Tissue Characterization By Combining Delayed Hyperenhancement And Percent Edema Mapping – A R2-map Based MRI Method In Canine Myocardial Infarction

P. Surányi[1,2], B. Ruzsics[1], P. Kiss[1,2], B. C. Brott[3], T. Simor[1,2], N. H. Saab-Ismail[2], R. A. Baker[4], G. A. Elgavish[1,2]

[1]Biochemistry and Molecular Genetics, University of Alabama at Birmingham, Birmingham, Alabama, United States, [2]Elgavish Paramagnetics Inc., Hoover, Alabama, United States, [3]Department of Medicine, Division of Cardiovascular Disease, University of Alabama at Birmingham, Birmingham, Alabama, United States, [4]Animal Resources Program, University of Alabama at Birmingham, Birmingham, Birmingham, Alabama, United States

INTRODUCTION A Tissue-Characterization-Mapping (TCM) method is introduced here which combines delayed hyperenhancement (DE) and Percent-Edema-Mapping (PEM). The latter is based on changes in transverse relaxation properties of the myocardium due to changing water content over the course of infarct healing, and, where present, due to intramyocardial hemorrhage. TCM can assess the relative extent of edema, necrosis, hemorrhage and mature scar and infarct age.

Elevation of myocardial T2 (i.e. the decrease in R2) has been shown following varying durations of coronary occlusion.[1,2] The decrease in R2 has been correlated with elevated tissue water content which occurs with acute ischemia.[3] Intramyocardial hemorrhage can be a confounder of edema detection, as deoxyhemoglobin and/or methemoglobin induces an increase in R2 in the center of the infarcted region.[4] Thus, it can partly mask the R2-reducing effect of edema. Hemorrhage, however, only occurs in severely injured areas, is always surrounded by necrotic tissue, and does not impede delayed hyperenhancement.[5,6]

PEM Percent Edema Value	DE Enhancement	DIAGNOSIS	COLOR CODE
PE=0	NO	healthy myocardium	
PE>0	NO	acute ischemic injury (edematous, viable)	
PE>0	YES	acute non-hemorrhagic infarct	
PE=0	YES	acute hemorrhagic infarct	
PE<0	YES	chronic maturing scar	

Figure 1. The Tissue-Characterization-Mapping (TCM).

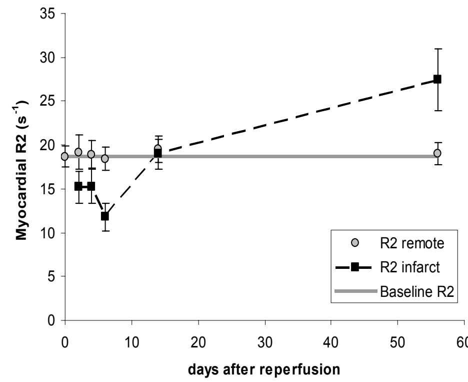

Figure 2. Average R2 values in infarcted regions. Infarct R2 was significantly different from remote R2 throughout the first week. Lowest infarct R2 was detected on day 6 ($11.8\pm1.6s^{-1}$), which represents the peak edema. Edema retreated and R2 retuned to baseline by day 14. Highest R2 was detected in mature scar at 8 weeks ($27.4\pm3.5s^{-1}$). Remote R2 was constant (horizontal line) ($18.7\pm1.2s^{-1}$).

METHODS In dogs (n=6), four days following closed-chest coronary occlusion(180min) and reperfusion, pixel by pixel R2-mapping was carried out. Conventional IR-prepared fast-gradient-echo delayed contrast-enhanced (DE) images were then acquired using 0.05mmol/kg Gd-(ABE-DTTA), an infarct-avid tissue persistent contrast agent.[7,8] Four dogs were sacrificed after this point. Two dogs were followed for eight weeks with repeat R2-maps and were subjected to the TCM imaging protocol at eight weeks using 0.2mmol/kg Gd(DTPA). Six short axis images covered the entire left ventricle. R2-maps were acquired using a double-IR fast-spin-echo sequence during breathholds, with varying echo-times (TE). with the following parameters: FOV/matrix/flip-angle/TE/ETL/inversion-time/recycle-time =300mm/256x256/90°/12-120ms/450ms/24/two cardiac cycles. The image with a TE of 60ms was used as a T2w image. DE imaging parameters were: FOV/matrix/flip-angle/TE/VPS/inversion-time/recycle-time = 300mm/256x256/25°/3.32ms/250-300ms/16/two cardiac cycles. MRI image analysis was semiautomated. The only manual input was tracing the endo- and epicardial contours in all slices. R2 was calculated pixel-by-pixel by nonlinear curve fitting applied to the SI vs. TE dependence. Percent-edema(PE)=100% was defined as the R2 of pure water ($0.27s^{-1}$) and PE=0% was defined as the R2 of intact myocardium ($18.7s^{-1}$). A PE value was calculated for each voxel from the measured R2. Edema yielded positive PE values (increased water content and decreased R2) while mature scar yielded negative PE (decreased water content and increased R2). In acute hemorrhage the R2-decreasing effect of edema was masked by the R2-increasing effect of extravasated blood, and therefore, in these cases, in the center of the infarct normal PE values were obtained. The TCM algorithm is shown in Figure 1. Postmortem, TTC staining was carried out. Hemorrhagic regions observed with TTC-staining as purple-brown spots were verified using hematoxyllin-eosin stained light-microscopy.

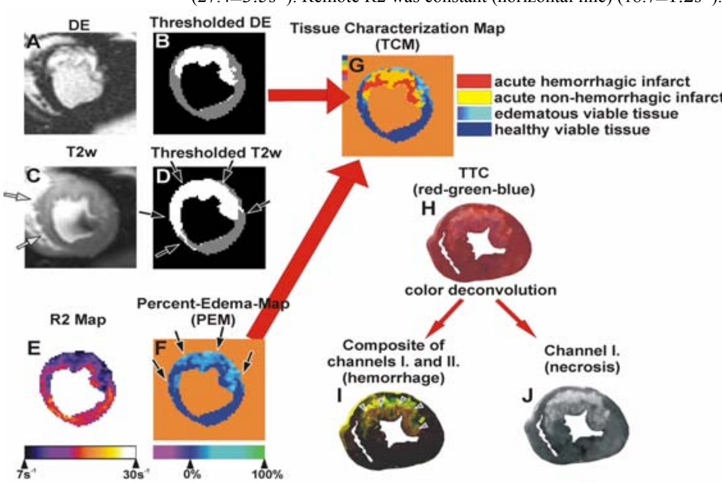

Figure 3. MRI images and post-processed maps 4 days following hemorrhagic infarction are shown. **A**. DE. **B**. Thresholded DE. **C**. T2-weighted (T2w) image. Increased signal in the septum is due mainly to the closeness of the coil (white arrows). **D**. Thresholded T2w image. Gray pixels are classified intact, white pixels are classified as edematous (black arrows). The thresholded T2w image overestimates the edematous region and is unable to differentiate regions with varying extent of edema or hemorrhage from non-hemorrhagic infarct. **E**. Parametric R2 map not influenced by field inhomogeneity or proton density. In edematous regions, R2 is decreased due to increased water content. **F**. Percent-Edema-Map (PEM) calculated from the R2 map. The region at risk is shown by black arrows. Note the apparent lack of edema in the center of the infarct due to acute hemorrhage in the infarct. **G**. Tissue-Characterization-Map (TCM) generated from F. and B. Note that the edematous region surrounds the non-hemorrhagic part of the necrotic tissue, and the hemorrhagic region is in the center of the infarcted region (mainly subendocardially). **H**. Corresponding TTC-stained slice. Purple-brown region in the center of the infarct is hemorrhagic. **I**. Post-processed TTC-photo (see **METHODS**), where hemorrhage can be delineated clearly as a light brown region within the infarct(gray arrowheads). **J.** The red channel of TTC photo, showing infarct borders most accurately.

RESULTS Serial changes in myocardial R2 values are shown in Figure 2, in agreement with other investigators' ex vivo findings. [1,2]. Examples for the steps in generating the TCM in an acute hemorrhagic infarct (Figure 3.) and in a chronic infarct are also shown (Figure 4.) Quantitative comparison of the amount of myocardial hemorrhage (ml of tissue) determined using TCM yielded significant correlation (R=0.9, $p<0.05$, linear regression line: $y=1.12x+0.1$) with that determined with TTC-staining. Average overestimation of the per slice amount of hemorrhage was 0.2±0.4ml (1.4±5.1%).

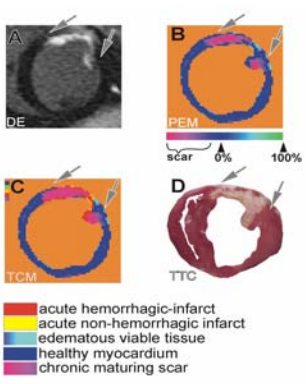

Figure 4. Generation of a TCM is shown at 8 weeks (A-C), and corresponding TTC-photo (D).

CONCLUSIONS Our data suggest that the TCM method is feasible in vivo. Results were in good agreement with TTC-staining in both acute and chronic infarction regarding localization of acute necrosis, hemorrhage and mature scar. TCM is capable of quantifying hemorrhage accurately.

1. Johnston DL, et al. *Magn Reson Med*. 1988;8:363-79.
2. McNamara MT, et al. *Radiology*. 1986;158:765-9.
3. Canby R, et al. *J Am Coll Cardiol*. 1987;10:412-20.
4. Lotan CS, et al. *Magn Reson Med*. 1992;23:346-55.
5. Fishbein M, et al. *Circulation*. 1980;62:1274-1279.
6. Shishido T, et al. *Journal Am. Col.Card*. 1997;30:585-591.
7. Surányi P, et al. *Proc. Intl. Soc. Magn. Reson. Med.* 2004;12:172.
8. Surányi P, et al. *Proc. Intl. Soc. Magn. Reson. Med.* 2004;12:1836.