to obtain more than two echoes in a fast-spin-echo sequence. With these limitations in mind, two four-echo sequences were run with echo times of 16,32,48,64ms and 20,40,60,80ms. In both cases, TR=2000ms, FOV=38cm, thickness=3.5mm and matrix=256x256. These series were collected with fat saturation turned on and again with fat saturation turned off. In addition, the series were collected as a single slice and as a multi-slice acquisition. In addition to the four-echo spin-echo sequences, three dual-echo fast-spin-echo sequences were obtained. All FSE series used TR=4500ms, FOV=38cm, thickness=3.5mm, ETL=8, matrix=256x256, and fat saturation turned on. The three series had echo times of 16 and 82ms, 24 and 59ms, and 16 and 99ms.

In addition to the phantom study, a bovine study was carried out using the same imaging parameters on a bovine knee.

**Results:** For the phantom study, the ground truth results were compared with the T2 decay times calculated from each of the series. A regression was performed for all vials that had a ground truth T2 value of less than 200ms (56 of the 70 vials). When estimating the T2 values using all four of the four-echo spin-echo sequence with echo times of 16,32,48 and 64ms, the slope is 0.5628 and R-squared is 0.9808. It has been shown that dropping the first echo when estimating T2 provides significantly better results. By using only the echoes at 32, 48 and 64ms, the slope is 0.8816 and the R-squared is 0.9702. With the use of 32 echo times, the slope is 0.8677 and R-squared is 0.9759. These two results do not differ substantially, although the slope is slightly closer to one for the shorter echo times.

This was compared to the single-slice data for 32, 48 and 64ms echoes. The slope was 0.4496, the intercept was 18.293ms and R-squared was 0.9835.

For the dual-echo sequences, the best results were obtained from the echoes at 16 and 82ms echoes. The slope was 0.9015, the intercept was 5.8687ms and R-squared was 0.9971.

**Conclusions:** From the results of the phantom study, the dual-echo fast-spin-echo sequence with echo times of 16 and 82ms provided the most accurate and consistent results for the vials with echo times below 200ms. Large magnetization transfer contrast effects were observed in the 4-echo spin-echo sequences by comparing the single slice acquisitions to the multi-slice acquisitions. The results were substantially worse for the single-slice acquisition. This same phenomena was not observed in the dual-echo sequence. Our hypothesis is that the magnetization transfer contrast counteracts the stimulated and additional spin echoes that occur in the 4-echo multi-slice sequences.

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**HEME OXYGENASE-1 DOWN-REGULATES MICROSMAL PROSTAGLANDIN E SYNTHASE-1 IN OSTEOARTHRITIC CHONDROCYTES**

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**Purpose:** Pro-inflammatory cytokines are believed to play a role in the pathogenesis of osteoarthritis (OA). We have previously shown that these cytokines down-regulate heme oxygenase-1 (HO-1) in OA cartilage and chondrocytes. We have also shown a protective effect of HO-1 induction on cartilage degradation. Pro-inflammatory cytokines induce the coordinated expression of cyclooxygenase-2 (COX-2) and microosomal prostaglandin E synthase-1 (mPGES-1) leading to PGE2 overproduction. Recent data indicate that the predominant effects of this prostanoid in OA chondrocytes are catabolic. We have examined the effects of HO-1 on the production of oxidative stress and PGE2 in OA chondrocytes and the mechanisms involved.

**Methods:** Chondrocytes were isolated by digestion with collagenase and used in primary culture. Cells were stimulated with IL-1β. HO-1 was induced by incubation with 10 μM cobalt protoporphyrin IX (CoPP), PGE2 was measured by RIA. Gene expression was analyzed by real-time PCR. Protein expression was investigated by Western blot, ELISA and immunocytochemistry. Apoptosis and oxidative stress were determined by LSC. The activation of nuclear factor-κB (NF-κB), activating protein-1 (AP-1) and early growth response (EGR) was assayed by the luciferase method. To determine the effects of HO-1 overexpression, three-dimension cultures of chondrocytes were transduced with a lentiviral vector (LV-HO-1).

**Results:** Induction of HO-1 by CoPP augmented viability and agar-agar content, and decreased the production of oxidative stress and PGE2. This effect was not dependent on the inhibition of COX-2/mPGES-1 enzyme activity. HO-1 induction did not modify COX-2 expression but it significantly decreased mPGES-1 at the protein and mRNA levels. Induction of HO-1 resulted in a significant reduction of EGR-1-luc and NF-κB-luc promoter activation. In cells transduced with LV-HO-1, mPGES-1 expression and PGE2 production were significantly inhibited.

**Conclusions:** HO-1 decreases the production of inflammatory mediators in primary OA chondrocytes stimulated with IL-1β. The inhibition of PGE2 production would be dependent on mPGES-1 down-regulation. The inhibition of EGR-1 activation provides a basis for this effect of HO-1.

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**THYMOQUINONE INHIBITS INFLAMMATORY AND CATABOLIC RESPONSES AND LIPID PEROXIDATION IN RHEUMATOID ARTHRITIS**

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**Purpose:** Tymoquinone (TQ) is the major active compound derived from the medicinal Nigella sativa. Few studies have been shown that TQ exhibits anti-inflammatory activities in experimental model of rheumatoid arthritis (RA) through mechanisms that are not fully understood. The aim of this study was to evaluate the in vitro and in vivo effects of TQ and to investigate its influence on the major signaling pathways involved in RA pathophysiologic changes.

**Methods:** Isolated human RA synoviocytes were pre-incubated with increasing concentration of TQ (0-20 μM) and then incubated with 1 μM lipopolysaccharide (LPS) for 24 h. Experimental model of RA was induced by 0.5 mg native chick collagen II (CII) solubilized in 0.1 M acetic acid and emulsified in incomplete Freund’s adjuvant and scores of arthritis were recorded. RA rats were randomly distributed into 2 groups and treated orally with 1) water + 0.1% ethanol, or 2) 5 mg/kg/day of TQ. Pro-inflammatory cytokines, matrix metalloproteinase-1 (MMP-1), prostaglandin E2 (PGE2) were measured in blood media and serum by commercial kits. Cyclooxygenase (COX-2) and phosphorylated levels of mitogen activated protein kinases (MAPKs) and nuclear factor-kappaB (NF-κB) were assayed by Western blot. mRNA levels of pro-inflammatory cytokines, MMP-1, COX-2 were assessed by real-time reverse transcriptase-polymerase chain reaction (RT-PCR). To investigate bone metabolism and resorption, serum pro-inflammatory cytokines, alkaline phosphate (ALPase),...