analysis of areas enhanced in late gadolinium enhancement (LGE) imaging in a patient who had suffered a myocardial infarction, the strain thresholds were found to be lower in the late-enhanced interventricular septum,[11] indicating that the strain parameter values were lower in the infarcted areas than in normal areas.

Cine MRI images of the same patient as in Figure 2, who had severe calcification and renal failure, were also acquired, and myocardial strain analysis was performed using MR-WMT. The strain values were found to be lower in the ischemic RCA area (Figures 10, 11).

As discussed above, myocardial strain analysis using non-invasive MRI provides superior spatial resolution as compared to echocardiography and is useful for cardiac function analysis in patients with ischemic heart disease as well as other diseases associated with phase differences. Although conventional myocardial strain analysis using tagging MRI is useful for quantitative cardiac function analysis, it involves complicated and time-consuming imaging procedures and data processing. Myocardial strain analysis using MR-WMT is a simple method that can be completed in a shorter time as compared to the conventional method. This means that cardiac function analysis can now be performed in routine clinical practice, and the results obtained can serve as useful indices for risk stratification in patients with heart failure.

Summary

The diagnostic capabilities of MRCA are comparable to those of CTCA, and it can be used to evaluate the coronary arteries in patients who cannot be examined using CTCA. In addition, MRCA can be used to evaluate patients after placement of a next-generation BVS stent.

In myocardial strain analysis using MR-WMT, analysis can be performed easily using cine MRI images in routine clinical practice. This new approach in myocardial strain analysis enables the quantitative evaluation of cardiac functional impairment that may not be reflected in changes in the LVEF, allowing the patient's prognosis to be assessed with greater accuracy.

Figure 8 MR-WMT screen on the Vitrea workstation.

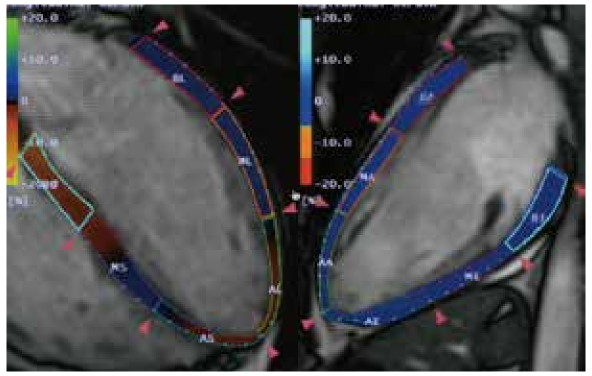


Figure 9 Myocardial strain analysis using cine MRI.

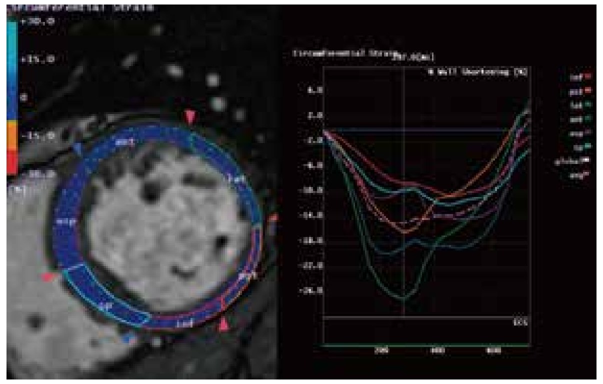


Figure 10 MR-WMT - Circumferential strain in the same patient as in Figure 2 (with severe calcification and renal failure).

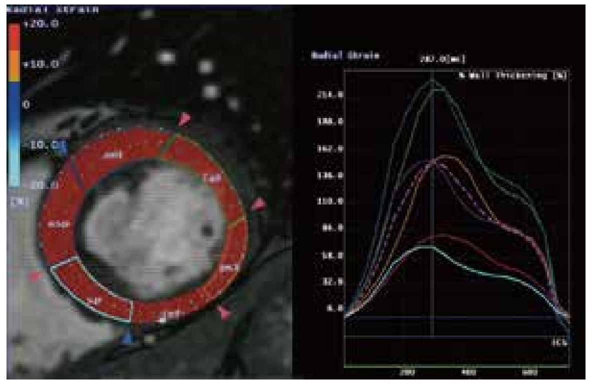


Figure 11 MR-WMT - Radial strain in the same patient as in Figure 2 (with severe calcification and renal failure).

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