for the global estimate, and increased for the segmental estimates for all SSFP estimates (5% vs. 9%, respectively). The variability between masked and original SSFP estimates was largest for ExMyo and Contour estimates.

Through-plane motion is likely to introduce errors in strain. Because tags are created orthogonal to the image plane, the tagging strain estimate is more robust to through-plane motion. A 3-dimensional analysis may give better agreement between untagged and tagged estimates. Limitations include differences in slice thickness (6 mm for SSFP and 8 mm for tagging), which may give rise to small differences in strain. Masking the myocardium also introduces different endocardial and epicardial image edge features, which may influence the feature tracking results. However, Figure 1B shows that the Myo mask did not significantly change segmental estimates.

Our results support the conclusions that global strain is primarily determined by changes in the circumference, and that features outside the myocardium greatly influence segmental strain estimates. Because the anterior insertion point of the RV free wall into the interventricular septum curves around the left ventricle, through-plane motion gives rise to apparent deformation. Also, relative motions of papillaries and trabeculae give rise to strain artifacts. The pericardium also creates a potential discontinuity between myocardial and extracardiac motion.

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[68Ga]Pentixafor-PET/CT for Imaging of Chemokine Receptor 4 Expression After Myocardial Infarction

Due to the inability of myocytes to regenerate, acute and sustained ischemia usually results in irreversible myocardial damage and subsequent remodeling processes. Chemokine receptor 4 (CXCR4)/stromal cell-derived factor (SDF)-1α play a pivotal role in the recruitment and homing of stem and progenitor cells to the infarct zone (1). Prolonged myocardial SDF-1α expression after infarction has been demonstrated to result in beneficial outcomes (2) Additionally, CXCR4 is normally expressed on various immune cells and therefore is involved in the orchestration of post-infarct inflammation and its resolution (3).

Recently, a radiolabeled CXCR4 ligand ([68Ga] Pentixafor) for positron emission tomography (PET) imaging has been developed (4). This is the first report of noninvasive detection of CXCR4 expression in the human myocardium after acute myocardial infarction.

Seven patients (4 men and 3 women, mean age 62 ± 14 years) with (sub)acute myocardial infarction underwent imaging with cardiac magnetic resonance (CMR) (n = 6) and Pentixafor-PET (all, 126 to 161 MBq/patient) within 5 to 10 days after symptom onset (mean 8 ± 2 days; delay between PET and CMR 1.0 ± 0.5 days). All patients gave written informed consent before imaging. Static PET scans were acquired 60 min post-injection using an integrated PET/computed tomography (CT) scanner (Siemens Biograph mCT 64, Siemens, Knoxville, Tennessee). CMR was performed on a 1.5-T scanner (Achieva 1.5T, Philips Healthcare, Best, the Netherlands) including steady-state free precession cine, T2-weighted turbo spin echo, and multishot inversion recovery turbo field echo sequences.

Images were first inspected visually. For quantification of increased tracer uptake, a visual score using the terms mild, moderate, and intense was employed. Affected areas were documented using the 17-segment American Heart Association heart model. For semiquantitative analysis, a 15-mm circular region was placed over the infarcted areas to derive maximum standardized uptake value (SUVmax) and
mean standardized uptake value ($SUV_{\text{mean}}$). For reference, a second region of interest (diameter of 15 mm) was placed in a remote region of the left ventricular wall. Signal-to-background ratios were calculated.

Acute myocardial infarction was diagnosed by elevated cardiac enzymes, ST-segment elevations, and coronary angiography. The left anterior descending coronary artery was affected in 5 patients, and the right coronary artery, in 2 subjects. All patients were on antihypertensive medications (including beta-blockers, hydrochlorothiazide, and calcium channel blockers) and underwent mechanical revascularization within 20 h after symptom onset. On CMR, infarcts comprised 7% to 30% of the myocardium; left ventricular ejection fractions ranged from 37% to 67%.

Pentixafor-PET was visually positive in 3 of 7 patients (CMR available in 2 of 3). Overall, retention of the radiotracer was rated mild (5 segments) or moderate (5 segments). No segment was rated intense. CXCR4-PET and CMR were concordantly positive in 9 of 10 segments with no PET-positive, CMR-negative segments (Figure 1). The remaining 4 patients did not show increased tracer accumulation.

Of note, there was no substantial difference between the “positive” (days 5, 8, and 8) and “negative” (days 6, 8, 9, and 10) patients regarding the timing of imaging after onset of clinical symptoms.

$SUV_{\text{mean}}$ in infarced areas ranged from 2.0 to 3.3, and $SUV_{\text{max}}$ from 2.1 to 3.7, respectively. The $SUV_{\text{mean}}$ and $SUV_{\text{max}}$ ratios of lesion to remote myocardium were 2.1 ± 0.2 and 2.0 ± 0.4, respectively. Median troponin T and maximum creatine kinase levels were 2,106 pg/ml (range 1,285 to 13,058 pg/ml) and 1,065 U/l (range 631 to 3,570 U/l) in PET-positive patients compared with 670 pg/ml (range 36 to 1,936) and 538.5 U/l (range 386 to 1,933 U/l) in PET-negative subjects.

This is the first report to our knowledge of in vivo imaging of CXCR4 in the human heart after myocardial infarction. Enhanced chemokine expression could be observed in 3 of 7 patients, with tracer uptake 2-fold higher in the infarcted myocardium as compared with remote myocardium. Of note, PET-positive patients presented with higher troponin and creatine kinase levels than negative subjects. One might speculate that increased myocardial damage with hypoxia leads to CXCR4 up-regulation in order to initiate healing processes of the damaged myocardium (5). Interestingly, 4 patients proved Pentixafor negative in the presence of acute myocardial damage on CMR.

However, given the very limited number of observations, as well as the lack of histological proof, no final conclusions can be drawn yet, especially as the true source of the signal detected by Pentixafor-PET has not been identified yet. In general, both hematopoietic stem cells and neutrophils are potential cellular origins. Neutrophils are known to outnumber hematopoietic progenitors in acutely inflamed myocardium and may therefore be the likely source of the imaging signal. However, the timing of PET was somewhat late (mean 8 ± 2 days after onset of symptoms) because neutrophils are thought to dominate very early. Additionally, up-regulation of CXCR4 by cardiac myocytes has been demonstrated to occur after 36 to 48 h after acute infarction (5). Future studies including serial imaging starting at earlier time points are warranted.
Although the data would benefit from corroboration, further pre-clinical support is prevented by high specificity of the tracer for the human CXCR4, limiting all investigation to the human setting. New ligands enabling experiments in another species are not yet available.

In summary, this first proof-of-concept investigation demonstrates the general possibility to examine and quantify alterations in CXCR4 receptor density after myocardial infarction by means of Pentixafor-PET/CT.

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Evidence of a Direct Effect of Myocardial Steatosis on LV Hypertrophy and Diastolic Dysfunction in Adult and Adolescent Obesity

Previous studies have shown that myocardial steatosis occurs with age, diabetes, and the metabolic syndrome and that myocardial triglyceride content (MTGC) is related to concentric left ventricular hypertrophy (LVH) (1) and diastolic dysfunction (2), suggesting a direct negative effect on the heart. Despite this, whether a relationship between MTGC, concentric LVH, and diastolic function exists in obesity per se is unclear and in childhood obesity remains unknown.

¹H-magnetic resonance spectroscopy (¹H-MRS) is a technique that can measure MTGC noninvasively (3). We used ¹H-MRS and cardiovascular magnetic resonance imaging to explore the relationship between increasing body fat and MTGC; the relationship between MTGC, LVH, and diastolic dysfunction; and whether any changes were present in an adolescent population.

A total of 128 adult subjects (71 female; body mass index [BMI], 18.5 to 53.0 kg/m²) and 22 male adolescents (10 to 15 years of age, BMI percentile 8 to 100) underwent ¹H-MRS and left ventricular (LV) studies, as previously described (4,5). Total body fat content (DXA, GE Lunar system, GE Healthcare, New York, New York) and abdominal visceral fat mass (fourth/fifth lumbar water-suppressed turbo spin echo) were also assessed. Age, BMI, systolic blood pressure (SBP), and diastolic blood pressure were similar in men and women. All subjects were normotensive (adults, 121 ± 11/74 ± 8 mm Hg; children, 113 ± 13/67 ± 10 mm Hg), normoglycemic (adults, 5.0 ± 0.5 mmol/l; children, 4.8 ± 0.6 mmol/l), and normcholesterolemic (adults, 5.1 ± 0.8 mmol/l; children, 3.9 ± 0.5 mmol/l). The mean homeostatic model assessment of insulin resistance (HOMA-IR) was 2.7 ± 1.3 (adult population). All subjects had normal LV ejection fraction (>58%).

In adults, although MTGC was positively correlated with all measures of obesity (BMI, r = 0.59; visceral fat, r = 0.46; total fat, r = 0.60; females; BMI, r = 0.53) (Figure 1), only total fat mass (+0.013%/kg fat, p < 0.001) was an independent predictor of MTGC. No sex difference in the regression coefficient for the associations of obesity with MTGC was seen. In adolescents, MTGC was also positively correlated with BMI percentile (r = 0.45, p = 0.035).

Increasing BMI was associated with LV cavity dilation in both males (r = 0.32, p = 0.014) and females (LV end-diastolic volume, r = 0.39, p < 0.001). In contrast, with increasing BMI, concentric LV remodeling was only seen in males (LV mass, volume ratio; r = 0.44, p = 0.01) and was positively correlated with MTGC (r = 0.39, p = 0.003), a relationship that remained after adjustment for SBP and HOMA-IR (r = 0.40, p < 0.005). In adolescent male subjects, increasing BMI percentile was not related to cavity dilation (r = 0.32, p = 0.14), but again was positively correlated with indexed LV mass (g/m²², r = 0.54,