A 50-year-old man presented with acute chest pain that had started about 6 hours prior to admission to our emergency department. His resting ECG revealed an ST-elevation myocardial infarction with typical ST-segment elevation in the leads V1 through V4 and reciprocal ST-segment depression. Consequently, immediate coronary angiography was performed and revealed a proximally occluded left anterior descending artery (Figure 1). The left anterior descending artery was recanalized and a bare-metal stent was implanted. Postinterventional blood analysis revealed a peak total creatine kinase level of 2962 U/L (normal, <190 U/L), a peak creatine kinase–muscle-brain type level of 231 U/L (normal, <25 U/L), a peak high-sensitivity troponin T level of 5705 pg/mL (normal, <14 pg/mL), and a slightly elevated N-terminal pro-brain natriuretic peptide level of 882 pg/mL (normal, <450 pg/mL).

After coronary angiography, the patient was enrolled in an ongoing clinical trial (Non-invasive myocardial inflammation imaging study 2 [NIMINI-2]) that is attempting to evaluate whether myocardial infarct imaging using ultrasmall superparamagnetic iron oxide nanoparticles (USPIO) and multiparametric cardiovascular magnetic resonance (CMR) techniques allow an improved characterization of infarct as well as peri-infarct pathology (compared with conventional gadolinium-based necrosis/fibrosis imaging). Therefore, multiparametric CMR studies were performed before and after intravenous ferumoxytol (Feraheme, a USPIO; 17 mL IV/510 mg Fe) administration.

The first CMR (pre-Feraheme) was performed 3 days after acute presentation with acute ST-elevation myocardial infarction. Serial CMR studies were then performed 6 hours, 24 hours, 48 hours, 96 hours, and 3 months after intravenous Feraheme administration (post-Feraheme). Only the first (pre-Feraheme) and last CMR study (3 months post-Feraheme) comprised additional late-gadolinium enhancement (LGE) images 10 minutes after intravenous administration of a gadolinium-based contrast agent (0.15 mmol/kg Magnevist). Cine-CMR, T2-weighted edema imaging (using a T2-weighted short tau inversion recovery [STIR] black-blood segmented turbo spin echo sequence [T2-weighted STIR-SE]) and T2*-mapping sequences (using a T2*-weighted multiecho/gradient echo sequence) were obtained in all CMR studies. In addition, 3-dimensional magnetic resonance angiography without gadolinium contrast of the aorta was performed (using a breath-hold gradient-echo sequence with time-of-flight technique) at the following time points: 6 hours, 24 hours, 48 hours, and 96 hours after intravenous Feraheme administration.

During the first CMR study, 3 days after acute presentation, LGE images revealed a transmural myocardial infarction in the anterior wall (Figure 2). There were only very small foci of subendocardial dark zones within the infarcted LGE-positive segments indicative of microvascular obstruction. Hyperenhancement, which was not present during the first CMR study prior to Feraheme administration, was observed on the steady-state free precession (SSFP)-cine-CMR images in the region of myocardial infarction and the peri-infarct zone during the second CMR study 6 hours after Feraheme administration (Figure 2 and Movie I in the online-only Data Supplement). The observed hyperenhancement in the region of myocardial infarction and the peri-infarct zone had disappeared 96 hours after Feraheme administration. Global systolic function was only slightly impaired (left ventricular ejection fraction, 57%). Moreover, hyperenhancement and signal void, which were not present during the first CMR study prior to Feraheme administration, were detected in the infarcted myocardium based on T2-weighted STIR-SE and T2*-mapping images, respectively, at CMR 6 hours after Feraheme administration, and had disappeared almost completely 96 hours after Feraheme administration (Figure 2). Last, 3-dimensional magnetic resonance angiography following intravenous Feraheme administration enabled robust visualization of the aorta at 6 hours, 24 hours, and even 48 hours after Feraheme administration (Figure 3 and Movie II in the online-only Data Supplement).

To the best of our knowledge, this is the first case that evaluates the diagnostic value of a USPIO (Feraheme) for in...
vivo CMR imaging in a patient with acute myocardial infarction.1 Our results suggest that USPIO-based contrast agents may open up new vistas in (1) characterization of infarct as well as peri-infarct pathology by causing hyperenhancement in SSFP-cine-CMR images versus hypoenhancement in T2-weighted STIR-SE images and signal void in T2*-mapping images, and in (2) visualization of the aorta by causing bright blood for at least 48 hours after Feraheme administration without the need of correct timing of contrast injection to ensure synchronization between the transit of contrast material and scanning. Three-dimensional magnetic resonance angiography following intravenous administration of Feraheme could become an alternative technique compared with gadolinium-based 3D-magnetic resonance angiography—in particular, in patients with renal disease—for evaluation of aortic diseases such as aortic aneurysm, congenital malformation, (chronic) dissection, and potentially aortitis.

The reason for the observed hyperenhancement in the area of myocardial infarction as well as in the peri-infarct zone in contrast material and scanning.
SSFP-cine-CMR images is, so far, unclear. The SSFP signal depends on T2 as well as T1, unless measures are taken to destroy signal refocusing and to prevent the development of steady-state free precession. In principle, contrast agents such as USPIO decrease both the T1 and T2 relaxation times. Although a decrease in T1 leads to an increase of signal, a decrease of T2 results in signal loss. Hence, in case of a predominant T2 effect of Feraheme, one would expect a hyperenhancement in SSFP-cine-CMR images. However, hyperenhancement was observed in the area of myocardial infarction and the peri-infarct zone in (balanced) SSFP-cine-CMR images. Consequently, a predominant T1 effect has to be assumed. Considering the fact that (1) the r2/r1 relaxation ratio of Feraheme (reflecting the T1/T2 ratio) is 5.9, and thus substantially lower than the T1/T2 ratio of healthy myocardium, which is $\approx 27.0$, and that (2) the intramyocardial concentration of Feraheme is expected to be significantly higher in the area of infarction and the peri-infarct zone (compared with healthy myocardium) as a result of the swelling of the ischemic myocardium caused by acute inflammation, edema, and/or hemorrhage, a substantial decrease of the T1/T2 ratio is expected in the area of myocardial infarction and the peri-infarct zone. Consequently, a decrease of the myocardial T1/T2 ratio comes along with an increasing T1 effect and an increase in signal intensity (while the T2 effect is decreasing).

USPIO-based contrast agents not only allow the accurate detection of the infarct core by causing hyperenhancement in T2-weighted STIR-Se images and signal void in T2*-mapping images, but also possibly enable accurate detection of the peri-infarct zone by causing hyperenhancement in SSFP-cine-CMR images, which is still a difficult challenge with gadolinium-based techniques. Hyperenhancement in T2-weighted STIR-SE images and signal void in T2*-mapping images may reflect different aspects of the infarct core compared with LGE-positive areas in LGE images.

Considering the blood half-life of Feraheme of $\approx 15$ hours, the disappearance of Feraheme–induced effects already 96 hours ($\approx 6 \times$ the blood half-life) after Feraheme administration suggests a direct Feraheme effect. Thus, Feraheme, which is already approved by the Food and Drug Administration for iron replacement therapy in patients with anemia resulting from chronic renal failure, is also an attractive contrast agent for CMR because of its magnetic relaxivity properties. Moreover, in contrast to gadolinium-based contrast agents, there is no renal elimination of Feraheme. Therefore, Feraheme can even be applied to patients with advanced kidney disease (compared with gadolinium-based compounds).

The current case report suggests that a USPIO such as Feraheme may allow (1) noninvasive detection of the region of myocardial infarction and the peri-infarct zone based on a multiparametric CMR approach and (2) noninvasive visualization of the aorta and aortic diseases even in patients with advanced kidney disease. These first results could be of paramount and far-reaching consequences for future developments of USPIO-based contrast agents.

Sources of Funding
This work was supported by a grant from the German Federal Ministry of Education and Research (BMBF; grant No. 01EZ0818, to Dr Yilmaz and Dr Sechtem).

Disclosures
None.

References
First Multiparametric Cardiovascular Magnetic Resonance Study Using Ultrasmall Superparamagnetic Iron Oxide Nanoparticles in a Patient With Acute Myocardial Infarction: New Vistas for the Clinical Application of Ultrasmall Superparamagnetic Iron Oxide

Ali Yilmaz, Sabine Rösch, Handan Yildiz, Siegfried Klumpp and Udo Sechtem

_Circulation_. 2012;126:1932-1934
doi: 10.1161/CIRCULATIONAHA.112.108167

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/126/15/1932

Data Supplement (unedited) at:
http://circ.ahajournals.org/content/suppl/2012/10/05/126.15.1932.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/