# 7 Summary

**Determination of myocardial perfusion and vitality by MRI with P792 in comparison to Gd-DOTA in a pig model after creating an acute myocardial infarction**

Determination of myocardial perfusion and vitality has evolved into a standard procedure of great clinical relevance in evaluating coronary heart disease and its complications.

The aim of the present study was to investigate the potential of the blood pool contrast medium P792 for evaluating myocardial perfusion and vitality by magnetic resonance imaging (MRI) in a pig model. P792 was compared with the low-molecular weight contrast medium Gd-DOTA.

P792 is a macrocyclic blood pool contrast medium with a molecular weight of 6.47 kDa and a diameter of 5.05 nm. It is based on a Gd-DOTA core, which is substituted by four rigid hydrophilic arms. This is why P792 cannot diffuse through capillary walls while it is small enough to be eliminated by the kidneys. Gd-DOTA consists of a gadolinium ion forming a complex with the macrocyclic ligand DOTA. It has a molecular weight of 0.56 kDa and a diameter of 0.9 nm.

Since the R1 relaxivity of P792 (measured at 60 MHz in 37 °C water) is ten times that of Gd-DOTA, P792 was administered at a dose of 13 µmol/kg body weight and Gd-DOTA at 100 µmol/kg body mass. MR imaging was performed on a 1.5 T MRI scanner (Magnetom Sonata).

The animal experiments were performed in ten minipigs (mini LEWE) with a body weight of 20-30 kg. In five animals each, reperfused and non-reperfused myocardial infarction was created in a closed chest manner. The animals were examined by MRI with both contrast media two and three days after induction of infarction. As P792 is still in the early phase of clinical trial, P792 was only used in the animals with non-reperfused myocardial infarction (group 2).

Perfusion imaging was performed with an SR-trueFISP sequence with a TR of 2.83 ms, a TE of 1.1 ms, and a flip angle (α) of 50°. This sequence has a high temporal resolution with three images per cardiac cycle. Vitality was examined with a 2D-IR-FLASH sequence using the following parameters: TR = 5.7 ms, TE = 4.3 ms, α = 25°. Inversion time ranged from 270 to

500 ms. All images were acquired along the short heart axis with ECG triggering and during breath-hold.

Both contrast media investigated generated pronounced late enhancement in infarcted areas. All infarctions showed transmural extension on at least one slice. The onset of late enhancement was significantly later with Gd-DOTA ($p < 0.041$ for group 1 and $p < 0.043$ for group 2). The difference between reperfused and non-reperfused infarction was significant for P792 (22 min vs. 40 min) and for Gd-DOTA (5 min vs. 10 min).

Comparison of infarction volumes measured with the 2D-IR-FLASH sequence during late enhancement demonstrated very good agreement between P792 and Gd-DOTA ($p = 1$). The volumes measured by MRI were smaller as compared with the sizes determined histomorphometrically in TTC-stained sections. The results obtained with the SR-trueFISP sequence showed less good agreement. With regard to the SNRs and CNRs, the differences between both contrast agents were not significant or just barely significant. Altogether, the SNRs and CNRs in the infarcted areas were slightly higher with Gd-DOTA than with P792.

The perfusion studies yielded the following results: The perfusion deficit of the infarcted area was seen as a low-intensity zone immediately after contrast medium arrival with both media investigated and in all animals. With P792, the perfusion deficit was visible throughout the imaging period of 10 minutes. The PSIC curves of the infarcted area and healthy myocardium have a nearly parallel course but approach each other significantly from 30 seconds onwards. The CNR for P792 is markedly lower than for Gd-DOTA (<1 vs. 3.6), which is also confirmed by the more difficult visual analysis. The perfusion deficit is seen more clearly with Gd-DOTA but only for a short period <2 min. The curves of the infarcted area and healthy myocardium cross each other highly significantly at around 140 seconds. At this time, the contrast medium starts accumulating in the infarcted area and the perfusion deficit becomes invisible. There was no good agreement between the areas with reduced perfusion at MRI and the sizes determined histomorphometrically. The sizes determined by MRI were much lower with the diagnostic yield of P792 being slightly better than that of Gd-DOTA.

In conclusion, the blood pool contrast medium P792 is suitable for performing a comprehensive cardiac MRI examination including evaluation of perfusion and vitality. Using P792, the perfusion deficit is visible not only during first pass but also in the equilibrium phase. There is good agreement in infarction sizes determined with P792 and Gd-DOTA during late enhancement.