Molecular MRI of Thrombosis using Novel Fibrin-Specific Contrast Agent: Initial Results in Humans at 3.0 T

M. Katoh[1,2], A. Wiethoff[3], R. Sparing[4], R. W. Gunther[4], and E. Spuentrup[4]

[1]Department of Diagnostic and Interventional Radiology, University Hospital Saarland, Homburg, Germany, [2]University Hospital RWTH Aachen, Aachen, Germany, [3]Philips Medical Systems, Netherlands, [4]University Hospital RWTH Aachen, Germany

Introduction

Recently, the value of a gadolinium based fibrin-specific contrast agent (EP-2104R; Epix Pharmaceuticals, Cambridge, MA, USA) for molecular MRI of thrombosis has been demonstrated in several animal studies including selective visualization of coronary and carotid thrombosis, pulmonary embolism and thrombi in the left atrium (1-5). In these studies a fairly low dose of the novel fibrin-specific contrast agent allowed for selective and high-contrast delineation of fresh and chronic thrombi at 1.5 T. High-field MRI, however, may be advantageous for molecular MRI due to the basically longer T1 relaxation time of tissue and higher signal output.
In this study, first data in patients for selective visualization of thrombi in variable regions of the cardiovascular system using EP-2104R are presented. The following data are part of a multi-center clinical phase II trial with patients investigated at 3.0 T.

Materials and Methods

Four patients with known thrombus in the heart chambers, carotid arteries or aorta were investigated on a 3.0 T whole-body MR-system (Achieva, Philips Medical Systems, Best, NL) after systemic (i.v.) adminstration of EP-2104R (4.0 µmol per kg body weight). Imaging was performed using a breath-hold or navigator-gated cardiac-triggered fat-suppressed inversion-recovery gradient-recalled-echo (IR-GRE) sequence (heart and aorta) or a RF-spoiled fat-suppressed 3D GRE sequence (carotid artery). Optimal inversion time to suppress the blood signal was determined using a *Look-Locker* sequence. As EP-2104R binds specifically to fibrin, imaging at 3.0 T was performed 24h after contrast agent administration to allow the wash out of the non-bound contrast agent from the blood pool. Images obtained were assessed by to two radiologists in terms of selective contrast enhancement.

Results

MRI at 3.0 T was successfully completed in all four patients without any complications and side effects. All thrombi were selectively visualized with a high contrast to the surrounding tissue and the blood pool. The first patient demonstrated a ventricular thrombus after myocardial infarction at the hypocinetic apex (Fig. 1). The second patient with known carotid artery stenosis showed a thrombus layer on the stenotic lesion (Fig. 2). This patient underwent surgery to prevent cerebral infarction. In the third patient suffering from non-Hodgkin-lymphoma, a new mass at the descending aorta was seen by CT. EP-2104R allowed identification of a thrombus layer covering the mass (Fig. 3). Finally, a thrombus in the left atrial appendage was selectively visualized, and deemed likely to be responsible for the two cerebral infarctions experienced by the patient within the week before imaging (Fig. 4). In this patient, who recently underwent bypass surgery, contrast enhancement was also seen at the pericardium and pleura indicative for a fibrinoid pericarditis and pleuritis, respectively.

Conclusion

Molecular MRI of thrombosis in patients using EP-2104R is feasible at 3.0 T and allows for selective and high-contrast visualization of thrombi. The detection of thrombi may be of high clinical impact, especially in patients with embolic stroke and unknown origin of embolism.

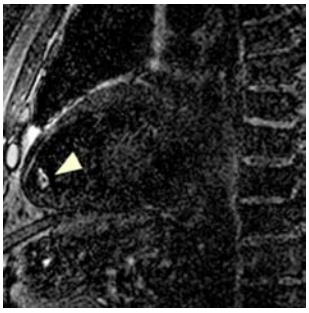

Fig. 1: Ventricular thrombus (arrowhed) at the hypocinetic apex shown in the two-chamber-view.

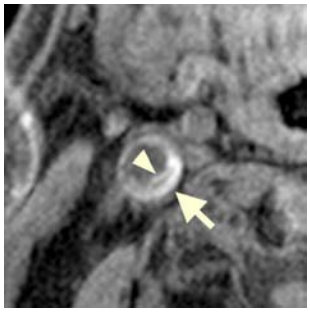

Fig. 2: A thrombus layer (arrowhead) was seen on the surface of the carotid artery stenosis. The arrow indicates additional intraplaque haemorrhage, which is also seen with high signal.

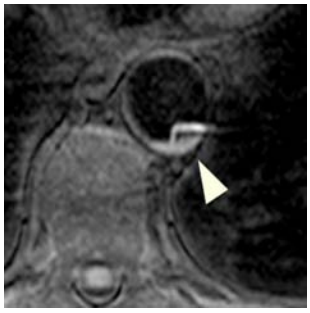

Fig. 3: CT showed a new lesion within the aortic wall. MRI using EP-2104R clearly identified thrombus (arrowhead) attached to the wall.

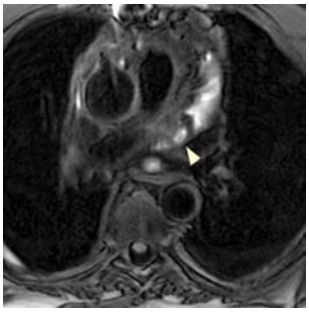

Fig. 4: Thrombus in the left atrial appendage (arrow head). In addition, contrast enhancement was seen at the pericardium, which may represent fibrinoid pericarditis.

1. Botnar RM et al. Circulation 2004
2. Spuentrup E et al. Circulation 2005
3. Spuentrup E et al. Am J Respir Crit Care Med 2005
4. Spuentrup E et al. Circulation 2005
5. Sirol M et al. Circulation 200