INTRODUCTION: Contrast enhanced arthrography has become an important tool for evaluation of musculoskeletal disorders. It is used clinically for assessment of capsular pathology in the shoulder, intercarpal ligament tears in the wrist, and labral pathology in the hip. The procedure entails intraarticular injection of both an iodinated contrast agent and a gadolinium-based contrast agent.

Although there has much recent work done to characterize the renal toxicity of these agents, there has been little published data examining effects on cartilage or chondrocytes. However, one past study did find that gadodiamide, a gadolinium based contrast agent, induced low levels of chondrocyte apoptosis [1].

The goal of our study was to examine chondrocyte viability following exposure to iodinated and gadolinium-based contrast agents used in arthrography: gadopentetic acid (Gd-DPTA), iopamidol, diatrizoate sodium, and iohexol.

METHODS: Primary chondrocytes were harvested from fresh bovine articular cartilage using collagenase digestion and grown in monolayer culture at high density. First passage chondrocytes were plated on 96 well plates at a density of 1 x 10^5 cells/cm². After overnight incubation in standard tissue culture conditions, contrast agents were introduced to wells in varying concentrations: Gd-DPTA (Bayer Healthcare Pharmaceuticals, Belt Wayne, NJ), diluted to 0.9 mg/mL, 2.3 mg/mL, or 23.4 mg/mL in PBS; iopamidol (Bracco Diagnostics, Princeton, NJ), diluted to 102 mg/mL, 204 mg/mL, or 408 mg/mL in PBS; iohexol (GE Healthcare, Chalfont St. Giles, Buckinghamshire, United Kingdom), diluted to 129.5 mg/mL, 259 mg/mL, or 518 mg/mL in PBS; diatrizoate sodium (Amersham Health Inc., Chalfont, Buckinghamshire, United Kingdom), 75 mg iodine/mL, 150 mg iodine/mL, or 300 mg iodine/mL in PBS; Gd-DPTA/iopamidol, diluted to 0.9 mg/102 mg/mL, 2.3 mg/204 mg/mL, or 23.4 mg/387.6 mg/mL in PBS. The midrange dilution for each contrast agent was chosen to correspond to the dosage commonly used for arthrography at our institution. PBS was introduced to control wells. Following 16 hour incubation with PBS and contrast agents, chondrocyte viability was assessed using the Live/Dead stain kit (Invitrogen, San Diego, CA) and quantified using the CellTiter-Glo Luminescent Cell Viability Assay (Promega, Madison, WI). Manufacturer protocols were followed for viability assays. Statistical analysis was performed using unpaired two-tailed t-tests. Results were presented as percentage difference in chondrocyte viability [number of viable control cells – number of viable treated cells]/(number of viable control cells) ± standard error of the mean (s.e.m.).

RESULTS: At clinical doses, chondrocyte viability was reduced after exposure to all iodinated contrast agents tested (figure 2). Compared with controls, the percentage difference in viable cell number was 26.0% ± 6.4% for iohexol-treated chondrocytes and 60.0% ± 2.3% for diatrizoate sodium-treated chondrocytes. Chondrocytes treated with a combination of Gd-DPTA and iopamidol demonstrated changes in cell viability similar to chondrocytes treated with iopamidol alone [37.0% ± 4.3% for Gd-DPTA/iopamidol, 36.5% ± 3.7% for iopamidol-treated chondrocytes]. All percentage differences for chondrocytes treated with clinical doses of iopamidol contrast were determined to be statistically significant with p<0.05. There was a trend towards decreased chondrocyte viability as contrast agent concentration increased. This is demonstrated by significant differences (p<0.05) between percentage difference in viability at low concentrations and percentage difference in viability at high concentrations for all contrast agents tested. Furthermore, diatrizoate sodium and iopamidol showed significant differences (p<0.05) in percentage difference in viability between the clinical (midrange) dose and the high dose as well as between the low dose and the clinical (midrange) dose.

Staining with the Live/Dead kit confirmed the cell viability changes measured by the CellTiterGlo assay (figure 1).