Figure 3. Kinetic friction coefficient ($\mu_{\text{kinetic, Neq}}$) at Tps = 1.2 s of PRG4 deficient Flare-SF with 450 μg/mL PRG4 and 1.0 mg/mL 1.5 MDa HA supplementation, and NLSF.

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CHANGE IN MRI SYNOVITIS CORRELATES WITH CHANGE IN PAIN FOLLOWING INTRA-ARTICULAR STEROID INJECTION

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Purpose: Synovitis is a well recognised finding in knee osteoarthritis. It can be identified on Magnetic Resonance Imaging (MRI) as synovial thickening, although injection of contrast material is required to distinguish synovial tissue from synovial fluid. The aim of this analysis was to determine whether change in synovial tissue volume as assessed using gadolinium (Gd) enhanced MRI imaging correlates with change in knee pain following intra-articular steroid therapy.

Methods: Men and women aged 40 years and older who met ACR criteria for the disease, were recruited for participation in an ongoing open label clinical trial of intra-articular steroids. Subjects who took part in the study had significant knee pain and grade 2 or higher knee OA. At baseline visit they completed a questionnaire about their symptoms including KOOS pain scale (100 = no pain to 0 = extreme pain) and also a VAS score (0 = no pain) to 10 = extreme pain) for pain on a nominated activity (VASnA). They subsequently had a Gd enhanced MRI immediately prior to having an intra-articular steroid injection with repeat questionnaire and Gd-enhanced MRI scan at follow up visit to assess synovial response usually within 2 weeks after the injection. To assess synovial tissue volume, sagittal (post CE T1W Fat Suppressed images: TR 500ms, TE 17ms; FoV 15.9 x 15.9cm; slice thickness 3mm) scans were obtained. Manual segmentation of the synovial tissue layer was performed on the post contrast knee image by a single observer. Using computer imaging analysis we excluded cartilage within the segmented space, by thresholding in the associated sagittal (3D WAT5c: TR 20ms, TE 7.7ms, FoV 15cm, 288x228) scan. The rest of the segmented space was assumed to be a mixture of fluid and synovial tissue. We calculated the proportion of synovial tissue in every voxel using P = (1 - mf) / (ms - mf) truncated to [0,1], where l is the voxel intensity and mf, ms are the means of the intensity distributions of fluid and synovial tissue volume respectively. We looked at mean synovial volume before and after the steroid injection and looked at the Spearman Rank correlation coefficient between change in synovial volume and change in the level of KOOS-pain and also VASnA.

Results: We analysed data from 41 patients. Their mean age was 62.4 years (SD 10.5 years), and 21 were female (51.2%). The median time between baseline and follow up scan was 9 days (IQR 7 to 14 days). The median synovial tissue volume at baseline was 7,556 mm$^3$ (IQR 4,670mm$^3$ to 11,269 mm$^3$), and at follow up was 7,078 mm$^3$ (IQR 3,642mm$^3$ to 8,541mm$^3$); median difference -1,007 mm$^3$ (95% CI -1,909mm$^3$ to -320mm$^3$). Both KOOS pain (24.7pts; 95% CI 18.4 pts to 31.0) and VASnA (2.3cm, IQR 3.2cm to 1.5cm) improved significantly between baseline and follow up. The change in synovial tissue volume correlated with change in VASnA ($r_s = 0.39; p = 0.01$) though not with KOOS-pain ($t_s = -0.11; p = 0.50$). Change in VASnA did not appear to correlate with synovial tissue volume at baseline ($r_s = -0.03; p = 0.85$); nor did change in KOOS pain ($r_s = 0.17; p = 0.30$).

Conclusions: Synovial tissue volume in knee osteoarthritis, assessed with Gd-enhanced MRI correlates with change in pain assessed as pain on a nominated activity, though not KOOS, in response to intra-articular steroid injection.

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A SYSTEMATIC REVIEW OF WHERE AND HOW TO INJECT IN THE KNEE?

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Purpose: The knee can be injected at different anatomic sites with or without image-guidance. We undertook a systematic review to determine i) the accuracy of intra-articular knee injection (IAKI) and whether this varied by site, use of image-guidance and clinician experience, and ii) whether accuracy of IAKI was linked with improved therapeutic response.

Methods: Medline, Embase, AMED, CINAHL, Web of Knowledge and the Cochrane Central Registers for Controlled Trials up to July 2012 were searched including additional hand searches of relevant articles. Studies included were those that evaluated accuracy of steroid injection at one or more IAKI sites performed either blinded or using image-guidance. We pooled data across studies to determine accuracy and also differences in accuracy by injection site when injections were delivered blind or guided by imaging. Using data from the small number of studies which permitted within-study comparisons, we performed meta-analyses (fixed effect model with forest plot) to determine differences in accuracy of blind and guided injections.

Results: Data from 26 publications were included in the review. Only 5 studies were available for within-study comparison for 4 out of the 8 injection sites. The within-study analyses found guided IAKIs at supramedial patellar (SMP), medial midpatellar (MMP), supralateral patellar (SLP) and lateral suprapatellar bursa (LSB) had greater accuracy using image-guidance than given blind [pooled risk difference 0.09-0.19]. Using between-study analyses, for blinded IAKIs, the SLP site was the most accurate [87%] through SMP and lateral joint line injection sites. The anteromedial mid-patellar (LMP) and LSB were also accurate [pooled accuracies 82-84%]. Overall about one in five blinded IAKIs were inaccurate. Using data pooled across studies the SMP [Absolute Risk Difference (ARD) 0.22, 95% Confidence Interval (CI) 0.10-0.33] and the anterolateral joint line injection approaches [ARD 0.28, 95% CI 0.20-0.35] were least accurate when performed blinded compared to when performed guided. Overall there was no significant difference in accuracy between the lateral injection sites and the medial sites [Blinded: ARD 0.04, 95% CI 0.00 to 0.08; Guided: ARD 0.01, 95%CI -0.01 to 0.03]. Adverse events associated with IAKI at different sites were uncommon, though compared to the lateral approach, the medial approach was associated with a higher frequency of adverse events. There was some evidence that experience of the injector was linked with improved accuracy for blinded though not image-guided injections. There was no association between accuracy of IAKIs and treatment outcome though there was a paucity of data.

Conclusions: IAKIs are safe and can be accurate when performed blind depending on injection site. The use of image guidance improves accuracy of IAKI at all sites. Further studies are required to address the question whether accurate localisation is linked with a better outcome.

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COMPARATIVE EFFECTIVENESS OF TWO HYALURONIC ACID FORMULATIONS ON PERCEIVED FUNCTIONAL PERFORMANCE

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Purpose: Intra-articular hyaluronic acid (HA) injections are a non-surgical treatment for knee osteoarthritis (OA) that have the potential to reduce pain and improve functional ability. Despite potential benefits,
not all patients that receive HA injections have an optimal response. Several different HA formulations are available and a comparative analysis of outcomes is lacking in the literature. Therefore, the purpose of this study was to quantify the functional benefit of two different HA formulations for individuals with knee OA.

**Methods:** The Knee Outcome Survey (KOS) and Global Rating Score (GRS) from patients who received HA injections for knee OA were analyzed. Patients with bilateral injections completed a questionnaire for each limb. Baseline KOS and GRS scores prior to injection and scores 4-6 weeks after the last injection were compared between subjects who received 5 Sodium Hyaluronate (Supartz) injections (n = 226) or a single Hylan G-F 20 (Synvisc-One) injection (n = 368). "Responders" to the HA injections were operationally defined as 1) Patients who had a KOS change score greater than 10 points or 2) Patients who showed any increase in KOS scores. Self-reported knee function, ranked as "Severely Abnormal", "Abnormal", "Nearly Normal", or "Normal" was evaluated at baseline to stratify groups if a significant interaction effect was found. "Normal" subjects were subjects without functional limitations, but may have had pain or were known to have chondral lesions. A repeated measures ANOVA was used to assess change in KOS score between injection types and over time. Chi-square analysis was used to determine differences in the responder rate between injection types and determine if there was a relationship between change perception of function (KOS and GRS) and baseline self-reported knee function.

**Results:** 594 knees were assessed and time between first injection and follow-up was 78 +/- 13 days for patients who received Sodium Hyaluronate and 46 +/- 15 days for patients who received Hylan G-F 20. There was a significant Self-Function by Time interaction effect (p=0.002) and those with lower reported self-functional score (abnormal, severely abnormal) demonstrated greater improvement in KOS and GRS scores at follow-up (Figures 1 and 2). There was no Injection Type by Time interaction effect and no difference in responder rates when stratified by injection type suggesting no difference in outcomes between the multi or single injection (p=0.453). Most patients patients demonstrated some improvement on the KOS at follow-up, although a smaller number of individuals achieved a 10 point change on the KOS (Table 1).

**Conclusions:** HA injections offer small, but significant improvements in self-reported function for the majority of patients with OA. There was no additional functional benefit to using one particular formulation. Patients who report their knee function as abnormal or severely abnormal at baseline are most likely to have a larger response at follow-up, although a smaller number of individuals achieved a 10 point change on the KOS.

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**588 INTRARTICULAR DRUG DELIVERY THROUGH AN IN-SITU GELLING SYSTEM**

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**Purpose:** Our aim was to develop a biodegradable, in situ forming gel suitable for prolonged, i.e. several weeks, intra-articular drug delivery. Gel degradation kinetics, visualization, drug release and intra-articular biocompatibility were tested.

**Methods:** Gel synthesis: PCLA-PEG-PCLA synthesis was performed by ring opening polymerization of 1-lactide and ε-caprolactone in solution using PEG1500-diol as macrorinitiator and tin(II) 2-ethylhexanoate as catalyst. To gain radiopacity, TIBO-capping of the PCLA-PEG-PCLA was performed using an excess of TIBO chloride. In-vitro gel behavior: Phosphate buffer was added to the polymer (25wt %) and the resulting gel was kept at 37 °C for the duration of the experiment. At predetermined time points, residual gel weight was measured. In-vivo experiments: Group 1 (n=6 male Wistar rats): 100μl radiopaque gel was injected subcutaneously (n=4) or in the knee joint (n=2) and scanned regularly to visualize in vivo gel degradation longitudinally. Attenuation and volume of the gels were calculated. Group 2 (n=10): 50 μl non-radiopaque gel was injected in the left knee, the right knee served as a control (50μl saline). μCT arthographies were acquired before injection, after 6 and 12 weeks to monitor cartilage quality (sGAG content is correlated inversely to Hexabrix influx) and quantity over time. After the last scan, knees were harvested for histology. Group 3 (n=5); 500 μl of Celecoxib loaded gels (60 mg/g) were injected subcutaneously and blood samples were taken regularly to analyze drug release with UPLC.

**Results:** In-vitro gel degradation: Complete gel degradation took ~ 130-140 days. Gel attenuation corresponded well with the measured polymer concentration over time, proving that μCT is indeed a good technique to quantify the amount of polymer present. In-vivo experiments: Group 1: Total gel volume directly after subcutaneous injection by μCT was set at 100% and for all following time points the percentage of residual volume was calculated (figure 1). A controlled degradation was observed for period of twelve weeks. Upon intra-articular injection, the