Manganese as a Contrast Agent for Articular Cartilage

G. Navon[1,2], H. Shinar[1], K. Keinan-Adamsky[1], G. Saar[1], A. H. Aletras[2]

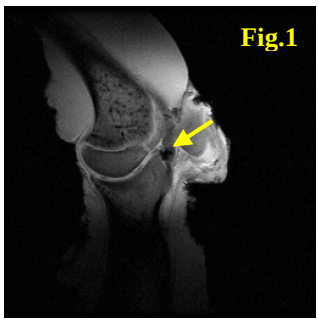
[1]School of Chemistry, Tel Aviv University, Tel Aviv, Israel, [2]NHLBI, Lab of Cardiac Energetics, National Institute of Health, Bethesda, MD, United States

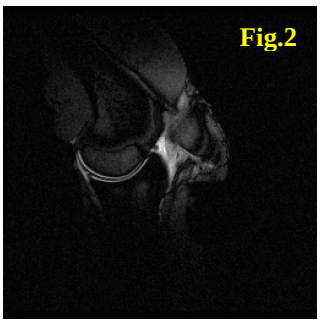
Introduction: The early stages of osteoarthritis are characterized by depletion of proteoglycans (PG), which play an important role in the mechanical properties of cartilage. The proteoglycans are highly negatively charged and thus attract sodium and calcium ions to preserve electroneutrality. Burstein and her group (1) developed the dGMERIC method, which is based on the idea that the penetration of the negatively charged $Gd(DTPA)^{2-}$ to the articular cartilage is enhanced upon the depletion of the proteoglycans. Kusaka et al (2) reported the enhancement of cartilage images by the addition of Mn^{+2} solutions.

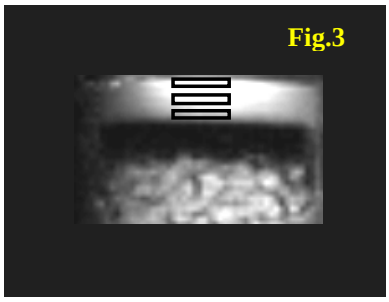
In this study we have measured the rate of enhancement of the image intensity by manganese solutions on the cartilage in porcine knee joints as well as in intact and PG depleted bovine articular cartilage plugs. The effect was compared with that of $Gd(DTPA)^{2-}$.

Material and Methods: Images of intact excised porcine knee joints taken from front legs of about 2 years old pigs and measured 1-3 days after excision. Measurements were done using a GE Signa 1.5 T scanner using a 3 inch surface coil, inversion-recovery gradient-echo sequence, FOV 14x14 cm, slice thickness 3 mm, TR/TE=2000/3.7 ms, 256x256. Recovery delay times were t_1 =37, 70, 150, 300, 600 ms and $t_1 = \infty$ obtained by eliminating the 180^o inversion pulse.

8 mm cartilage bone plugs were excised from bovine condoyles. Intact plugs were equilibrated in saline and then wiped dry and immersed in saline solutions containing either 0.3 mM $MnCl_2$ or 1.0 mM Gd(DTPA). For PG depletion intact plugs were equilibrated in 0.4 mg/ml trypsin in PBS for 12 h, at 25 ^{0}C. Plugs were then re-equilibrated in saline and treated like the intact plugs. T_1 weighted SE images (FOV=2x2 cm, 128x128, TR/TE=300/3.7 ms, 8.45T) were collected as a function of time.

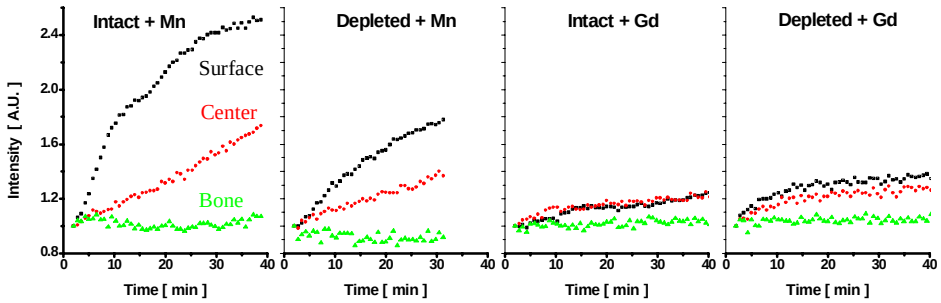






Results: The experiments on the porcine knee joints were performed by first inserting a non-magnetic titanium needle into the joint (shown by the arrow in Fig.1). Control T_1 values were measured and 3 ml of 1.0 mM $MnCl_2$ solution in saline were injected and the needle was removed. In a typical experiment the T_1 value dropped from 510±10 ms to 300±50 ms 4 minutes after the injection and to 160±20 ms 10 minutes after the injection. An image of the joint 46 minutes after the injection with a recovery delay time of 300 ms is shown in Fig. 2. An excellent delineation of the cartilage from the synovial fluid and from the bone was obtained.

The time course of the penetration of the contrast agents into intact and PG depleted cartilage-bone plugs was followed by a series of T_1 weighted images. The intensities at three regions of interests (Fig. 3), near the surface, at the center and close to the bone are plotted in Fig. 4. The 0.3 mM Mn^{2+} solution produced a much larger intensity enhancement than the 1.0 mM $Gd(DTPA)^{-2}$ solution, for the intact as well as the depleted plugs. As expected, depletion of the proteoglycans had an opposite effect on the relaxation enhancement caused by the two contrast agents. The difference in the intensity of the intact vs the depleted plug after the penetration of the relaxation reagent was much larger for the manganese solution. Moreover, the rate of intensity change was twice as fast in the case of the manganese penetration to the intact cartilage as compared to the depleted one.



Conclusions: Intraarticular injection of manganese solutions should be considered as a possible diagnostic tool for enhancing the contrast of articular cartilage and for monitoring proteoglycans depletion.

References: 1) A. Bashir et al. MRM **36**, 665, 1996. 2)Y.Kusaka et.al, MRM,**24**,137, 1992.