In Vivo T1 Mapping of Canine Hearts Using Gd(ABE-DTTA) in an Ischemia-Reperfusion Model

P. Kiss1, P. Suranyi1, T. Simor1, 2, N. Saab-Ismail1, 2, A. Elgavish1, 2, L. Hejfel1, 2, G. A. Elgavish1, 2
1University of Alabama at Birmingham, Birmingham, Alabama, United States, 2Elgavish Paramagnetics Inc, Birmingham, Alabama, United States

Synopsis
To determine the level and distribution of the MRI signal enhancement induced by the contrast agent Gd(ABE-DTTA) in myocardial tissue, T1 mapping experiments were carried out using an ischemia-reperfusion model in seven dogs. Exploiting the relatively long tissue life time of this contrast agent, no fast T1 measurement technique was needed. Myocardial perfusion was determined with non-radioactive dye microspheres. Excellent correlation was found between the myocardial perfusion, T1, and wall thickening values in the same areas.

Introduction
Ischemic heart disease is still the leading cause of death in the United States and the western world. Early non-invasive diagnosis and early institution of effective medical or surgical therapy is highly desirable. Magnetic resonance imaging (MRI) has been successfully used for cardiac imaging in the last fifteen years [1]. Gd(ABE-DTTA) induces signal enhancement in well-perfused myocardial tissue for a longer duration than the currently used contrast agents. In our present study, we have quantified its effect in vivo by carrying out cardiac T1 mapping experiments in seven mongrel dogs.

Materials and Methods

Contrast Agent Preparation: Gd(ABE-DTTA) was synthesized as described by Saab-Ismail et al [2].
Canine Preparation: Seven male mongrel dogs weighing 17-19 kg underwent surgical preparation as described in Simor et al [3].

MRI Protocol: The "delayed enhancement" GE sequence, performing a non-selective 180° preparation pulse, was used in our experiments. This provides the maximum dynamic range for determination of T1. Using a variable spin-evolution period (TI = inversion time) a series of images were obtained where signal intensity (SI) values were predominantly T1 weighted. The imaging parameters were: FOV: 200mm, imaging matrix: 192·128, NEX: 1, readout flip: 25°, TE: 5.3ms, TR: 11.4ms. Views per segment: 16, Recycle time: 1500-2000ms (varied according to individual canine heart rate). To reduce saturation, only every third or fourth heartbeat was used as a trigger signal. One short-axis (4 dogs) or one long-axis (3 dogs) slice was imaged, covering the main ischemic area determined by the coronary anatomy of the ligated vessel.

Ischemia-Reperfusion Protocol: After obtaining control MRI images and microsphere administration for the control period, a 30 minute zero-flow ischemia was induced. A second color of microspheres was administered, and late enhancement images and FIESTA movies were obtained. Ischemia was terminated by removing the snare from the LAD.

Data analysis: Images were analyzed with MASS 5.0 (MEDIS, Netherlands). In the short axis images we selected a mid-wall myocardial ring around the LV chamber avoiding epicardial and endocardial artifacts. The entire circumference was divided clockwise into 16 equal segments, starting at the posterior groove. The long axis images were traced for SI-analysis in a similar way, avoiding the epicardial and endocardial areas. The long axis view was divided into 9 segments, one apical and 4 each of anterior and posterior segments.

At the end of the imaging session, tissue samples for regional myocardial perfusion assay using colored microspheres (Triton Technology Inc., San Diego, CA, USA) were harvested by bread-slicing the heart (4 slices) perpendicular to the short axis. Each slice was cut into 4, 8 or 16 segments for digestion and spectrophotometric analysis. Since the entire heart was bread-sliced, it was also possible to reconstruct the MP in the long axis planes for comparison with the long-axis image intensities.

Using the software Origin 6.1 (Originlab Corporation, Northampton, MA, USA) we applied a three-parameter exponential curve fit to obtain T1 values from the TI dependence of the signal intensities.

Results
In 7 dogs, with varying extent of ischemia, abnormal wall motion was detected and T1 values in the ischemic segments (850-910ms) remained close to the control values (1000 ms). In the well-perfused segments myocardial T1 values decreased to 600-650ms due to the paramagnetic effect of the contrast agent administered (Table 1). Data from the myocardial perfusion (MP) assay and the T1-mapping in the 7 ischemic dogs were pooled and correlation analysis was carried out using the statistical package SigmaStat, Version 2.03 (SPSS, Inc). Pearson product moment correlation resulted in a correlation coefficient of 0.729 between MP and 1/T1 values (R=1.68·10-19). Linear regression analysis showed that for the MP=0 extrapolation (i.e., theoretical total ischemia), a 1/T1=1.09s-1 would obtain. This value corresponds well to our experimental finding of 1s-1 for the control 1/T1. These results suggest that the extent of the severity of the ischemia is well represented in the T1 values obtained in the presence of our contrast agent.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>T1, ms</th>
<th>Non-Ischemic Zones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1037.65±20.45</td>
<td>999.73±14.2</td>
</tr>
<tr>
<td>Ischemia</td>
<td>883.74±31.57</td>
<td>621±13.37</td>
</tr>
<tr>
<td>Reperfusion</td>
<td>632.03±9.61</td>
<td>680.94±9.92</td>
</tr>
</tbody>
</table>

Discussion
Gd(ABE-DTTA) is a MRI contrast agent with long lifetime in the myocardial tissue. This special attribute made possible the accurate T1 mapping of myocardium ranging from the ischemic to well-perfused. Significant differences were found between the T1 values of the ischemic vs. non-ischemic regions. These values showed close correlation with the myocardial perfusion and wall thickening data. Thus, Gd(ABE-DTTA) proves well suited to serve as a cardiac MRI contrast agent.

References