VI Congresso Nazionale SINUT

Focus sull'impiego clinico dei nutraceutici in medicina preventiva

La condroprotezione articolare nell'artrosi: nuove evidenze e linee guida terapeutiche

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Symptomatic slow acting drugs for OA (SYSADOA)

- Symptomatic slow acting drugs for OA (SYSADOA) have a slow onset of action but have additional benefits such as global efficacy similar to NSAIDs and a carry-over effect (the effect lasts for months even after treatment suppression).
- Moreover, these drugs have a high safety profile and the ratio cost/effectiveness is low.
- The main SYSADOAs are chondroitin sulfate (CS), glucosamine sulfate (GLU) and hyaluronic acid (HA).They are specially indicated in elderly patients, often polymedicated.
- SYSADOAs, apart from their symptomatic effect, also have a structure disease modifying effect slowing OA progression.

Recommendation for use of symptomatic slow-acting drugs for osteoarthritis (SYSADOAs) in the treatment of OA

	SySADOAs	Level of evidence or ES	Final recommendation
EULAR (2003)	Chondroitin sulfate and glucosamine sulfate	Highest level of evidence (1A), highest strength of recommendation (A)	Recommended for symptomatic effect and might modify structure
OARSI (2007, 2008, and 2010)	Chondroitin sulfate	Pain ES = 0.75 (0.5–1.01)	Recommended for OA symptoms
	Glucosamine sulfate	Pain ES = 0.58 (0.3–0.87)	Recommended for OA symptoms
	Glucosamine HCl	Pain ES = −0.02 (−0.15 to 0.11)	Not recommended
ACR (2012)	Chondroitin sulfate and glucosamine		Conditional recommendation NOT to use
OARSI (2014)	Chondroitin sulfate	Pain ES = 0.13 (0.00–0.27) to 0.75 (0.50–0.99)	Recommendation for symptom modification: uncertain
		mJSW[a] ES = 0.26 (0.14–0.38) to 0.30 (0.00–0.59)	Recommendation for disease modification: not appropriate
	Glucosamine	Pain ES = 0.17 (0.05–0.28) to 0.47 (0.23–0.72)	Recommendation for symptom modification: uncertain
		mJSW[a] ES = 1st year: 0.08 (−012 to 0.27); 3rd year: 0.43 (0.24–0.63)	Recommendation for disease modification: not appropriate
ESCEO (2014)	Glucosamine sulfate	Pain ES = 0.27; function ES = 0.32	Recommended as a background treatment in the initial pharmacological management
	Chondroitin sulfate	Pain ES from mild to moderate	

Is there any scientific evidence for the use of glucosamine in the management of human osteoarthritis?

Yves Henrotin*[1], Ali Mobasheri[2] and Marc Marty[3]

. *Arthritis Research & Therapy* 2012, **14**:201

GLUCOSAMINE SULFATE ACTION MECHANISMS

STIMULATES:

-↑ proteoglycans

EFFECT:

- Anti-inflammatory activity
- Membrane stabilising activity

INHIBITS:

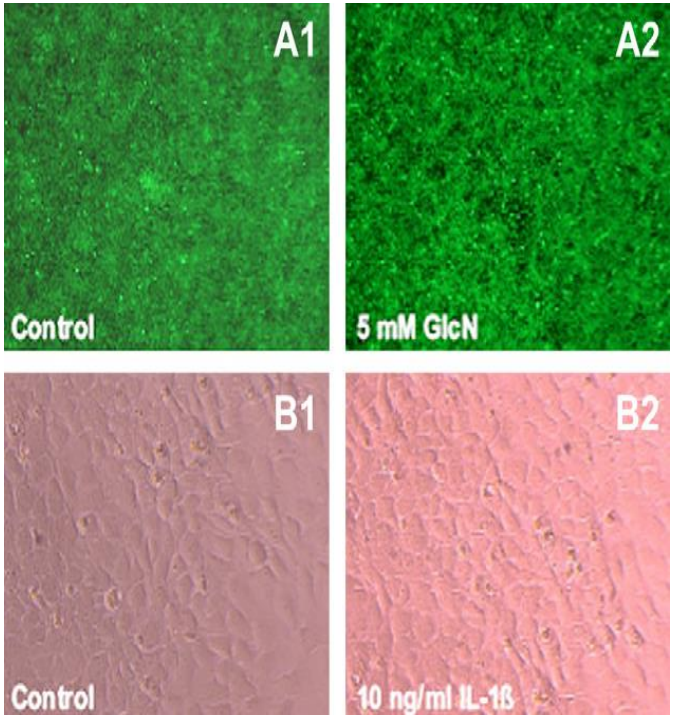
↓ cartilage degradative enzymes (collagenase, aggrecanase, phospholipase A2, etc.)
↓ MMP-3, MMP-2, MMP-9
↓ free radicals
↓ PGE2
↓ IL-1
↓ NF-kB

Comparison between chondroprotective effects of glucosamine, curcumin, and diacerein in IL-1β-stimulated C-28/I2 chondrocytes

S. Toegel M.Pharm.S., Ph.D.†*, S. Q. Wu M.Pharm.S.†, C. Piana M.Pharm.S.†,
F. M. Unger Ph.D., Professor†, M. Wirth M.Pharm.S., Ph.D., Professor†,
M. B. Goldring Ph.D., Professor‡, F. Gabor M.Pharm.S., Ph.D., Professor†
and H. Viernstein M.Pharm.S., Ph.D., Professor†

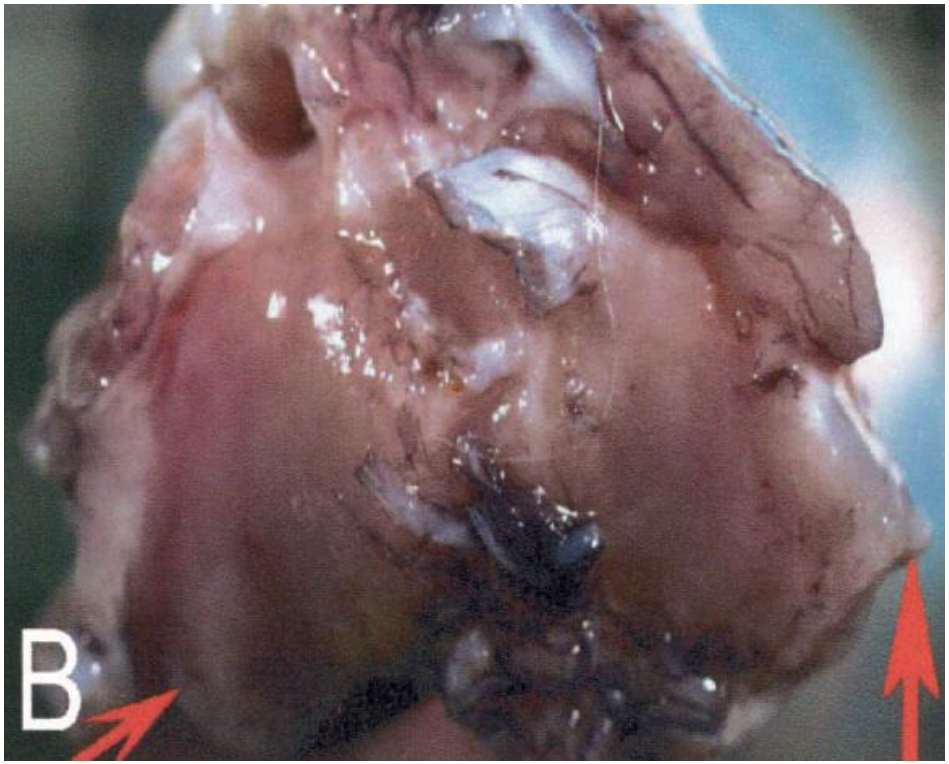
Osteoarthritis and Cartilage (2008) **16**, 1205–1212

Both glucosamine (GlcN) and diacerein promoted a differentiated chondrocytic phenotype of immortalized human C-28/I2 chondrocytes by altering proliferation, morphology, and collagen type I COL2/COL1 mRNA ratios. Moreover, both agents antagonized inhibitory effects of IL-1b by enhancing aggrecan and COL2 as well as by reducing COL1 mRNA levels.



The Effects of Glucosamine Hydrochloride on Subchondral Bone Changes in an Animal Model of Osteoarthritis

Susanne X. Wang,[1] Sheila Laverty,[2] Mircea Dumitriu,[1] Anna Plaas,[3] and Marc D. Grynpas[1]



This study shows that subchondral bone turnover, structure, and mineralization are significantly altered in the early stages of experimental OA, and that these changes are attenuated by glucosamine treatment.

ARTHRITIS & RHEUMATISM
Vol. 56, No. 5, May 2007, pp 1537–1548

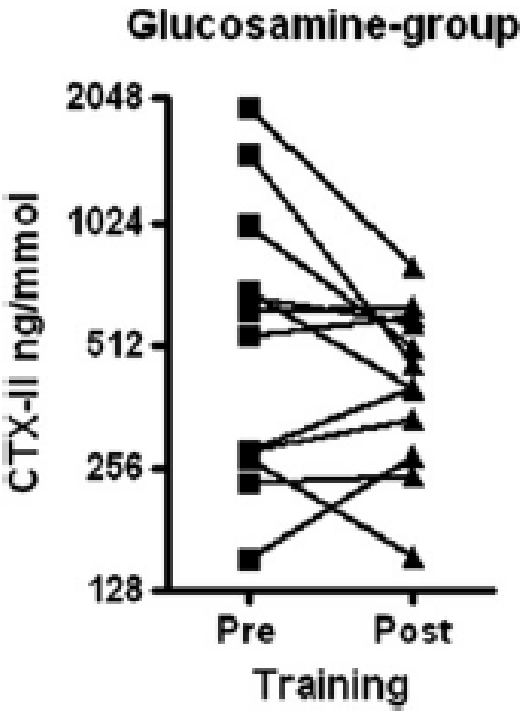
Glucosamine but not ibuprofen alters cartilage turnover in osteoarthritis patients in response to physical training[1]

S. G. Petersen†*, T. Saxne‡, D. Heinegard§, M. Hansen†, L. Holm†, S. Koskinen†, C. Stordal†, H. Christensen‖, P. Aagaard¶ and M. Kjaer†

Osteoarthritis and Cartilage (2010) 18, 34–40

Serum cartilage oligomeric matrix protein (COMP) decreased significantly over the 12-week training period when treatment with glucosamine.

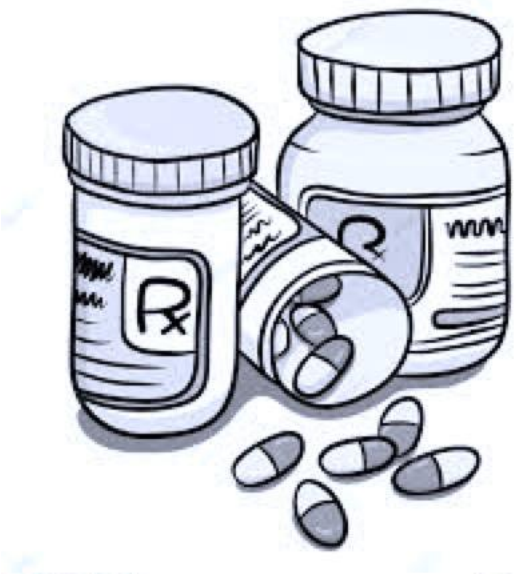
This suggests an effect by glucosamine on the response of the OA cartilage to a period of joint loading in humans with knee OA.



An algorithm recommendation for the management of knee osteoarthritis in Europe and internationally: A report from a task force of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO)

Olivier Bruyère, PhD[a,*], Cyrus Cooper, MD, PhD[b,c], Jean-Pierre Pelletier, MD, PhD[d],

Seminars in Arthritis and Rheumatism 44 (2014) 253–263

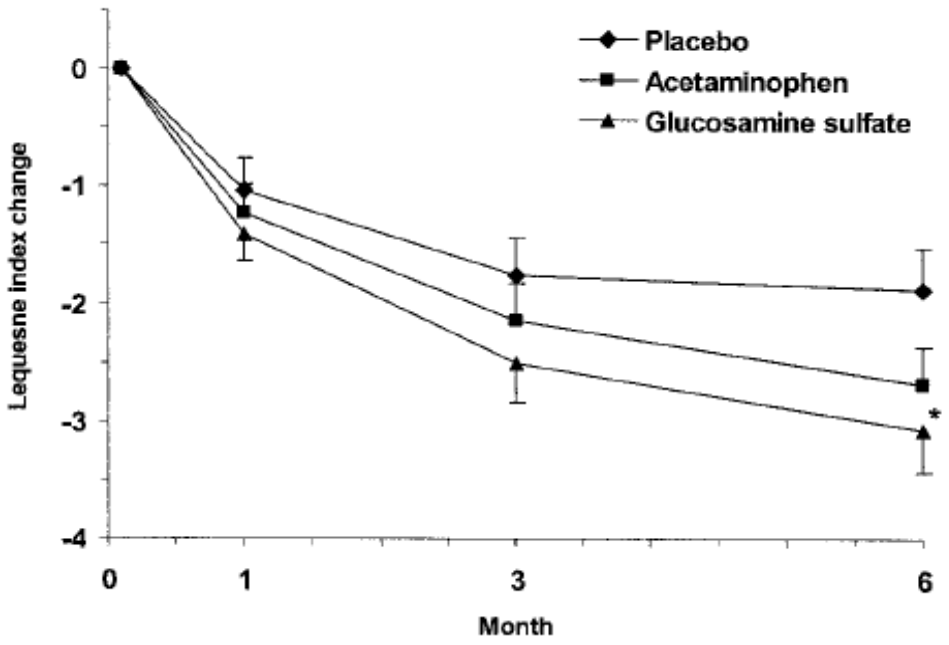


Both glucosamine sulfate and chondroitin are safe medications, with no difference in adverse effects compared with placebo, which would also strengthen their role as chronic background treatments.

Glucosamine Sulfate in the Treatment of Knee Osteoarthritis Symptoms

A Randomized, Double-Blind, Placebo-Controlled Study Using Acetaminophen as a Side Comparator

Gabriel Herrero-Beaumont,[1] José Andrés Román Ivorra,[2] María del Carmen Trabado,[3] Francisco Javier Blanco,[4] Pere Benito,[5] Emilio Martín-Mola,[6] Javier Paulino,[7] José Luis Marenco,[8] Armando Porto,[9] Armando Laffon,[10] Domingos Araújo,[11] Manuel Figueroa,[12] and Jaime Branco[13]



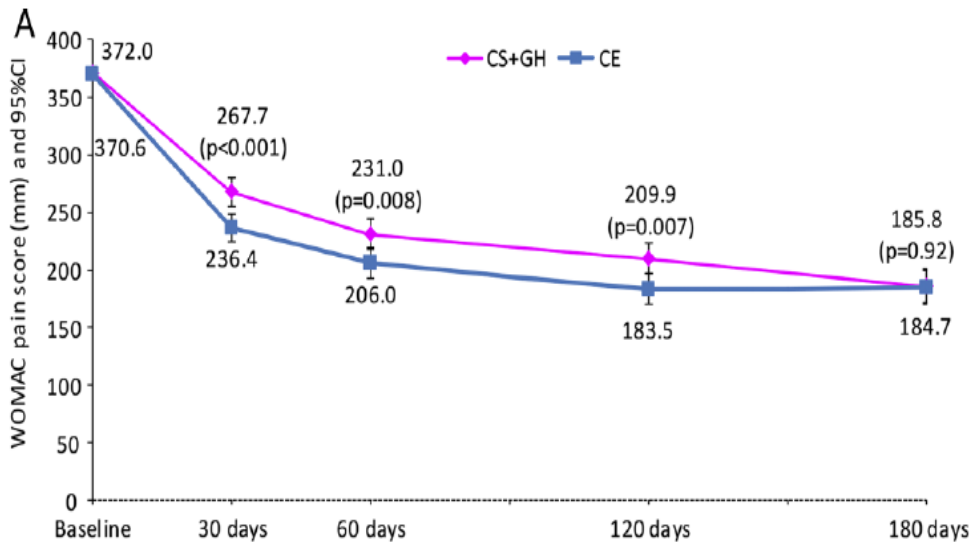
The findings of this study indicate that glucosamine sulfate at the oral once-daily dosage of 1,500 mg is more effective than placebo in treating knee OA symptoms.

ARTHRITIS & RHEUMATISM
Vol. 56, No. 2, February 2007, pp 555–567

Combined chondroitin sulfate and glucosamine for painful knee osteoarthritis: a multicentre, randomised, double-blind, non-inferiority trial versus celecoxib

Ann Rheum Dis 2016;**75**:37–44.

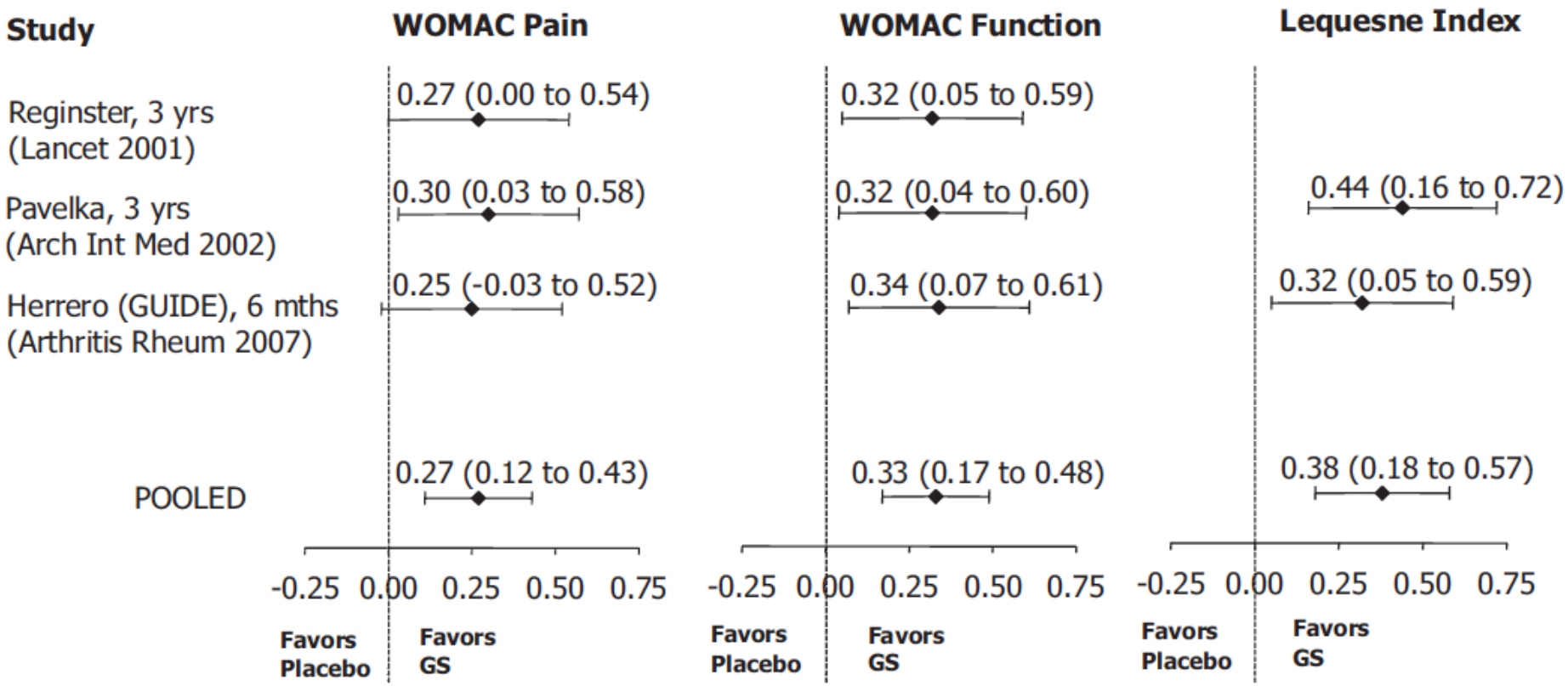
Marc C Hochberg,[1] Johanne Martel-Pelletier,[2] Jordi Monfort,[3,4] Ingrid Möller,[5] Juan Ramón Castillo,[6] Nigel Arden,[7,8,9] Francis Berenbaum,[10] Francisco J Blanco,[11] Philip G Conaghan,[12] Gema Doménech,[13] Yves Henrotin,[14,15] Thomas Pap,[16] Pascal Richette,[17,18] Allen Sawitzke,[19] Patrick du Souich,[20] Jean-Pierre Pelletier,[2] on behalf of the MOVES Investigation Group



Chondroitin sulfate plus glucosamine hydrochloride (CS+GH) has comparable efficacy to celecoxib in reducing pain, stiffness, functional limitation and joint swelling/effusion after 6 months in patients with painful knee osteoarthritis, with a good safety profile.

Efficacy and safety of glucosamine sulfate in the management of osteoarthritis: Evidence from real-life setting trials and surveys

Olivier Bruyère, PhD[a,*], Roy D. Altman, MD[b], Jean-Yves Reginster, MD, PhD[c]



Seminars in Arthritis and Rheumatism 45 (2016) S12–S17

Structural and Symptomatic Efficacy of Glucosamine and Chondroitin in Knee Osteoarthritis

A Comprehensive Meta-analysis

Florent Richy, MSc; Olivier Bruyere, MSc; Olivier Ethgen, MSc; Michel Cucherat, MSc, PhD; Yves Henrotin, MSc, PhD; Jean-Yves Reginster, MD, PhD

Arch Intern Med. 2003;163:1514-1522

VAS Pain				
Bourgeois et al,[12] 1998	0.89	0.43	1.34	<.001
Bucsi and Poor,[13] 1998	0.57	0.13	1.01	.01
Conrozier,[14] 1998	0.39	0.00	0.78	.05
L'Hirondel,[18] 1992	0.35	0.00	0.71	.05
Mazieres et al,[15] 1992	0.38	0.00	0.76	.05
Mazieres et al,[16] 2001	0.28	−0.07	0.63	.12
Pavelka et al,[19] 1999	0.98	0.47	1.48	<.001
Uebelhart et al,[17] 1998	1.02	0.39	1.66	<.001
Hughes and Carr,[29] 2002	0.03	−0.41	0.48	.89
Pujalte et al,[25] 1980	1.23	0.19	2.28	.01
Rindone et al,[28] 2000	0.06	−0.34	0.46	.77
Rovati,[27] 1997	0.53	0.21	0.86	<.001
Combined	0.45	0.33	0.57	<.001
Mobility				
Uebelhart et al,[17] 1998	0.78	0.16	1.40	.01
Hughes and Carr,[29] 2002	0.52	0.07	0.98	.02
Pujalte et al,[25] 1980	0.42	−0.53	1.37	.34
Combined	0.59	0.25	0.92	<.001

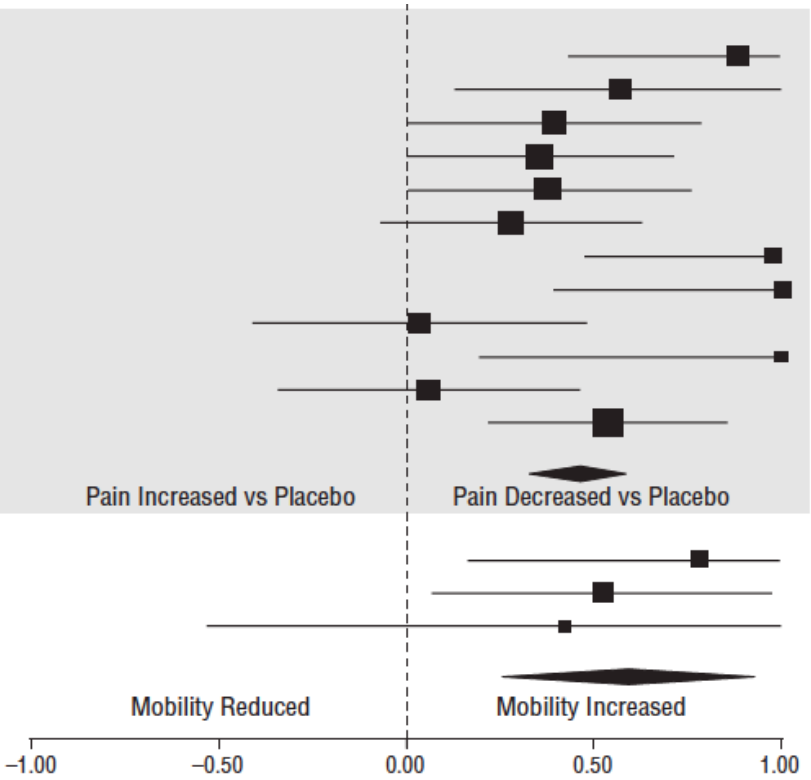


Figure 2. Effect sizes of symptomatic outcomes. LI indicates Lequesne Index; WOMAC, Western Ontario MacMaster University Osteoarthritis Index; and VAS, visual analog scale.

Efficacy and safety of glucosamine, diacerein, and NSAIDs in osteoarthritis knee: a systematic review and network meta-analysis

Jatupon Kongtharvonskul[1*], Thunyarat Anothaisintawee[1], Mark McEvoy[2], John Attia[3], Patarawan Woratanarat[4] and Ammarin Thakkinstian[1]

European Journal of Medical Research (2015) 20:24

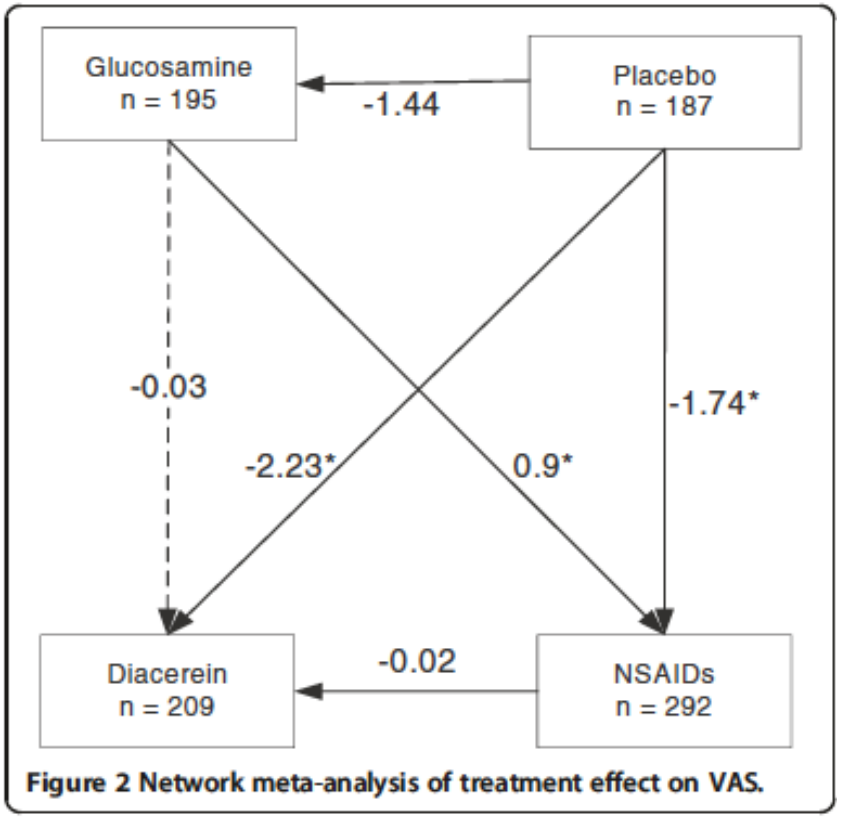


Figure 2 Network meta-analysis of treatment effect on VAS.

Compared to placebo, glucosamine showed a significant improvement with unstandardized mean differences in total WOMAC, pain WOMAC, function WOMAC, and Lequesne score

Effects of glucosamine sulfate on the use of rescue non-steroidal anti-inflammatory drugs in knee osteoarthritis: Results from the Pharmaco-Epidemiology of GonArthroSis (PEGASus) study☆

Lucio C. Rovati, MD[a,*], Federica Girolami, PharmD, MSc[b], Massimo D'Amato, MD[a], Giampaolo Giacovelli, PhD[c]

Seminars in Arthritis and Rheumatism 45 (2016) S34–S41

The Pharmaco-Epidemiology of GonArthroSis (PEGASus) Was a cohort study of continuous recruitment o fpatients with "dynamic" exposure to the investigated SYSADOA (crystalline glucosamine sulfate,glucosamine hydrochloride,chondroitin sulfate, diacerein,and avocado–soybean unsaponifiables, all a tapproved dosages)

Crystalline glucosamine sulfate was the only SYSADOA that decreased the use of NSAIDs in this study in patients with knee OA

A Clinical Study on Glucosamine Sulfate versus Combination of Glucosamine Sulfate and NSAIDs in Mild to Moderate Knee Osteoarthritis

The Scientific World Journal
Volume 2012, Article ID 902676, 5 pages

Tamil Selvan,[1] Kingston Rajiah,[2] M. Sundara-Moorthi Nainar,[3] and Elizabeth M. Mathew[4]

The objective of this study was glucosamine sulfate versus combination of glucosamine sulfate and Non-Steroidal anti inflammatory drugs (NSAID) in mild to moderate knee osteoarthritis.

Study results may suggest that the Glucosamine Sulfate has a carryover effect like Disease-modifying agents. Long-term treatment of Glucosamine Sulfate may reduce the dependence of NSAIDs usage and delay the disease progression. Thereby we can reduce the NSAIDs side effects and improve the patient's quality of life.

Efficacy and safety of glucosamine sulfate in the management of osteoarthritis: Evidence from real-life setting trials and surveys

Olivier Bruyère, PhD[a,*], Roy D. Altman, MD[b], Jean-Yves Reginster, MD, PhD[c]

Real-life pharmacoeconomic studies demonstrate a long term reductionin the need for additional pain analgesia and non-steroidal anti-inflammatory drugs (NSAIDs) with pCGS,with a significant reduction of over 50% in costs associated with medications, healthcare consultations and examinations over 12 months.

Mean costs, € (US$)[a]	Placebo (n = 43)	pCGS (n = 58)
Cost of analgesics	59 (77)	19 (25)
Cost of NSAIDs	116 (151)	63 (82)
Total cost of OA drugs (including analgesics, NSAIDs, etc.)	204 (265)	108 (140)
Total cost calculated for OA-related resources[b]	605 (786)	292 (380)[c]

Mean costs associated with use of OA medication and OA-related healthcare resources per patient per year among OA patients who had received patented crystalline glucosamine sulfate (pCGS) 5 years previously versus placebo

Seminars in Arthritis and Rheumatism 45 (2016) S12–S17

Conventional medical therapy for osteoarthritis: current state of the evidence

Allan C. Gelber

Curr Opin Rheumatol 2015, 27:312–317

- From the NIH Osteoarthritis Initiative, we learn that a combination of glucosamine and chondroitin was associated with a structural benefit to the knee, though we are not informed about the dose of glucosamine and chondroitin consumed, the formulation used, or the compliance rate with the supplement.

Efficacy and safety of glucosamine sulfate in the management of osteoarthritis: Evidence from real-life setting trials and surveys

Olivier Bruyère, PhD[a,*], Roy D. Altman, MD[b], Jean-Yves Reginster, MD, PhD[c]

Evidence for a disease-modifying effect of patented crystalline glucosamine sulfate (pCGS): prevention of joint space narrowing in knee osteoarthritis

Reginster et al. [24]	Placebo (n = 106)	pCGS (n = 106)	Difference	p Value
JSW at enrollment, mm (mean ± SD)	3.95 ± 1.24	3.82 ± 1.32	-	-
3-year JSN, mm (mean and 95% CI)	−0.40 (−0.56 to −0.24)	−0.07 (−0.22 to 0.07)	0.33 (0.12–0.54)	0.003
Pavelka et al. [25]	**Placebo (n = 101)**	**pCGS (n = 101)**	**Difference**	**p Value**
JSW at enrollment, mm (mean ± SD)	3.63 ± 1.57	3.89 ± 1.48	-	-
3-year JSN, mm (mean and 95% CI)	−0.19 (−0.29 to −0.09)	0.04 (−0.06 to 0.14)	0.23 (0.09–0.37)	0.001

CI, confidence interval; JSN, joint space narrowing; JSW, joint space width; pCGS, patented crystalline glucosamine sulfate; SD, standard deviation.

Seminars in Arthritis and Rheumatism 45 (2016) S12–S17

Glucosamine and chondroitin for knee osteoarthritis: a double-blind randomised placebo-controlled clinical trial evaluating single and combination regimens

Marlene Fransen,[1] Maria Agaliotis,[1] Lillias Nairn,[1] Milana Votrubec,[2] Lisa Bridgett,[1] Steve Su,[3] Stephen Jan,[4] Lyn March,[5] John Edmonds,[6] Robyn Norton,[4] Mark Woodward,[4] Richard Day,[7] on behalf of the LEGS study collaborative group

A double-blind randomised placebo-controlled clinical trial with 2-year follow-up. 605 participants, reporting chronic knee pain and with evidence of medial tibio-femoral compartment narrowing Were randomised to once daily: glucosamine sulfate 1500 mg, chondroitin sulfate 800 mg, both dietary supplements or matching placebo capsules .

Allocation to the glucosamine–chondroitin combination resulted in a statistically significant reduction in JSN at 2 years.

Ann Rheum Dis 2015;**74**:851–858.

The Effect of Glucosamine and/or Chondroitin Sulfate on the Progression of Knee Osteoarthritis

A Report from the Glucosamine/Chondroitin Arthritis Intervention Trial

Allen D. Sawitzke,[1] Helen Shi,[2] Martha F. Finco,[1] Dorothy D. Dunlop,[3] Clifton O. Bingham, III,[4] Crystal L. Harris,[5] Nora G. Singer,[6] John D. Bradley,[7] David Silver,[8] Christopher G. Jackson,[1] Nancy E. Lane,[9] Chester V. Oddis,[10] Fred Wolfe,[11] Jeffrey Lisse,[12] Daniel E. Furst,[13] Domenic J. Reda,[2] Roland W. Moskowitz,[6] H. James Williams,[1] and Daniel O. Clegg[1]

A 24-month, double-blind, placebocontrolled study, conducted at 9 sites in the United States as part of the Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT), enrolled 572 patients with knee OA treatment effects on K/L grade 2 knees, but not on K/L grade 3 knees, showed a trend toward improvement relative to the placebo group.

Knees with K/L grade 2 radiographic OA appeared to have the greatest potential for modification by these treatments.

ARTHRITIS & RHEUMATISM
Vol. 58, No. 10, October 2008, pp 3183–3191

The role of diet and exercise and of glucosamine sulfate in the prevention of knee osteoarthritis: Further results from the PRevention of knee Osteoarthritis in Overweight Females (PROOF) study

Jos Runhaar, PhD[a,*], Rita Deroisy, PhD[b], Marienke van Middelkoop, PhD[a], Francesco Barretta, MSc[c,d], Beatrice Barbetta, PhD[d], Edwin H. Oei, MD, PhD[e], Dammis Vroegindeweij, MD, PhD[f], Giampaolo Giacovelli, PhD[d], Olivier Bruyère, PhD[b], Lucio C. Rovati, MD[d], Jean-Yves Reginster, MD, PhD[b], Sita M.A. Bierma-Zeinstra, PhD[a,g]

The PRevention of knee Osteoarthritis in Overweight Females (PROOF) study described a trend for a decrease in the incidence of knee osteoarthritis (OA) by a tailored diet and exercise program (DEP) or by oral glucosamine sulfate in women at risk for the disease, using a composite clinical and/or radiological outcome.

Glucosamine sulfate decreased the risk of developing radiographic knee OA over 2.5 years in overweight, middle-aged women at risk, as determined by medial mJSN progression.

Seminars in Arthritis and Rheumatism 45 (2016) S42–S48

Total joint replacement after glucosamine sulphate treatment in knee osteoarthritis: results of a mean 8-year observation of patients from two previous 3-year, randomised, placebo-controlled trials

O. Bruyere Ph.D.†*, K. Pavelka M.D.‡, L. C. Rovati M.D.§, J. Gatterová M.D.‡, G. Giacovelli Ph.D.§, M. Olejarová M.D.‡, R. Deroisy Ph.D.† and J. Y. Reginster M.D.†

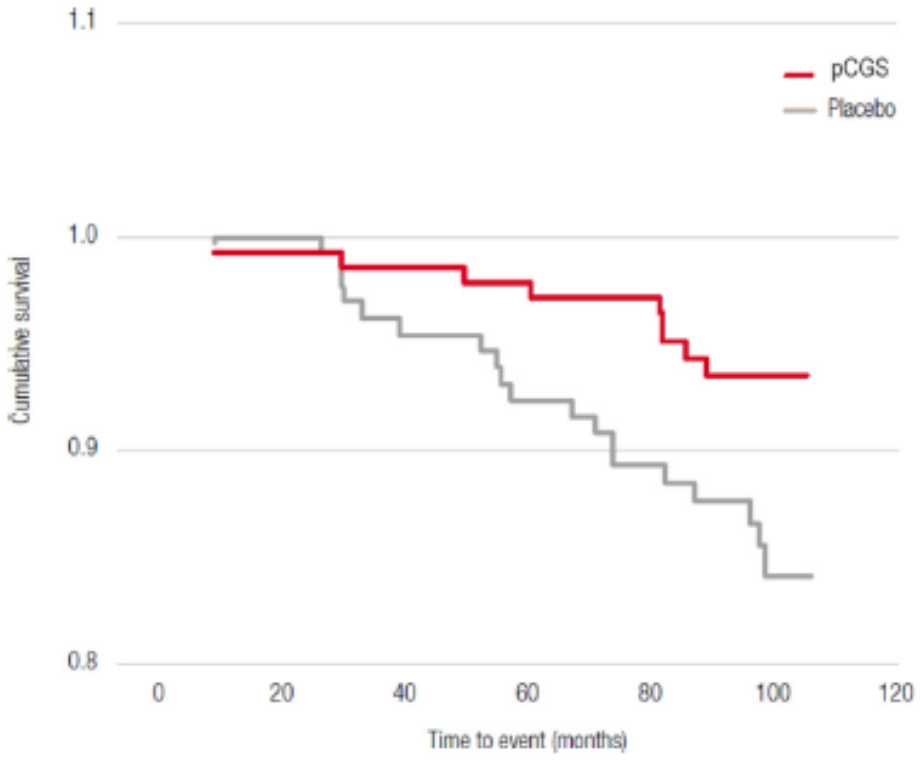


Fig. 2. Effect of prior patented crystalline glucosamine sulfate (pCGS) treatment on cumulative incidence of total joint replacement surgery for up to 5 years following treatment [37]. (Adapted with permission from Bruyere et al. [37].)

Real-life patient cohort follow-up studies have demonstrated that the structure-modifying effects of pCGS appear to translate into clinically relevant benefits in knee OA,i.e., a delay in the need for total joint replacement

Osteoarthritis and Cartilage (2008) **16,** 254–260

A consensus statement on the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) algorithm for the management of knee osteoarthritis—From evidence-based medicine to the real-life setting

Olivier Bruyère, PhD[a,*], Cyrus Cooper, MD, PhD[b,c], Jean-Pierre Pelletier, MD[d],

Seminars in Arthritis and Rheumatism 45 (2016) S3–S11

Only patented crystalline glucosamine sulfate (pCGS)
Only pCGS is given as a highly bioavailable once-daily dose (1.500 mg) with a proven pharmacological effect that equates to a clear clinical benefit in trials and real-life studies of knee OA.

An algorithm recommendation for the management of knee osteoarthritis in Europe and internationally: A report from a task force of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO)

BASIC PRINCIPLE AND CORE SET

Combination of treatment modalities, including non-pharmacological and pharmacological therapies is strongly recommended

Core set: - Information/Education
- Weight loss if overweight
- Exercise program (aerobic, strengthening)

STEP 1: Background treatment

if symptomatic

- (Paracetamol on a regular basis)
  OR
- Chronic SYSADOA: prescription glucosamine sulfate and/or chondroitin sulfate ± as needed paracetamol

if still symptomatic ADD

- Topical NSAIDs
  (OR)
- (Topical capsaicin)

Referral to physical therapist for:
if needed
(to control malalignment)

- Knee braces
- (Insoles)

if symptomatic ADDITION at any time

- ✓ Walking aids
- ✓ Thermal agents
- ✓ Manual therapy
- ✓ Patellar taping
- ✓ Chinese acupuncture
- ✓ TENS

Difficulties with assessing the benefit of glucosamine sulphate as a treatment for osteoarthritis

Nikki Burdett MBBS and Julian David McNeil MBBS FRACP FRCP PhD

Int J Evid Based Healthc 2012; **10:** 222–226

Abstract

Osteoarthritis is a chronic disease with a major impact on quality of life for a large proportion of the population. It is a disease for which to date there has been no disease-modifying therapy identified. As a result of its physiological role in articular cartilage, glucosamine sulphate has been postulated as a treatment for osteoarthritis. Claims have included symptomatic relief and even reduction in the rate of disease progression. Despite promising *in vitro* studies, however, the role of glucosamine sulphate in the management of osteoarthritis remains unclear. Studies addressing this issue have generated a wide range of conclusions, and these are discussed here. Methodological issues need to be addressed in order to gauge whether there is true benefit. On current evidence, it would appear that the benefits of dietary supplementation with glucosamine sulphate are limited to mild symptomatic relief, while a disease-modifying agent for this disease remains elusive.

OA IN THE PAST

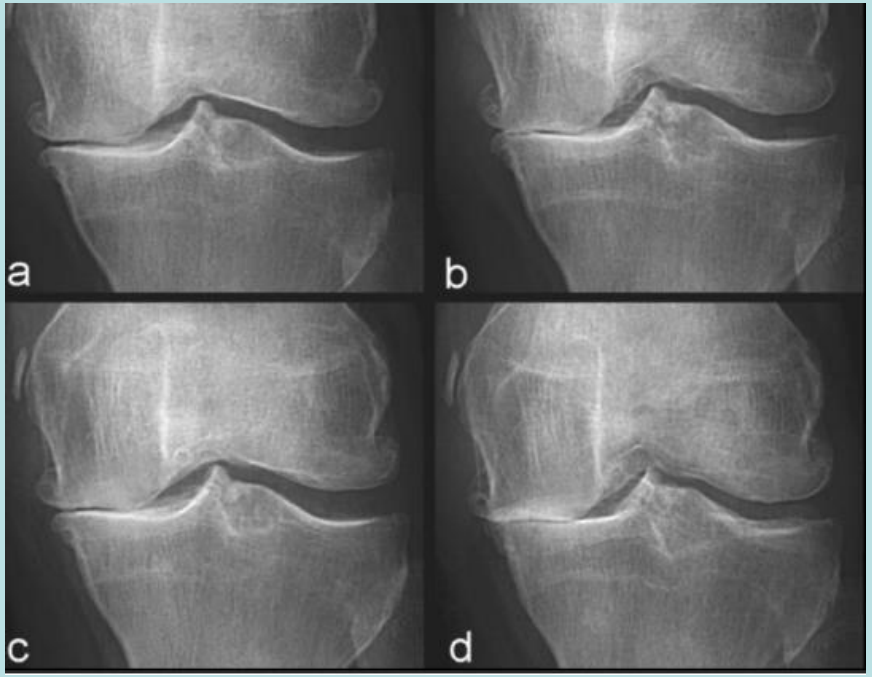
A disease of cartilage and bone

↓

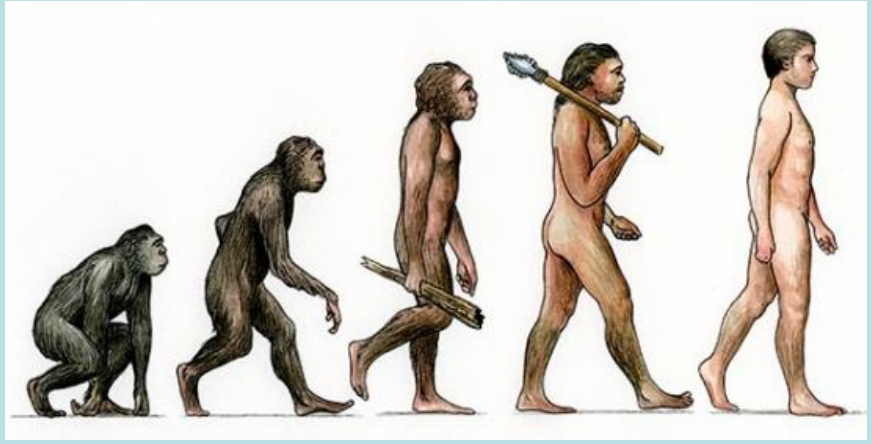
RADIOGRAPHS

↓

RADIOGRAPHIC CHANGES:
-OSTEOPHYTES
-JOINT SPACE NARROWING
-SCLEROSIS
-SUBCHONDRAL CYSTS



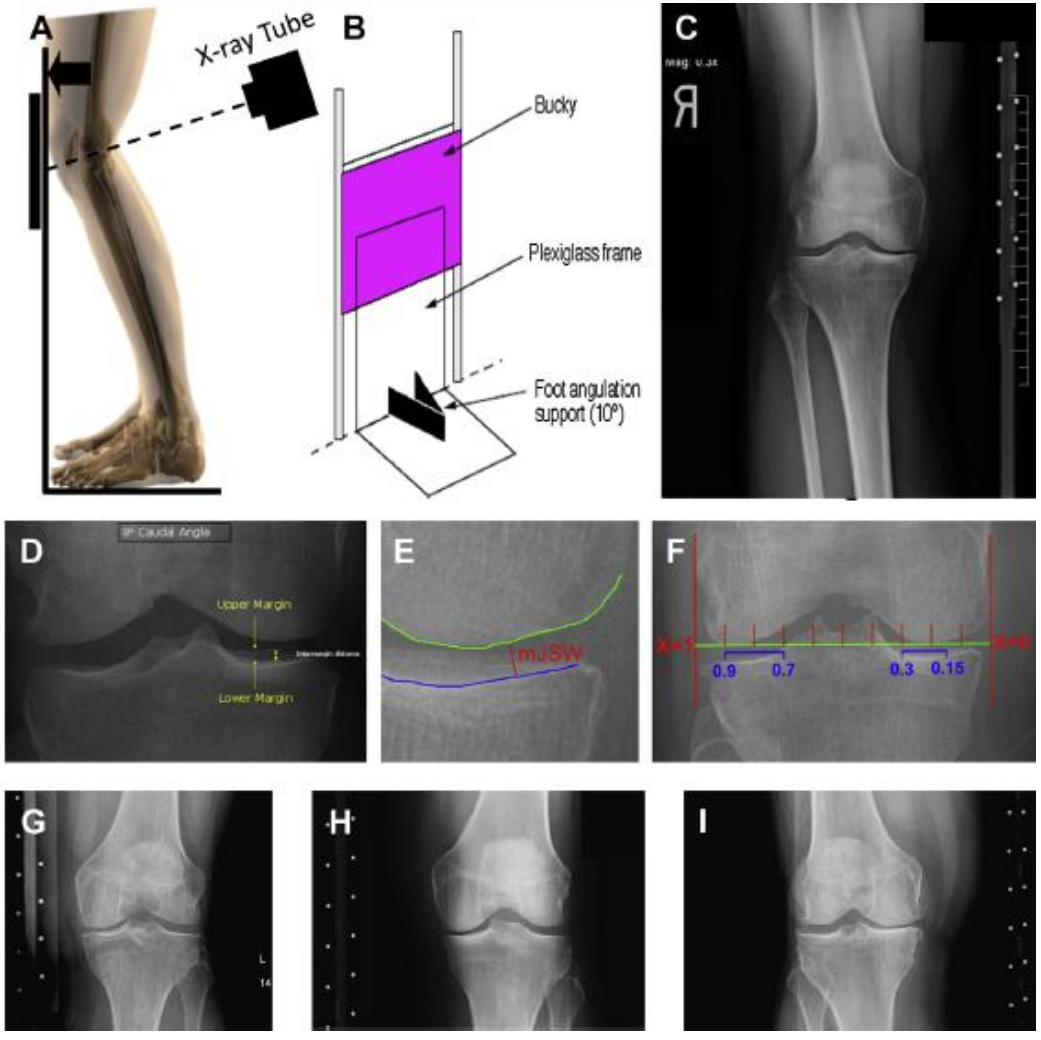
Conventional radiographs



Imaging of cartilage and bone: promises and pitfalls in clinical trials of osteoarthritis

Osteoarthritis and Cartilage 22 (2014) 1516–1532

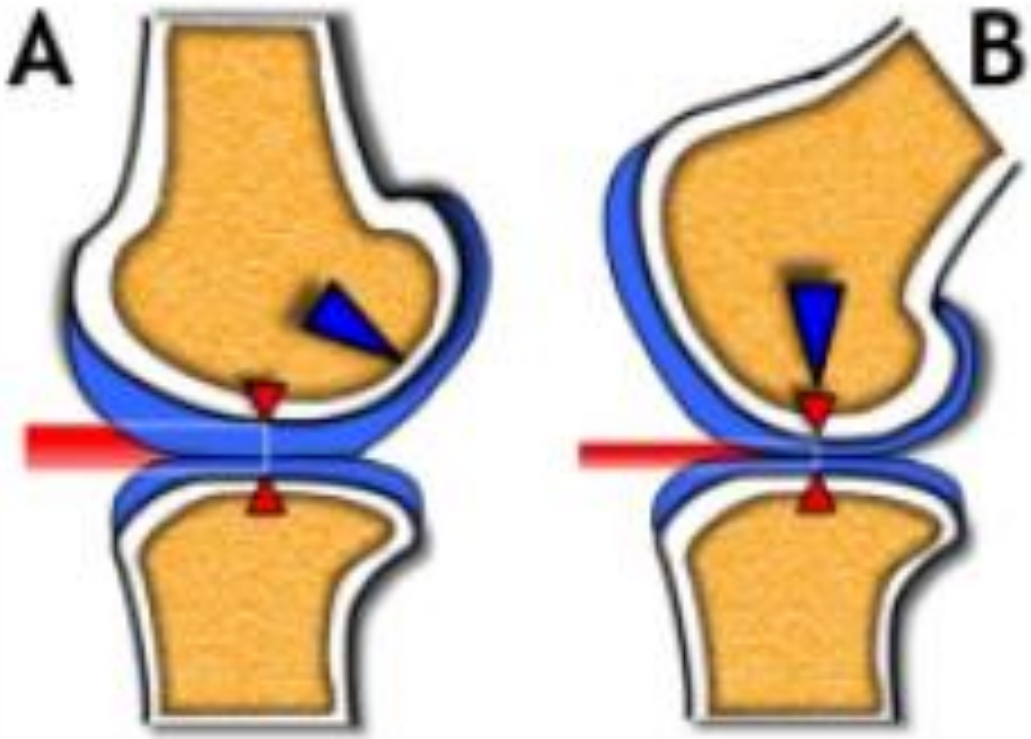
F. Eckstein † ‡ *, A. Guermazi § ||, G. Gold ¶, J. Duryea #, M.-P. Hellio Le Graverand ††, W. Wirth † ‡, C.G. Miller ‡‡



Radiography

- Standards of knee positioning (weight-bearing and fixed flexion) are important.
- Each of both knees should be imaged separately to ensure minimal X-ray beam divergence.
- The X-ray beam must be aligned with the medial tibial plateau; the IMD should be ≤1.0 mm.
- Several modifications of radiographic classification systems exist, these should therefore be clearly defined and documented.
- In fixed flexion radiographs of OA knees, central fixed location JSW measurements may be more responsive than that of minimum JSW.

Effetti della variazione dell'angolo femoro-tibiale sulla valutazione dell'ampiezza della rima articolare e dello spessore della cartilagine articolare.



Apparente assottigliamento della cartilagine e riduzione della rima articolare in corrispondenza della parte posteriore del condilo femorale (freccia blu) in caso di posizionamento del paziente con ginocchio in semi-flessione (B), rispetto all'immagine ottenuta con il ginocchio in completa estensione (A).

OA IN THE PRESENT

A whole joint disease

↓

MRI
ARTHROSCOPY
ULTRASOUND

↓

PRE-RADIOGRAPHIC STRUCTURAL TISSUE CHANGES:

-CARTILAGE DEFECTS
-MENISCUS LESIONS
-BONE MARROW LESIONS
-SYNOVITIS

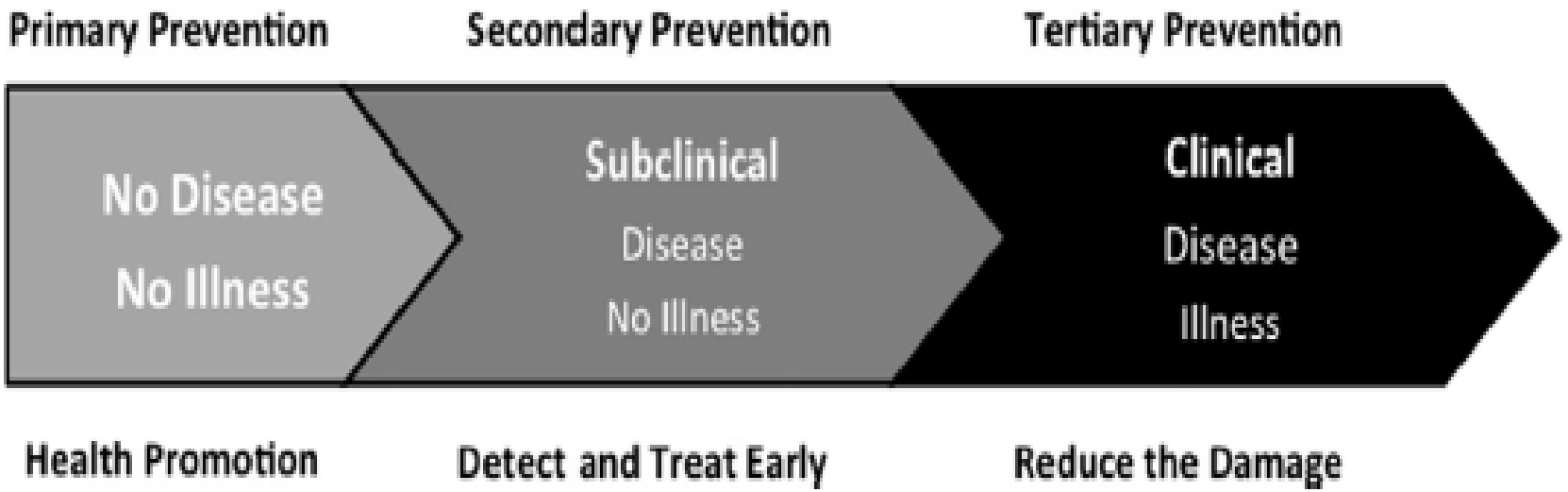
↓

EARLIER DIAGNOSIS OF OA

Call for standardized definitions of osteoarthritis and risk stratification for clinical trials and clinical use

V.B. Kraus †*, F.J. Blanco ‡, M. Englund §||, M.A. Karsdal ¶, L.S. Lohmander §#

Osteoarthritis and Cartilage 23 (2015) 1233–1241



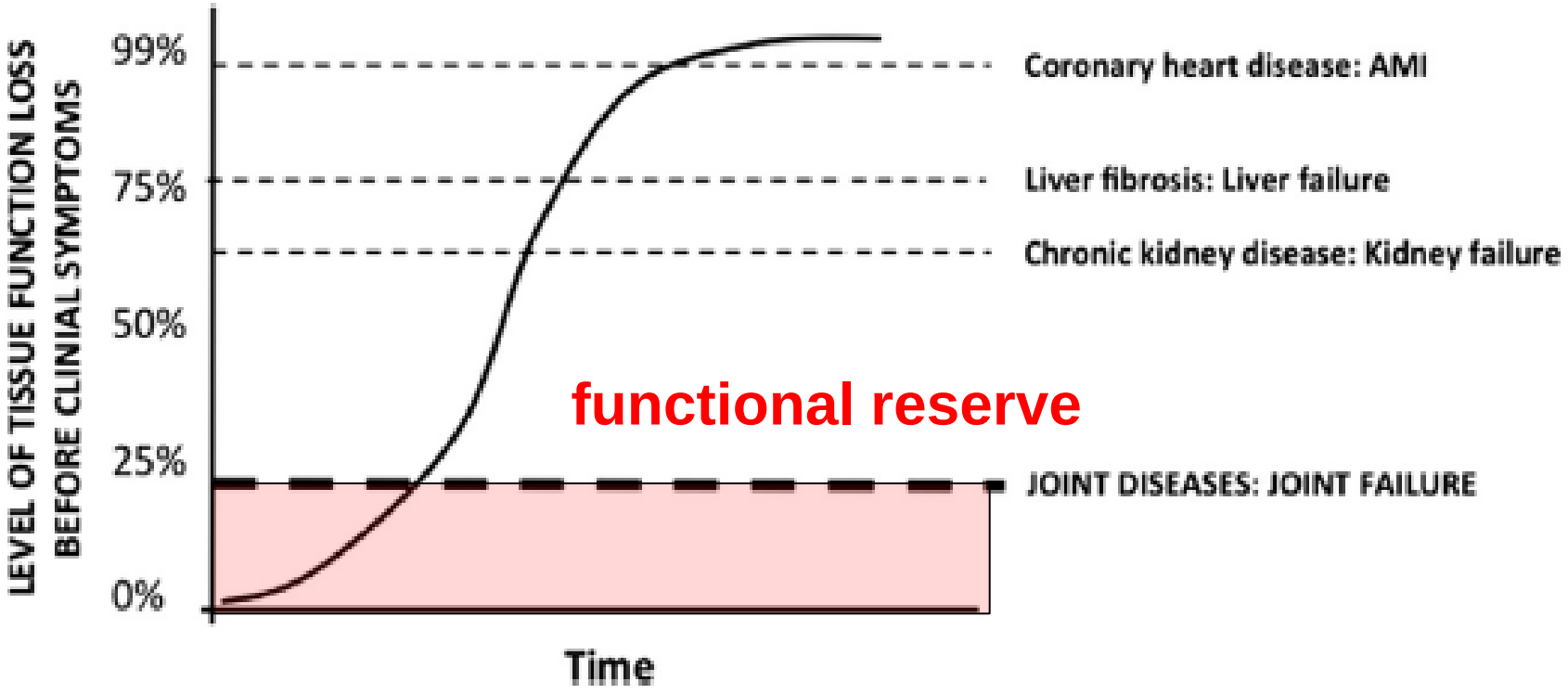
Stages of OA incorporating the new taxonomy. Three stages can be imagined e a no disease/no illness stage, a subclinical stage (with disease manifestations only) and a clinical stage (with illness manifestations).

Call for standardized definitions of osteoarthritis and risk stratification for clinical trials and clinical use

Osteoarthritis and Cartilage 23 (2015) 1233–1241

V.B. Kraus †*, F.J. Blanco ‡, M. Englund §‖, M.A. Karsdal ¶, L.S. Lohmander §#

Disease vs illness.



The tissue functional threshold for establishment of a clinical symptomatic disease differs by organ system. The horizontal dashed lines depict the transition from disease to illness for different diseases. The threshold is relatively high in heart, liver and kidney disease but anticipated to be relatively low for the transition of joint disease to illness (symptoms, disability and joint failure). It is possible that the threshold will vary according to type of joint disease. Both the kidney and liver have a large "functional reserve".

Plain radiography or magnetic resonance imaging (MRI): Which is better in assessing outcome in clinical trials of disease-modifying osteoarthritis drugs? Summary of a debate held at the World Congress of Osteoarthritis 2014

Seminars in Arthritis and Rheumatism 45 (2015) 251–256

Felix Eckstein, MD[a,b,*], Marie-Pierre Hellio Le Graverand, MD, PhD[c]

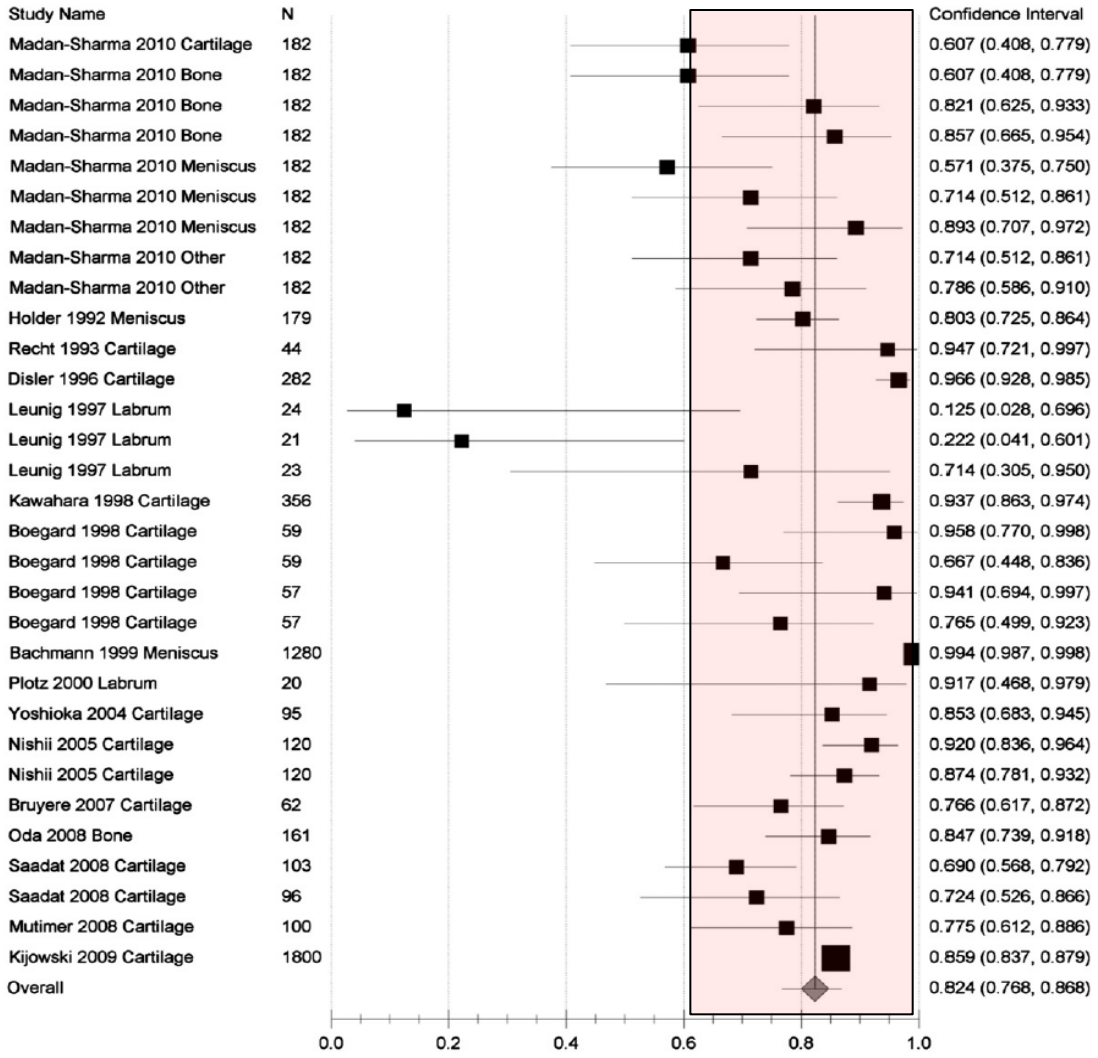
A B S T R A C T

Osteoarthritis (OA) is the most common disease of synovial joints and currently lacks treatment options that modify structural pathology. Imaging is ideally suited for directly evaluating efficacy of disease-modifying OA drugs (DMOADs) in clinical trials, with plain radiography and MRI being most often applied. The current article is based on a debate held on April 26, 2014, at the World Congress of Osteoarthritis: The authors were invited to contrast strengths and limitations of both methods, highlighting scientific evidence on reliability, construct-validity, and correlations with clinical outcome, and comparing their sensitivity to change in knee OA and sensitivity to DMOAD treatment. The authors concluded that MRI provides more comprehensive information on articular tissues pathology, and that implementation of radiography in clinical trials remains a challenge. However, neither technique has thus far been demonstrated to be strongly superior over the other; for the time being it therefore appears advisable to use both in parallel in clinical trials, to provide more evidence on their relative performance. Radiographic JSW strongly depends on adequate positioning; it is not specific to cartilage loss but also to the meniscus. MRI provides somewhat superior sensitivity to change compared with the commonly used non-fluoroscopic radiographic acquisition protocols, and has recently provided non-location-dependent measures of cartilage thickness loss and gain, which are potentially more sensitive in detecting DMOAD effects than radiographic JSW or region-specific MRI. Non-location-dependent measures of cartilage thickness change should thus be explored further in context of anabolic and anti-catabolic DMOADs.

The diagnostic performance of MRI in osteoarthritis: a systematic review and meta-analysis

Osteoarthritis and Cartilage 20 (2012) 13–21

L. Menashe †‡, K. Hirko ‡, E. Losina §, M. Kloppenburg ||, W. Zhang ¶, L. Li ‡, D.J. Hunter ‡#*



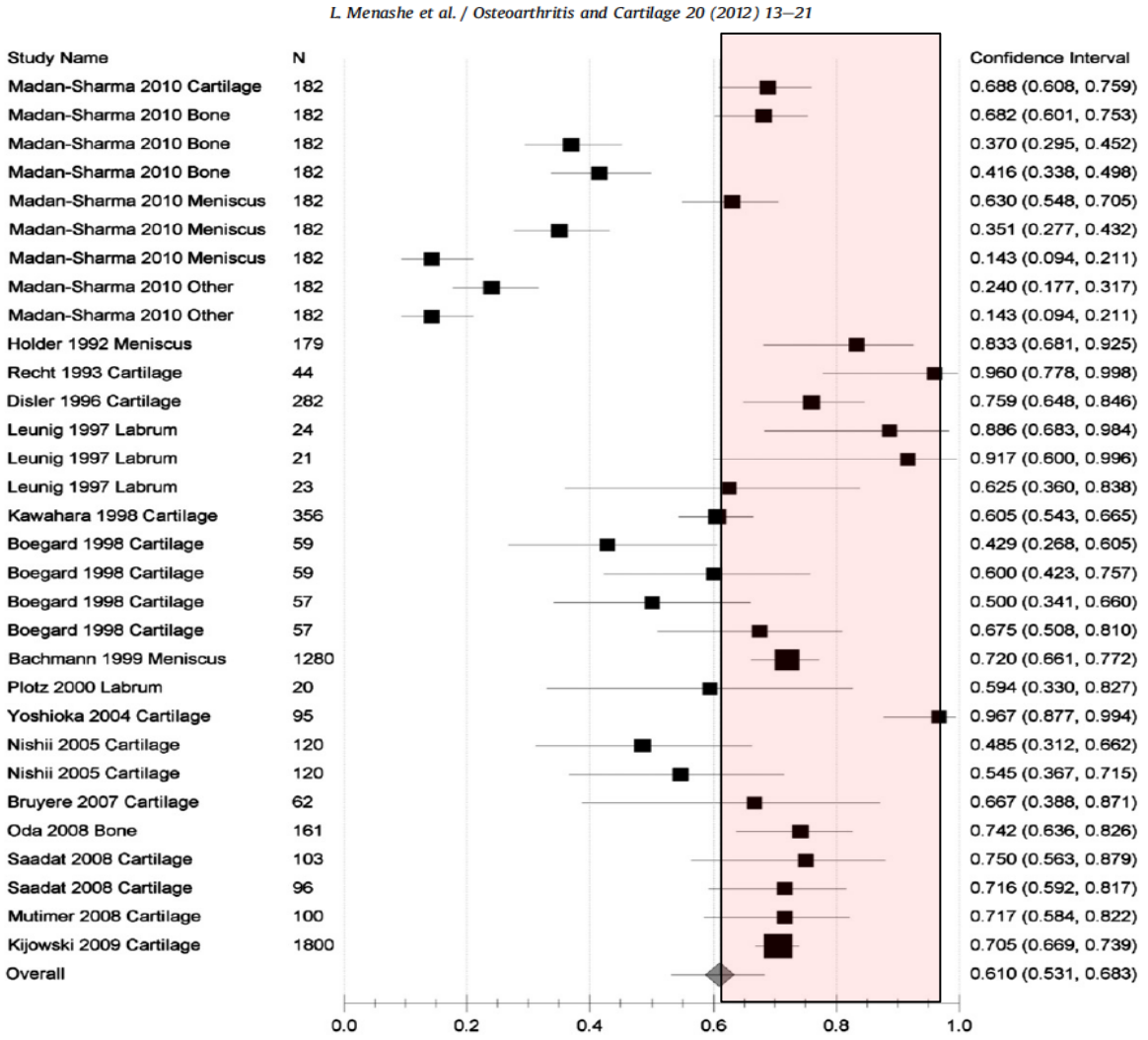
MRI can detect OA with an overall high specificity and moderate sensitivity when compared with various reference standards

Plot showing specificity of MRI use in OA viewing various tissue types in the 16 studies

The diagnostic performance of MRI in osteoarthritis: a systematic review and meta-analysis

Osteoarthritis and Cartilage 20 (2012) 13–21

L. Menashe †‡, K. Hirko ‡, E. Losina §, M. Kloppenburg ||, W. Zhang ¶, L. Li ‡, D.J. Hunter ‡#*

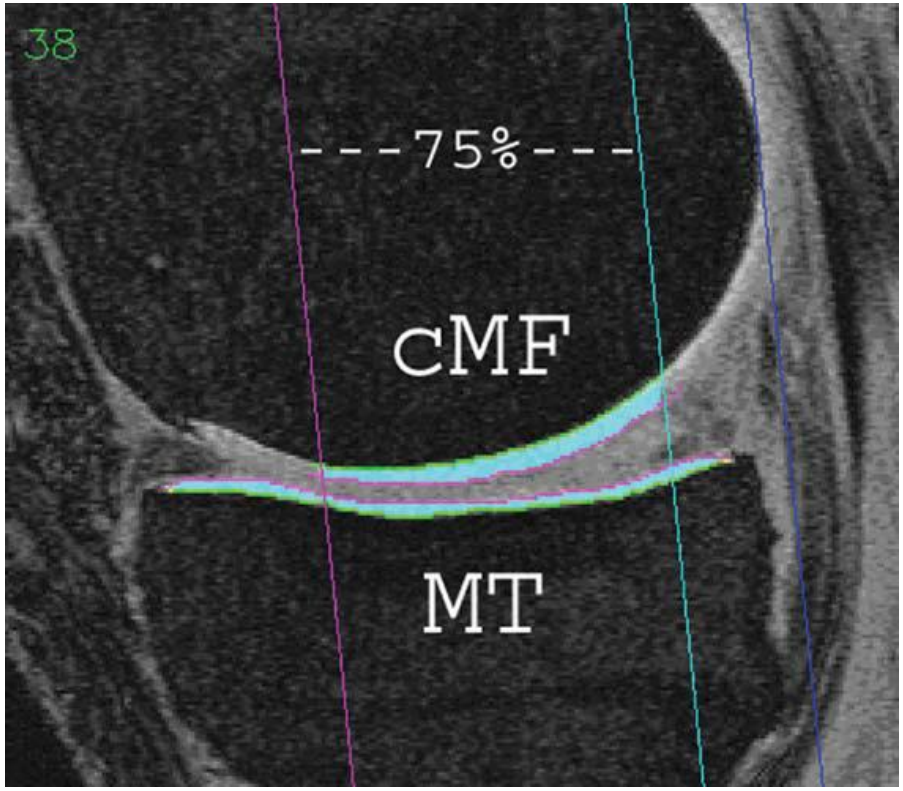


MRI can detect OA with an overall high specificity and moderate sensitivity when compared with various reference standards

Plot showing sensitivity of MRI use in OA viewing various tissue types in the 16 studies

Responsiveness of Quantitative Cartilage Measures Over One Year in Knee Osteoarthritis: Comparison of Radiography and MRI Assessments

Megan S. Cromer, BAppSc,[1,2*] Roger M. Bourne, PhD,[2] Marlene Fransen, PhD,[3] Roger Fulton, PhD,[2,4,5] and Shih-Chang Wang, BSc(Med)[1,6]



The MRI approach proved to be a superior analysis tool for detecting changes in cartilage morphology over a 1-year period.

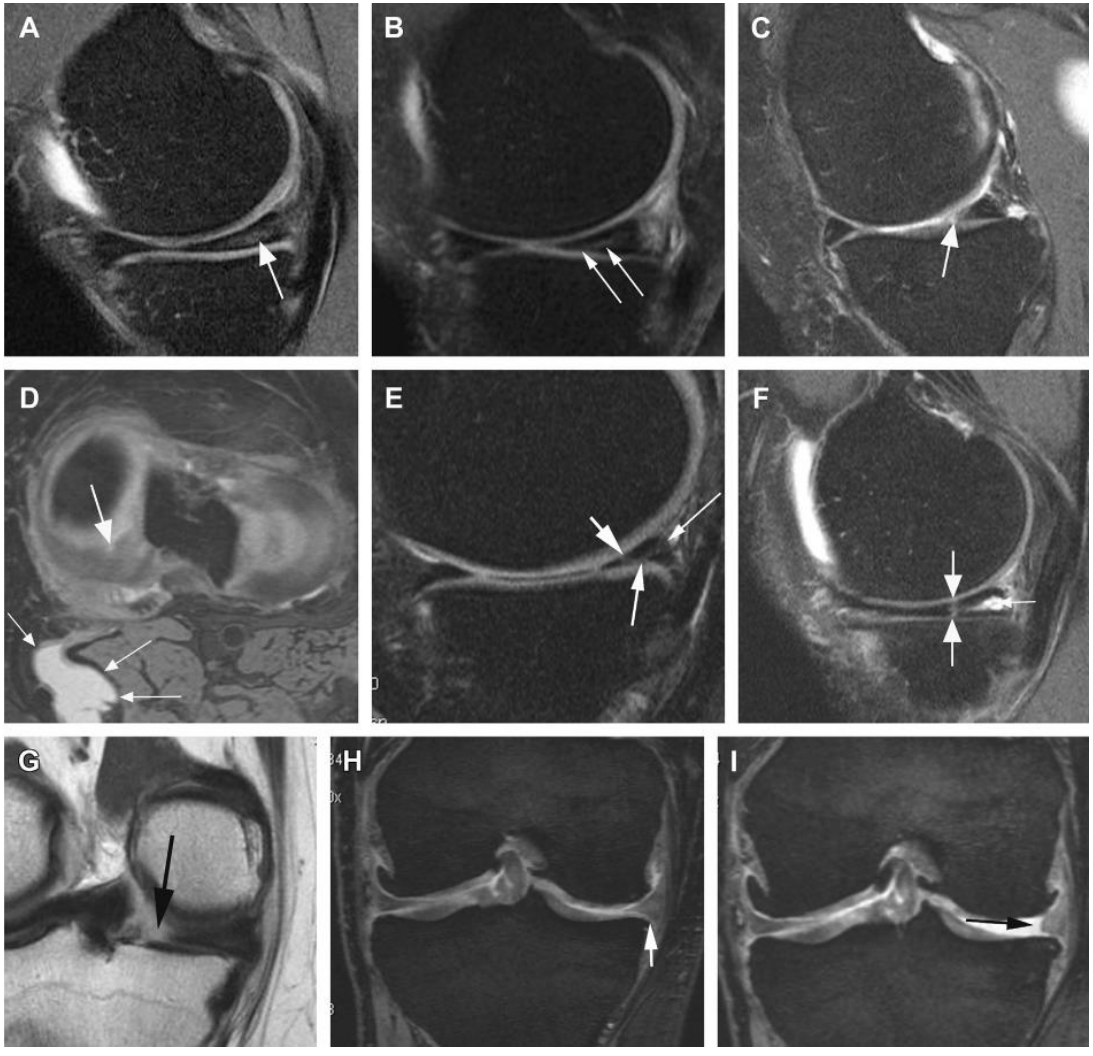
Radiographically defined JSN was found to be the least responsive measurement method of knee OA disease progression.

JOURNAL OF MAGNETIC RESONANCE IMAGING 39:103–109 (2014)

An illustrative overview of semi-quantitative MRI scoring of knee osteoarthritis: lessons learned from longitudinal observational studies

F.W. Roemer †‡*, D.J. Hunter §‖, M.D. Crema †¶#, C.K. Kwoh ††, E. Ochoa-Albiztegui ‡‡, A. Guermazi †

Osteoarthritis and Cartilage 24 (2016) 274–289



Evidence suggests that semiquantitative (SQ) assessment of OA by MRI is valid, reliable and responsive, which helps investigators to understand the natural history of this complex disease and to evaluate potential new drugs in OA clinical trials.

What is the predictive value of MRI for the occurrence of knee replacement surgery in knee osteoarthritis?

Ann Rheum Dis 2013;**72**:1594–1604

J-P Pelletier,[1] C Cooper,[2,3] C Peterfy,[4] J-Y Reginster,[5] M-L Brandi,[6] O Bruyère,[5] R Chapurlat,[7] F Cicuttini,[8] P G Conaghan,[9] M Doherty,[10] H Genant,[11] G Giacovelli,[12] M C Hochberg,[13] D J Hunter,[14] J A Kanis,[15] M Kloppenburg,[16] J-D Laredo,[17] T McAlindon,[18] M Nevitt,[19] J-P Raynauld,[1] R Rizzoli,[20] C Zilkens,[21] F W Roemer,[22,23] J Martel-Pelletier,[1] A Guermazi[23]

Box 1 Economic aspects of osteoporosis and osteoarthritis statements on the predictive value of MRI for hard outcomes in knee osteoarthritis

Statement 1: Medial compartment cartilage volume/thickness loss may be a valid structural endpoint in RCT in knee osteoarthritis involving patients with late-stage osteoarthritis.
Statement 2: Other MRI outcomes including assessment of cartilage defects, bone marrow lesions, meniscal lesions and synovitis may also predict knee replacement, and may potentially serve as structural endpoints in clinical trials.
Statement 3: Integration of the information contained in MRI could eventually lead to a predictive tool for knee replacement.

MRI may prove to be a good alternative to radiography in definitions of knee replacement.

Prognostic factors for progression of clinical osteoarthritis of the knee: a systematic review of observational studies

Alex N. Bastick[1*], Jos Runhaar[1], Janneke N. Belo[2] and Sita M.A. Bierma-Zeinstra[1]

The best evidence synthesis showed strong evidence that age, ethnicity, body mass index, co-morbidity count, magnetic resonance imaging (MRI) - detected infrapatellar synovitis, joint effusion and baseline OA severity (both radiographic and clinical) are associated with clinical knee OA progression.

Recommendations for an update of the 2010 European regulatory guideline on clinical investigation of medicinal products used in the treatment of osteoarthritis and reflections about related clinically relevant outcomes: expert consensus statement

J.-Y. Reginster † *, S. Reiter-Niesert ‡, O. Bruyère †, F. Berenbaum § ||, M.-L. Brandi ¶, J. Branco # ††, J.-P. Devogelaer ‡‡, G. Herrero-Beaumont §§, J. Kanis |||, S. Maggi ¶¶, E. Maheu ##, P. Richette ††† ‡‡‡, R. Rizzoli §§§, C. Cooper |||| ¶¶¶

MRI may become the imaging modality of choice in the future. MRI measures currently investigated include quantitative cartilage morphometry, bone marrow lesions and other joint structure changes on semi-quantitative analysis, bone shape/attrition and subchondral bone area.

Medicinal products intended to slow or prevent structural damage

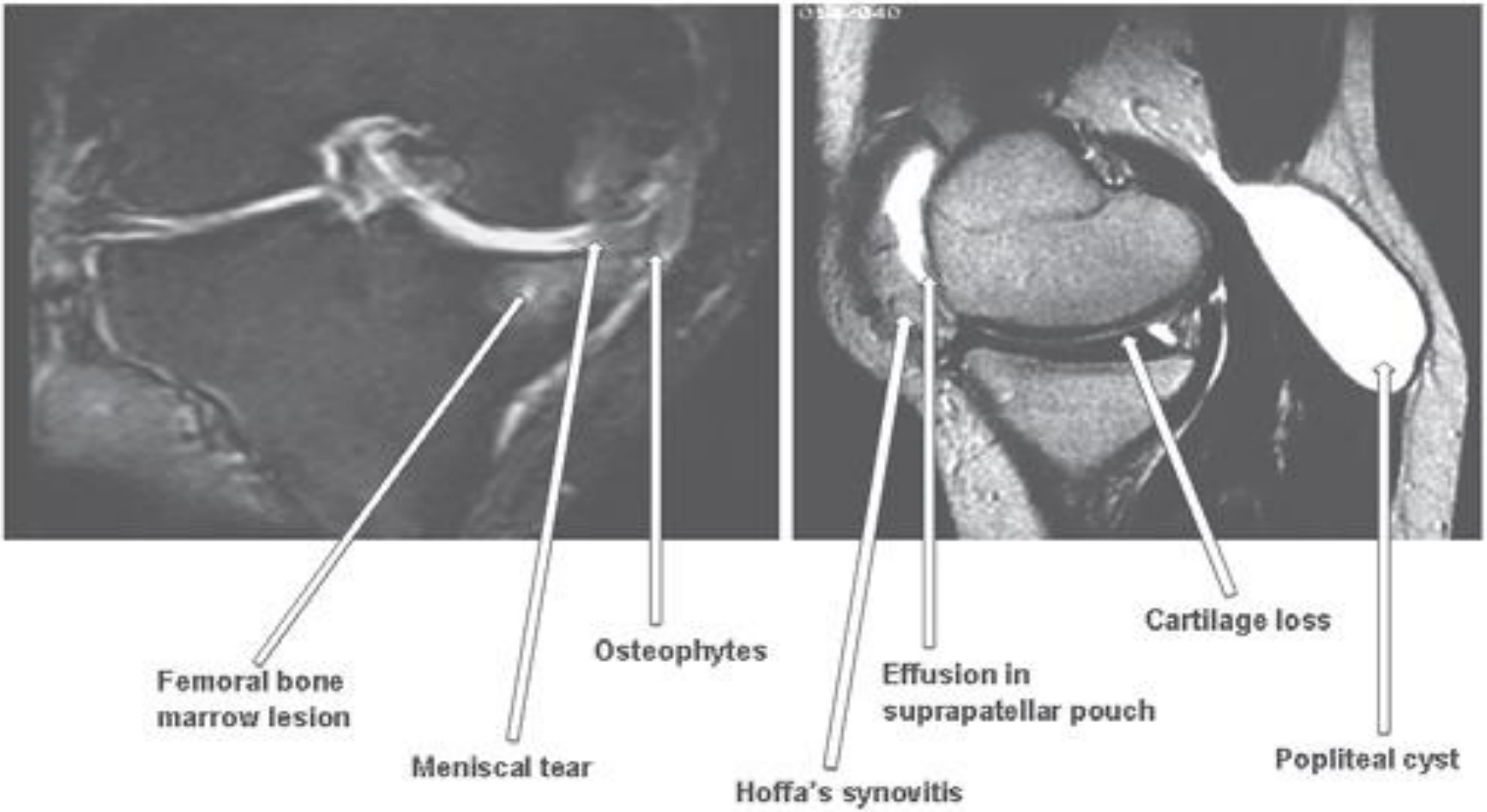
- Watch out for ongoing initiatives to qualify biochemical markers and especially MRI as an imaging biomarker offering surrogacy over shorter periods and in smaller trials than with JSN.

Osteoarthritis and Cartilage 23 (2015) 2086–2093

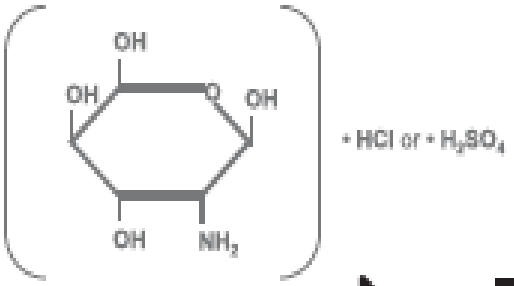
The sources of pain in osteoarthritis: a pathophysiological review

Reumatismo, 2014; 66 (1): 57-71

F. Salaffi[1], A. Ciapetti[1], M. Carotti[2]



Glucosamine hydrochloride or sulfate



Cartilage

Anti-inflammatory

↓ PLA_2
↓ iNOS, COX-2
↓ pro-inflammatory cytokines and chemokines
↓ NF-κB
↑ GRP78

Anti-catabolic and anabolic

↓ MMPs
↓ ADAMTS-5
↑ GAG and HA production

Subchondral bone

Anti-resorptive

↓ RANKL
↑ OPG

Synovial membrane

Anti-inflammatory

↓ TNFa and IL-1β
↓ NO and PGE_2
↑ IL-10

Anti-catabolic

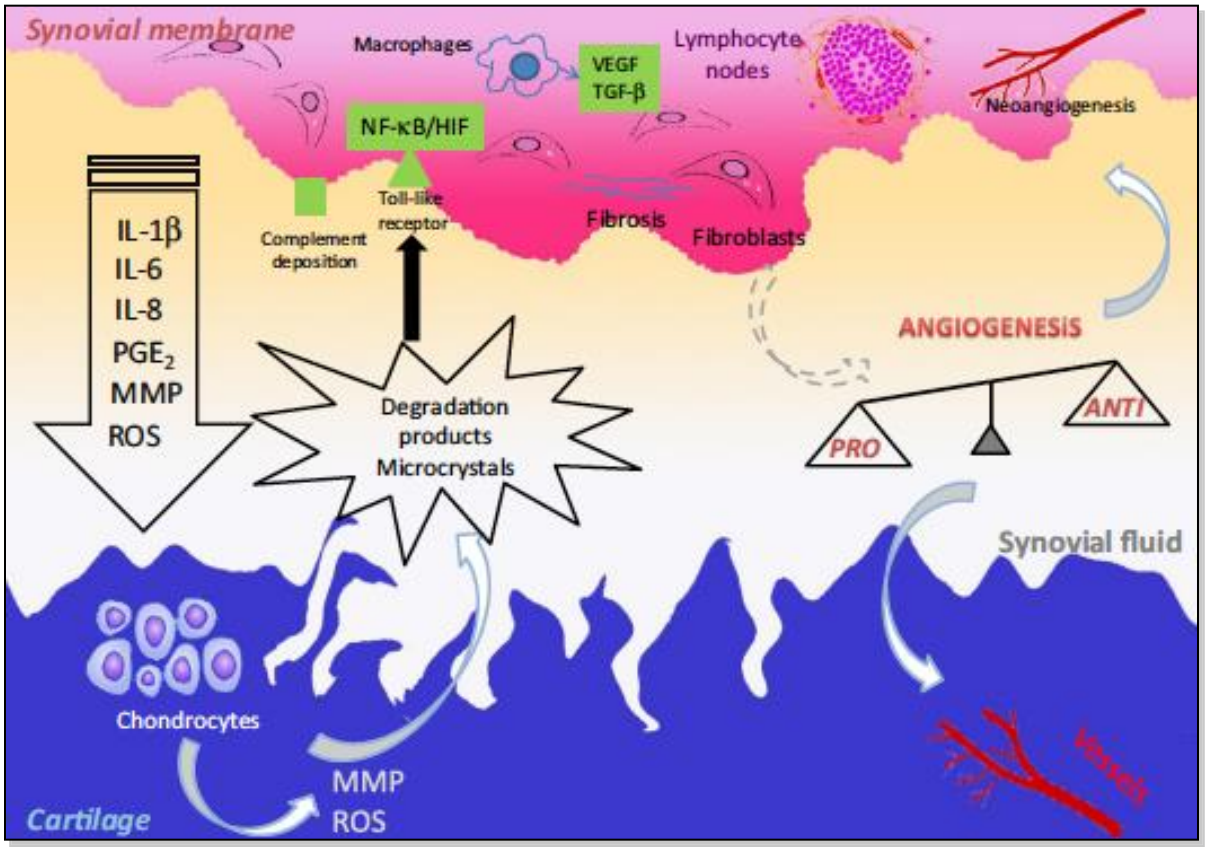
↑ HAS, HA and GAG production
↓ MAPK signaling pathway

Pro and anti-angiogenic

Importance of synovitis in osteoarthritis: Evidence for the use of glycosaminoglycans against synovial inflammation

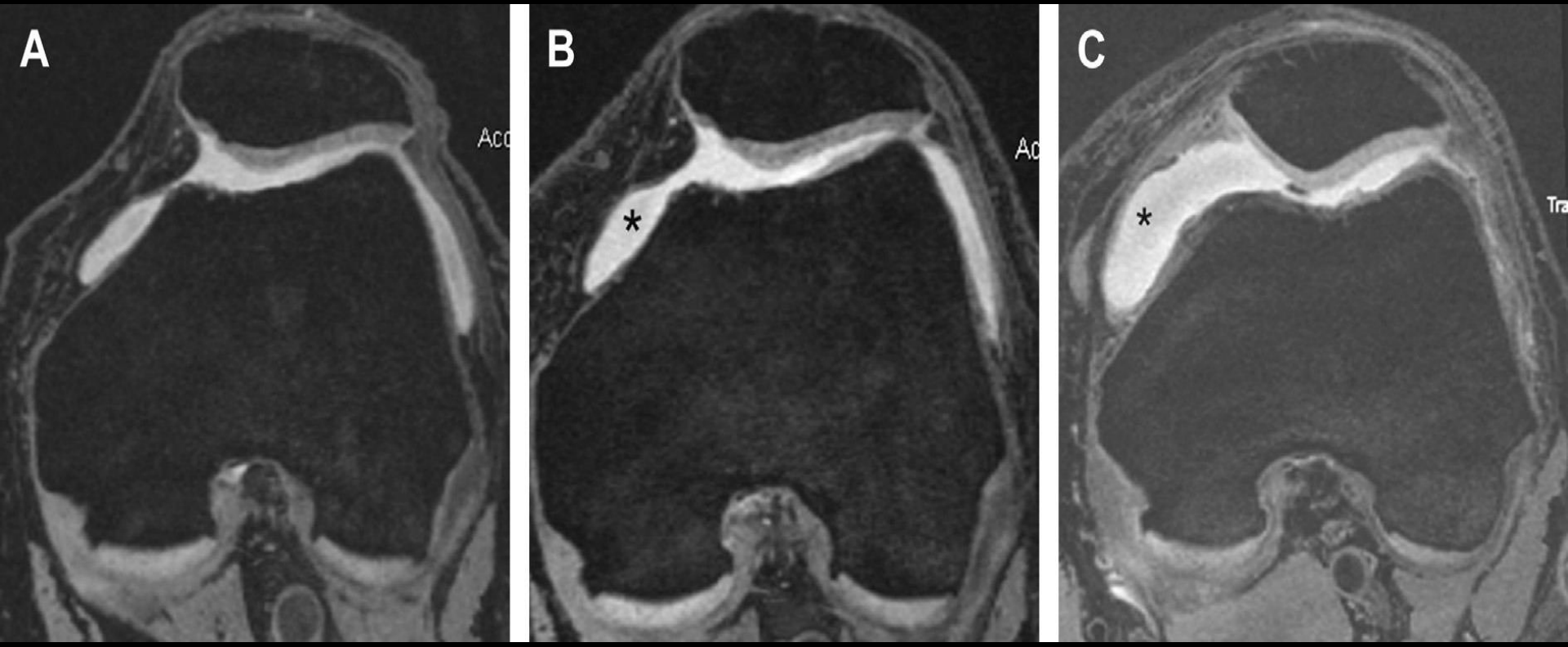
Yves Henrotin, PhD[a,*], Cécile Lambert, PhD[a], Pascal Richette, MD, PhD[b,c]

Seminars in Arthritis and Rheumatism 43 (2014) 579–587



The inflamed SM is the source of pain in the OA joint. There are changes in nociception, sensitization by inflammatory mediators, and production of specific neuropeptides

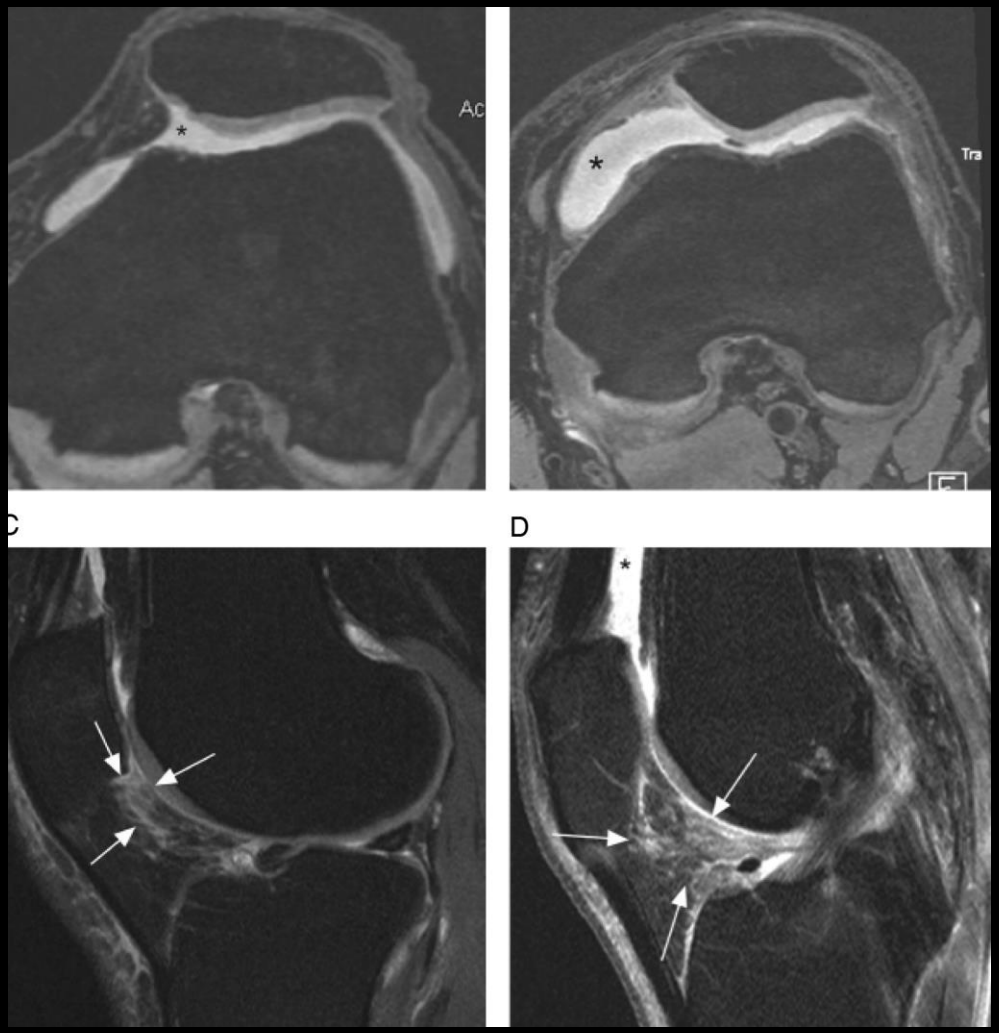
MRI of markers of inflammation in OA



Fluid sensitive sequences are capable of delineating intraarticular joint fluid. However, a distinction between true joint effusion and synovial thickening is not possible as both are visualized as hyperintense signal within the joint cavity. For this reason the term effusion-synovitis has been introduced (T2 fat sat)

Synovitis in knee osteoarthritis: a precursor of disease?

I Atukorala,[1,2] C K Kwoh,[3] A Guermazi,[4] F W Roemer,[4,5] R M Boudreau,[6] M J Hannon,[6] D J Hunter[1]

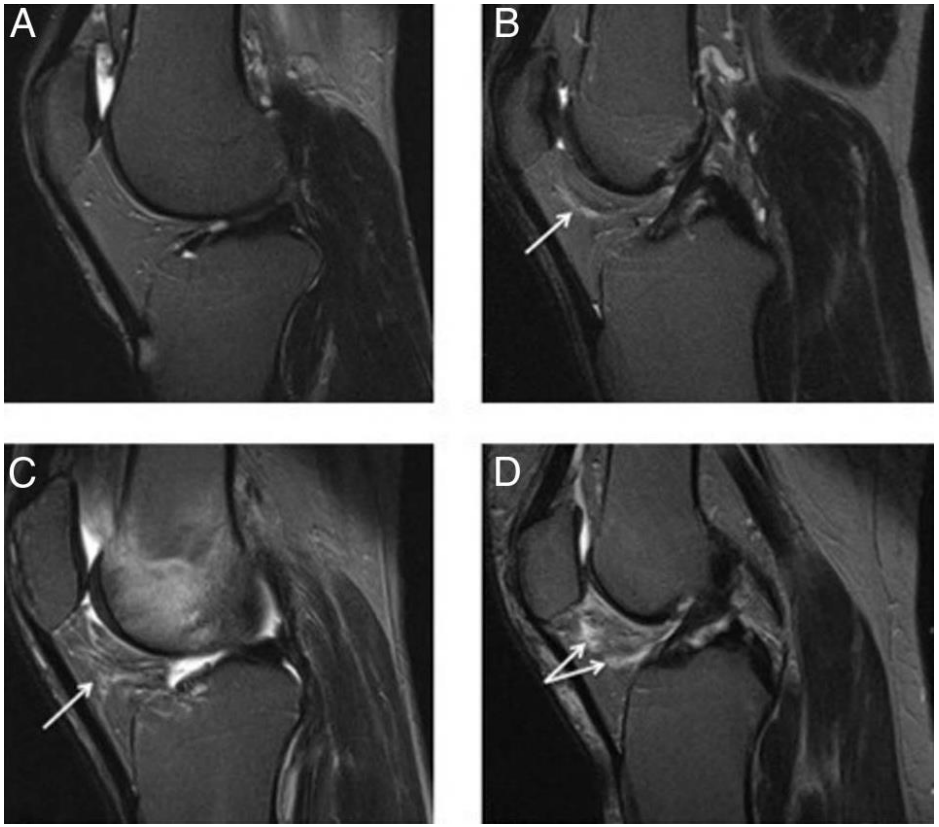


Effusion-synovitis strongly predicted the development of radiographic knee OA (ROA).

Ann Rheum Dis 2016;**75**:390–395.

Signal intensity alteration in the infrapatellar fat pad at baseline for the prediction of knee symptoms and structure in older adults: a cohort study

Weiyu Han,[1,2] Dawn Aitken,[1] Zhaohua Zhu,[1] Andrew Halliday,[3] Xia Wang,[1] Benny Antony,[1] Flavia Cicuttini,[4] Graeme Jones,[1] Changhai Ding[1,4,5]



Infrapatellar fat pad (IPFP) signal intensity alteration at baseline was associated with knee structural abnormalities and clinical symptoms cross-sectionally and longitudinally in older adults, suggesting that it may serve as **an important imaging biomarker in knee OA.**

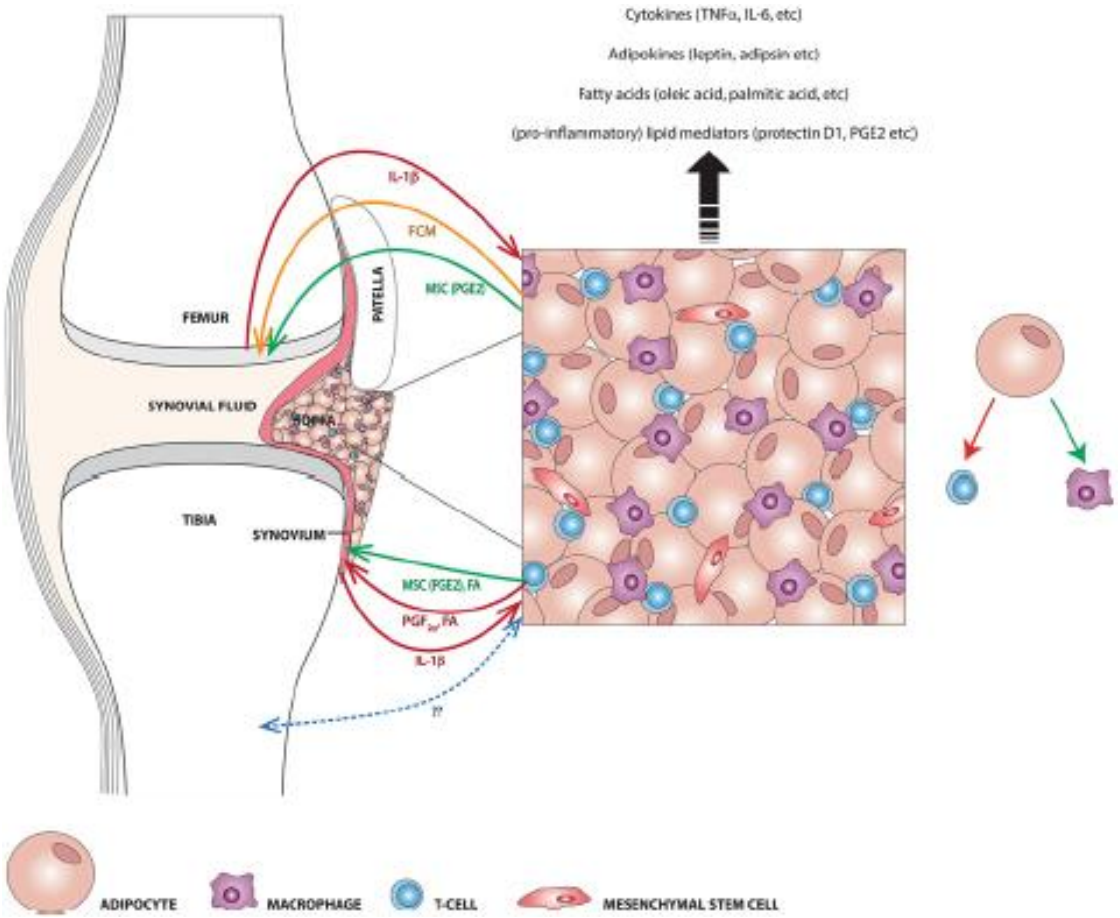
Ann Rheum Dis 2015;**0**:1–6.

An emerging player in knee osteoarthritis: the infrapatellar fat pad

Arthritis Research & Therapy 2013, 15:225

Andreea Ioan-Facsinay* and Margreet Kloppenburg

Current view of the infrapatellar fat pad (IFP) and its interaction with other joint tissues

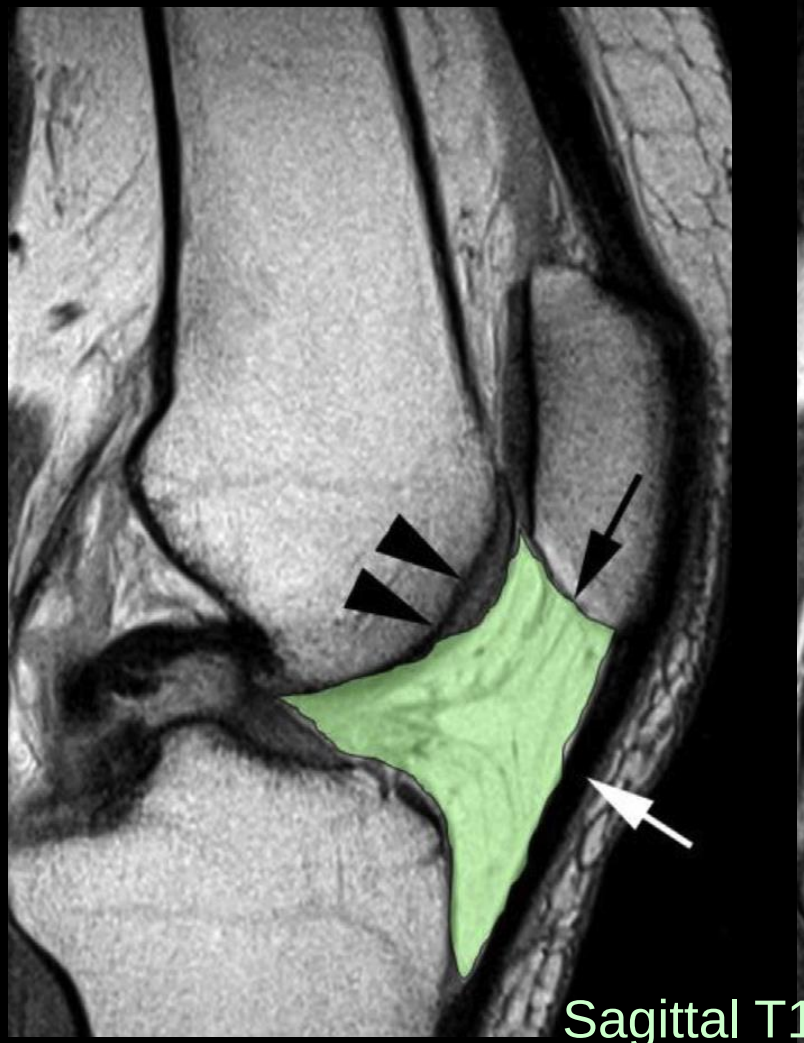


The IFP (Hoffa) is a source of several soluble factors. Moreover, it is composed of adipocytes and stromal vascular cells, such as macrophages, T cells, and mesenchymal stem cells (MSCs). Cellular interactions have been described within the IFP, such as between adipocytes and macrophages or T cells but also between IFP and other joint tissues.

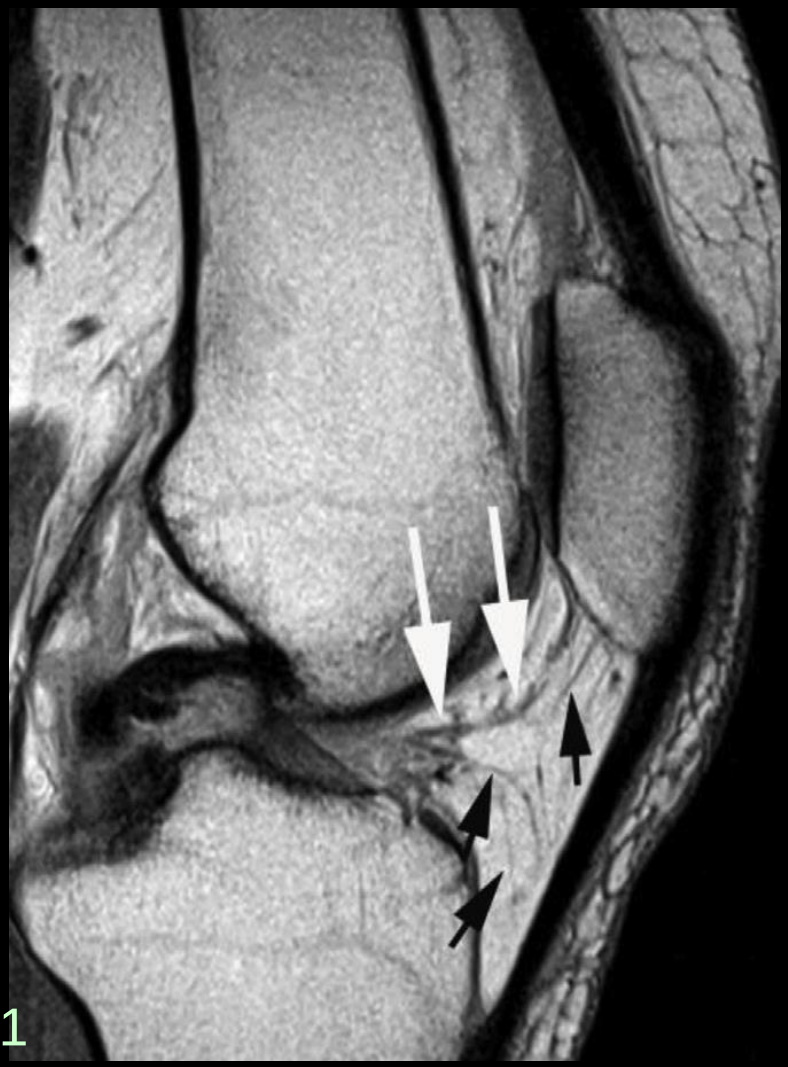
Magnetic resonance imaging of Hoffa's fat pad and relevance for osteoarthritis research: a narrative review

Osteoarthritis and Cartilage 24 (2016) 383–397

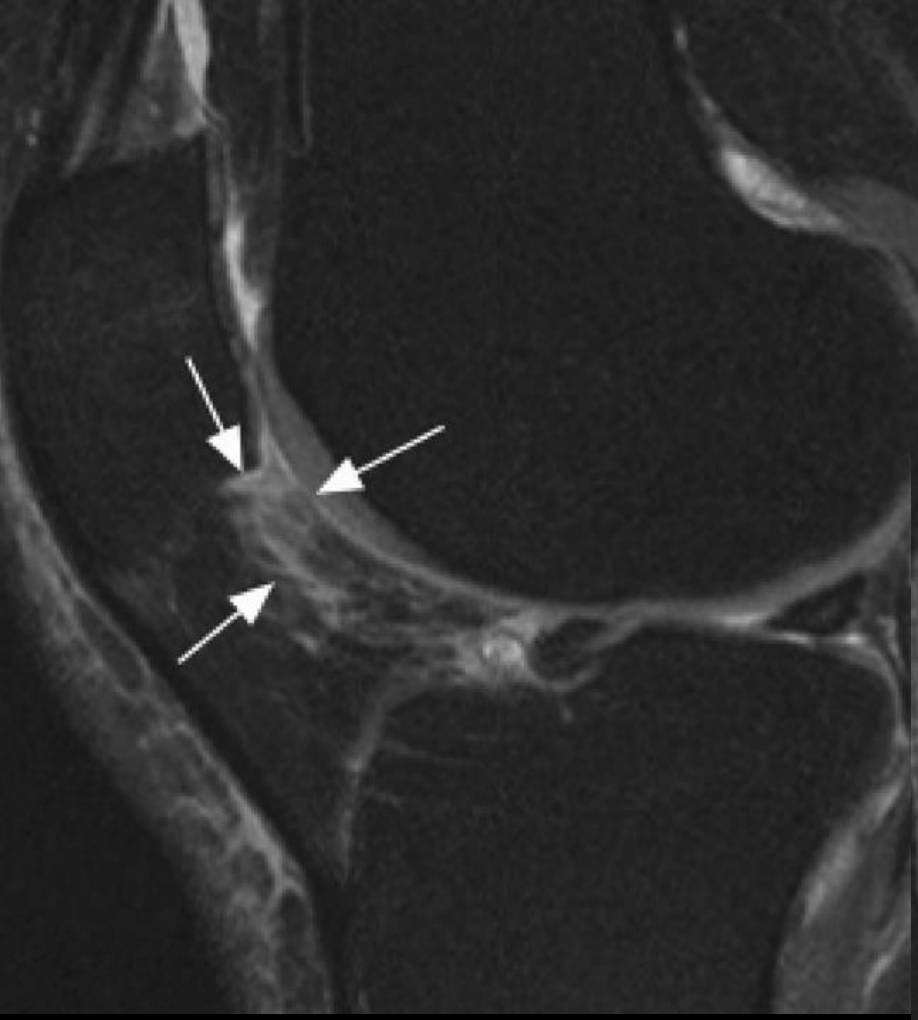
F.W. Roemer † ‡ *, M. Jarraya ‡ §, D.T. Felson ||, D. Hayashi ‡ ¶, M.D. Crema ‡ #, D. Loeuille ††, A. Guermazi ‡



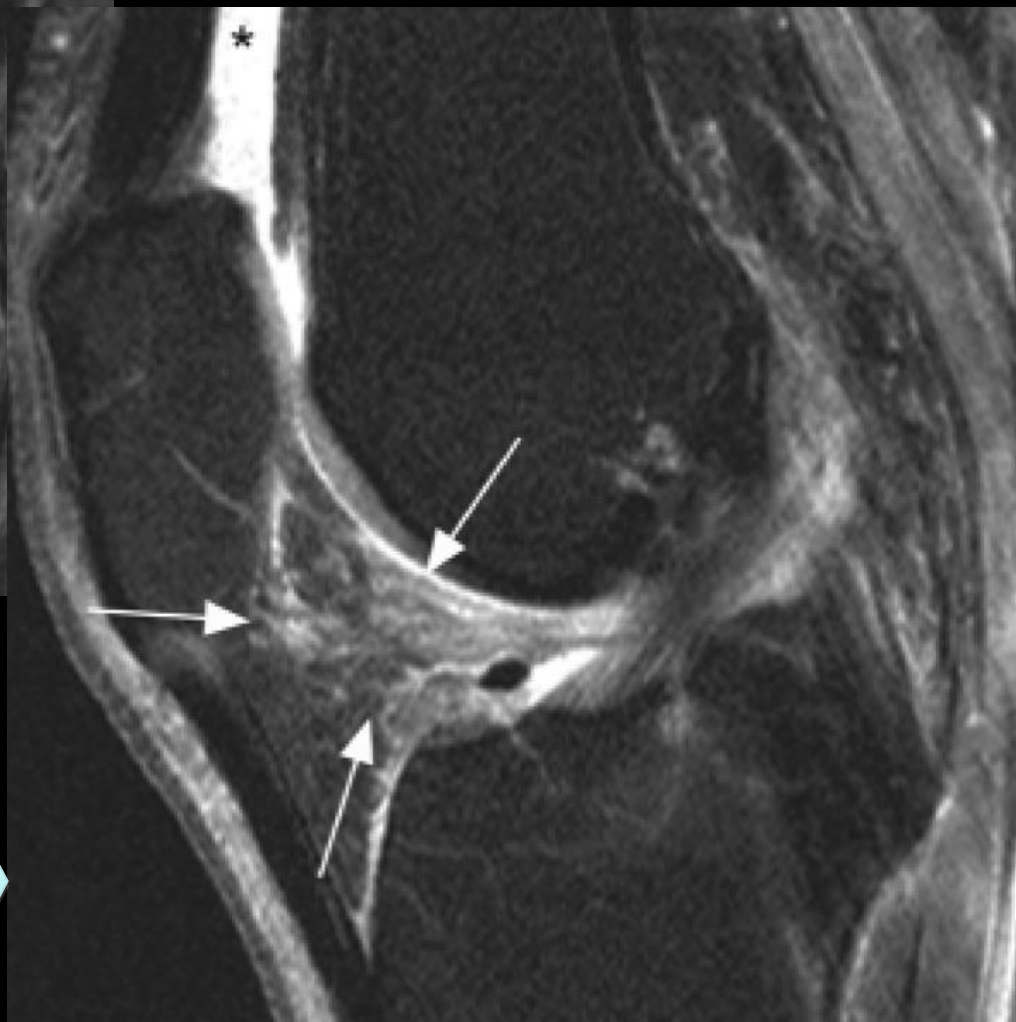
Sagittal T1



Anatomy of Hoffa's fat pad



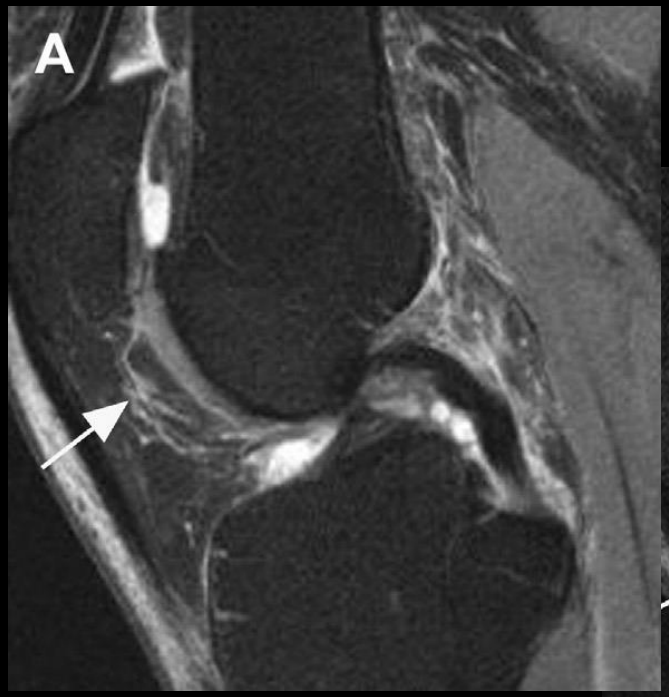
Hoffa-synovitis: intermediate-weighted fat suppressed image shows infrapatellar areas of hyperintensity within Hoffa's fat pad (grade 2).



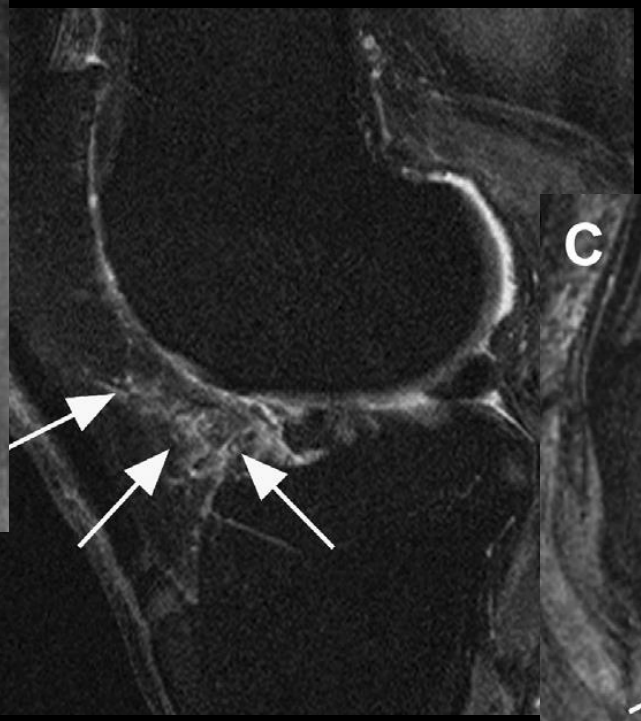
Hoffa-synovitis: Another knee exhibits marked signal alterations within Hoffa's fat pad representing grade 3 Hoffa-synovitis (arrows)

Signal changes in Hoffa's fat pad are commonly used as a surrogate for synovitis on non contrast-enhanced MRI.

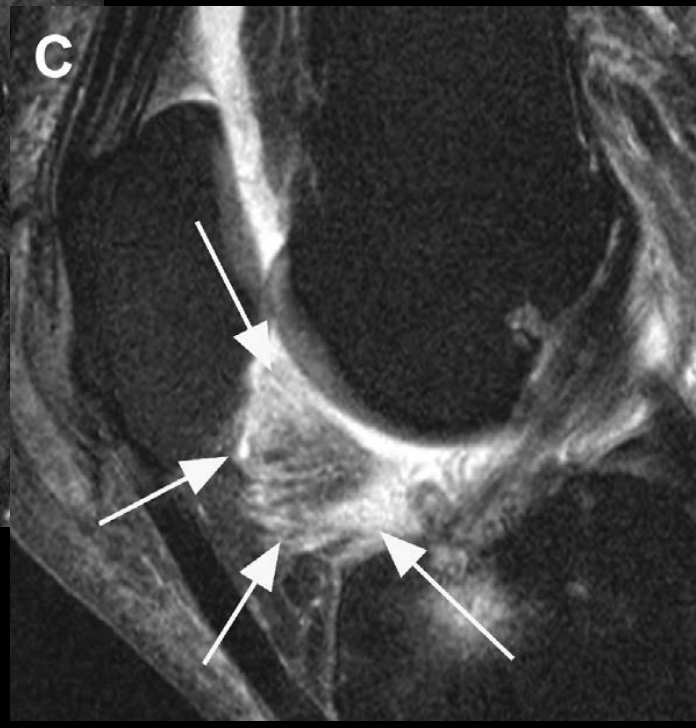
Sagittal T2 fat sat



Grade 1



Grade 2



Grade 3

Hoffa-synovitis

Synovitis detected on magnetic resonance imaging and its relation to pain and cartilage loss in knee osteoarthritis

C L Hill, D J Hunter, J Niu, M Clancy, A Guermazi, H Genant, D Gale, A Grainger, P Conaghan, D T Felson

Ann Rheum Dis 2007;**66**:1599–1603. doi: 10.1136/ard.2006.067470

Change in synovitis was correlated with change in knee pain.

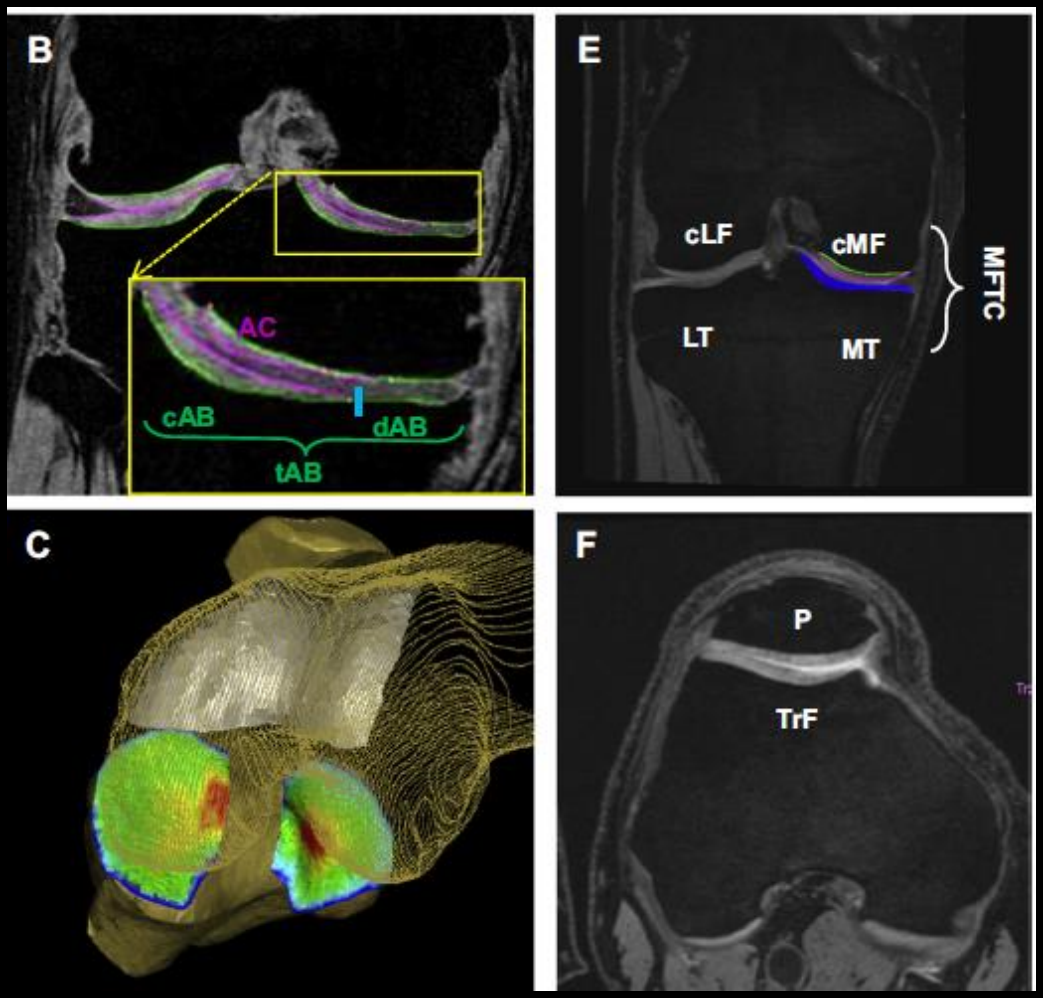
Treatment of knee osteoarthritis (OA) needs to consider treatment of synovitis.

Of the 3 locations for synovitis, changes in the infrapatellar fat pad were most strongly related to pain change.

Imaging of cartilage and bone: promises and pitfalls in clinical trials of osteoarthritis

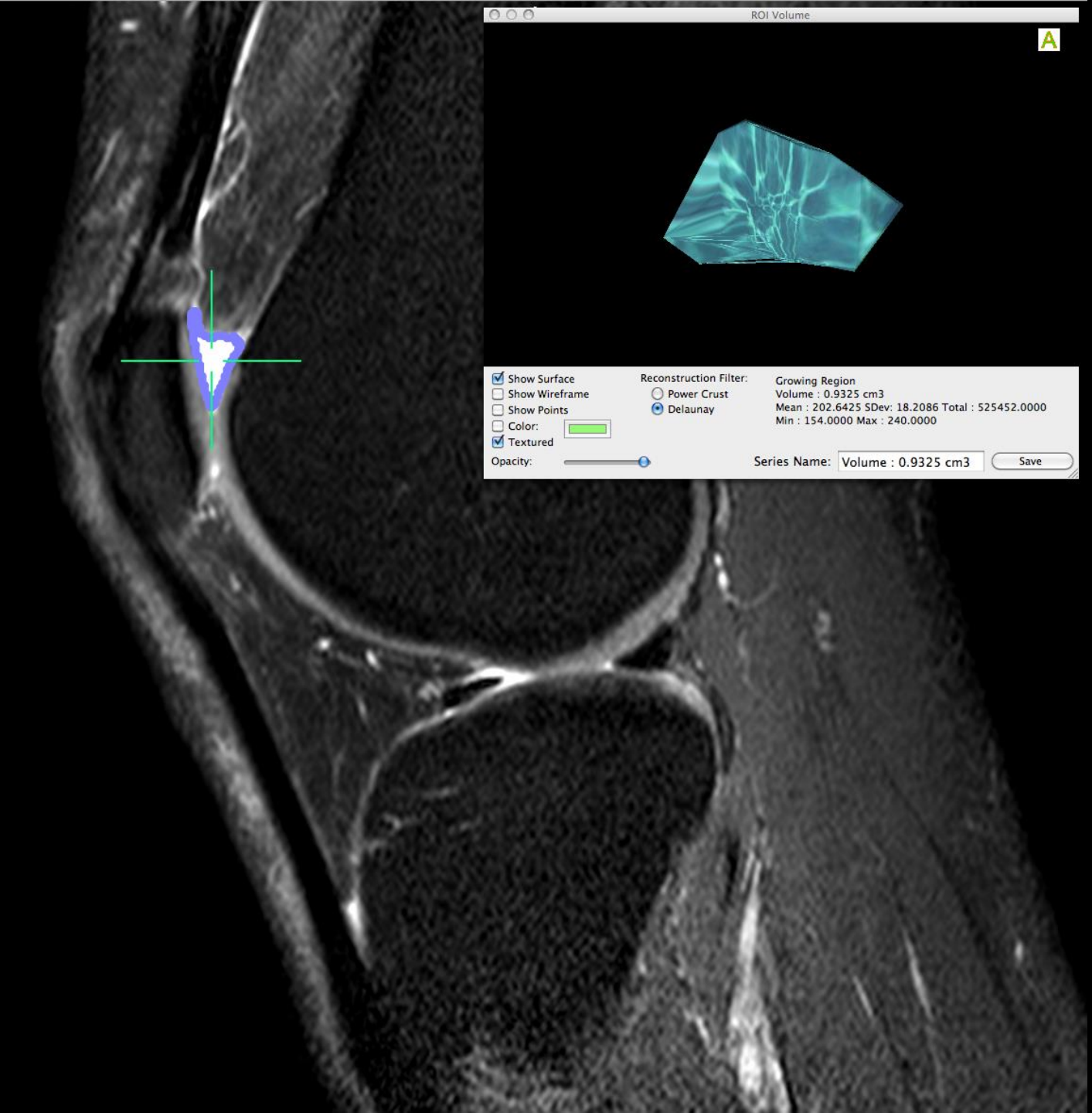
Osteoarthritis and Cartilage 22 (2014) 1516–1532

F. Eckstein † ‡ *, A. Guermazi § ||, G. Gold ¶, J. Duryea #, M.-P. Hellio Le Graverand ††, W. Wirth † ‡, C.G. Miller ‡‡



Magnetic resonance imaging (MRI) provide powerful tools for scoring and measuring morphological and compositional aspects of most articular tissues, capturing longitudinal change with reasonable to excellent sensitivity.

Effusion-synovitis volume



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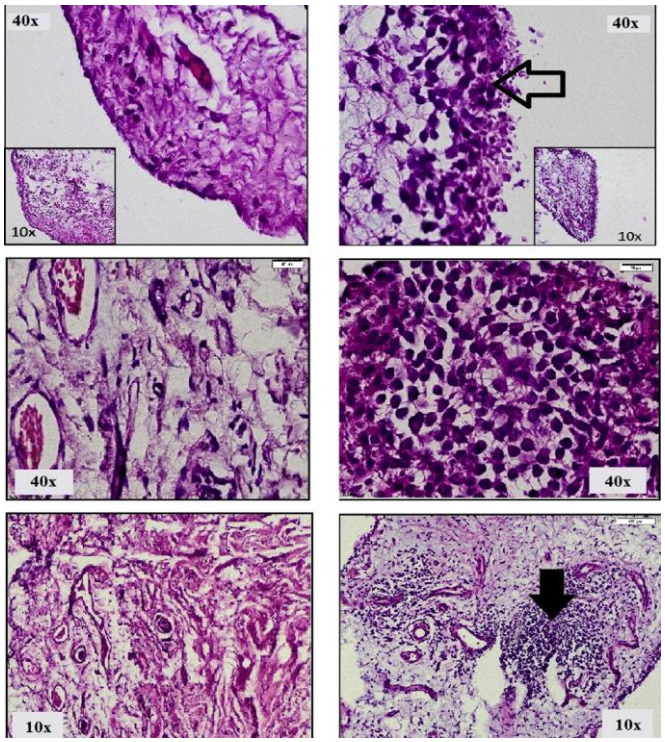
World's fastest DICOM viewer

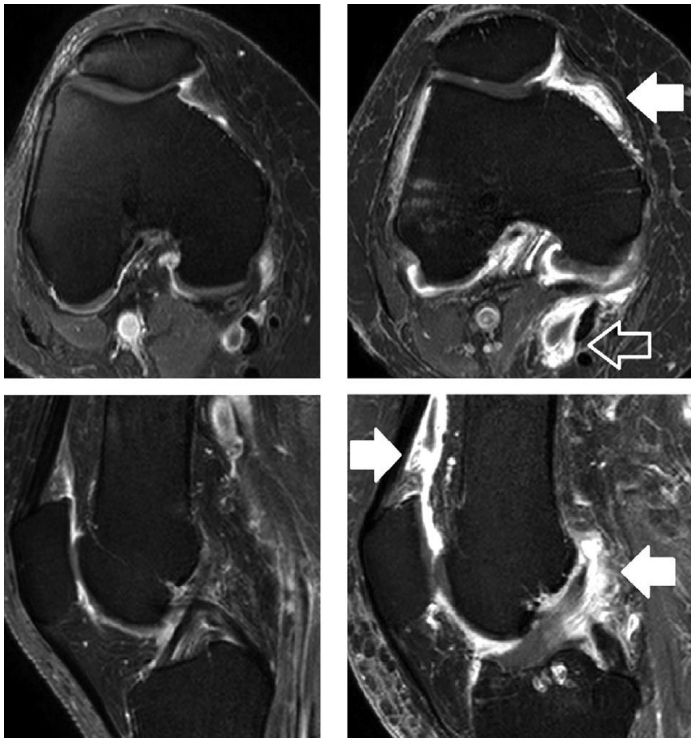
Salaffi F et al. in press 2016

Degree of synovitis on MRI by comprehensive whole knee semi-quantitative scoring method correlates with histologic and macroscopic features of synovial tissue inflammation in knee osteoarthritis

B.J.E. de Lange-Brokaar †*, A. Ioan-Facsinay †, E. Yusuf †, A.W. Visser †, H.M. Kroon ¶, S.N. Andersen †, L. Herb-van Toorn †, G.J.V.M. van Osch ‡, A.-M. Zuurmond §, V. Stojanovic-Susulic ||, J.L. Bloem ¶, R.G.H.H. Nelissen #, T.W.J. Huizinga †, M. Kloppenburg †††

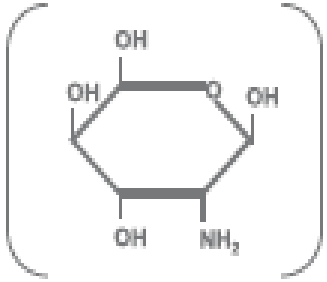
Osteoarthritis and Cartilage 22 (2014) 1606–1613





Synovitis severity on contrast enhanced (CE-MRI) assessed by a new whole knee scoring is a valid, non-invasive method to determine synovitis as it is significantly correlated with both macroscopic and microscopic features of synovitis in knee OA patients.

Glucosamine hydrochloride or sulfate



+ HCl or + H_2SO_4

Cartilage

Anti-inflammatory

↓ PLA_2
↓ iNOS, COX-2
↓ pro-inflammatory cytokines and chemokines
↓ NF-κB
↑ GRP78

Anti-catabolic and anabolic

↓ MMPs
↓ ADAMTS-5
↑ GAG and HA production

Subchondral bone

Anti-resorptive

↓ RANKL
↑ OPG

Synovial membrane

Anti-inflammatory

↓ TNFα and IL-1β
↓ NO and PGE_2
↑ IL-10

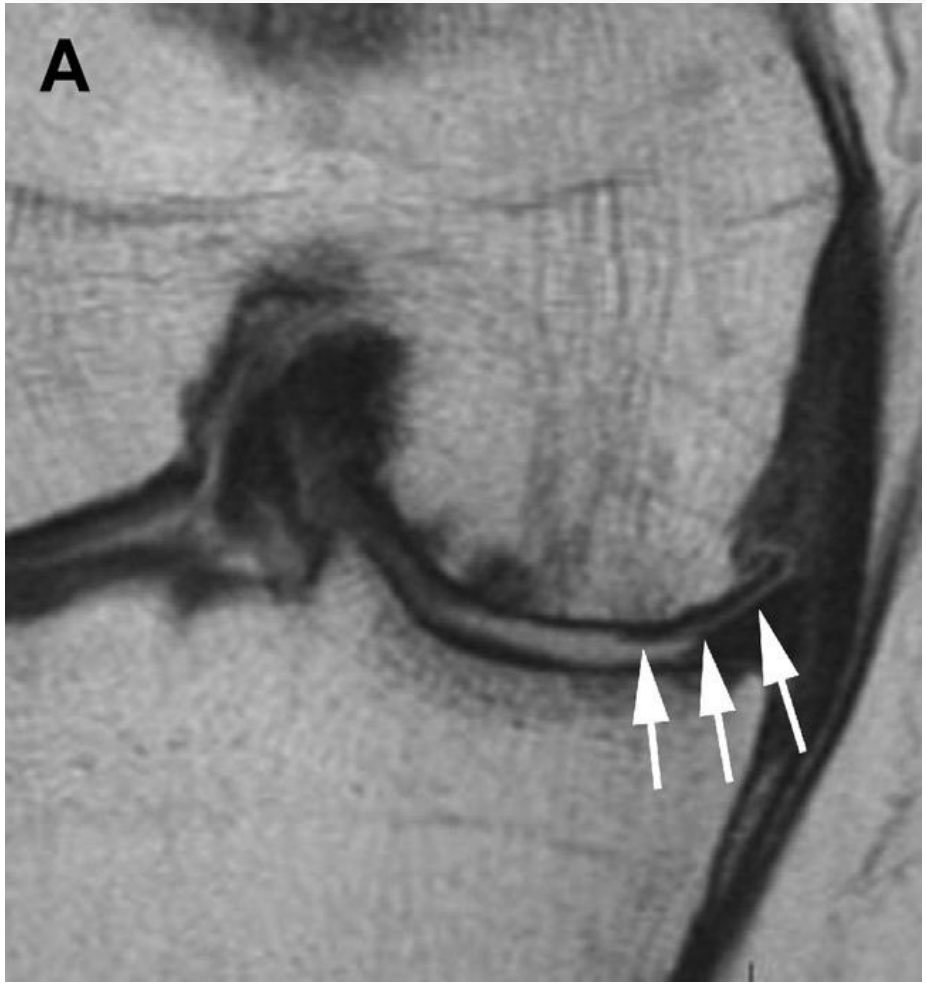
Anti-catabolic

↑ HAS, HA and GAG production
↓ MAPK signaling pathway

Pro and anti-angiogenic

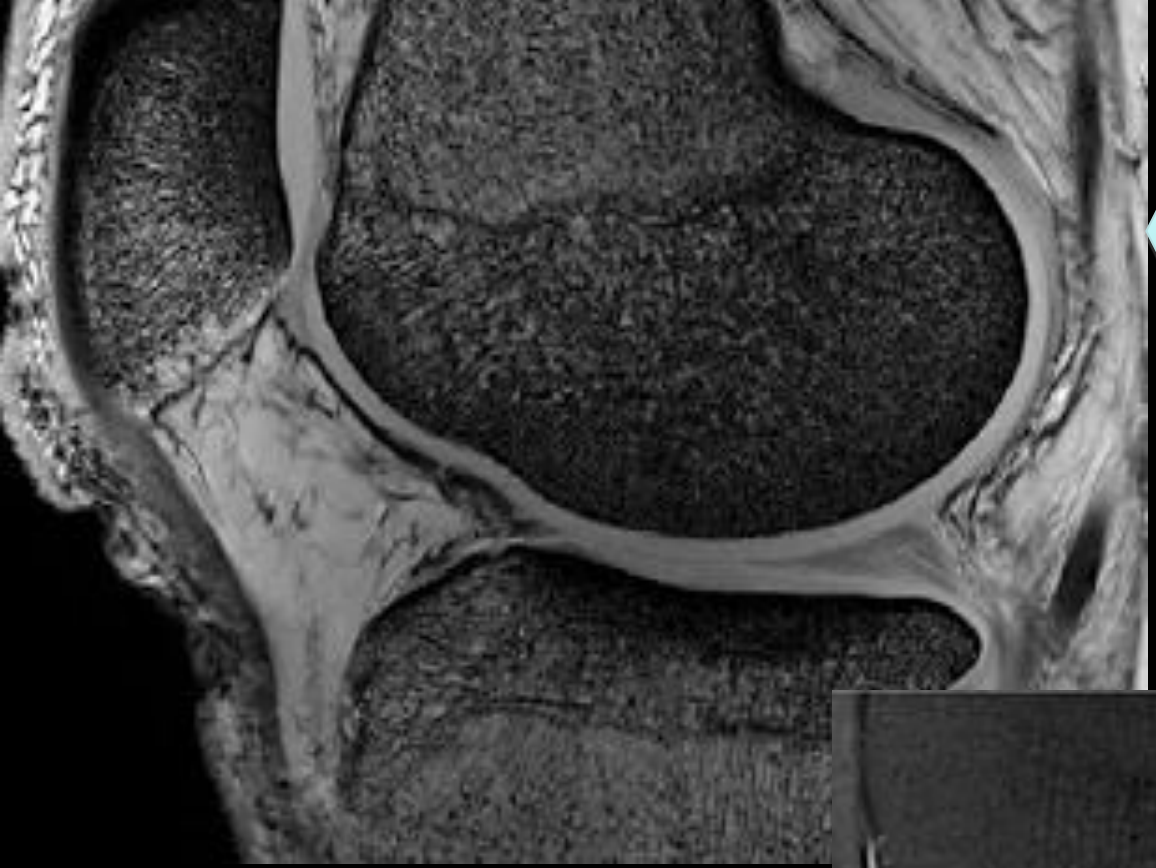
Cartilage Thickness Change as an Imaging Biomarker of Knee Osteoarthritis Progression: Data From the Foundation for the National Institutes of Health Osteoarthritis Biomarkers Consortium

F. Eckstein,[1] J. E. Collins,[2] M. C. Nevitt,[3] J. A. Lynch,[3] V. B. Kraus,[4] J. N. Katz,[2] E. Losina,[2] W. Wirth,[1] A. Guermazi,[5] F. W. Roemer,[6] and D. J. Hunter,[7] for the FNIH OA Biomarkers Consortium



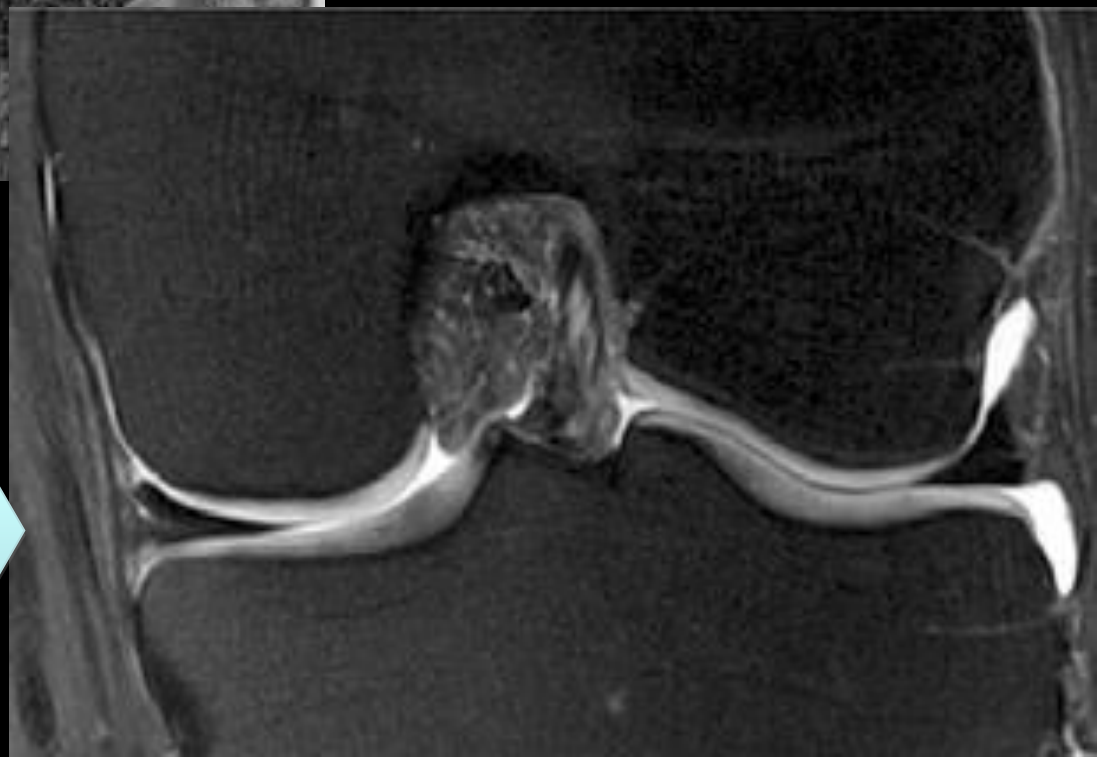
A reduction in central medial femoro-tibial compartment cartilage thickness was strongly associated with radiographic progression (OR 4.0 P < 0.0001)

ARTHRITIS & RHEUMATOLOGY
Vol. 67, No. 12, December 2015, pp 3184–3189

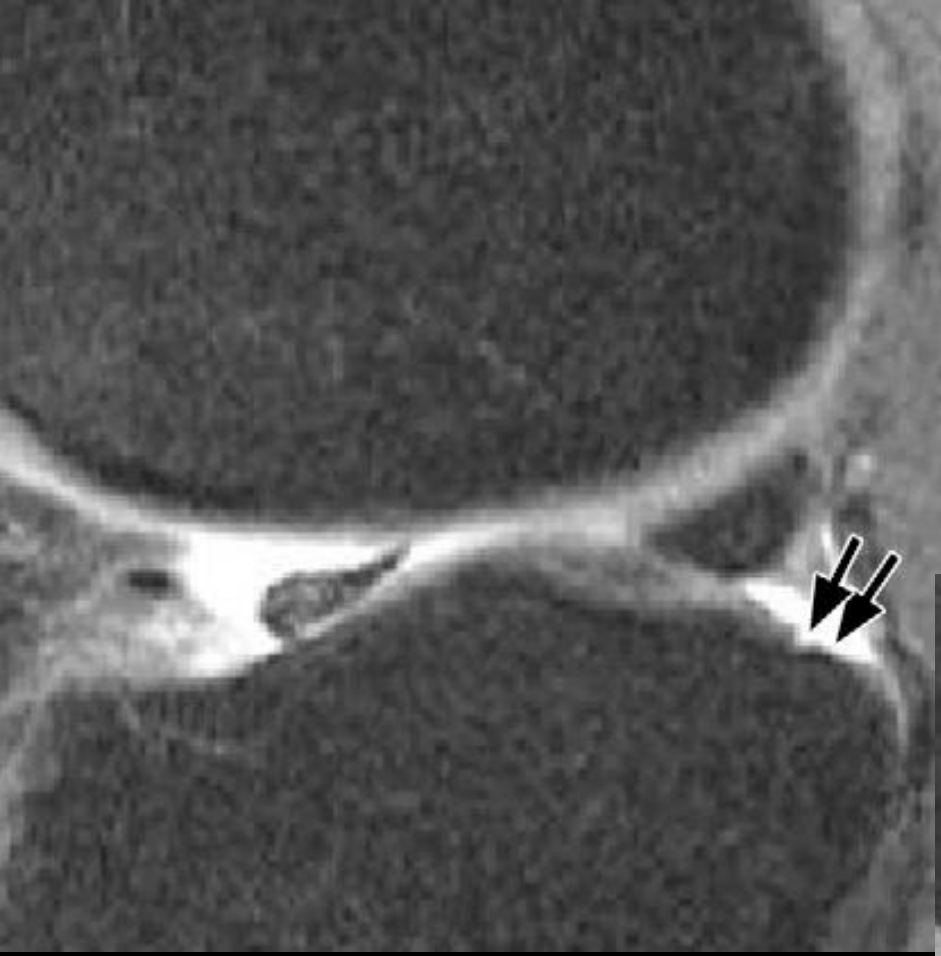


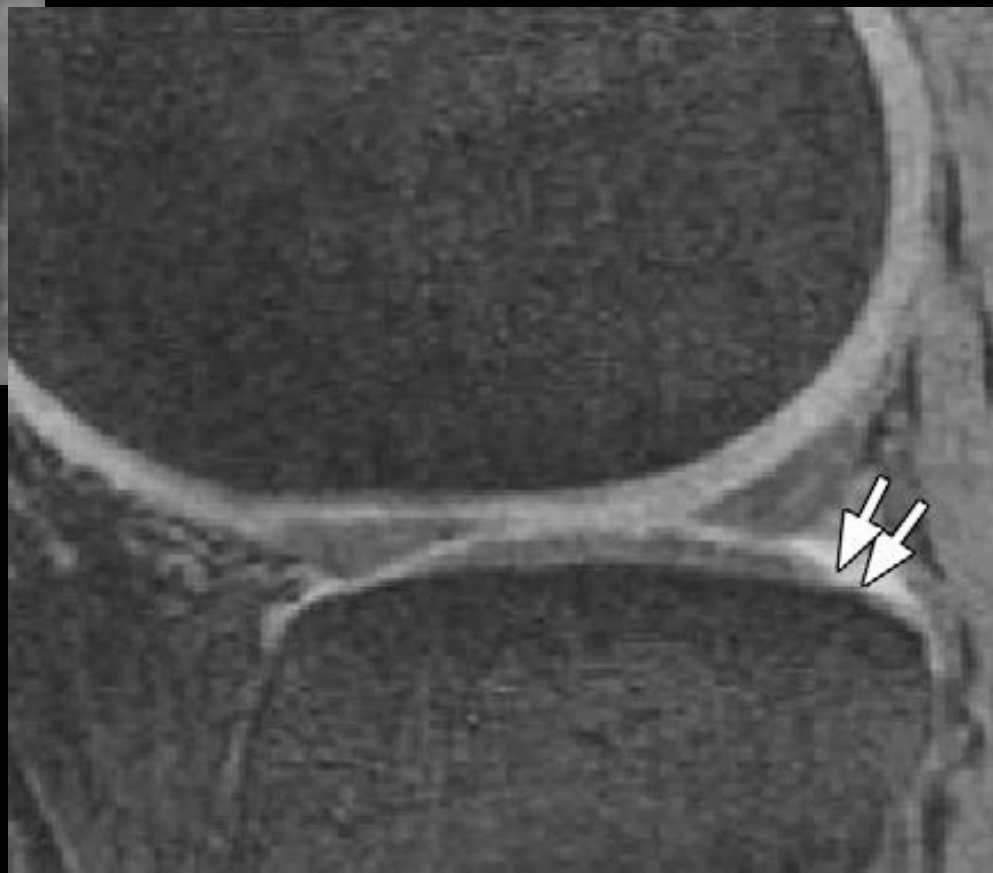
Sagittal proton density-weghted suppressed 3D fast low-angle shot

Coronal proton density–weighted fat-suppressed image shows excellent differentiation of articular cartilage, subchondral bone, and intraarticular joint fluid.

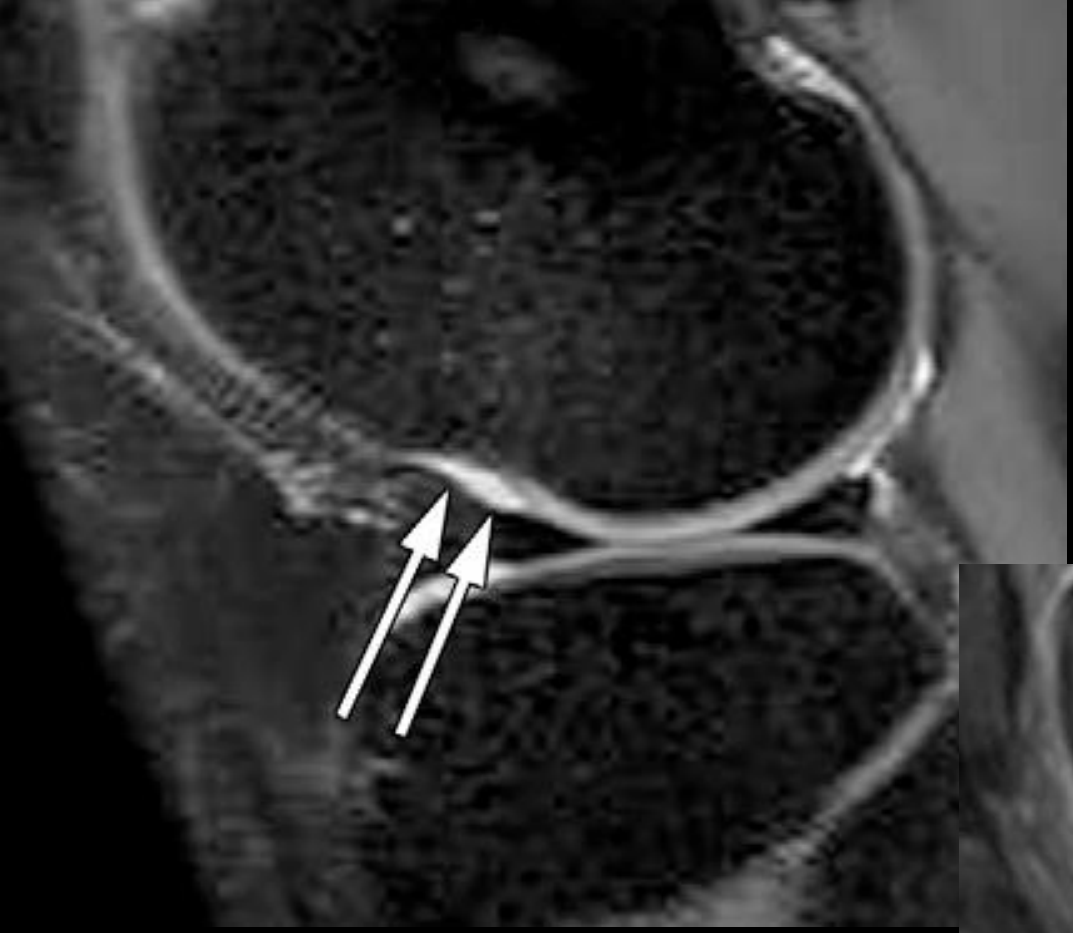


Focal fullthickness cartilage defect

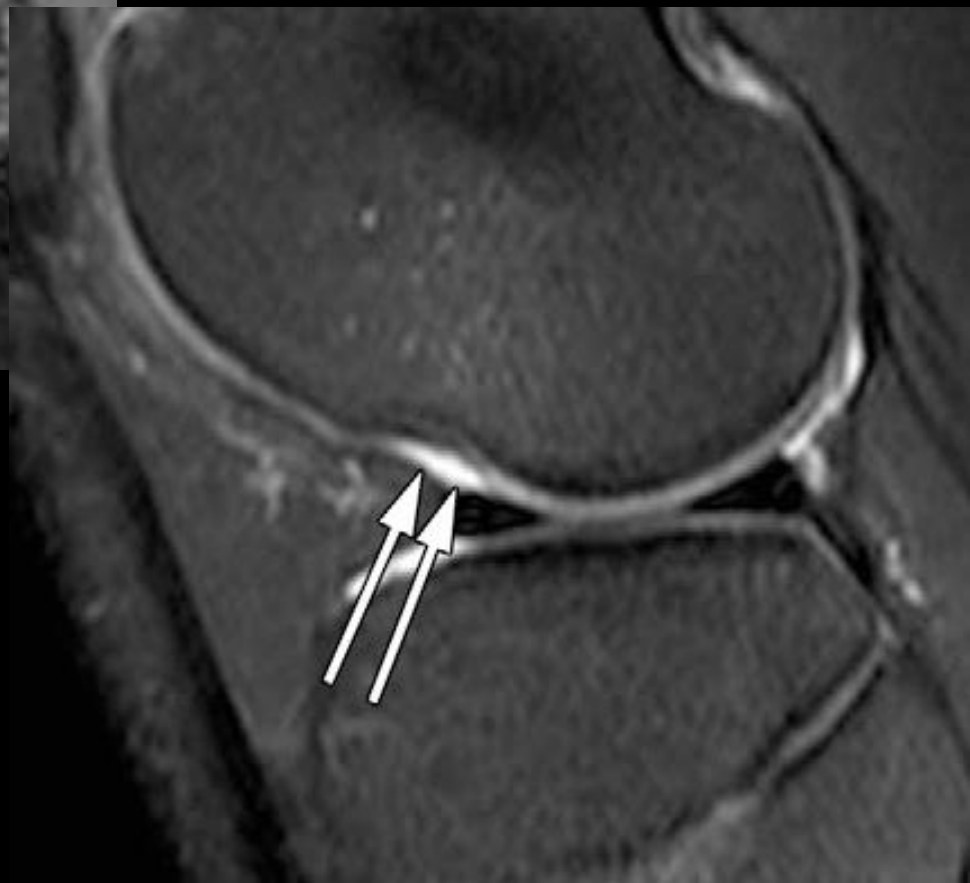




Sagittal intermediate-weighted fat suppressed image) shows focal fullthickness cartilage defect (arrows) on posterior aspect of lateral tibial plateau. Defect is well delineated because of high contrast between intraarticular fluid and cartilage surface

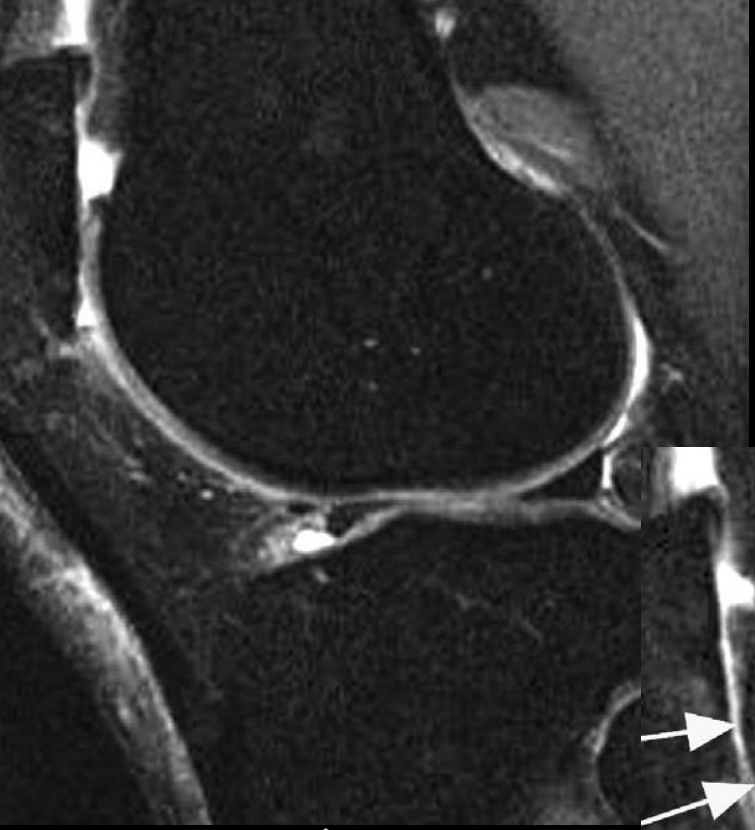


Sagittal T2 fat sat 3D image depicts full-thickness chondral defect (arrows). Accompanying osteochondral depression at the lateral femoral condyle.

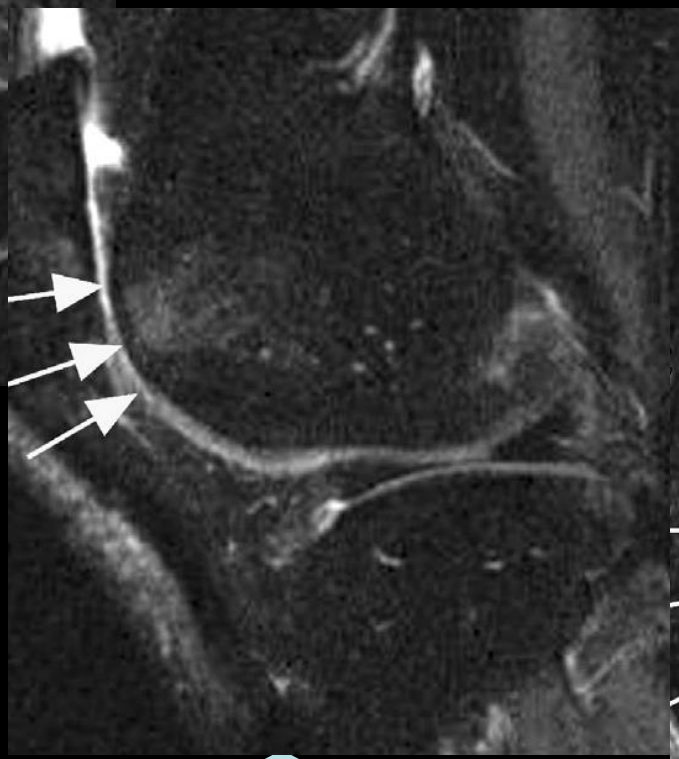


Standard sagittal T2 fat sat 2D Image shows defect (arrows) in similar fashion.

Evolution of cartilage damage over time

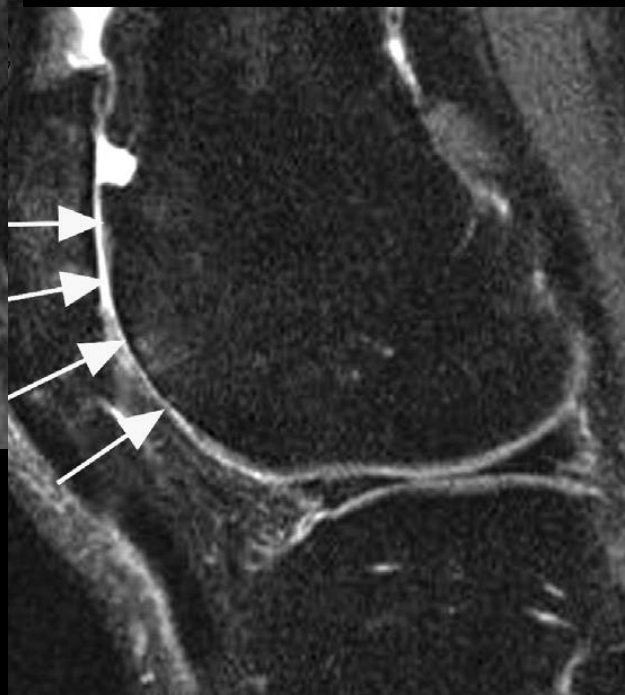


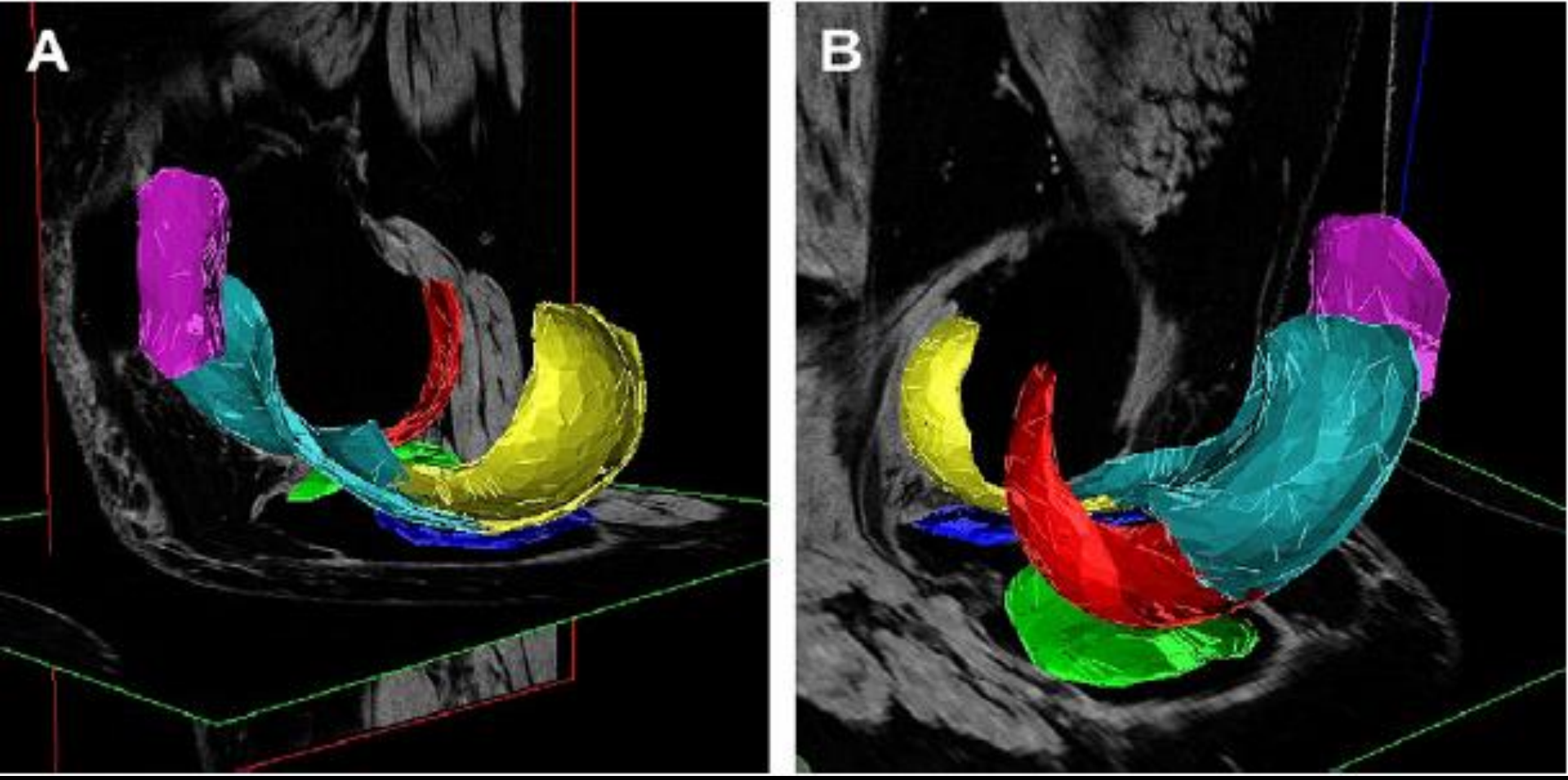
Baseline fat-suppressed intermediate-weighted MRI shows an intact articular cartilage surface



12 months later areas of partial and full thickness cartilage damage

Another 12 months later there is definite increase in area extent of lesion





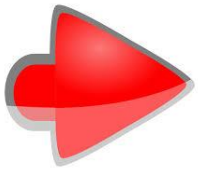
3D reconstruction and visualization of knee cartilage plates from a sagittal MR imaging data set: medial tibial cartilage marked blue, medial femoral cartilage marked yellow, lateral tibial cartilage marked green, lateral femoral cartilage marked red, femoral trochlear cartilage marked turquoise, and patellar cartilage marked magenta.

Impact of disease treatments on the progression of knee osteoarthritis structural changes related to meniscal extrusion: Data from the OAI progression cohort

Camille Roubille, MD[a,1], Johanne Martel-Pelletier, PhD[a,1], François Abram, PhD[b], Marc Dorais, MSc[c], Philippe Delorme, MSc[a], Jean-Pierre Raynauld, MD[a], Jean-Pierre Pelletier, MD[a,*]

Seminars in Arthritis and Rheumatism 45 (2015) 257–267

In summary, this study argues for a structural beneficial effect of treatment with Glu/CS in subsets of knee OA patients, as assessed by qMRI. This study is the first to describe, using qMRI, the impact of medial meniscal extrusion on the Glu/CS treatment response.



Glu/CS has a positive effect on cartilage volume loss assessed by quantitative MRI in symptomatic knee OA patients.

LONG-TERM EFFECTS OF GLUCOSAMINE/CHONDROITIN SULFATE ON THE PROGRESSION OF STRUCTURAL CHANGES IN KNEE OSTEOARTHRITIS: 6-YEAR FOLLOW-UP DATA FROM THE OSTEOARTHRITIS INITIATIVE

Jean-Pierre Raynauld, MD[1], Jean-Pierre Pelletier, MD[1], François Abram, PhD[2], Philippe Delorme, MSc[3], Johanne Martel-Pelletier, PhD[1]

Treatment with combined glucosamine (Glu) and chondroitin sulfate (CS) significantly reduced the cartilage volume loss in the global knee, associated with the lateral compartment. Multivariate analysis further demonstrated that the extent of the treatment's positive effect was related to exposure time to treatment, the protective effect at 6 years being significant in participants exposed to two or more years of treatment

Arthritis Care & Research
DOI 10.1002/acr.22866

First-line analysis of the effects of treatment on progression of structural changes in knee osteoarthritis over 24 months: data from the osteoarthritis initiative progression cohort

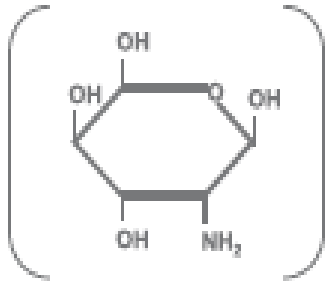
Johanne Martel-Pelletier,[1] Camille Roubille,[1] François Abram,[2] Marc C Hochberg,[3] Marc Dorais,[4] Philippe Delorme,[1] Jean-Pierre Raynauld,[1] Jean-Pierre Pelletier[1]

In analgesic/NSAIDs groups and – analgesic/NSAIDs groups, participants who took Glu/CS had reduced loss of cartilage volume over 24 months in subregions when assessed with qMRI, arguing for a disease-modifying effect of Glu/CS which could not be identified by X-rays.

These data are consistent with the hypothesis that individuals with milder structural changes would benefit more from structure-modifying agents, such as Glu/CS, than those with a more advanced disease.

Ann Rheum Dis 2015;**74**:547–556.

Glucosamine hydrochloride or sulfate



+ HCl or + H_2SO_4

Cartilage

Anti-inflammatory

↓ PLA_2
↓ iNOS, COX-2
↓ pro-inflammatory cytokines and chemokines
↓ NF-κB
↑ GRP78

Anti-catabolic and anabolic

↓ MMPs
↓ ADAMTS-5
↑ GAG and HA production

Subchondral bone

Anti-resorptive

↓ RANKL
↑ OPG

Synovial membrane

Anti-inflammatory

↓ TNFα and IL-1β
↓ NO and PGE_2
↑ IL-10

Anti-catabolic

↑ HAS, HA and GAG production
↓ MAPK signaling pathway

Pro and anti-angiogenic

Evaluation of bone marrow lesion volume as a knee osteoarthritis biomarker - longitudinal relationships with pain and structural changes: data from the Osteoarthritis Initiative

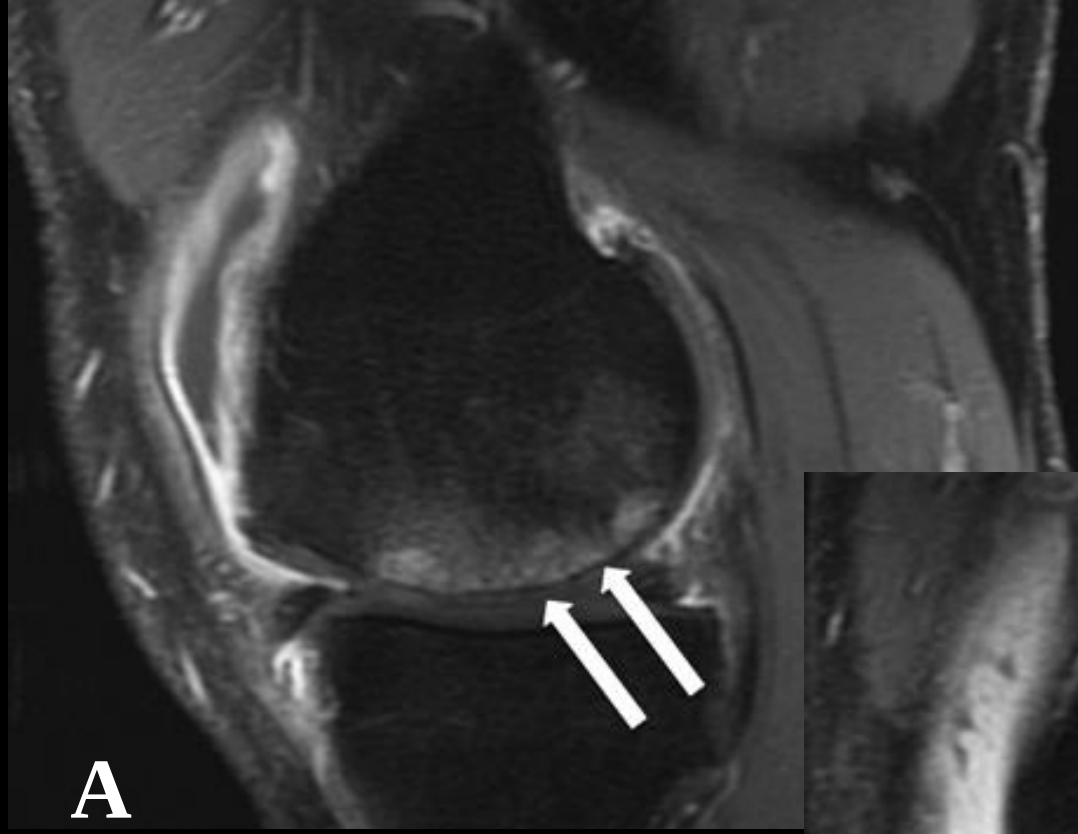
Jeffrey B Driban[1*], Lori Lyn Price[2], Grace H Lo[3,4], Jincheng Pang[5], David J Hunter[6], Eric Miller[5], Robert J Ward[7], Charles B Eaton[8], John A Lynch[9] and Timothy E McAlindon[1]

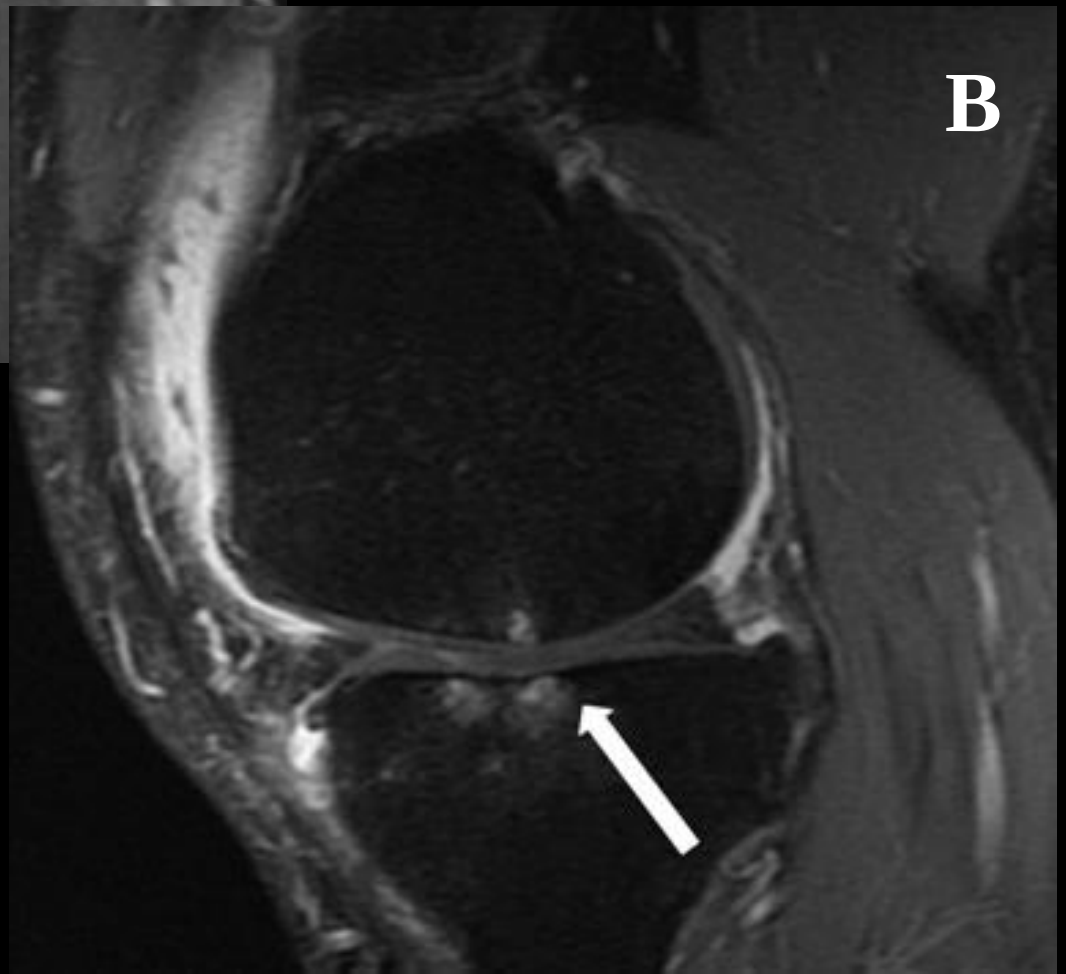
Driban *et al. Arthritis Research & Therapy* 2013, **15**:R112

Large baseline BMLs are associated with greater baseline knee pain, the presence of JSN at baseline, and disease progression. Additionally, BML regression is associated with decreased knee pain but not a reduced risk of concurrent JSN progression.

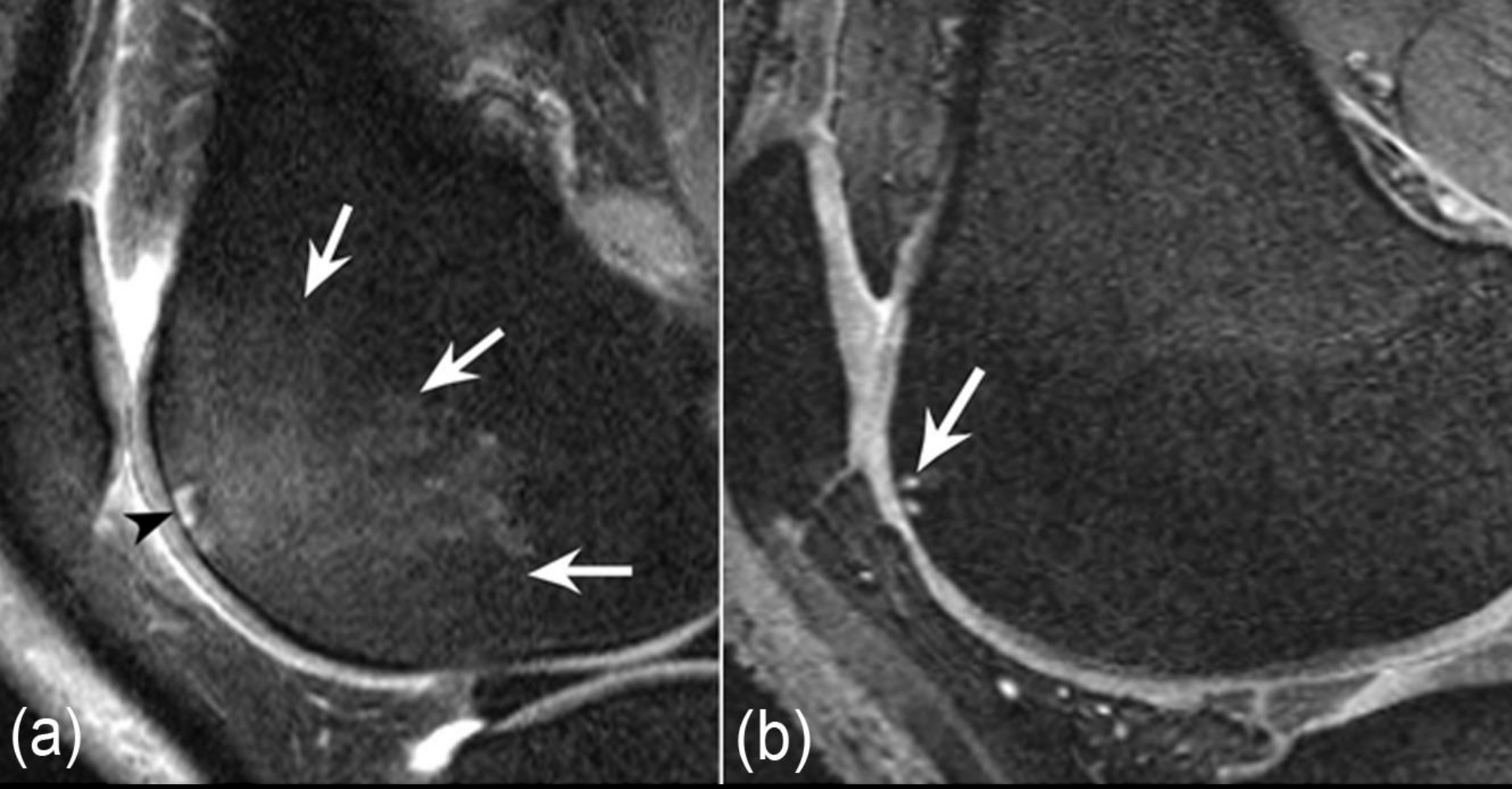
Bone marrow lesion (BML) size may be an important imaging biomarker for osteoarthritis-related clinical trials and reducing BML size may be an important therapeutic goal.

Bone marrow edema in OA



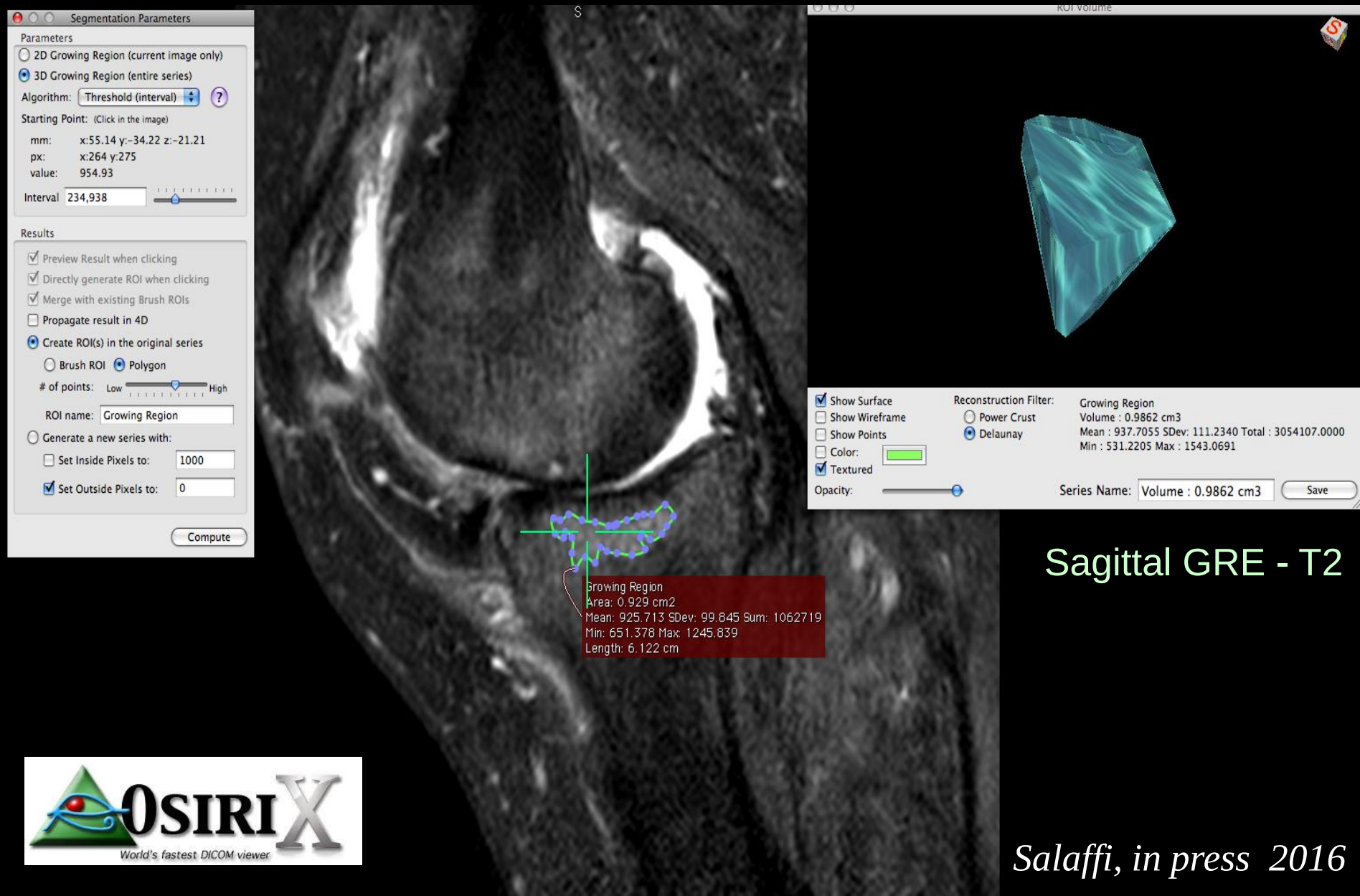


Bone marrow edema and bone marrow lesions depicted on the medial femur on a T2-weighted fat suppressed MRI (A) and medial tibial plateau on an intermediate-weighted fat suppressed MRI (B).



a: Sagittal intermediate-weighted (IW) fat-suppressed (fs) image shows a large (grade 3) subchondral bone marrow edema-like lesion at the lateral femoral trochlea (white arrows). Within this lesion, there is a small subchondral cyst (grade 1) directly adjacent to the subchondral plate (black arrowhead). b: Corresponding sagittal Dual Echo Steady-State (DESS) image only shows the small cyst (white arrow).

SEGMENTAZIONE SEMIAUTOMATICA CON OSIRIX



Sagittal GRE - T2

OSIRIX
World's fastest DICOM viewer

Salaffi, in press 2016

Frank W. Roemer, MD
Michel D. Crema, MD
Siegfried Trattnig, MD
Ali Guermazi, MD

Advances in Imaging of Osteoarthritis and Cartilage[1]

radiology.rsna.org ▪ ***Radiology:*** Volume 260: Number 2—August 2011

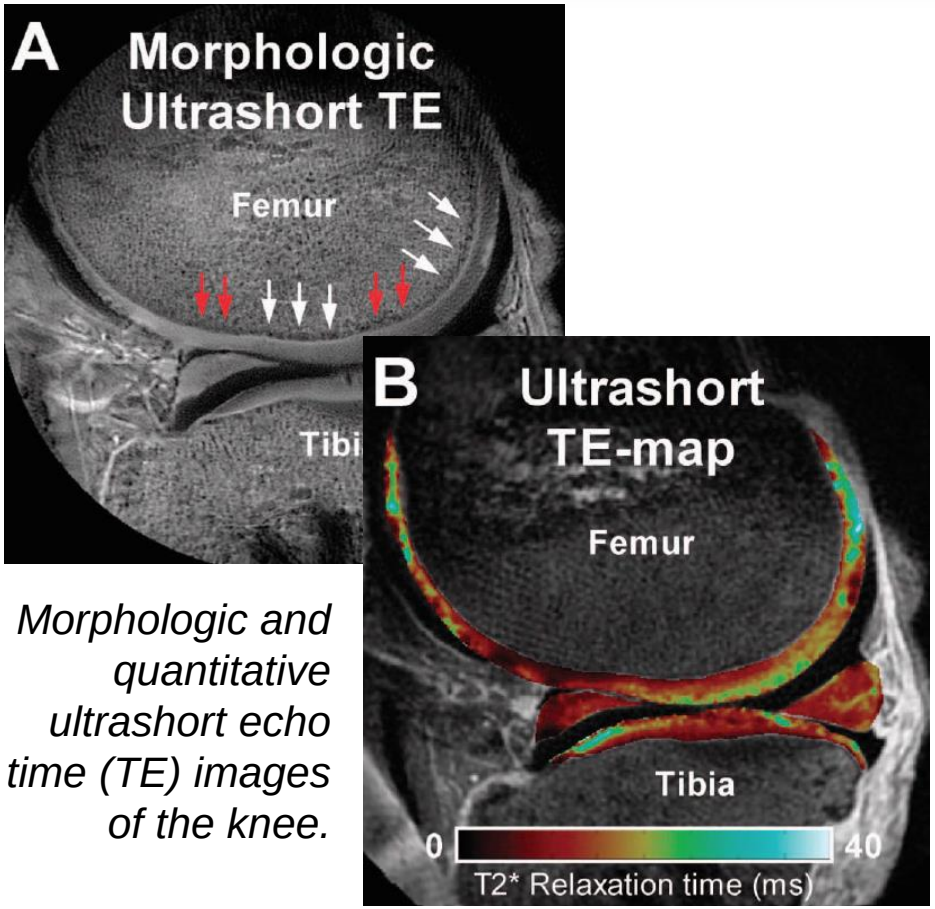
- Whole-organ semiquantitative MR imaging-based knee assessment is a reliable instrument to evaluate all tissues involved in the osteoarthritic disease process and may be applied in cross-sectional and longitudinal studies.

MR Imaging of Biochemical Properties of Articular Cartilage

- Quantitative 3D cartilage morphometry is a validated and reliable tool to assess several cartilage parameters cross sectionally and in a longitudinal fashion and is complementary to other evaluation techniques.
- Compositional MR imaging might play an important role in the assessment of early and potentially reversible cartilage damage, and several techniques are available and applicable in a clinical setting.

Quantitative Radiologic Imaging Techniques for Articular Cartilage Composition: Toward Early Diagnosis and Development of Disease-Modifying Therapeutics for Osteoarthritis

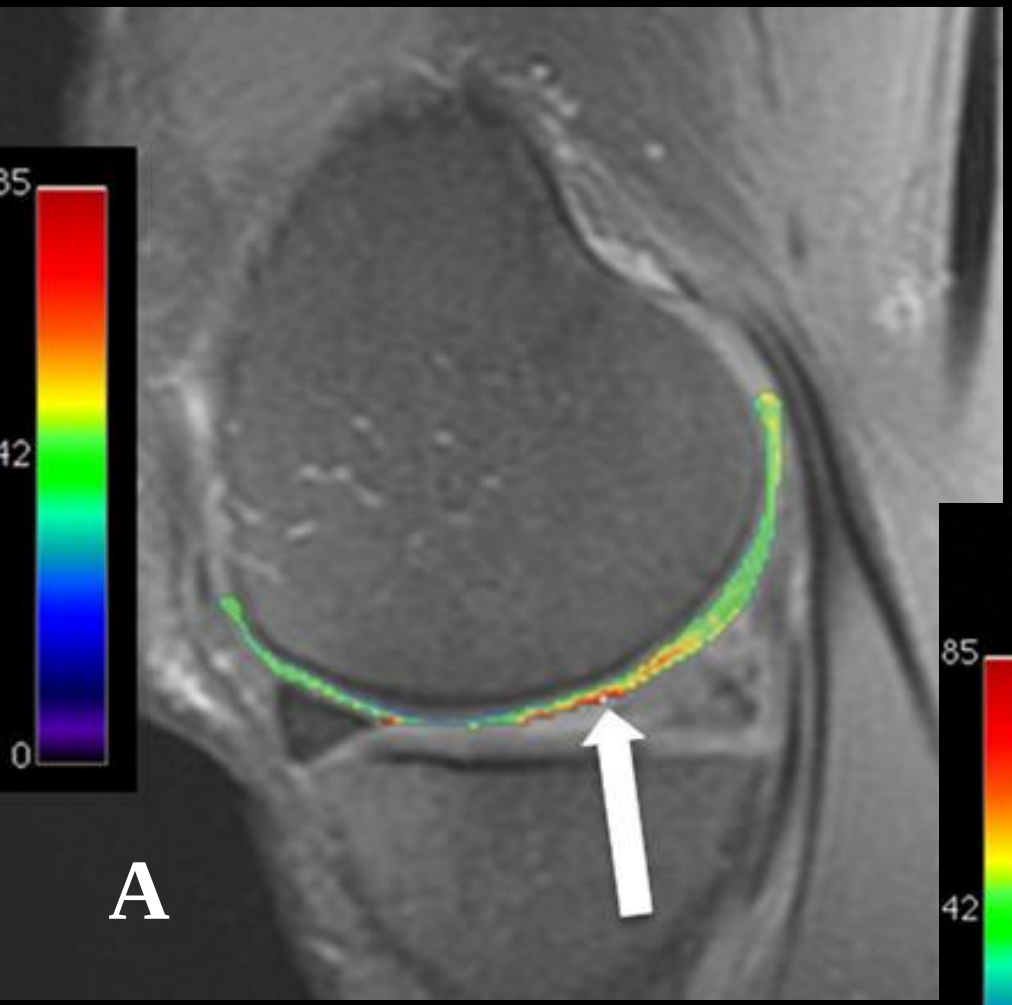
EDWIN H. G. OEI,[1] JASPER VAN TIEL,[2] WILLIAM H. ROBINSON,[3] AND GARRY E. GOLD[4]



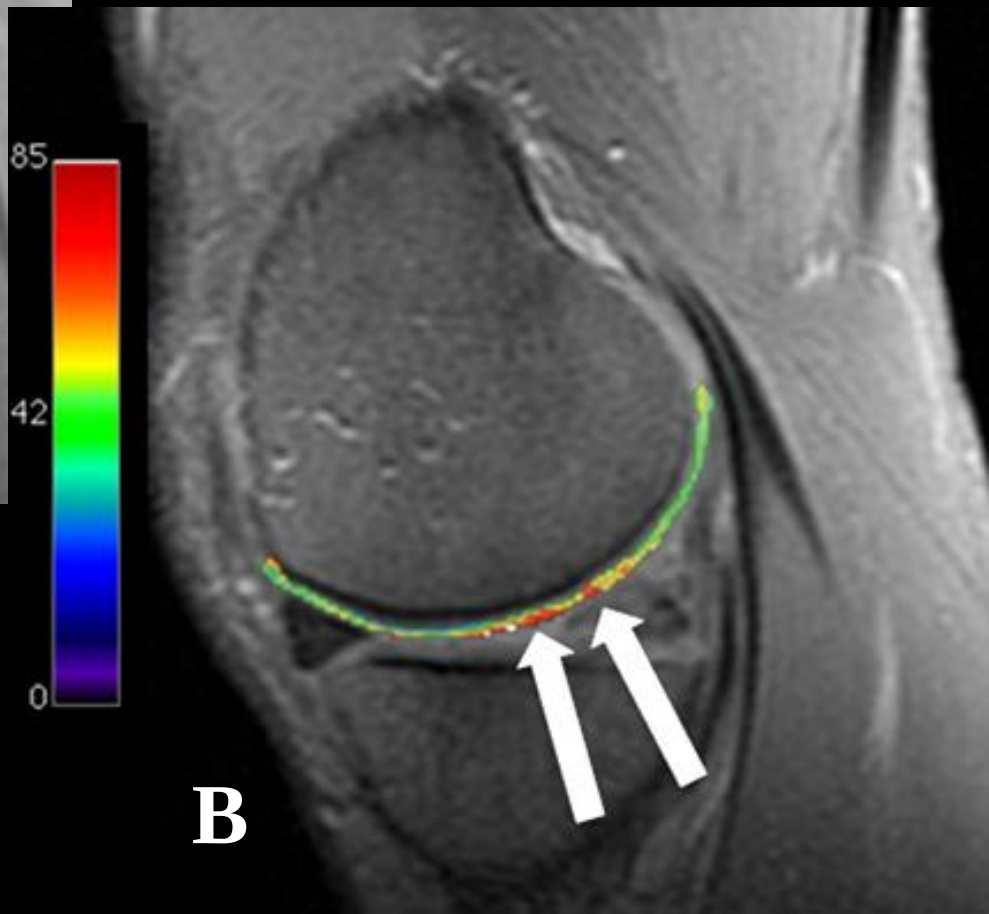
Morphologic and quantitative ultrashort echo time (TE) images of the knee.

- The role of quantitative imaging techniques in OA is emerging because they detect cartilage disease at earlier stages than radiography and conventional MRI, and provide outcome measures that can be used as imaging biomarkers in clinical research.
- Quantitative imaging techniques for cartilage composition are likely to play a pivotal role in future research and development of disease-modifying therapy for arthritis.

Arthritis Care & Research
Vol. 66, No. 8, August 2014, pp 1129–1141

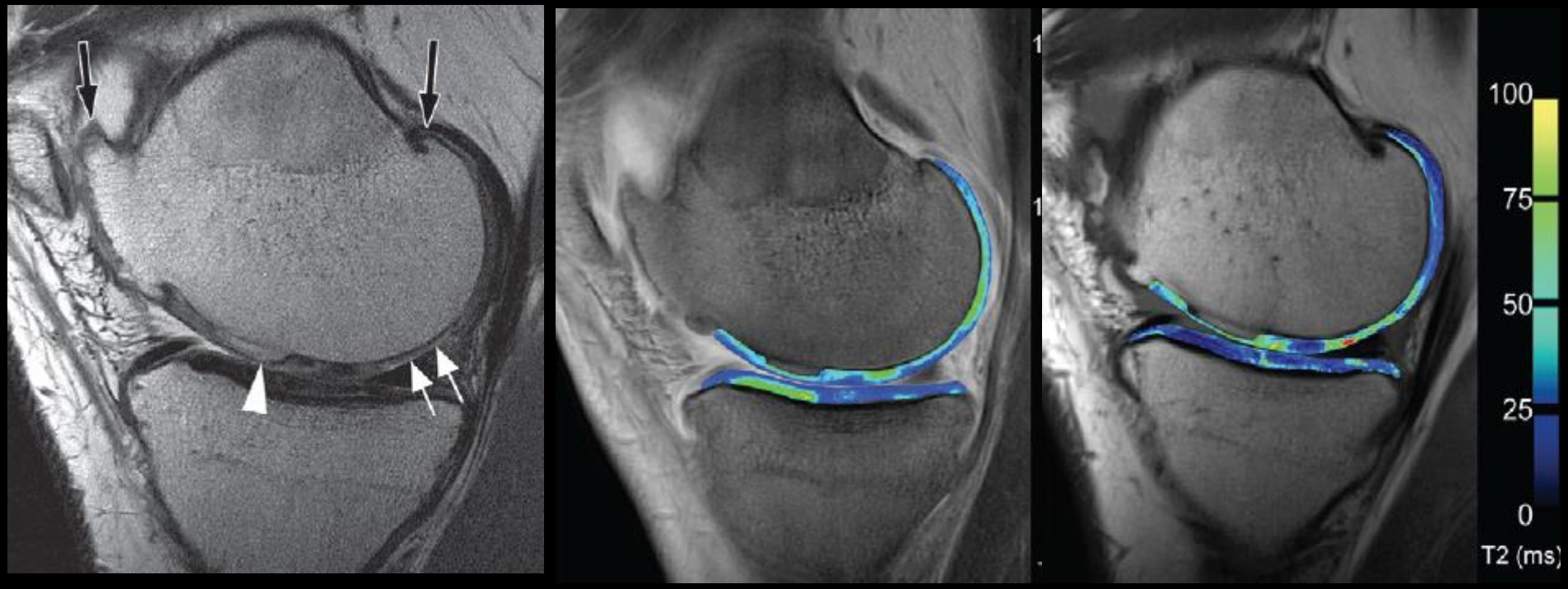


T2 mapping of articular cartilage in the medial femur of a patient with osteoarthritis at two time points.



Mapping software allows visualization of the spatial distribution; notice the increased T2 relaxation times in Fig. B. The T2 relaxation time is overlaid on the images using a color map, with the scale in milliseconds.

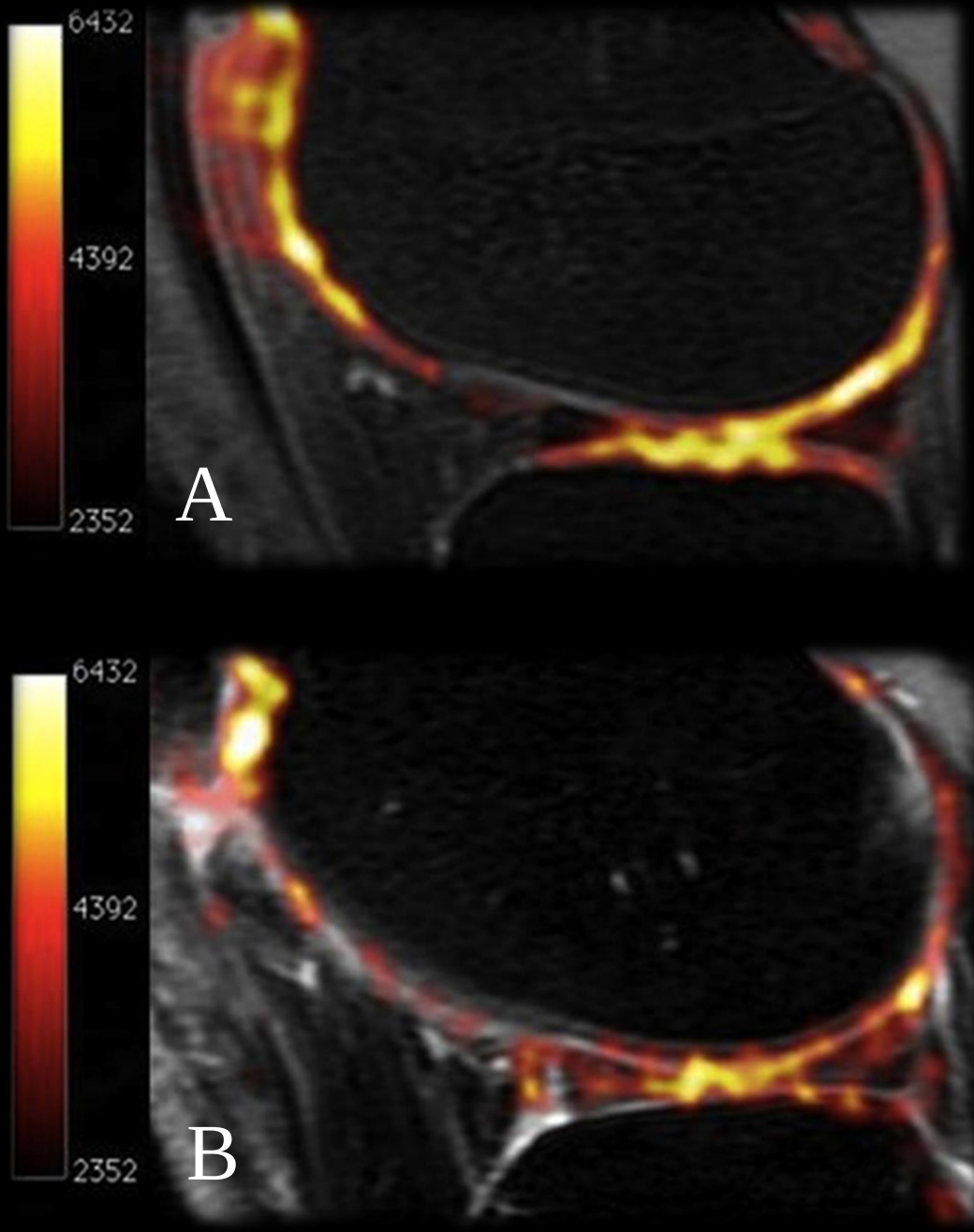
Compositional MR imaging.



A) Sagittal proton density–weighted high-spatial-resolution 3-T MR image of medial compartment of a knee with tibiofemoral OA shows peripheral (black arrows) and central (arrowhead) osteophytes.

B) (B) Delayed gadolinium-enhanced MR imaging of cartilage (dGEMRIC) T1 map corresponding to a shows multiple areas with low T1 values, corresponding to low GAG content in superficial layers of femoral cartilage and in posterior part of tibial cartilage (dark blue).

C) Sagittal T2 map corresponding to a reveals several areas of increased T2 values in femoral medial condyle.

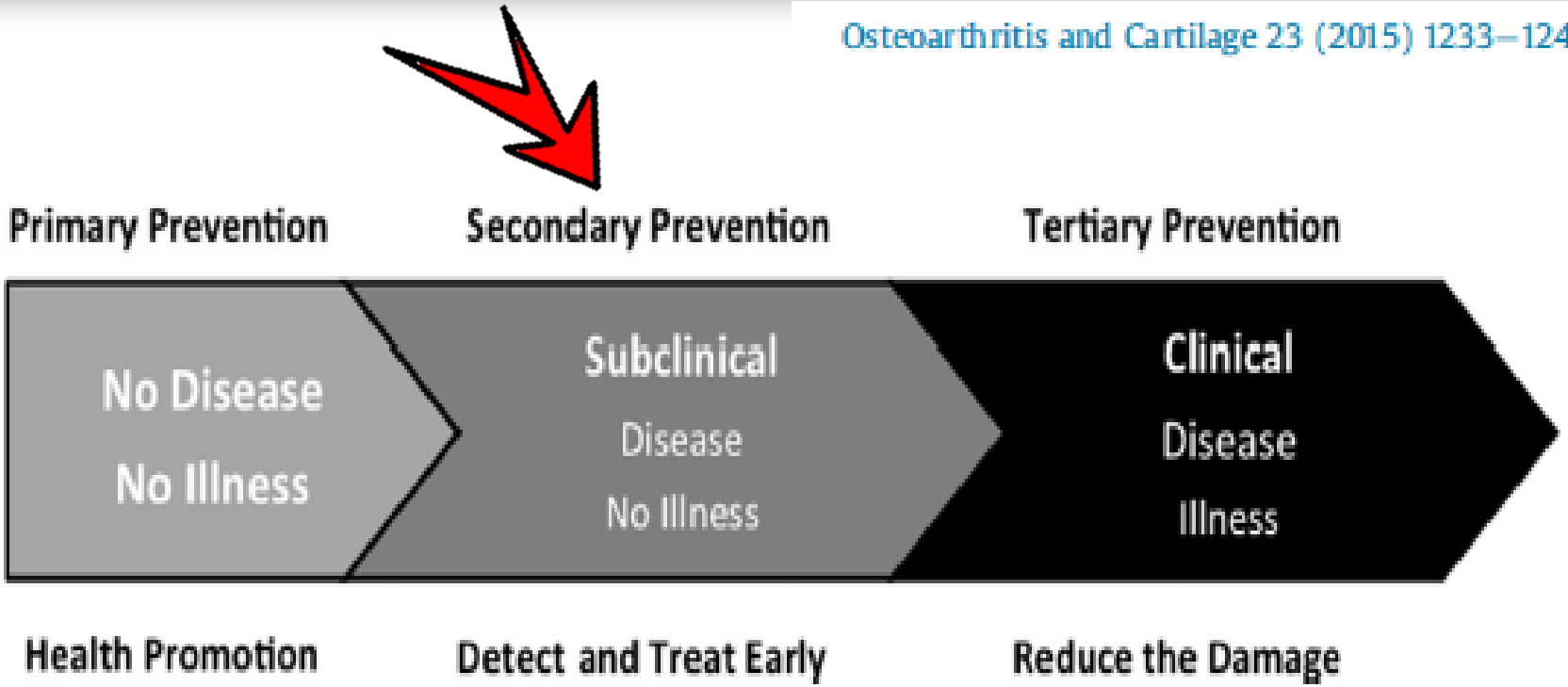


Sodium maps of articular cartilage in a healthy volunteer (A) and a patient with OA (B) overlaid onto proton images. The increased sodium signal correlates with higher glycosaminoglycan (GAG) concentration. As cartilage degenerates and GAG concentration decreases, sodium signal declines

Call for standardized definitions of osteoarthritis and risk stratification for clinical trials and clinical use

V.B. Kraus †*, F.J. Blanco ‡, M. Englund §||, M.A. Karsdal ¶, L.S. Lohmander §#

Osteoarthritis and Cartilage 23 (2015) 1233–1241

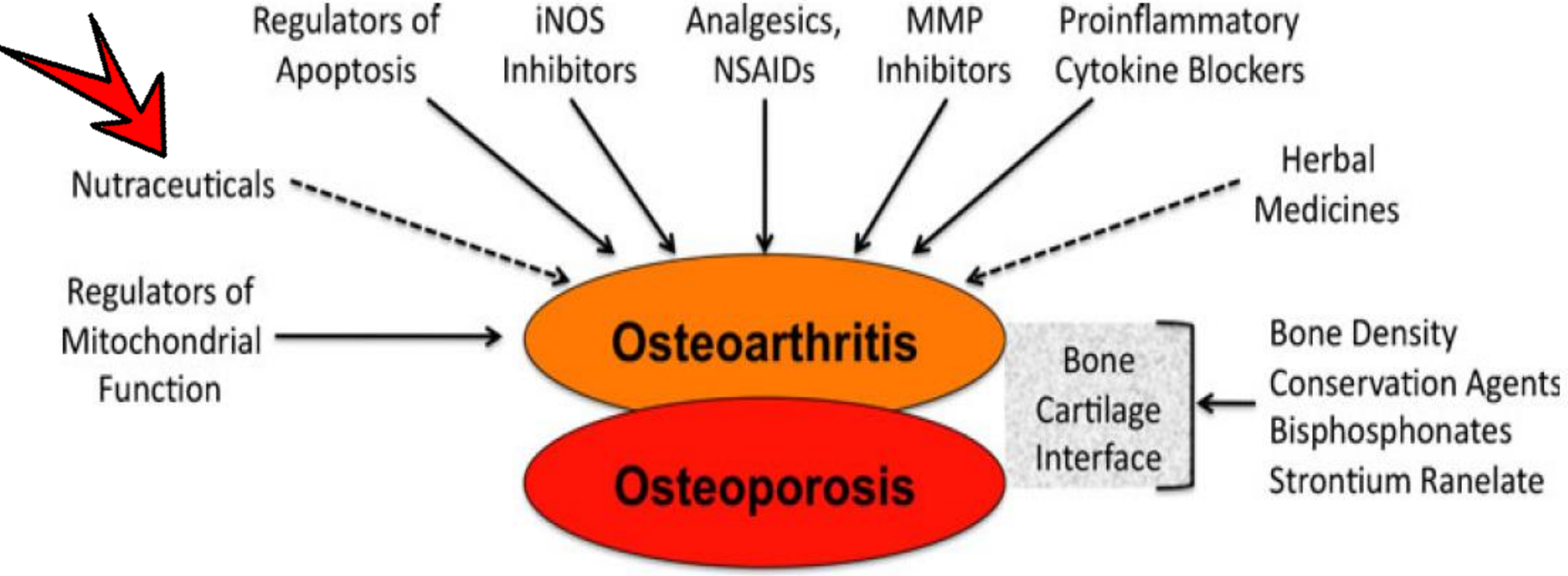


Stages of OA incorporating the new taxonomy. Three stages can be imagined e a no disease/no illness stage, a subclinical stage (with disease manifestations only) and a clinical stage (with illness manifestations).

The Future of Osteoarthritis Therapeutics: Targeted Pharmacological Therapy

A. Mobasheri

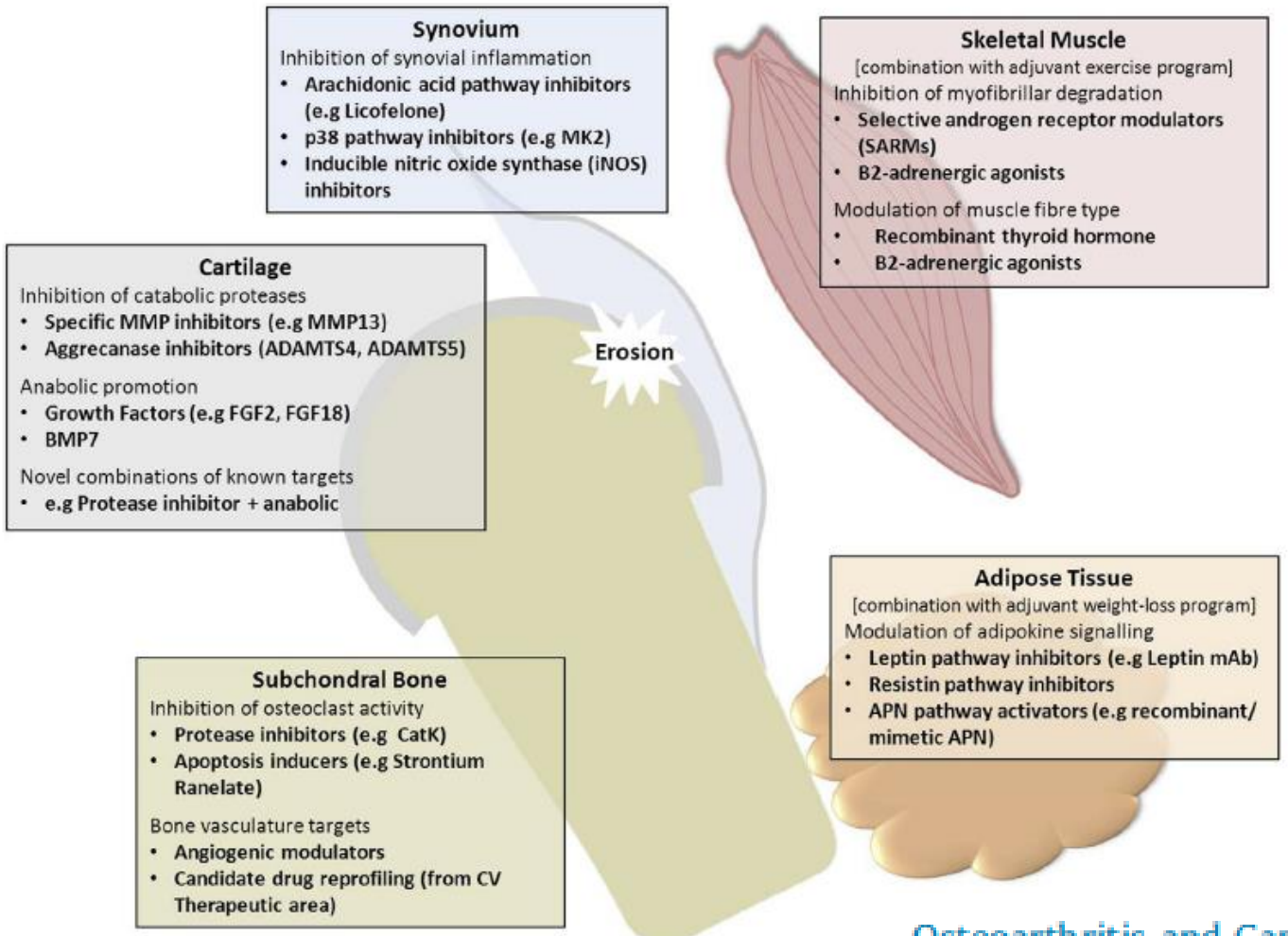
Curr Rheumatol Rep (2013) 15:364



Schematic diagram summarizing current concepts in pharmacological treatment of OA

The hallmarks of osteoarthritis and the potential to develop personalised disease-modifying pharmacological therapeutics

D.P. Tonge ‡, M.J. Pearson †, S.W. Jones †*



Representation of the multiple biological effect areas within the OA joint and key pathways to exploit for the development of pharmacological DMOADs.

Osteoarthritis and Cartilage 22 (2014) 609–621