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CASE REPORT
Cardiac imaging

Non-lipid-rich low attenuation plaque with intraplaque haemorrhage assessed by multimodality imaging: a case report

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Background The lipid-rich necrotic core is a major pathological hallmark of acute coronary syndrome. Low attenuation plaque (LAP) on coronary computed tomography angiography (CCTA), defined as plaque CT attenuation of <30 Hounsfield units, is commonly believed to correspond to the lipid component. This report presents a non-lipid-rich LAP with intraplaque haemorrhage of the left main coronary artery (LM), as assessed by CCTA, near-infrared spectroscopy (NIRS), and non-contrast magnetic resonance imaging (MRI) using coronary atherosclerosis T1-weighted characterization with integrated anatomical reference technique, recently developed by our group.

Case summary A 75-year-old woman presented with chest discomfort on exertion. Coronary computed tomography angiography revealed severe stenosis of the mid-left circumflex coronary artery and minimal stenosis with a large eccentric LM plaque. The LM lesion had an LAP, with a minimum plaque attenuation of 25 Hounsfield units. On non-contrast T1-weighted MRI, a high-intensity plaque with a plaque-to-myocardium signal intensity ratio of 3.02 was observed within the vessel wall, indicating intraplaque haemorrhage. Near-infrared spectroscopy categorized the lesion as non-lipid-rich, with a maximum lipid core burden index in 4 mm of 169.

Discussion Intraplaque haemorrhage is a key feature of plaque instability, which is different from the lipid-rich necrotic core. Non-contrast T1-weighted MRI is ideal for detecting intraplaque haemorrhage with short T1 values. The imaging findings suggest that LAP on CCTA may represent not only lipid-rich plaques but also intraplaque haemorrhage. Magnetic resonance imaging provides a unique insight into plaque vulnerability from a different perspective than lipid assessment. Multimodality imaging, including MRI, facilitates the understanding of complicated plaque morphologies.

Keywords Atherosclerosis • Case report • Computed tomography • Intraplaque haemorrhage • Lipid-rich plaque • Magnetic resonance imaging • Near-infrared spectroscopy-intravascular ultrasound

ESC Curriculum 2.3 Cardiac magnetic resonance • 3.1 Coronary artery disease • 2.1 Imaging modalities • 2.4 Cardiac computed tomography

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Learning points

- Low attenuation plaque (LAP) on coronary computed tomography angiography is not unique to lipid-rich plaque.
- Intraplaque haemorrhage, a different key feature of plaque instability from the lipid, may also appear as LAP on computed tomography.
- Non-contrast T_1-weighted magnetic resonance imaging offers a different perspective on plaque vulnerability from near-infrared spectroscopy and computed tomography, aiding in understanding complicated plaque morphologies.

Introduction

The lipid-rich necrotic core is a major pathological hallmark of high-risk atherosclerotic plaques that are prone to rupture.[1] Low attenuation plaque (LAP) on coronary computed tomography angiography (CCTA), defined as plaque CT attenuation of <30 Hounsfield units, is commonly believed to indicate a lipid-rich plaque.[2,3] This report presents a non-lipid-rich LAP with intraplaque haemorrhage of the left main coronary artery (LM), as assessed by CCTA, near-infrared spectroscopy-intravascular ultrasound (NIRS-IVUS), and non-contrast magnetic resonance imaging (MRI) using coronary atherosclerosis T_1-weighted characterization with integrated anatomical reference (CATCH) technique, recently developed by our group.[4]

Timeline

2010 July	A 66-year-old woman underwent percutaneous coronary intervention on the left circumflex coronary artery and the left anterior descending artery for stable angina pectoris.
2019 October	At the age of 75, she visited her primary care doctor because of recurrence of chest discomfort on exertion.
	Blood tests, electrocardiogram, and echocardiography did not reveal any abnormal findings suggestive of acute coronary syndrome.
2020 November	Coronary computed tomography angiography demonstrated severe stenosis of the mid-left circumflex coronary artery and minimal stenosis of the left main coronary artery (LM) with high-risk plaque features.
	Non-contrast T1-weighted magnetic resonance imaging demonstrated high-intensity signals with a plaque-to-myocardium signal intensity ratio of 3.02 in the LM.
2019 December	*Ad hoc* percutaneous coronary intervention was performed for the mid-left circumflex coronary artery using a drug-eluting stent with near-infrared spectroscopy-intravascular ultrasound guidance.
	The LM lesion showed an eccentric plaque with extensive echo attenuation on grayscale intravascular ultrasound and a maximum lipid core burden index in 4 mm of 169 on near-infrared spectroscopy.
Present	The patient has been free from chest symptoms and cardiac events during the 18 months of follow-up.

Case presentation

A 66-year-old woman with dyslipidaemia and hypertension underwent percutaneous coronary intervention on the left circumflex coronary artery and left anterior descending artery for stable angina pectoris. She regularly received an intermediate dose of statin, a beta-blocker, an angiotensin II receptor blocker, and a $P2Y_{12}$ receptor inhibitor as a life-long single antiplatelet therapy after drug-eluting stent placement. At the age of 75, she visited her primary care doctor due to a recurrence of chest discomfort on exertion. Physical examination showed neither signs of congestive heart failure nor heart murmurs. Troponin I was below the detection limit (<10 pg/mL), and electrocardiography did not show ST-T changes. On echocardiography, left ventricular function was within the normal range, and no valvular disease corresponding to her symptoms was observed.

She was referred to our cardiology outpatient clinic for further work-up. In accordance with recent clinical guidelines that recommend CCTA as the initial investigation in symptomatic patients in whom obstructive coronary artery disease cannot be excluded by clinical assessment alone,[5,6] she underwent CCTA to examine the cause of her symptoms. Coronary computed tomography angiography was performed on a 192-slice dual-source scanner using prospectively ECG-triggered high-pitch spiral acquisition, 100-KV protocol, and body weight and kilovolt-adjusted iodine injection protocol.[7] The radiation dose was 0.9 mSv, and the contrast dose was 43 mL. On CCTA, high-grade stenosis was observed in the mid-left circumflex coronary artery. The LM had a large eccentric mixed plaque, despite minimal luminal narrowing (*Figure 1*). The LM plaque demonstrated high-risk features, including LAP with a minimum of 25 Hounsfield units and positive remodelling.[2] To further assess the high-risk plaque of the LM, non-contrast MRI was performed on a 1.5-T scanner using the CATCH technique (details in the Supplementary material online). CATCH MRI acquires whole-heart dark-blood T_1-weighted plaque images and bright-blood anatomical reference images simultaneously, allowing perfectly matched fusion images without any additional image registration steps (*Video 1*).[4] *Figure 2* displays the CATCH MR images. Bright-blood coronary MR angiography showed minor luminal narrowing of the mid-shaft of the LM. High-intensity signals with a plaque-to-myocardium signal intensity ratio (PMR) of 3.02 were observed on dark-blood T_1-weighted imaging. The fusion image confirmed that the high-intensity signals were located within the LM wall, indicating intraplaque haemorrhage. Taking the high-risk imaging features into account, the dosage of rosuvastatin was increased from 10 mg to 20 mg daily.

The CCTA findings suggested that the high-grade stenosis of the mid-left circumflex coronary artery accounted for her symptoms. Percutaneous coronary intervention was thus indicated and considering its high probability, dual antiplatelet therapy was initiated.[8] She

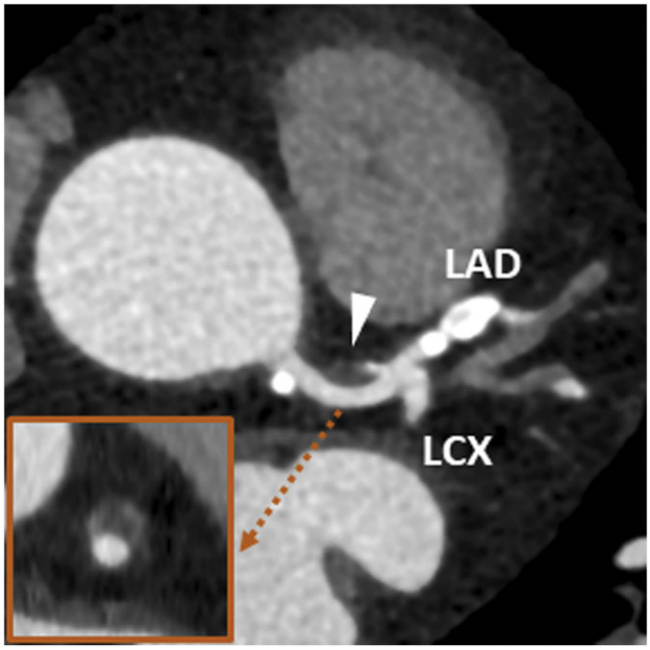
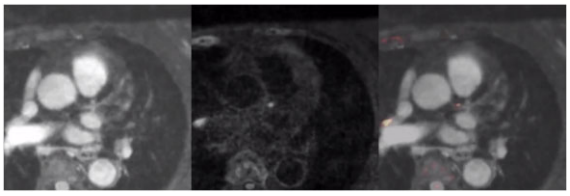


Figure 1 Coronary computed tomography angiography. Longitudinal and cross-sectional views of the multiplanar reformatted images are presented. The left main coronary artery had minimal stenosis with a large mixed plaque and positive remodelling (arrowhead). The minimum plaque attenuation was 25 Hounsfield units. LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery.

was referred to the catheter laboratory for invasive coronary angiography and percutaneous coronary intervention as clinically indicated. In line with the CCTA findings, invasive coronary angiography showed high-grade stenosis of the mid-left circumflex coronary artery and minor luminal narrowing of the LM (*Figure 3*). The mid-left circumflex coronary artery was considered indicated for revascularisation.[8] *Ad hoc* percutaneous coronary intervention using a drug-eluting stent was successfully performed with NIRS-IVUS guidance. *Figure 4* and *Video 2* display the pre-procedural NIRS-IVUS imaging of the LM. At the site with the minimal lumen area (13.8 mm^2), the plaque burden was 70%. Cross-sectional grayscale IVUS images showed an eccentric plaque with extensive echo attenuation and spotty calcification. Meanwhile, the NIRS chemogram categorized the LM lesion as non-lipid-rich, with a maximum lipid core burden index in 4 mm ($maxLCBI_{4mm}$) of 169.

After percutaneous coronary intervention, the patient was free from chest symptoms. Considering the multiple high-risk features of the LM lesion, which might cause a fatal cardiac event, ezetimibe was added to high-intensity statin therapy to further reduce low-density lipoprotein levels. Thereafter, no cardiac events occurred during the 18 months of follow-up.



Video 1 Whole-heart coronary atherosclerosis T1-weighted characterization with integrated anatomical reference magnetic resonance imaging images. Synchronized bright-blood anatomical reference, dark-blood T1-weighted plaque, and fusion images are shown. Note that the bright-blood images and dark-blood images were perfectly matched without any manual registration steps. (Left) Bright-blood anatomical reference images. Minor luminal narrowing was observed in the mid-shaft of the left main coronary artery. (Middle) Dark-blood T1-weighted plaque images. High-intensity signals were observed in the corresponding slice of the left main coronary artery. (Right) Fusion images. Fusion images were created by overlaying the dark-blood T1-weighted images onto the bright-blood anatomical reference images. High-intensity signals were located within the vessel walls. CATCH, coronary atherosclerosis T1-weighted characterization with integrated anatomical reference; MRI, magnetic resonance imaging.

Discussion

Pathological studies associated lipid-rich necrotic core with the acute coronary syndrome.[1] Imaging studies have, therefore, focused on identifying the lipid component. Near-infrared spectroscopy imaging specifically detects lipids within atherosclerotic plaques.[9] Near-infrared spectroscopy-derived $maxLCBI_{4mm}$ is a unique quantitative metric of lipids in atherosclerotic plaques. A minimum threshold of 400 is a reasonable cut-off for defining lipid-rich plaques and/or predicting adverse coronary events.

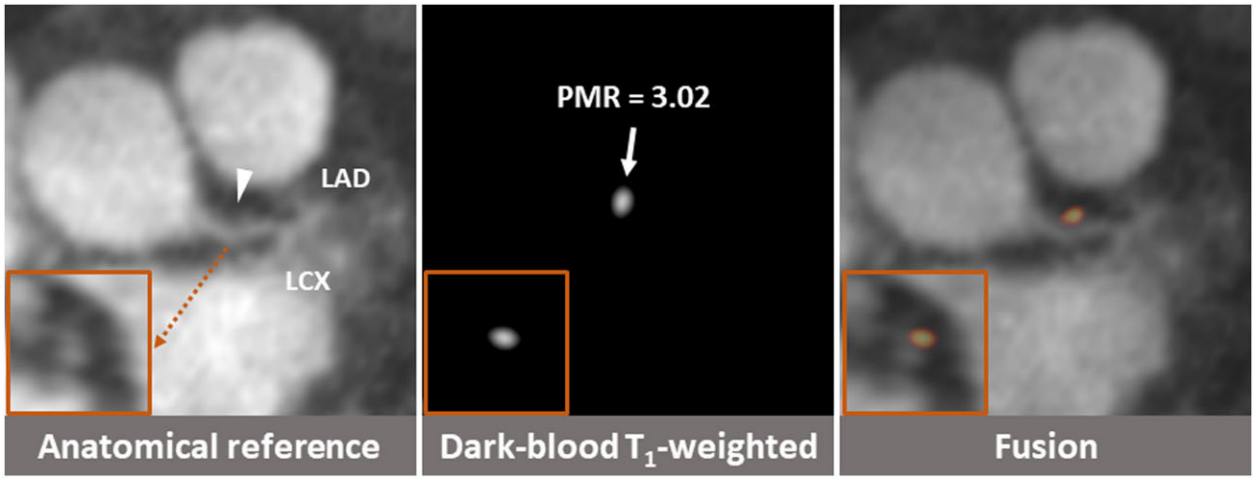


Figure 2 Coronary atherosclerosis T_1-weighted characterization with integrated anatomical reference magnetic resonance imaging. Longitudinal and cross-sectional multiplanar reformat images of non-contrast coronary atherosclerosis T_1-weighted characterization with integrated anatomical reference magnetic resonance imaging are displayed. On bright-blood coronary magnetic resonance angiography (left), minor luminal narrowing was observed in the mid-shaft of the left main coronary artery (arrowhead). The corresponding lesion on dark-blood T_1-weighted plaque imaging (middle) had high-intensity signals. Plaque-to-myocardium signal intensity ratio was 3.02. On the fusion image, the high-intensity signals were localized within the vessel wall. CATCH, coronary atherosclerosis T_1-weighted characterization with integrated anatomical reference; MRI, magnetic resonance imaging; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; PMR, plaque-to-myocardium signal intensity ratio.

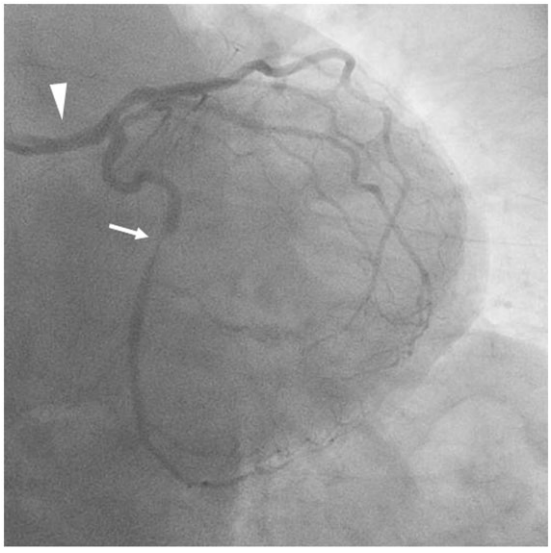


Figure 3 Invasive coronary angiography. Coronary angiogram demonstrated significant stenosis of the mid-left circumflex coronary artery (arrow) and minor luminal narrowing of the left main coronary artery (arrowhead).

Intraplaque haemorrhage is another key feature of plaque instability.[10] Following intraplaque haemorrhage, lipid-rich membranes from extravasated erythrocytes contribute to free cholesterol accumulation and macrophage infiltration within the plaque, triggering lipid-rich necrotic core enlargement.[10] Non-contrast T_1-weighted MRI is ideal for detecting intraplaque haemorrhage[11] because it is highly sensitive to methaemoglobin with short T_1 values that are contained in recent haemorrhage or thrombus.[12] In the coronary artery, high-intensity plaques defined as PMR ≥1.4 are associated with subsequent coronary events.[13] From a histopathological point of view, the categorical disagreement between a lipid-rich plaque on NIRS and a high-intensity plaque on T_1-weighted MRI is not surprising. Intraplaque haemorrhage occurs even in earlier lesions with less lipids, as well as in late fibroatheromas with a lipid-rich necrotic core. Even with a low to intermediate $maxLCBI_{4mm}$, a high PMR may portend plaque instability.

While the use of intracoronary imaging is limited to specific patient populations who undergo percutaneous coronary intervention, non-invasive imaging can be applied to a wide range of populations. Recent developments in CT technology have improved image quality and reduced radiation exposure. The updated National Institute for Health and Care Excellence guideline advocates the use of CCTA as first in line in the investigation of all patients suspected to have angina or silent myocardial ischaemia, irrespective of pre-test probability.[5] Low attenuation plaque is a major criterion of high-risk plaques on CCTA.[2] Autopsy studies revealed that lipid-rich necrotic cores appeared as LAP on CCTA, and the term 'LAP' has been used as a synonym of 'lipid-rich necrotic core' or 'lipid-rich plaque'.[2,3] Nonetheless, the discordance between NIRS (non-lipid-rich) and CCTA (LAP) questions whether LAP is always linked to the lipid. Although the CT features of coronary intraplaque haemorrhage are yet to be well understood, the imaging findings of this case suggest that intraplaque haemorrhage also appears as LAP, regardless of the lipid. In the carotid artery, both a lipid-rich necrotic core and intraplaque haemorrhage show similarly low CT attenuation; therefore,

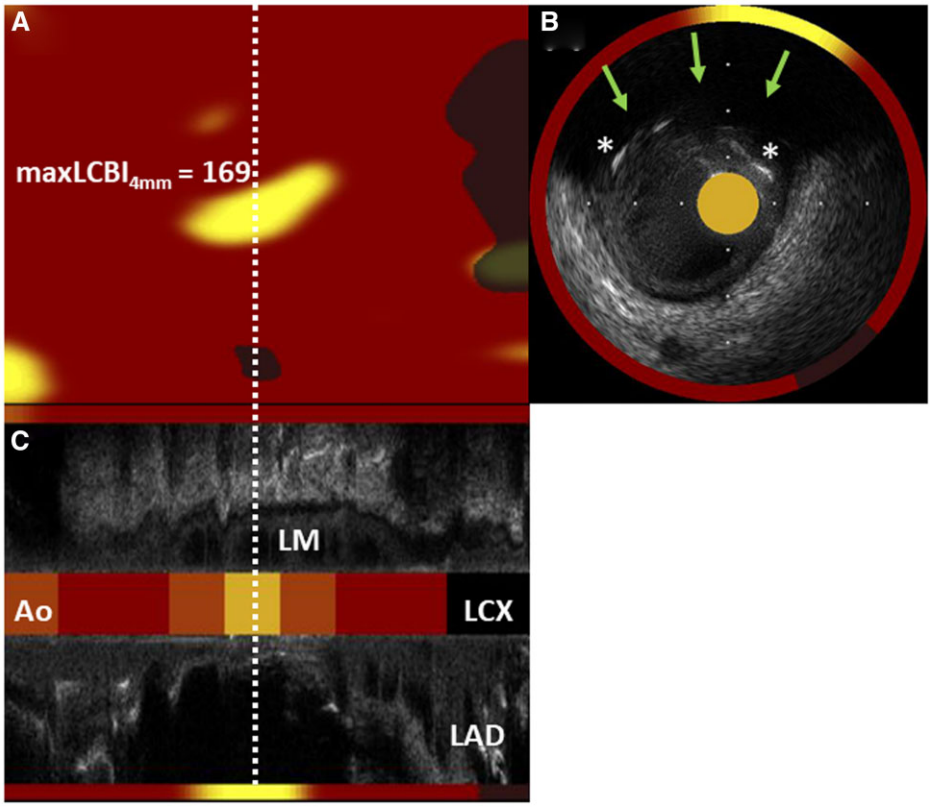


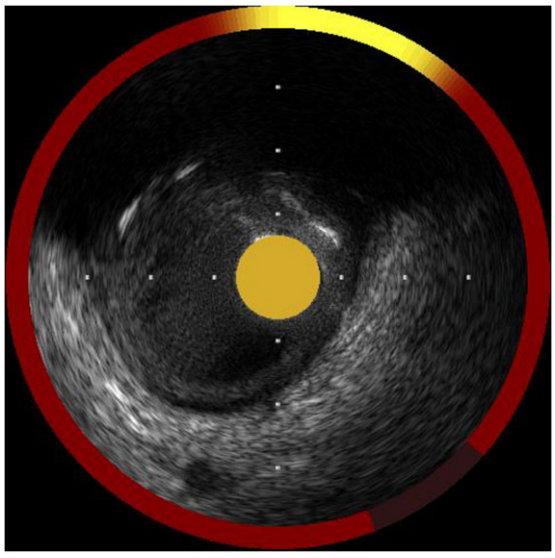
Figure 4 Near-infrared spectroscopy-intravascular ultrasound. Pre-procedural near-infrared spectroscopy-intravascular ultrasound imaging is shown. (*A*) Near-infrared spectroscopy chemogram. The near-infrared spectroscopy chemogram categorized the left main coronary artery lesion as non-lipid-rich ($maxLCBI_{4mm}$, 169). (*B*) Grayscale intravascular ultrasound longitudinal view. A longitudinal view of grayscale intravascular ultrasound image from the left circumflex coronary artery through the left main coronary artery is shown. (*C*) Grayscale intravascular ultrasound cross-sectional view. An intravascular ultrasound cross-section with $maxLCBI_{4mm}$ showed an eccentric plaque with echo attenuation (green arrows) and spotty calcification (asterisks). LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; $maxLCBI_{4mm}$, maximum lipid core burden index in 4 mm; NIRS-IVUS, near-infrared spectroscopy-intravascular ultrasound.

CCTA cannot discriminate between the two components.[14] Non-contrast T_1-weighted MRI in combination with CCTA yields complementary pathophysiological information on complicated coronary plaques. Without involving ionizing radiation or contrast media, CATCH MRI can be readily applied in daily clinical practice as a risk-free option for detecting coronary intraplaque haemorrhage. The combined use of CCTA and MRI could improve the predictive ability for adverse cardiac events. Despite the association of LAP with subsequent cardiac events, the reported positive predictive value remains limited.[15] Based on previous literature, HIP on T_1-weighted MRI is more frequently associated with adverse cardiac events than LAP on CCTA.[13,15] MRI may facilitate new preventive strategies for coronary events from a different perspective than lipid assessment, on which the cardiovascular science community has long focused.

This case illustrates the potential of multimodality imaging, including MRI, for characterizing complicated coronary plaques. Non-contrast T_1-weighted MRI provides a unique insight into plaque vulnerability from the standpoint of intraplaque haemorrhage, not the lipid, aiding in understanding complicated plaque morphology.

Lead author biography

Dr Hidenari Matsumoto graduated from Kobe University Graduate School of Medicine, Japan in 1994 and obtained a PhD at the Division of Cardiovascular Medicine, Kobe University Graduate School of Medicine in 2004. He is a cardiologist at the Division of Cardiology, Showa University School of Medicine and specializes in interventional cardiology and non-invasive cardiac imaging. He has published in the field of computed tomography, MRI, intracoronary cardiac imaging, and coronary physiology. His current research interests are standardizing non-invasive coronary plaque characterization.



Video 2 Near-infrared spectroscopy intravascular ultrasound. Automated pullback was performed from the left circumflex coronary artery through the left main coronary artery. Grayscale intravascular ultrasound demonstrated an eccentric mixed plaque with extensive echo attenuation. IVUS, intravascular ultrasound; NIRS, near-infrared spectroscopy.

Supplementary material

Supplementary material is available at *European Heart Journal—Case Reports* online.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text was obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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