enhancement of synovium during dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) correlate more strongly with reduction in pain severity than changes in static synovial volume. The aim of this analysis was to determine the impact of a PFJ brace on synovitis as assessed by change in synovial enhancement using DCE-MRI.

Methods: One hundred and twenty six people aged between 40 and 70 years with PFJ OA were recruited into a randomised clinical trial of a patellar brace. Participants were randomised to an intervention (wearing brace) and a control group (no brace) for six weeks. Subjects were assessed at baseline and at 6 weeks for pain using the KOOS questionnaire and also a visual analogue score (VAS) scored from 0-100mm for a nominated physical activity (VASNA). They also had DCE-MRI of the symptomatic knee performed at baseline and at 6 weeks. Dynamic synovial parameters were calculated based on the enhancement of synovium with contrast including; maximum rate of enhancement (max-grad), late relative enhancement (late-rel), maximum enhancement (max) and volume transfer coefficient (ktrans). We used a paired t-test to look at within group change in both pain and DCE-MRI parameters before and after intervention and an unpaired t-test to look at the between group difference in the change in these parameters.

Results: Subjects' mean age was 55.5 years (SD = 7.5) and 72 (57.1%) were female. Pain improved significantly within the intervention group though not the control group. There was a significant between group difference in the change in both KOOS and VASNA, see Table. Within controls there was a reduction in all of the dynamic parameters between baseline and follow up. This was significant for volume transfer coefficient (within group difference in ktrans = -0.003) and also maximum rate of enhancement (within group difference in max-grad = -0.198). Within the intervention group there was a small increase (worsening) in all of the dynamic MRI parameters between baseline and 6 weeks follow up though none of these differences was statistically significant. There was a significant difference in the change in maximum rate of enhancement (max) between the intervention and control groups.

Conclusions: Patellofemoral joint brace therapy for patients with symptomatic patellofemoral knee OA does not reduce synovitis as suggested by change in synovial enhancement using DCE-MRI. Pain reduction following brace therapy can not therefore be explained by change in synovitis.

Table 1
Changes in Dynamic MRI Factors Following Brace Intervention

Variables	No brace group (N=63)		Brace group (N=63)			
	Within group mean diff (95% CI)	p	Within group mean diff (95% CI)	p	Between-group mean diff (95% CI)	p
ktrans	−0.003 (−0.006 to 0.000)	0.05	0.001 (−0.003 to 0.005)	0.63	0.002 (−0.009 to 0.001)	0.11
max_grad	−0.198 (−0.345 to −0.050)	0.01	0.171 (−0.013 to 0.356)	0.07	0.116 (−0.599 to −0.139)	<0.01
late_rel	−0.102 (−0.280 to 0.076)	0.25	0.010 (−0.175 to 0.195)	0.91	0.128 (−0.367 to 0.142)	0.38
max	−0.161 (−0.357 to 0.036)	0.11	0.045 (−0.166 to 0.256)	0.67	0.143 (−0.491 to 0.079)	0.15
Pain on nominated activity VAS	−0.13 (−0.64 to 0.38)	0.61	−1.82 (−2.39 to −1.24)	<0.01	0.38 (0.93 to 2.44)	<0.01
KOOS Pain Subscale Score	1.71 (−1.66 to 5.08)	0.31	8.78 (4.36 to 13.20)	<0.01	2.75 (−12.51 to −1.61)	0.01

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PERCEIVED BARRIERS IN CARE FOR OSTEOARTHRITIS

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Purpose: While osteoarthritis (OA) is the most frequent type of arthritis in the population, relatively little attention has been paid to patients' perceptions of the impact of their disease and the barriers they face in receiving care. This study examined current treatments and barriers to treatment, as well as perceptions around decision making and the preferences of patients for physician input into their OA treatment.

Methods: A poll of people with arthritis was commissioned to gather data on patient perceptions with the purpose of improving the information presented on The Arthritis Society of Canada website. Respondents were asked for their disease diagnosis; impact of arthritis (e.g., pain, fatigue, disability with activities and social roles); barriers and challenges in getting care; and preferences for physician involvement in care decisions. Most questions were on a 1 to 5 scale ranging from 1 = no impact/importance to 5 = extreme impact/importance. Scores are reported as means or percentages unless otherwise stated.

Results: Of the 1715 respondents, 922 (53.8%) reported osteoarthritis (OA) and 588 (34.3%) reported OA as their sole type of arthritis. We focus on those with OA as a sole diagnosis. Eighty two percent were female; 57% were aged 5 years. The mean pain intensity was 5.9 on a 1-10 scale with 70% reporting pain at least once a week. The mean number of joints affected was 3.8 (out of 13). However, 44% of participants reported taking no medications for their OA. The impact of OA on daily activities was moderate with mean scores in the range of 2.2-3.0 out of 5 for family and social-related activities. The greatest impact of OA was for exercise (3.3) and intimate relations (4.4). Respondents reported controlling pain, mobility and stiffness, loss of strength, fatigue, low energy and difficulty sleeping as being of high importance (range of mean scores 4.1-4.4) with no differences by age. Overall 75% of respondents reported at least one challenge in getting treatment with the top 3 challenges being a lack of affordable treatment (30.1%), long wait times for appointments (28.3%), and a perceived absence of beneficial treatment (e.g., "don't think anything can be done") (26.3%). Costs for treatments like physiotherapy and over-the-counter medication were noted in particular. Respondents rated highly the importance of physicians considering their input when making decisions related to prescription medication (mean = 4.4) and treatments such as surgery or physiotherapy (mean = 4.4). However they expressed lower perceived importance for seeking physician input before deciding on treatments such as diet and exercise (mean = 3.7) and over-the counter-medications (mean = 3.8).

Conclusions: Despite pain, a moderate impact on valued roles and activities, and a high importance of controlling a range of symptoms, two-fifths of people with OA were not taking any medications, which is in line with findings from other studies. Of concern was that most respondents reported challenges and hardships with getting treatment, including costs not covered by the health care system and a perception that little was available to them in the way of efficacious care for OA. Moreover, clinician input was not always seen as important in management of all aspects of OA. There is a clear need for better information for patients on what can be done to control their illness and for interventions to minimize barriers in accessing appropriate treatments. Additional research on decision-making preferences related to OA treatment would be beneficial in addressing a patient-centred approach to OA management.

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FOLATE RECEPTOR POSITIVE MACROPHAGES IN OSTEOARTHRITIS AND EFFECTS OF TRIAMCINOLONE

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Purpose: Folate-based radiotracers have been used in patients with cancer and inflammatory diseases to visualize folate receptor expressing cells using PET or SPECT techniques. Activated macrophages express folate receptor beta (FR-β) and this allows specific imaging of these cells in-vivo. From previous work using SPECT imaging to visualize folate receptor expressing macrophages in both animal models and in patients with OA we know that macrophages are present in OA affected joints. However, it remains unclear what role these macrophages play in the

different stages of OA and whether they can be influenced by treatment with corticosteroids. Aim of the study. To understand which macrophage subtypes express the folate receptor and can be visualized using SPECT imaging and whether these macrophages are affected by treatment with corticosteroids (Triamcinolone).
Methods: In vivo. In twenty 16-week-old male Wistar rats severe osteoarthritis was induced using a low dose intra-articular papain injections in their left knee joints combined with exposure to a moderate exercise protocol. Animals were divided over two groups: ten rats served as untreated OA controls and ten rats were treated during the experiment with weekly intra-articular injections of triamcinolone acetonide (100ug in 70ul saline). After six weeks an in vivo folate SPECT/CT scan and ex vivo EPIC-μCT and histology was obtained. In vitro. We generated macrophages from human peripheral blood monocytes in vitro by culturing them for 7 days in the presence of GM-CSF (M1 proinflammatory phenotype) or M-CSF (M2 anti-inflammatory phenotype). Subsequently, we treated the macrophages with LPS, cytokines (IL-4, IL-10, IFN-y) or triamcinolone acetonide (1ug/ml). FR-β (FOLR2) and macrophage marker expression was measured using FACS.
Results: . Increased macrophage activation was seen on SPECT-scans in OA induced knees versus control knees. Interestingly, treatment with corticosteroids resulted in reduced OA severity but an increase in activated macrophages seen on folate-SPECT imaging (figure1). On human in vitro generated macrophages Folate receptor expression was high in M2 macrophages and very low in M1 macrophages. There were only small differences between M2 macrophages stimulated with IL-4 or IL-10 alone. But when M2 macrophages were stimulated with IL-4 and IL-10 simultaneously, the number of positive cells and the fluorescent intensity increased approximately 1.5 - 2 fold compared to unstimulated M2 macrophages (figure2). Triamcinolone acetonide significantly reduced TNF-α production by M1 macrophages but did not affect M1 or M2 surface markers or folate receptor expression.
Conclusions: Our data indicate that the increase in macrophage activation as seen on SPECT is most likely due to an increase in M2 anti-inflammatory macrophages. However, from these results we cannot infer which M2 subtype is present in our animal model. It is known that corticosteroids can influence macrophage subtypes but we were not able to show these effects in vitro, although in-vitro stimulation with IL4+Il10 induced a folate receptor positive subtype within the M2 population. Our study suggests that not all macrophage subtypes are detrimental. Maintaining the balance between the various macrophage subtypes may thus be the key to maintain healthy joint homeostasis and prevent osteophytosis.

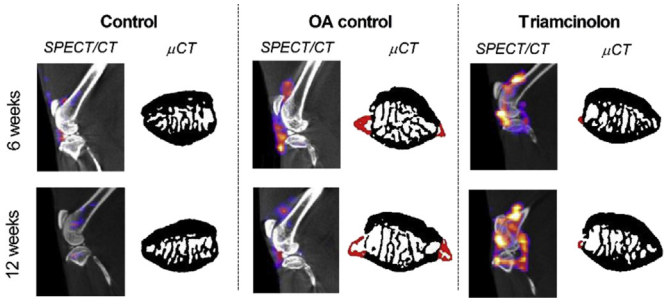

Figure 1. Macrophage activation determined after injection of 111In-DTPA-folate using SPECT/CT in Papaine induced osteoarthritis (OA) combined with moderate excercise. Representative sagittal SPECT/CT images of knee joints from representative animals per experimental group. CT images shown in black and white were used for anatomical reference, the SPECT images are shown in color. Patellar bone is shown with osteophyte formation highlighted in red.

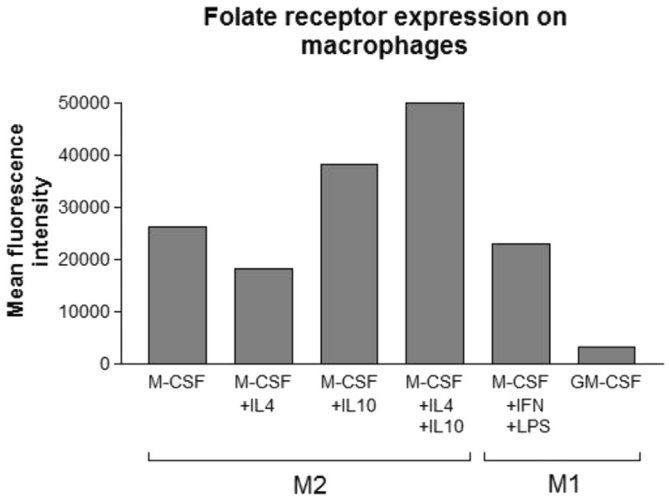

Figure 2. Fluorescent intensity of FOLR2 staining on human macrophages differentiated in vitro. Average results from two representative experiment are shown.

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S100 PROTEINS INDUCE CANONICAL WNT SIGNALING, WHICH CAUSES INCREASED EXPRESSION OF MMPS IN THE SYNOVIUM

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Purpose: Many osteoarthritis (OA) patients show synovial activation, which is thought to be involved in joint destruction. Previously, we found that the alarmins S100A8 and A9, and various members of the Wnt signaling pathway, including Wnt16, were highly increased in the synovium of knee joints during experimental OA. WISP1, a downstream protein of β-catenin-dependent canonical Wnt signaling, was increased in both synovium and cartilage. S100A9 KO mice showed strongly reduced pathology in experimental OA. Wnt signaling has been linked to OA through activation of β-catenin, but the role of the synovium in OA pathology under the influence of Wnt signaling is unclear. In this study we investigated whether S100 proteins induce Wnt signaling and determined the potency of Wnts to increase expression of cartilage-degrading enzymes in the synovium.
Methods: Pathway analysis of microarray data from synovium of a collagenase-induced OA was done using DAVID. Activation of Wnt signaling was determined with β-catenin immunostaining of whole knee joint sections. Gene expression was analyzed by qPCR. Human OA synovial specimens were collected from joint replacement surgery and stimulated with S100 or members of the Wnt signaling pathway or blocked with the Wnt inhibitors FrzB and DKK-1.
Results: Pathway analysis showed enrichment of Wnt signaling in the synovium during experimental OA. Because upregulation of both S100 and Wnt proteins during experimental OA showed comparable kinetics, we determined if S100 proteins could induce Wnt signaling. We found that injections of S100A8 into mouse knee joints led to increased expression of Wnt16 and WISP1 in the synovium and β-catenin accumulation in the synovium and in the cartilage. Underlining an interrelationship between Wnt signaling and S100A8/9, we found less β-catenin accumulation in both the synovium and cartilage during experimental OA in S100A9 KO mice, suggesting a decrease in canonical Wnt signaling. To determine the effects of canonical Wnt signaling in the synovium, we overexpressed Wnt8a and Wnt16 *in vivo* in the synovium with adenoviral vectors. This resulted in increased expression of various MMPs in the synovium. To translate these findings to a human situation, we stimulated human OA synovial tissues with Wnt3a, as a model for a canonical Wnt, and WISP1. This led to significantly increased expression of MMP1, MMP9 and MMP13, whereas the expression of the MMP inhibitors TIMP1 and 3 was not altered. Next, we hypothesized that if Wnt signaling was increased in OA synovium and that stimulation of synovium with members of the Wnt