knee osteoarthritis (OA). This analysis aimed to compare the proportion of patients in whom radiological OA progression was prevented between groups, considering different cut-offs of JSN.

Methods: SEKOIA study included patients with symptomatic primary knee OA (Kellgren and Lawrence [KL] grade 2 or 3, JSW:2.5–5 mm) randomly allocated to SrRan 1 or 2 g/day or placebo. Primary endpoint was JSW radiographic change over 3 years in the medial compartment. JSW was measured yearly with validated computer-assisted centralized reading method. Patients with no relevant radiological OA progression were defined as those with a JSW loss from baseline to End, lower than 0.1mm, 0.2 mm or 0.3 mm. Patients who withdrew from the study were counted as non-responder. Treatment groups were compared to placebo using a chi^2 test.

Results: ITT set included 1371 (82% of the randomized set) patients. Age was 63±7 years, BMI was 30±5 kg/m2, JSW was 3.5±0.8 mm. 61% were KL II. 69% were female. A significantly greater proportion of patients in SrRan1g and 2g groups had no radiological progression compared to placebo: 40.5% and 44.1% vs. 32.8% ($p=0.017$ and $p<0.01$) with the 0.3 mm threshold. It corresponds to a proportion of responders increased by 24% and 34% in the SrRan 1g and 2g groups compared to placebo, with a number of patients needed to be treated (NNT) of 13 and 9. Similar results were observed at additional JSN cut-offs:

	Strontium ranelate 1 g (N = 445)	Strontium ranelate 2 g (N = 454)	Placebo (N = 472)
Responders: JSN ≥ −0.1 mm			
Patients who responded, n (%)	130 (29.21)	136 (29.96)	101 (21.40)
p-value	**0.006**	**0.003**	
RRR	**36.0**	**40.0**	
NNT	13	12	
Responders: JSN ≥ −0.2 mm			
Patients who responded, n (%)	161 (36.18)	173 (38.11)	133 (28.18)
p-value	**0.009**	**0.001**	
RRR	**28.4**	**35.2**	
NNT	**13**	**10**	
Responders: JSN ≥ −0.3 mm			
Patients who responded, n (%)	180 (40.5)	200 (44.05)	155 (32.80)
p-value	**0.017**	**<0.001**	
RRR	**23.5**	**34.3**	
NNT	**13**	**9**	

Conclusion: Treatment with SrRan is associated with a significantly greater number of patients without OA radiological progression over 3 years.

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Impact On Cartilage Volume Changes Over Time Of Conventional Treatment and Of Glucosamine and Chondroitin Sulfate In Knee Osteoarthritis Patients: Data From The Osteoarthritis Initiative Cohort. Johanne Martel-Pelletier[1], Camille Roubille[1], Jean-Pierre Raynauld[1], François Abram[2], Pierre Dodin[2], Marc Dorais[3], Philippe Delorme[1] and Jean-Pierre Pelletier[1]. [1]Osteoarthritis Research Unit, University of Montreal Hospital Research Centre (CRCHUM), Montreal, QC, [2]Imaging Research & Development, ArthroLab Inc., Montreal, QC, [3]StatSciences Inc., Notre-Dame de l'Île Perrot, QC.

Background/Purpose: To explore, using data from participants enrolled in the progression cohort of the Osteoarthritis Initiative (OAI), the effects of conventional knee osteoarthritis (OA) pharmacological treatment and those of the SySADOA glucosamine and chondroitin sulfate (Glu/CS) on disease structural changes.

Methods: Six hundred knee OA subjects were included in a 24-consecutive-month follow-up study with annual knee X-rays and magnetic resonance imaging (MRI) of the most symptomatic (greatest WOMAC pain) knee. Participants were further stratified based on whether or not they received OA conventional pharmacological treatment and/or Glu/CS. The main outcomes were the loss of joint space width (JSW) and the loss of cartilage volume measured by MRI using a newly developed fully-automated system.

Results: Three hundred participants reported taking (+) (n=300) or not (−) (n=300) OA treatment (analgesic/NSAIDs) for 24 months, with or without Glu/CS. The +analgesic/NSAIDs subjects showed higher WOMAC scores ($p<0.0001$) and smaller JSW ($p=0.013$), reflecting a more severe disease at baseline vs. the -analgesic/NSAIDs participants. In the -analgesic/NSAIDs group, a reduction in the cartilage volume loss at 24 months in the medial central plateau ($p=0.007$ univariate and $p=0.03$ multivariate analysis) was found in those taking Glu/CS. In the +analgesic/NSAIDs group, the subjects receiving Glu/CS demonstrated less cartilage volume loss in the plateau at 12 months ($p=0.05$) and in the central plateau at 24 months ($p=0.05$). In addition, in the +analgesic/NSAIDs group, participants taking Glu/CS and having a JSW at baseline greater than the median (less severe disease) had less cartilage volume loss at both 12 and 24 months in the lateral plateau ($p=0.02$ and 0.03, respectively). By contrast, in all groups, no significant reduction in JSW over time was found.

Conclusion: In both the +analgesic/NSAIDs and -analgesic/NSAIDs groups, participants who received Glu/CS had reduced cartilage volume loss over 24 months mainly on the plateau when assessed with qMRI, arguing for a targeted DMOAD effect of Glu/CS, which could not be identified by X-ray alone.

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Effects Of Chondroitin Sulfate On Brain Response To Painful Stimulation In Knee Osteoarthritis Patients: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial. Jordi Monfort[1], Jesús Pujol[1], O Contreras-Rodriguez[1], Jone Llorente-Onaindia[1], M López-Solà[1], Laura Blanco-Hinojo[1], J Deus[1], H Ortiz[1], Francisco Montañés[1], M Campillo[1], Pere Benito[1], Laura Sánchez[2], Marta Herrero[2] and Josep Vergés[3]. [1]Hospital del Mar, Barcelona, Spain, [2]Bioiberica, Barcelona, Spain, [3]Pre-Clinical and Clinical R&D Area, Pharmascience Division, BIOIBERICA S.A., Barcelona, Spain.

Background/Purpose: Knee osteoarthritis (OA) is a degenerative joint disease causing symptoms in 12% of people over the age of 65. A variety of treatments have been tested to alleviate knee OA symptoms, most being focused on reducing pain through analgesic or anti-inflammatory actions. Clinical studies have reported a beneficial effect of pharmaceutical-grade chondroitin sulfate (CS) on knee pain, and a parallel reduction in the rate of decline in joint space width. Nevertheless, not all clinical trials have been successful and reports exist suggesting that CS is not equally effective in all clinical situations (Clegg 2006). Inherent problems with efficacy assessment of pain medication are the lack of objective pain measurements and the large variability of subjective pain ratings. The aim of the present fMRI study was to objectively identify the effects of CS treatment on the brain response to pressure painful stimulation in patients with symptomatic knee osteoarthritis.

Methods: Phase IV, randomized, double-blind clinical trial in which patients received CS (pharmaceutical-grade manufactured by Bioibérica) 800 mg/day or placebo for a 4-month treatment course. Patients were assessed at baseline and after four-month of treatment. Two fMRI tests were conducted in each session by applying painful pressure on the knee medial interline (pain sensitive maneuver) and on the patella surface (cartilage selective targeting). The main outcome measurement was attenuation of the response evoked by knee painful stimulation in the pain-processing brain system.

Results: Twenty-two evaluable patients received CS and 27 placebo. No effects of CS were detected using the knee interline pressure test. Patients receiving CS showed a tendency to report reduced subjective pain after treatment during patella pressure test ($p=0.077$), but no significant group by session interaction was demonstrated. fMRI of patella pain, showed a larger activation reduction in the CS group than in placebo in a

posterior mesencephalon region including the periaqueductal gray (PAG). The entire PAG cluster (238 voxels) with significant interaction showed a pre>post-treatment difference at $p<0.05$ (peak difference at $x=-10$, $y=-34$, $z=-16$; $t=2.4$, $p=0.007$). In this paired analysis, the CS group showed significant activation reduction in the primary somatosensory cortex (including the cortical representation of the leg) and extending to the primary motor cortex and posterior supplementary motor area. Group by session interaction consistently revealed a tendency for this cortical change to be larger in the CS than in placebo (peak interaction $x=2$, $y=-6$, $z=72$; $t=2.96$, $p=0.002$ and 43 voxels -subthreshold- with $p<0.01$).

Conclusion: fMRI was sensitive to objectify CS effects on brain response to knee painful stimulation. The current work yields further support to the utility of fMRI to objectify treatment effects on OA pain. The positive treatment effect of CS on brain was identified on pain elicited by pressure on patellofemoral cartilage, where the cartilage component of pain is a relevant factor. This result is consistent with the known CS mechanisms of action and the results obtained in previous clinical trials.

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Effect Of Fish Oil On Structural Progression In Knee Osteoarthritis: A Two Year Randomized, Double-Blind Clinical Trial Comparing High Dose With Low Dose. Catherine L. Hill[1], Graeme Jones[2], Susan Lester[3], Ruth Battersby[1], Tanya Fedorova[4], Kristen Hynes[5], Susanna Proudman[6], Leslie G. Cleland[6] and Lyn March[7]. [1]The Queen Elizabeth Hospital, Woodville, Australia, [2]Menzies Research Institute Tasmania, University of Tasmania, Hobart, 7000, Australia, [3]Queen Elizabeth Hospital, Woodville South, Australia, [4]University of Sydney, St Leonards, Australia, [5]University of Tasmania, Hobart, Australia, [6]Royal Adelaide Hospital, Adelaide, Australia, [7]University of Sydney Institute of Bone and Joint Research, Royal North Shore Hospital, St Leonards, Australia.

Background/Purpose: Fish oil is widely used for the symptomatic treatment of osteoarthritis. However, its effect on cartilage volume has not previously been investigated in an RCT. The objective of this study was to determine whether high dose fish oil is superior to low dose fish oil in retarding structural progression of symptomatic knee osteoarthritis.

Methods: Investigator initiated, government funded, randomized, double-blind, multicenter 24 month trial. Patients older than 40 years, with knee OA as defined by the ACR clinical criteria, suffering from regular knee pain were randomized 1:1 to (1) high dose fish oil liquid (EPA 18% and DHA 12%) 15mL/day or (2) low dose fish oil (blend of fish oil and sunola oil in a ratio of 1:9) 15mL/day. Each oil was also flavored with citrus to provide a comparable taste and ensure masking. Prior to randomization, a 4- week run in period with a similar oil was performed to exclude patients who were intolerant to liquid fish oil. Baseline knee radiographs were scored according to OARSI atlas. The co-primary end point was change in cartilage volume (medial tibial, lateral tibial, patellotibial) from baseline to 24 months. The co-primary endpoint of WOMAC pain score has previously been reported. Analysis of paired MRI data was performed, according to intention-to-treat and per-protocol analysis.

Results: Participants ($N=202$) were 49% female, mean age 60.9 yrs (SE 0.7), mean BMI 29.0 (SE 4.7). There was significantly greater and earlier dropout in the high dose group (34.6%, median 3 months), compared to the low dose group (19.8%, median 7.5 months). Participants from one site were excluded ($n=51$) due to technical MRI issue with baseline MRI data and a further 35 participants were excluded due to lack of paired MRI data. There was similar baseline characteristics in each group, except for gender (low dose group 38% female, high dose 58% female, $p=0.025$). The OARSI joint space narrowing and osteophyte scores were not different between groups. In intention to treat analysis ($n=116$), both groups demonstrated preservation or a slight increase in cartilage volume in each compartment over time with no significant difference seen between the two groups (Table 1). Similarly, per protocol analysis ($n=99$) demonstrated no decrease over time or difference between groups. There was no difference in results when males and females were analyzed separately.

Table 1.

		CHANGE FROM BASELINE (ITT)			Delta-Delta[1]		
MRI	Group	mean	sd	$p\text{-val}_{change}$	mean	sd	$p\text{-value}_{H\ vs\ L\ change}$
Lateral tibial	LowDose	0.015	0.027	0.58	0.000	0.038	1.00
	High Dose	0.015	0.026	0.57			
Medial tibial	LowDose	0.015	0.029	0.60	0.020	0.040	0.63
	High Dose	0.035	0.028	0.63			
Patellotibial	LowDose	0.027	0.040	0.50	0.030	0.055	0.59
	High Dose	0.003	0.039	0.94			

Conclusion: High dose fish oil supplementation for 2 years was not significantly different in its effect on cartilage volume in patients with symptomatic knee OA, when compared to low dose fish oil. The lack of a decrease in both groups is unexpected and may imply that both therapies have chondroprotective properties.

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Use Of Low Dose Aspirin Is Associated With Reduced Medial Tibial Cartilage Loss In Symptomatic Osteoarthritis: DATA From A Cohort Study. Anita Wluka[1], Changhai Ding[2], Yuanyuan Wang[1], Graeme Jones[3], Andrew Teichtahl[1] and Flavia Cicuttini[4]. [1]Monash University, Melbourne, Australia, [2]Menzies Research Institute Tasmania, University of Tasmania, Hobart, 7000, Australia, [3]Menzies Research Institute, Tasmania, Australia, [4]Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, 3004, Australia.

Background/Purpose: Inflammation and vascular disease have recently been shown to play a role in the pathogenesis of osteoarthritis (OA). Low dose aspirin is commonly used in the prevention of cardiovascular disease. Its effects have been attributed to a variety of actions, including anti-inflammatory effects and effects on platelet function (both anti-thrombotic and anti-inflammatory) and lipids. However whether it affects human joints has not been studied. The aim of this study was to examine whether the use of low dose aspirin affects change in knee cartilage volume over 2 years.

Methods: 117 people with symptomatic knee OA underwent magnetic resonance imasging of the knee at baseline and 2 years later. Medial and lateral tibial cartilage volumes were measured using validated methods. Annual absolute change and annual percentage change in cartilage volume were calculated. Information about regular low dose aspirin use was collected at baseline, 6, 12 and 24 months. Participants who reported taking regular low dose aspirin (< 150 mg per day) at more than 1 time point were defined as being aspirin users.

Results: Twenty six participants reported taking aspirin at more than one visit, with 91 not taking aspirin. At baseline, the only significant difference between the 2 groups was that those taking aspirin were older than those who did not ($p = 0.03$). In those taking aspirin, annual change in medial tibial cartilage volume and annual percentage change in cartilage volume was approximately half that seen in those not taking aspirin (−50 vs. −102 mm 3 and −2.5% vs. −5.5%, respectively, $P=0.04$ for both). These differences became more significant after adjusting for age, gender, body mass index, initial cartilage volume and severity of radiographic change in the medial compartment. The annual change in medial tibial cartilage volume was −40 mm 3 (95% confidence interval (CI) −83, 1.3) in aspirin users vs. −105 mm3 (95% CI −127, −82) in nonaspirin users ($P = 0.009$ for difference). The annual percentage change in medial tibial cartilage volume was −2.0% (95% CI −4.6, 0.53) in aspirin users vs. −5.6% (95% CI −6.9, −4.0) in non-aspirin users ($P=0.02$ for difference). There were no significant differences observed in change in lateral tibial cartilage volume.

Conclusion: This study showed that in people with knee OA, the use of low dose aspirin was associated with reduced medial tibial cartilage loss over 2 years. This requires confirmation in a randomised controlled trial. If this hypothesis were proven, aspirin may provide a cost effective disease modifying therapy for OA as it is a cheap medication that is already in common use and known to be well tolerated.

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