



# Tecniche Interventistiche In Reumatologia

## Simone Parisi

Azienda Ospedaliera Universitaria Città della Salute e della Scienza di Torino

Struttura Complessa Reumatologia

Emerging Euler Network - Social Media Co-Lead

Centro Studi – Società Italiana di Reumatologia





ABBVIE, BALDACCI, BIOGEN,  
CELGENE, CHIESI, GRUNENTHAL,  
BMS, JANSSEN, NOVARTIS, LILLY,  
SANOFI, UCB, MYLAN

SIMONE PARISI





# Artrocentesi ed esame del liquido sinoviale

---



# Il liquido sinoviale attraverso i secoli<sup>s</sup>

## *Synovial fluid over the centuries*

P. Marson

*Servizio di Immunoematologia e Trasfusionale, Azienda Ospedale Università di Padova*



In questa rassegna vengono analizzate le più significative tappe storiche nello studio del liquido sinoviale, partendo dalla **Medicina greco-romana, fino a Paracelso** (1493-1541), a cui è attribuita la paternità del termine “**sinovia**” per indicare il liquido intra-articolare.

Viene poi ripercorsa, alla luce di recenti indagini, la storia dell'intervento che permette il prelievo di liquido sinoviale, ovvero **l'artrocentesi**, che pare sia stata praticata per la prima volta **in Messico, nel periodo precoloniale**.

Ancora, si commentano **la prima analisi chimica del liquido sinoviale**, opera del francese **Jean-Louis Margueron (1792)**, ed il **primo studio sulla membrana sinoviale**, tratto dall'opera “*Traité des membranes*” di **Marie-François Xavier Bichat (1800)**.





La rassegna si conclude analizzando alcuni contributi dell'Ottocento, alla comparsa dei **primi studi di farmacologia "sinoviale"**, sull'eliminazione di diverse sostanze chimiche nel LS. Su questo tema è una comunicazione tenuta alla Regia Accademia Peloritana dal farmacologo siciliano **Gaetano Gaglio**.

*"De morborum principe tractatus"* (e si sa, *"princeps morborum"* è solo la gotta!) dell'autore tedesco Otto Tachenius (?-1670) In questo leggiamo:

*"Sperma ranarum, luna decrescente collectum, et ex Balneo ad siccitatem distillatum, prolicitam aquam alcali insipidi ditissimam dabit, ut Hippocr. Chemicus mechanice docet, quae tepida cum lineis pannis applicata calidae ignaeque podagrae optimum est refrigerium."*

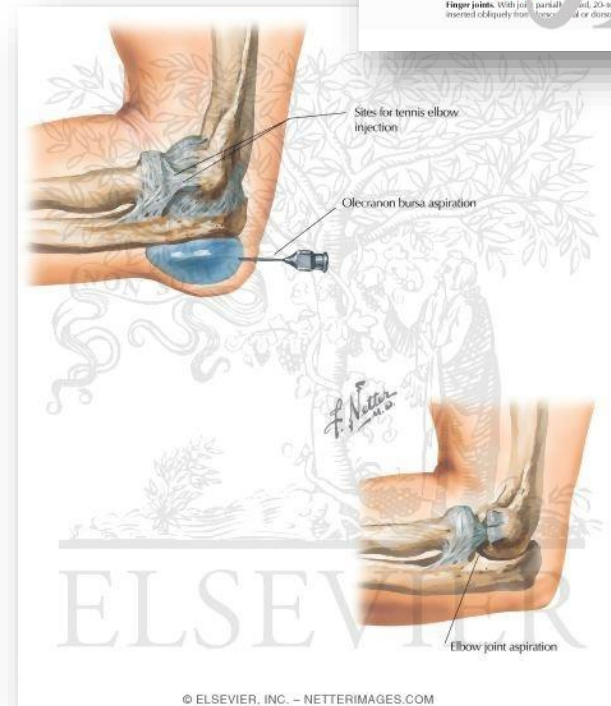
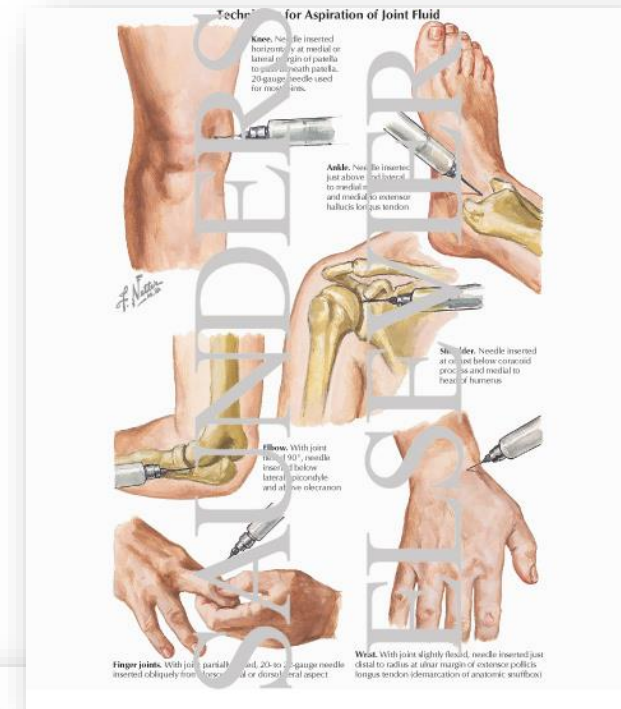
*"Multo promptius dolorem leniveris si aquae predicate alcali acueris, sive multiplicaveris addizione alcali urinae, tali proporzione, ut inflammata dolentemque partem applicata aqua non pungat, quod lingua facillime metiri potest."*



# L'ARTROCENTESI

Aspirazione di liquido presente nel cavo articolare e, per estensione, nelle borse e nelle guaine.

**Ha finalità sia diagnostiche sia terapeutiche**



# ARTROCENTESI

**DIAGNOSTICA**

**ESAME DEL  
LIQUIDO SINOVIALE**

**NON  
INFIAMMATORIO**

**OSTEOARTROSI**

**ARTRITI  
MICRO-  
-CRISTALLINE**

**INFIAMMATORIO**

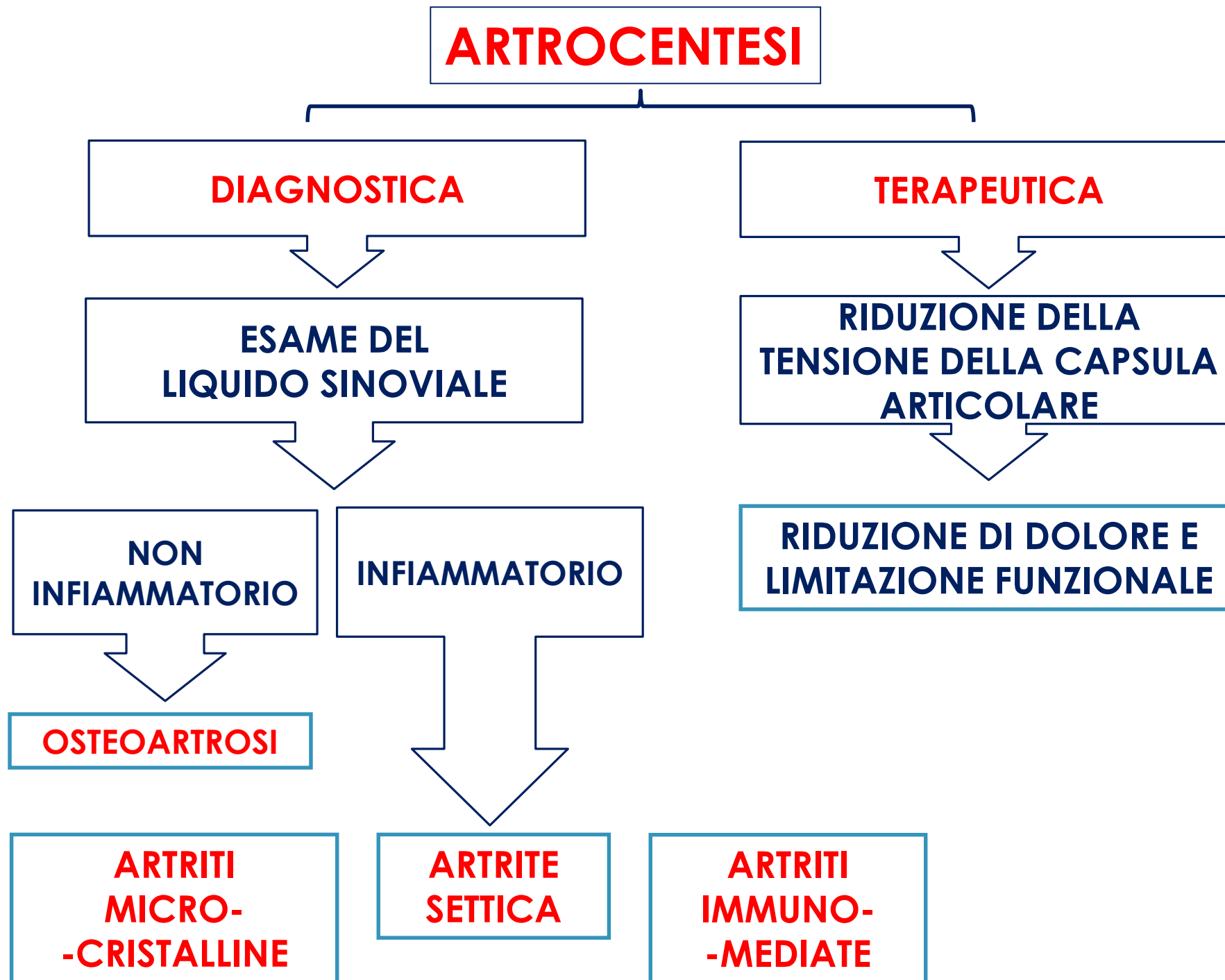
**ARTRITE  
SETTICA**

**ARTRITI  
IMMUNO-  
-MEDIATE**

**TERAPEUTICA**

**RIDUZIONE DELLA  
TENSIONE DELLA CAPSULA  
ARTICOLARE**

**RIDUZIONE DI DOLORE E  
LIMITAZIONE FUNZIONALE**



# Indicazioni

In tutte le condizioni in cui vi è una flogosi articolare di cui non è definita la natura:

Nelle monoartriti

Nel sospetto di artrite microcristallina o di artrite settica

Nelle condizioni predisponenti l'artrite settica:

Artrite reumatoide

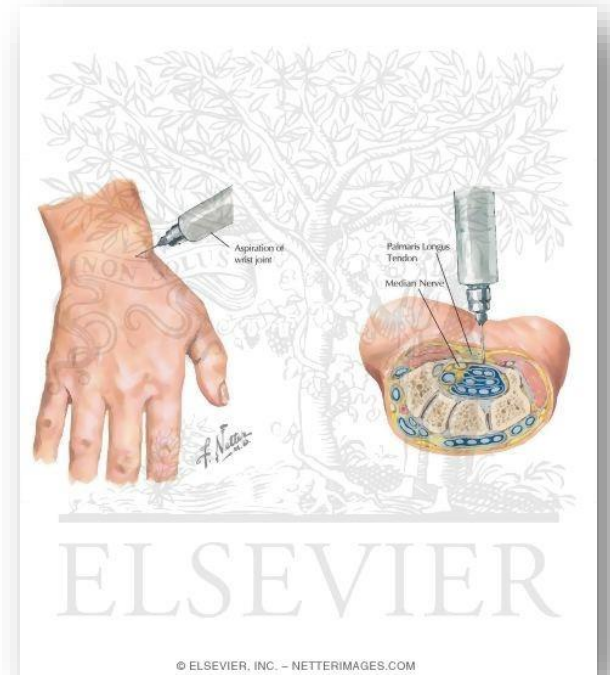
Artrite gottosa

Precedenti infiltrazioni

Precedenti interventi ortopedici

Sospetto di infezione protesica

Nell'emartro per prevenire l'organizzazione



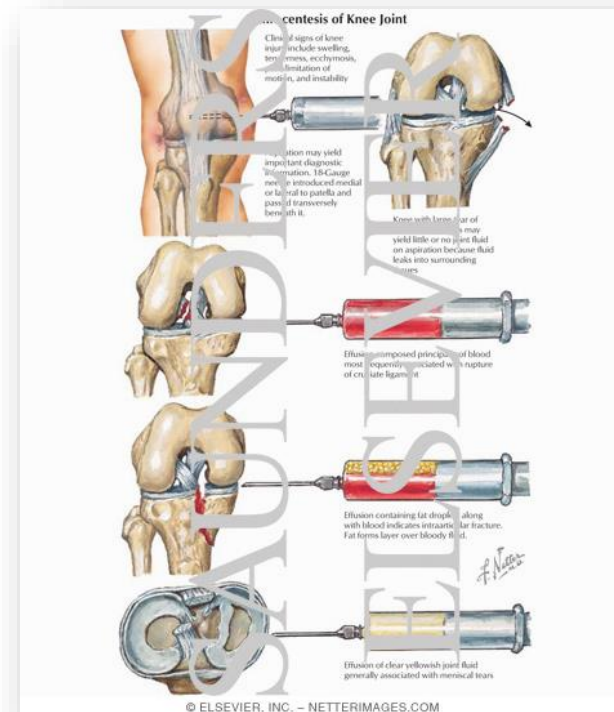


# Controindicazioni

Infezioni cutanee (erisipela) nella sede di iniezione

## Precauzioni (ma non controindicazioni)

- Diatesi emorragica
- Terapia anticoagulante orale



# Potenziiali rischi o complicazioni

Temporaneo «disconfort»

Puntura/lesione di tendini, vasi, nervi

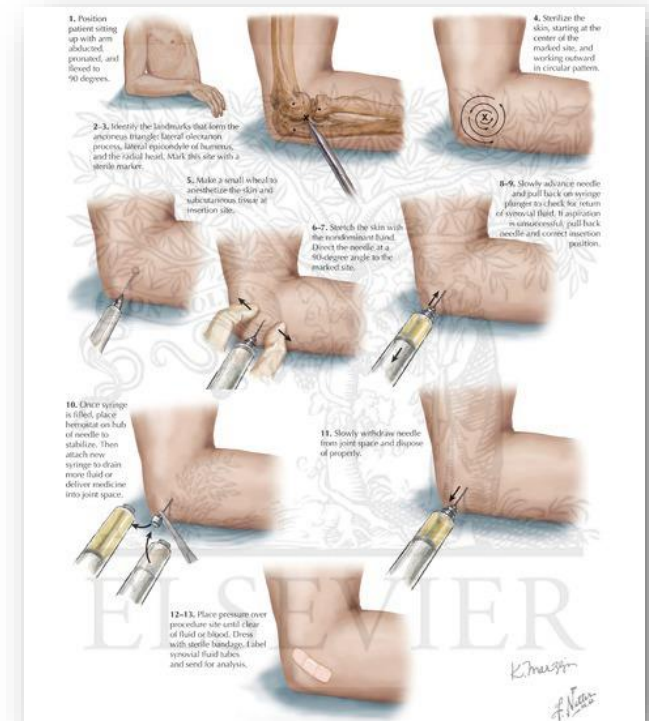
Allergie

Reazione vagale

Emartro

Sanguinamento nella sede di introduzione dell'ago

Infezione (0,01% dei casi)



# The Italian Society of Rheumatology clinical practice guidelines for the diagnosis and management of gout

**N. Ughi<sup>1,2</sup>, I. Prevete<sup>1,3</sup>, R. Ramonda<sup>4</sup>, L. Cavagna<sup>5</sup>, G. Filippou<sup>6</sup>, M. Manara<sup>1,2</sup>, A. Bortoluzzi<sup>1,6</sup>, S. Parisi<sup>1,7</sup>, A. Ariani<sup>1,8</sup>, C.A. Scirè<sup>1,6</sup>**

<sup>1</sup>Epidemiology Unit, Italian Society for Rheumatology, Milan, Italy; <sup>2</sup>Division of Clinical Rheumatology, Centro Specialistico Ortopedico-Traumatologico Gaetano Pini CTO ASST Gaetano Pini, Milano, Italy; <sup>3</sup>Rheumatology Unit, Azienda Ospedaliera San Camillo-Forlanini, Roma, Italy; <sup>4</sup>Rheumatology Unit, Department of Medicine-DIMED, University Hospital of Padua, Italy; <sup>5</sup>Department of Rheumatology, University and IRCCS Foundation Policlinico S. Matteo, Pavia, Italy; <sup>6</sup>Department of Medical Sciences, Rheumatology Section, University of Ferrara, Azienda Ospedaliero-Universitaria Sant'Anna di Cona, Ferrara, Italy; <sup>7</sup>Rheumatology Unit, Azienda Ospedaliera Città della Salute e della Scienza di Torino, Italy; <sup>8</sup>Department of Medicine, Internal Medicine and Rheumatology Unit, Azienda Ospedaliero-Universitaria di Parma, Italy

	The final set of 14 recommendations	Category of evidence	Grade of recommendation
1	Identification of MSU crystals should be performed for a definite diagnosis of gout; if not possible, a diagnosis of gout can be supported by classical clinical features such as podagra, tophi, rapid response to colchicine* and/or characteristic imaging findings <sup>§</sup> .	2*, 2 <sup>§</sup>	D*, B <sup>§</sup>





Needle is in  
into the joi  
fluid is with



# La manovra



## The Journal of Rheumatology

### Diagnostic Arthrocentesis for Suspicion of Gout Is Safe and Well Tolerated

William J. Taylor, Jaap Fransen, Nicola Dalbeth, Tuhina Neogi, H. Ralph Schumacher, Melanie Brown, Worawit Louthrenoo, Janitzia Vazquez-Mellado, Maxim Eliseev, Geraldine McCarthy, Lisa K. Stamp, Fernando Perez-Ruiz, Francisca Sivera, Hang-Korng Ea, Martijn Gerritsen, Carlo A. Scire, Lorenzo Cavagna, Chingtsai Lin, Yin-Yi Chou, Anne-Kathrin Tausche, Geraldo da Rocha Castelar-Pinheiro, Matthijs Janssen, Jiunn-Horng Chen, Ole Slot, Marco Cimmino, Till Uhlig and Tim L. Jansen

Table 1. Adverse events following diagnostic arthrocentesis (n = 887 patients).

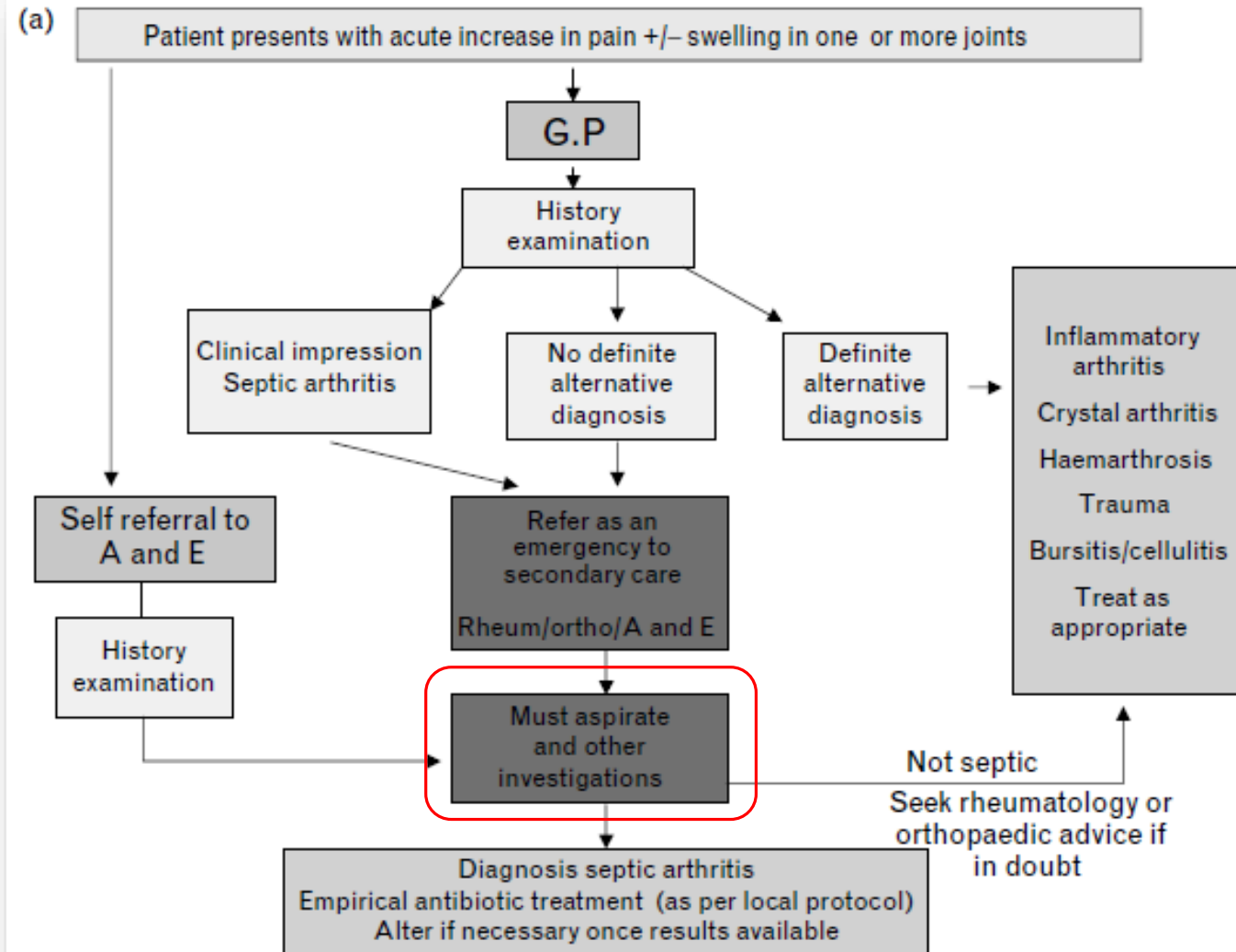
Adverse Events	n	95% CI*	% (95% CI)†	Serious	Attribution	Severity
Pain	5	1.6–11.7	0.6 (0.2–1.1)	None	Possible (n = 2), very likely (n = 3)	Mild (n = 4), moderate (n = 1)
Bruising	2	0.2–7.2	0.2 (0–0.6)	None	Very likely (n = 2)	Mild (n = 2)
Joint swelling	4	1.1–10.2	0.5 (0.1–0.9)	None	Doubtful (n = 3), possible (n = 1)	Mild (n = 3), moderate (n = 1)
Joint infection	1	0.03–5.6	0.1 (0–0.3)	Yes	Very likely (n = 1)	Severe (n = 1)

\* CI based on exact method from Poisson distribution. † CI estimated by bootstrapping.

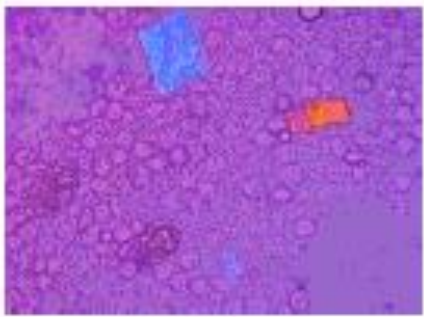
# Septic arthritis: current diagnostic and therapeutic algorithm

Catherine J. Mathews and Gerald Coakley

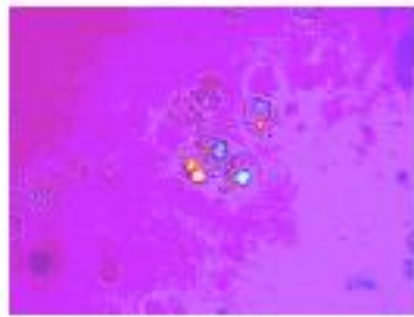
Current Opinion in Rheumatology 2008, 20:457–462







Cristalli di colesterolo.  
Microscopia ottica 40x



Cristalli di cortisone.  
Microscopia ottica 40x.



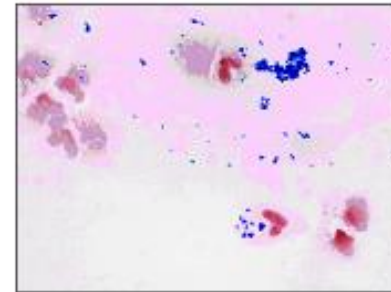
Cristalli di pirofosfato di calcio.  
Microscopia ottica 40x.



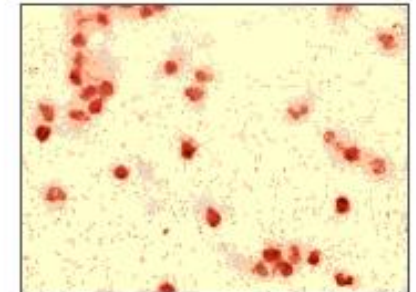
Cristalli di urato monopedico.  
Microscopia ottica 40x.

## ARTRITI MICROCRISTALLINE

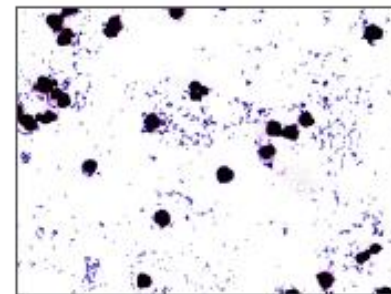
## ARTRITI INFETTIVE



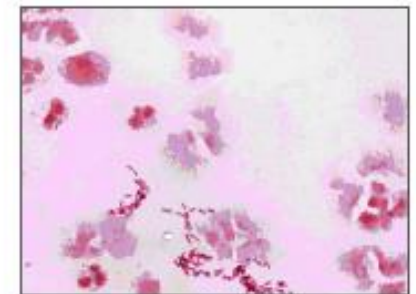
*Staphylococcus aureus*.  
Microscopia ottica 100x.



*Pseudomonas aeruginosa*.  
Microscopia ottica 100x.



*Streptococcus* spp.  
Microscopia ottica 100x.



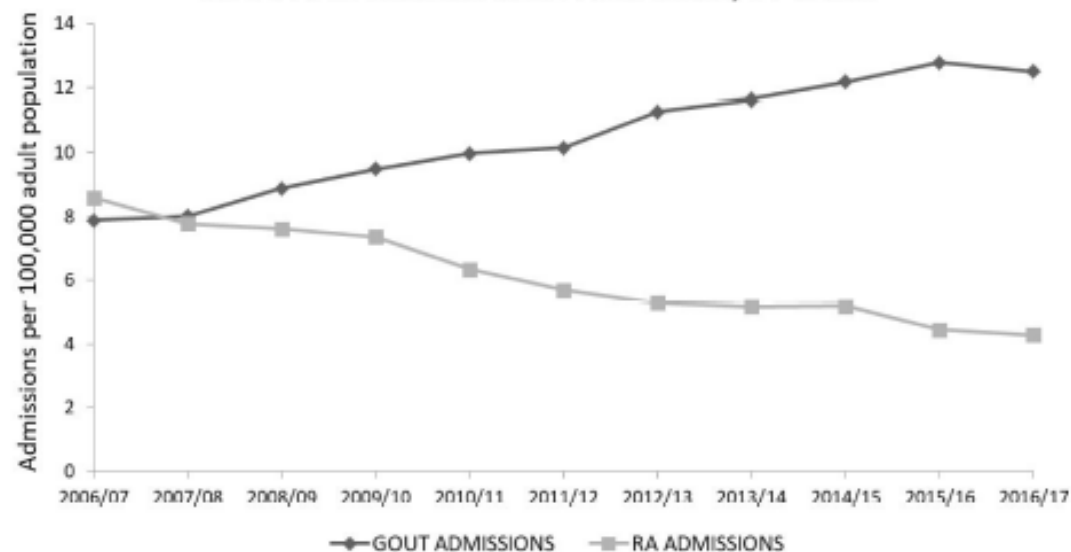
*Escherichia coli*.  
Microscopia ottica 100x.

Return of the King: Rising Incidence of Acute Hospital Admissions due to Gout

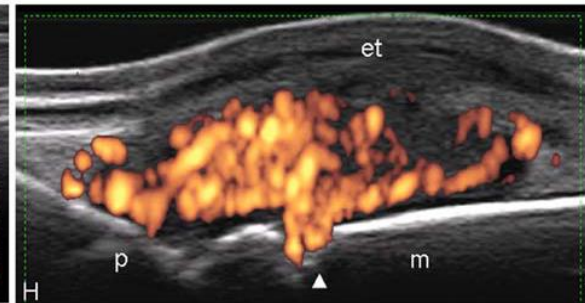
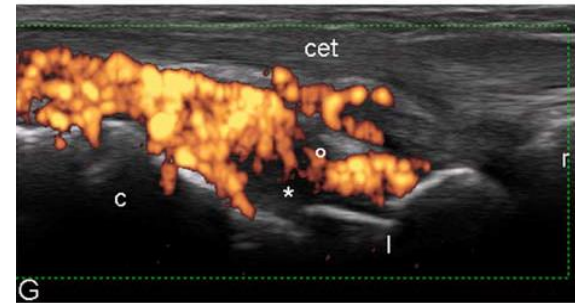
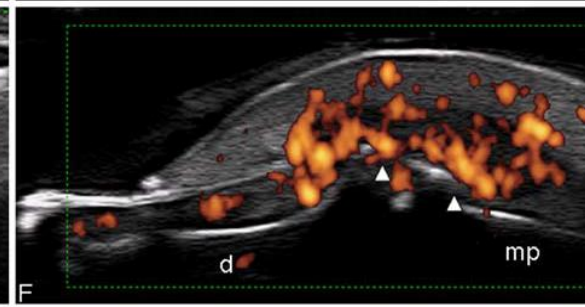
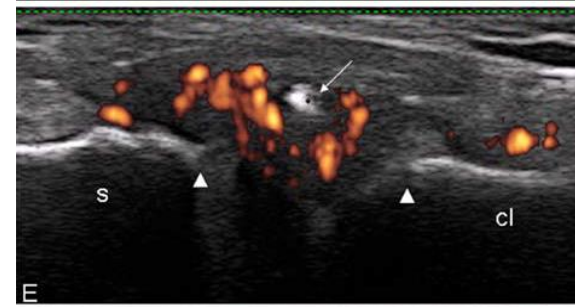
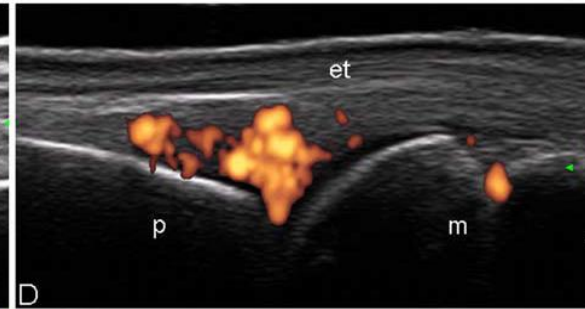
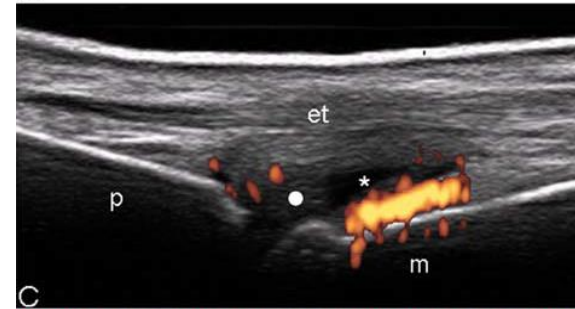
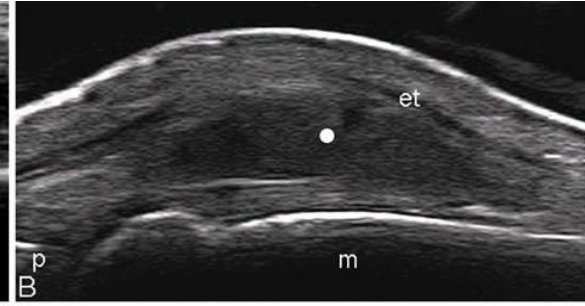
Mark Russell, Mark Yates, Katie Bechman, Andrew Rutherford, Sujith Subesinghe, Peter Lanyon and James Galloway



INCIDENCE OF ACUTE HOSPITAL ADMISSIONS DUE TO  
GOUT AND RHEUMATOID ARTHRITIS, BY YEAR



# IL RUOLO DELL'ECOGRAFIA





# TERAPIA INFILTRATIVA

## UTILITA' DELL' ECOGRAFIA

Nel 2007 la SIR raccomanda, nelle linee guida dell'artrocentesi, la metodica ecografica come supporto in casi selezionati (conformazione brachitipica, esito di fratture comminute, PAA ecc...)



# TERAPIA INFILTRATIVA

## Guida Ecografica



# Clinical utility of ultrasound guidance for intra-articular knee injections: a review

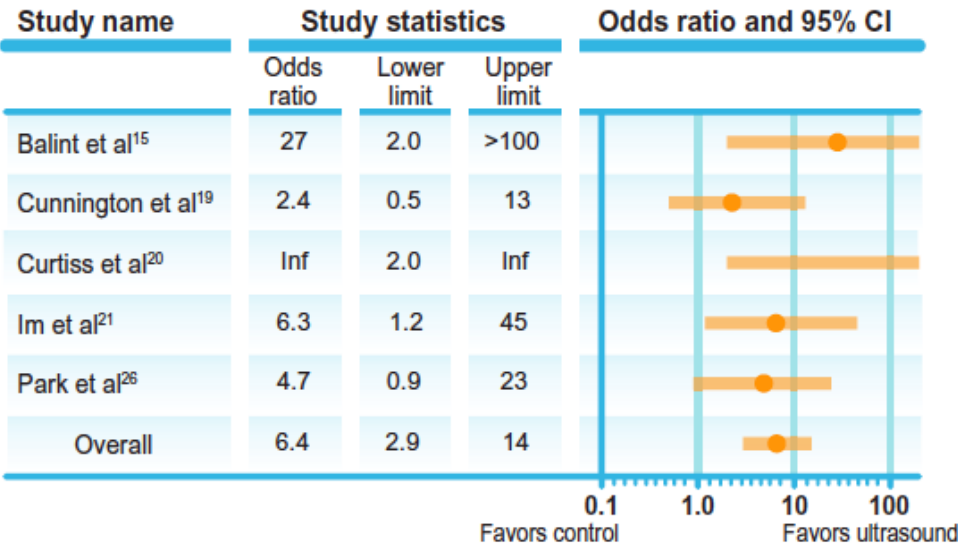


Figure 1 Accuracy of ultrasound guidance for intra-articular knee injections: forest plot of controlled studies.

Compared with anatomical guidance, ultrasound guidance reduced injection pain by 81% (P = 0.001) and increased therapeutic duration by 32% (P = 0.01)



# Osteoarthritis and Cartilage



Synovial pathology detected on ultrasound correlates with the severity of radiographic knee osteoarthritis more than with symptoms



M. Hall <sup>†‡\*</sup>, S. Doherty <sup>†</sup>, P. Courtney <sup>§</sup>, K. Latief <sup>§</sup>, W. Zhang <sup>†</sup>, M. Doherty <sup>†</sup>

<sup>†</sup> Academic Rheumatology, University of Nottingham, UK

<sup>‡</sup> School of Health Sciences, University of Nottingham, UK

<sup>§</sup> Nottingham University Hospitals NHS Trust, UK

- US features, particularly synovial hypertrophy, may well have a role to play in the development of painful OA.
- Synovial abnormalities are more common in those with painful knee OA compared to those with asymptomatic OA or normal knees.
- The presence of increased PD signal within the synovium is supported to represent more active inflammation.

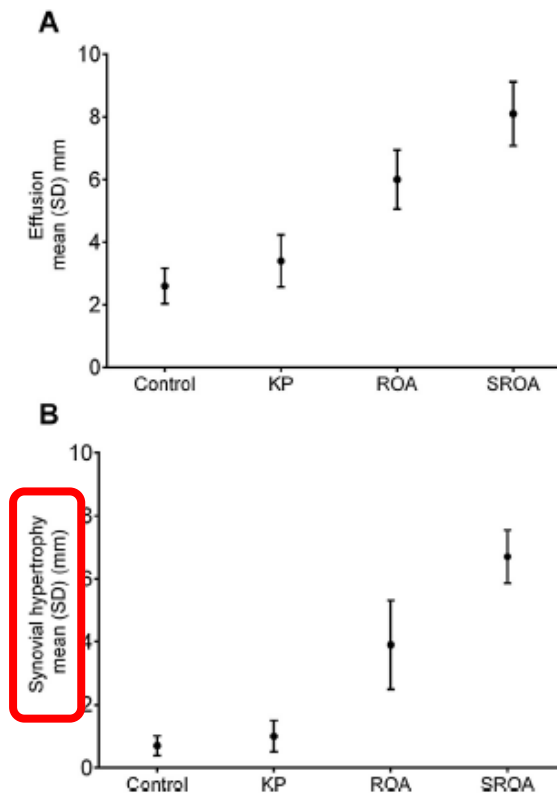


Fig. 2. US measures of (A) effusion and (B) synovial hypertrophy for each group.

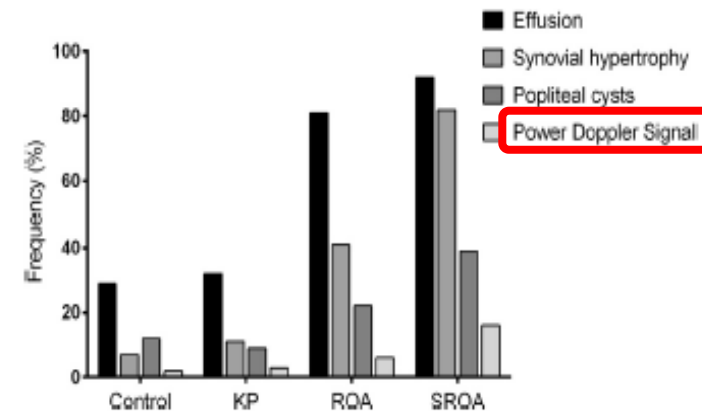


Fig. 1. Bar chart showing frequency (%) of US features within each comparison group.

## Concise report

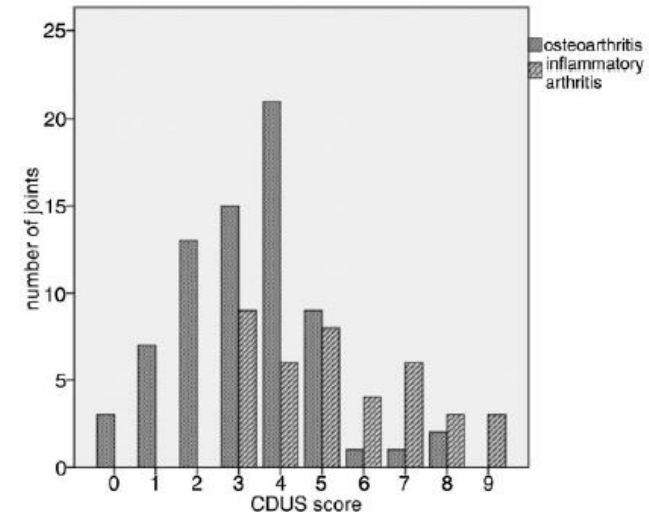
### The value of colour Doppler sonography of the knee joint: a useful tool to discriminate inflammatory from non-inflammatory disease?

Nelly Beitinger<sup>1</sup>, Boris Ehrenstein<sup>1</sup>, Benno Schreiner<sup>2</sup>, Martin Fleck<sup>1</sup>, Joachim Grifka<sup>2</sup>, Christian Lüring<sup>3</sup> and Wolfgang Hartung<sup>1</sup>

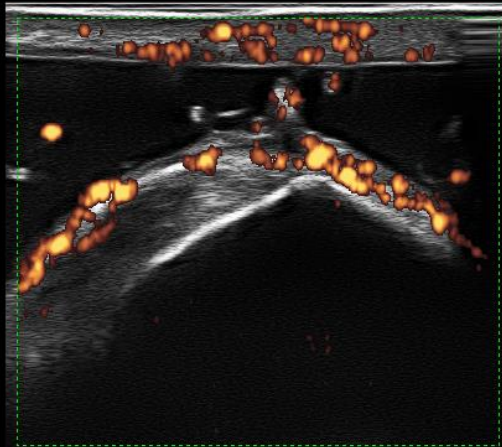
#### Rheumatology key messages

- PDUS is a useful tool to distinguish inflammatory from non-inflammatory knee swelling.
- There is no definitive PDUS threshold to allow for discrimination of inflammatory and non-inflammatory joint disease.

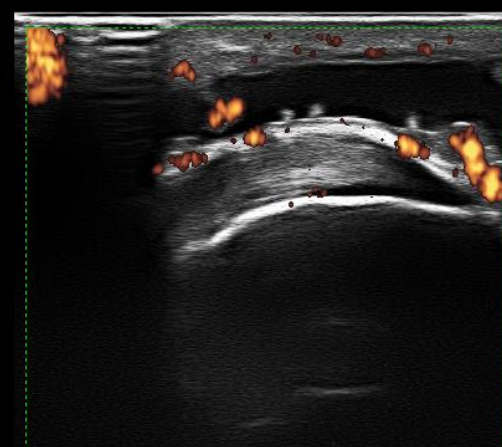
**FIG. 1** Distribution of CDUS sum scores in relation to OA and IA.



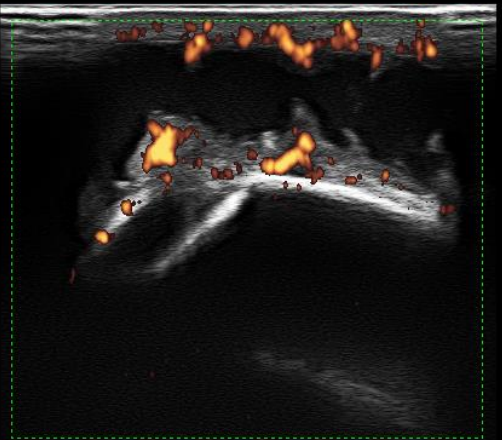
saote MyLab  
ID: BORSITE OLECRANICA,  
B RIS-A G 64%  
P 44mm XV 9  
PRC 12/6/2 PRS 2  
PST 3 C 2  
CFM F 9.1 MHz G 54%  
PRF 750 Hz  
PRC M/ 2 PRS 4  
FP 3  
6 SPEED 18 LA435



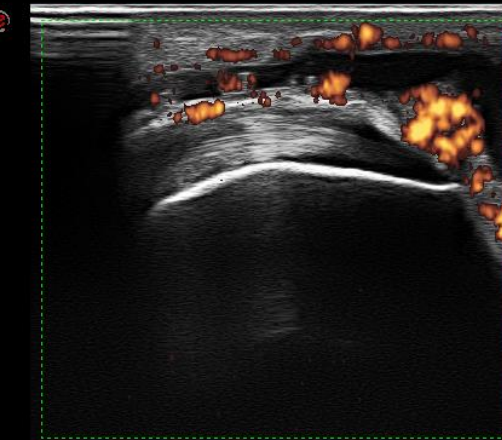
saote MyLab  
ID: BORSITE OLECRANICA,  
B RIS-A G 64%  
P 44mm XV 9  
PRC 12/6/2 PRS 2  
PST 3 C 2  
CFM F 9.1 MHz G 54%  
PRF 750 Hz  
PRC M/ 2 PRS 4  
FP 3  
6 SPEED 18 LA435



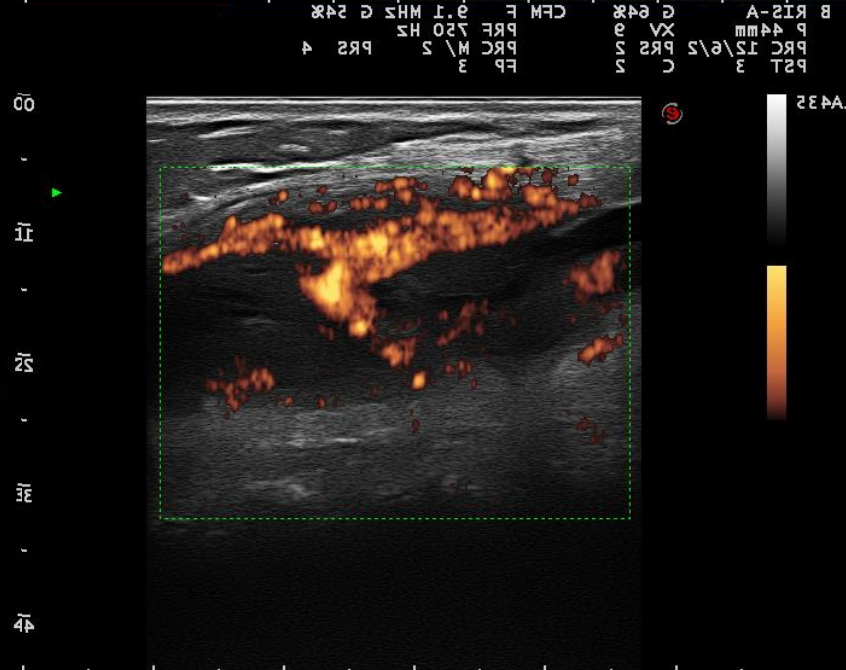
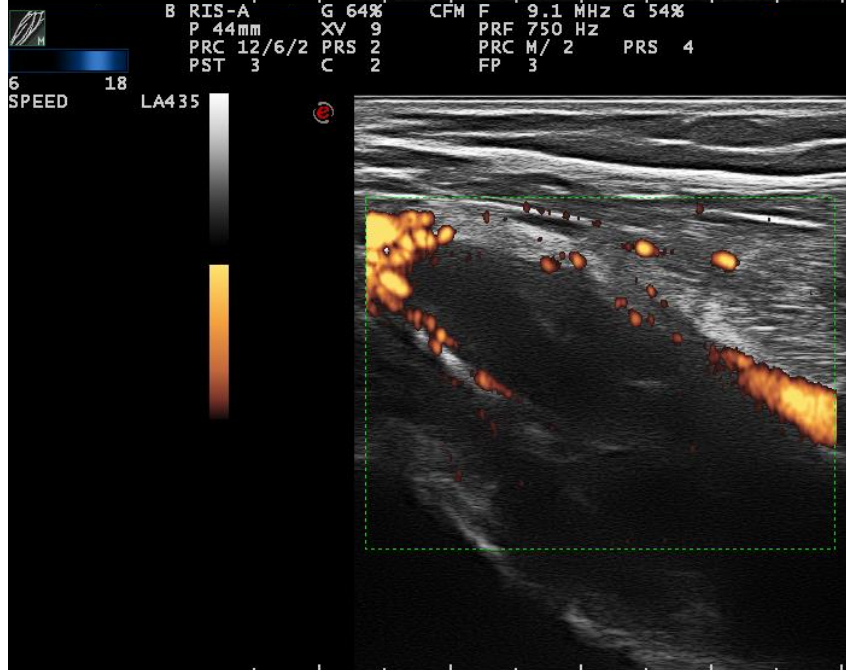
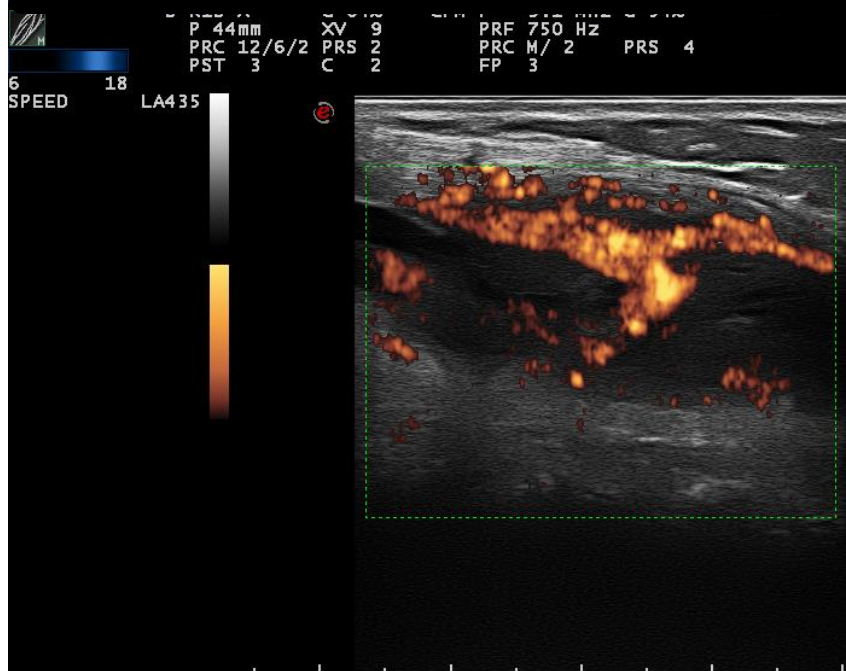
ID: BORSITE OLECRANICA,  
B RIS-A G 64%  
P 44mm XV 9  
PRC 12/6/2 PRS 2  
PST 3 C 2  
CFM F 9.1 MHz G 54%  
PRF 750 Hz  
PRC M/ 2 PRS 4  
FP 3  
6 SPEED 18 LA435



ID: BORSITE OLECRANICA,  
B RIS-A G 64%  
P 44mm XV 9  
PRC 12/6/2 PRS 2  
PST 3 C 2  
CFM F 9.1 MHz G 54%  
PRF 750 Hz  
PRC M/ 2 PRS 4  
FP 3  
6 SPEED 18 LA435







53 A, M,

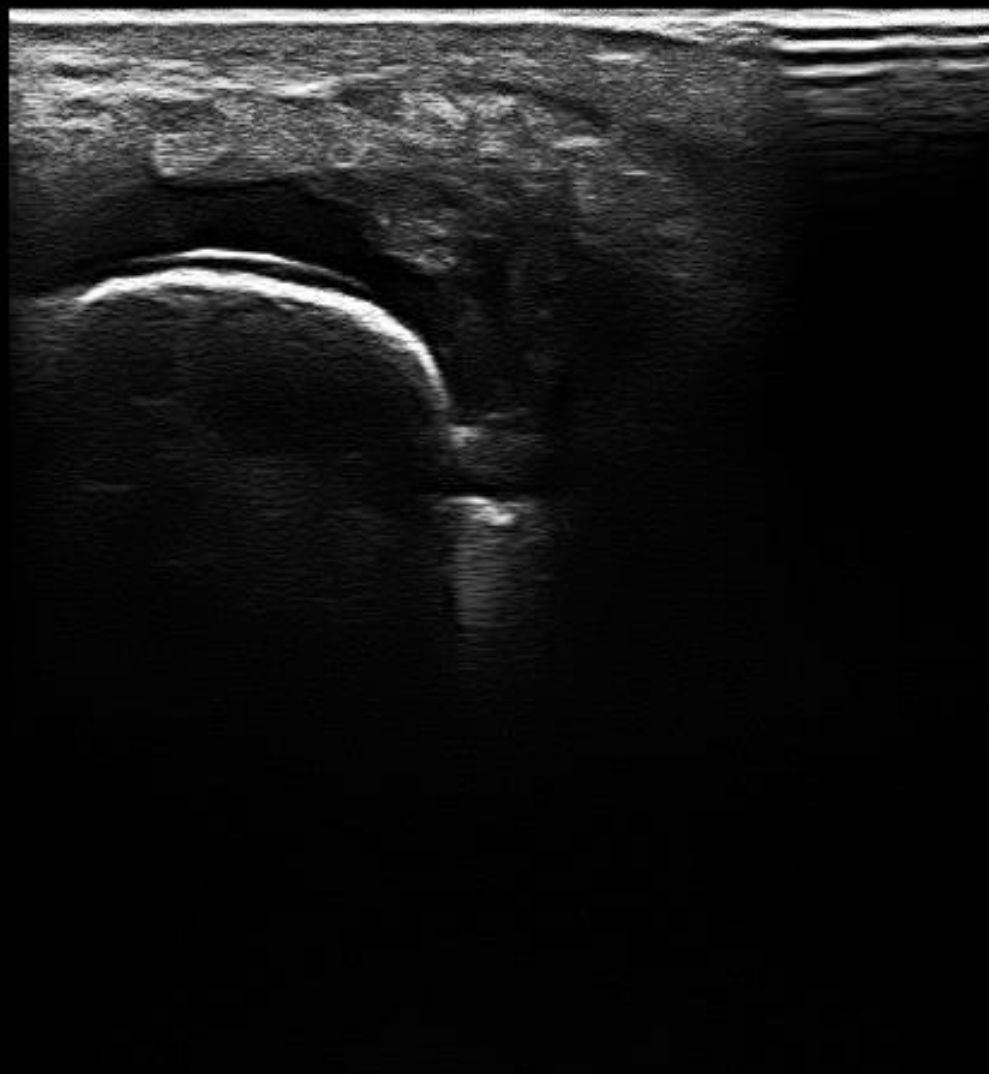
12 MAR 2018 17:07



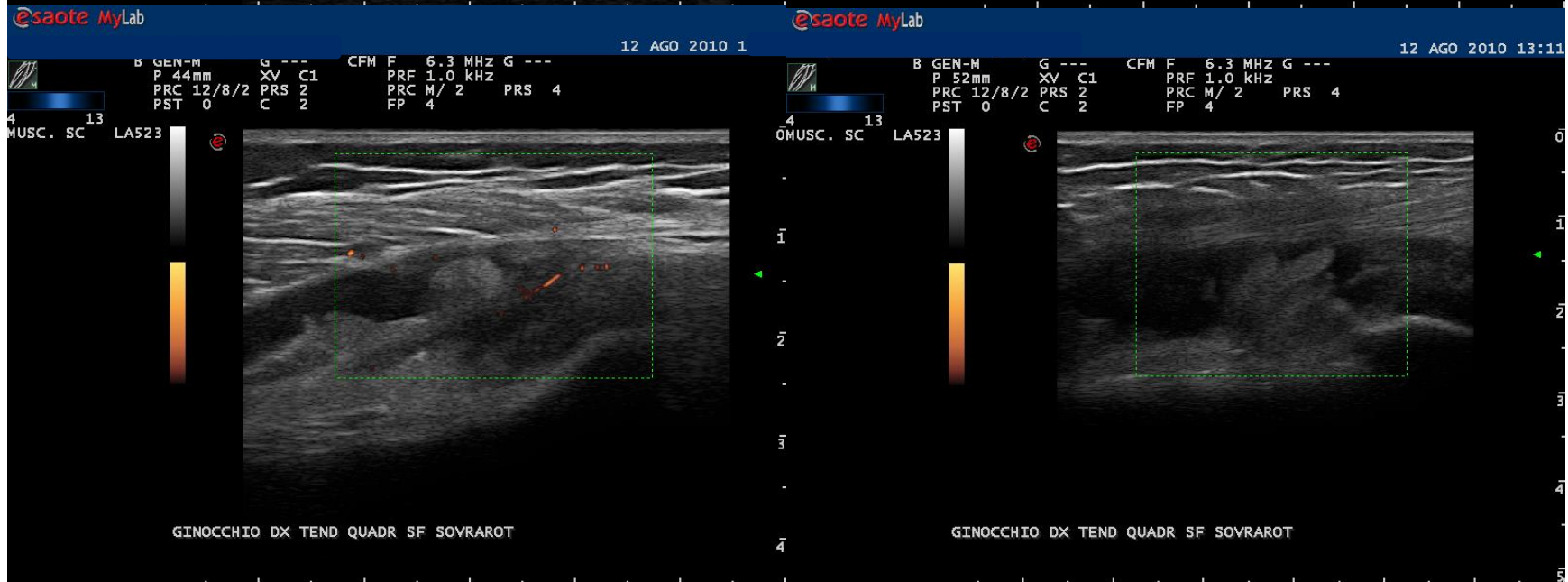
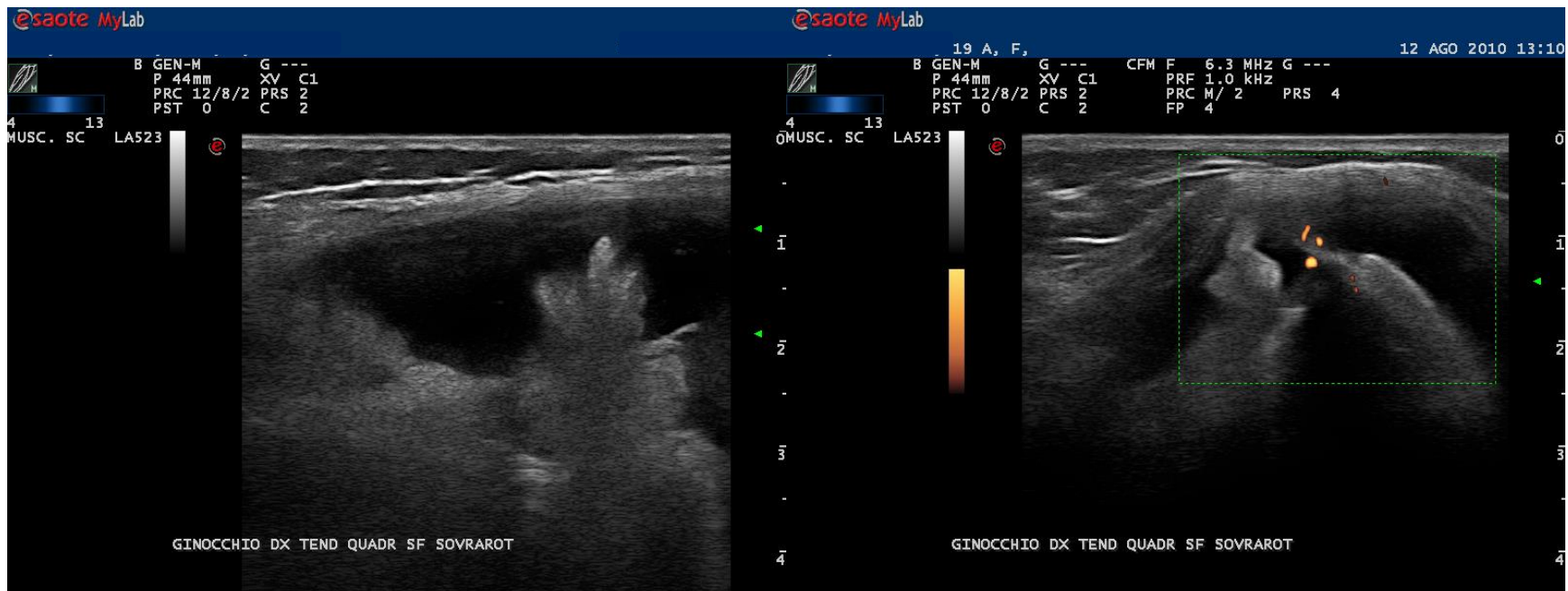
B RIS-A G 64%  
P 44mm XV 9  
PRC 12/6/2 PRS 2  
PST 3 C 2

6 SPEED 18

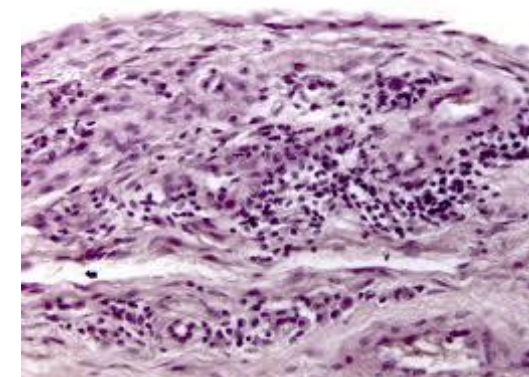
LA435



0  
1  
2  
3  
4







# BIOPSIA SINOVIALE ECOGUIDATA

---

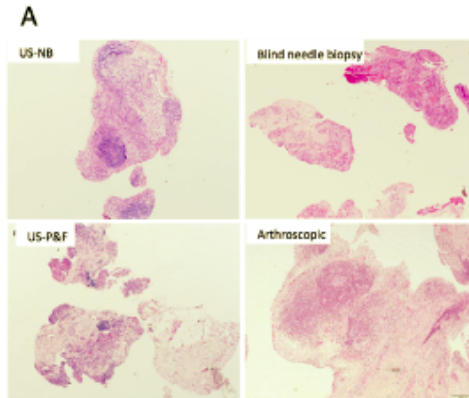


# MEDICINA DI PRECISIONE

# A Multicenter Retrospective Analysis Evaluating Performance of Synovial Biopsy Techniques in Patients With Inflammatory Arthritis

## Arthroscopic Versus Ultrasound-Guided Versus Blind Needle Biopsy

Frances Humby,<sup>1</sup> Vasco C. Romão,<sup>2</sup> Antonio Manzo,<sup>3</sup> Andrew Filer,<sup>4</sup> Serena Bugatti,<sup>3</sup> Elsa Vieira-Sousa,<sup>2</sup> Stephen Kelly,<sup>5</sup> Mihir Wechalekar,<sup>6</sup> Manzoor Ahmed,<sup>1</sup> Vidalba Rocher,<sup>1</sup> Rebecca Hands,<sup>1</sup> Carlomaurizio Montecucco,<sup>3</sup> Joao Fonseca,<sup>2</sup> and Costantino Pitzalis<sup>1</sup>



**C**

	Small Joint Biopsy				Large Joint Biopsy				
	US-NB (n=20)	US-P&F (n=11)	BN (n=10)	P value	ARTH (n=25)	US-NB (n=11)	US-P&F (n=17)	BN (n=13)	P value
Synovitis score	4.9 (3.2)	NA	3.4 (2.1)	0.59	4.5 (1.7)	8 (2.0)	4.5 (2.0)	5.2 (1.9)	0.58
CD20+ B cells	2 (1.7)	1.8 (1.3)	1 (0.9)	0.82	2 (1.2)	2 (1.6)	1.8 (1.1)	2 (0.8)	0.38
CD3+ T cells	2 (1.3)	NA	1 (1.1)	0.35	2 (1.2)	2.3 (1.3)	1.2 (1.1)	2 (0.7)	0.07
CD68+ Macrophages	2.9 (2.1)	1.9 (0.7)	1 (1.1)	0.29	1.9 (0.9)	2.9 (1.1)	2.1 (1.2)	2.2 (0.6)	0.06
Pathotype, no. (%)	lymphoid	8 (42)	7 (64)	1 (10)	0.18	15 (60)	7 (64)	6 (35)	0.07
	myeloid	6 (31)	3 (27)	4 (40)		5 (20)	3 (27)	9 (53)	
	fibroid	5 (26)	1 (9)	4 (40)		5 (20)	1 (9)	0 (0)	
	ungraded	1 (5)	0 (0)	1 (10)		0 (0)	0 (0)	2 (10)	

**B**

	Small joint biopsy				Large Joint Biopsy							
	US-NB (n=20)	US-P&F (n=11)	BN (n=10)	P value	ARTH (n=25)	US-NB (n=11)	US-P&F (n=17)	BN (n=13)	P value			
Proportion of graded synovial tissue fragments per procedure, mean % (SD)	77 (30.3)	91 (10.0)	61 (34.1)	0.057	94 (12.5)	94 (14.1)	85 (23.0)	73 (29.9)	0.048	0.89	0.012	0.011
Total graded synovial tissue area, mean mm <sup>2</sup> (SD)	8.76 (8.9)	7.95 (4.9)	7.88 (8.4)	0.57	14.7 (10.5)	5.67 (4.8)	2.24 (0.9)	35.57 (18.9)	<0.0001	0.0002	0.0062	0.0002
Synovial tissue area per graded tissue fragment, mean mm <sup>2</sup> (SD)	1.80 (1.9)	1.44 (0.8)	1.69 (1.4)	0.92	3.66 (2.9)	3.96 (2.8)	1.91 (1.6)	6.11 (2.8)	<0.0001	0.074	0.020	0.0094





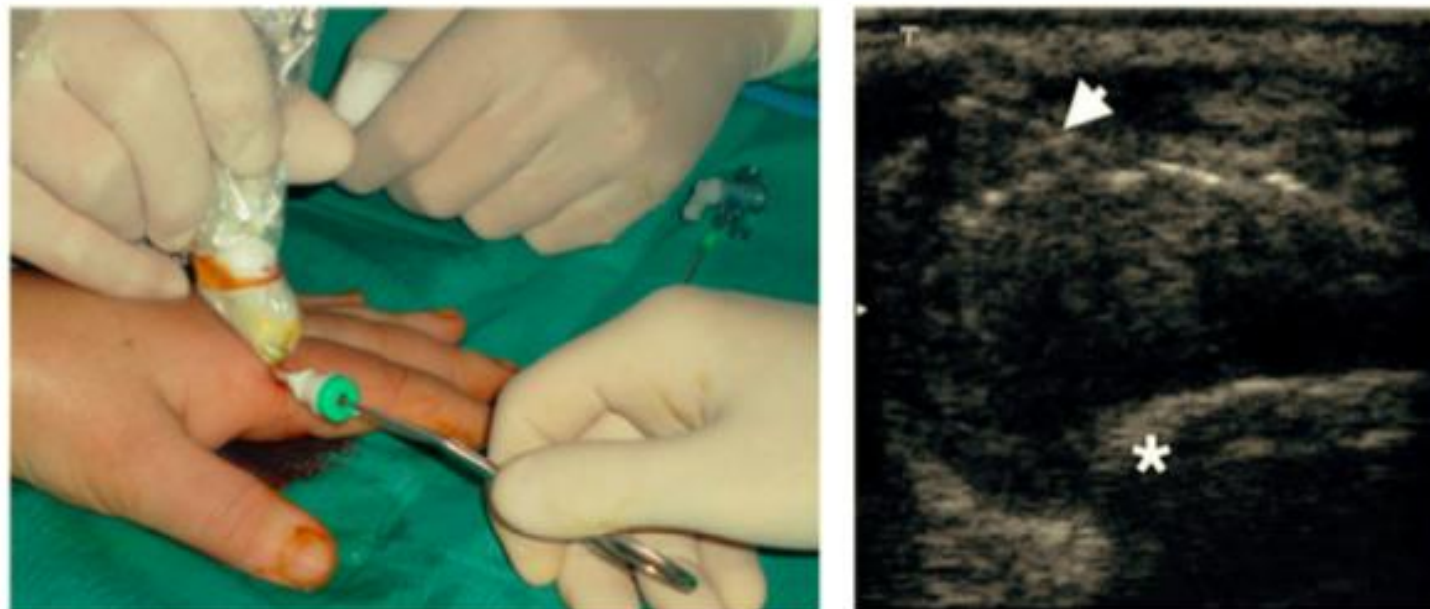
Research article

**Open Access**

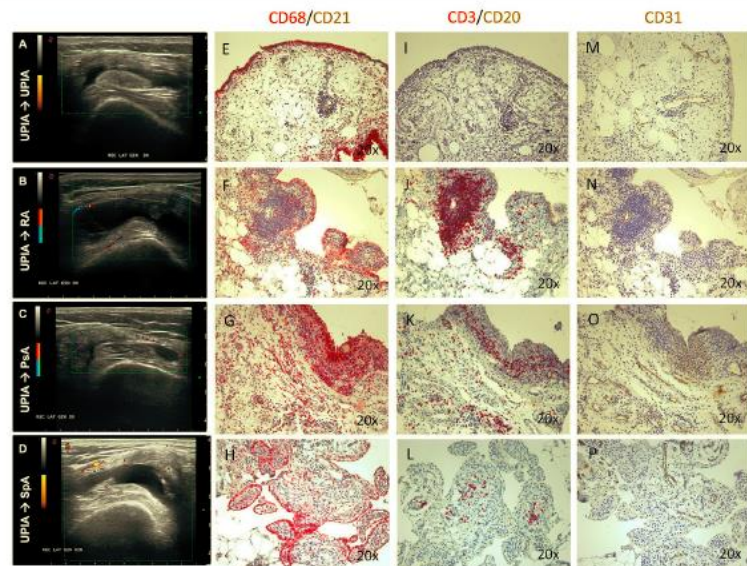
## **Immunohistological assessment of the synovial tissue in small joints in rheumatoid arthritis: validation of a minimally invasive ultrasound-guided synovial biopsy procedure**

Carlo Alberto Scirè<sup>1</sup>, Oscar Epis<sup>1</sup>, Veronica Codullo<sup>1</sup>, Frances Humby<sup>2</sup>, Patrizia Morbini<sup>3</sup>, Antonio Manzo<sup>2</sup>, Roberto Caporali<sup>1</sup>, Costantino Pitzalis<sup>2</sup> and Carlomaurizio Montecucco<sup>1</sup>

**Figure 1**



**Ultrasound-guided synovial biopsy of a second metacarpophalangeal joint using the portal and forceps technique.** Arrow, open forceps inside the joint; asterisk, metacarpal head.



**FIGURE 2 | (A–P)** Ultrasound assessment and immunohistochemistry for CD68<sup>+</sup>, CD21<sup>+</sup>, CD20<sup>+</sup>, CD3<sup>+</sup> cells and CD31<sup>+</sup> vessels of synovial tissue of enrolled UPIA patients based on the clinical differentiation. **(A)** Example photo of the ultrasound assessment of knee joint of UPIA patient who remained as UPIA afterwards; **(B)** Example photo of the ultrasound assessment of knee joint of UPIA patient who differentiated into RA afterwards; **(C)** Example photo of the ultrasound assessment of knee joint of UPIA patient who differentiated into PsA afterwards; **(D)** Example photo of the ultrasound assessment of knee joint of UPIA patient who differentiated

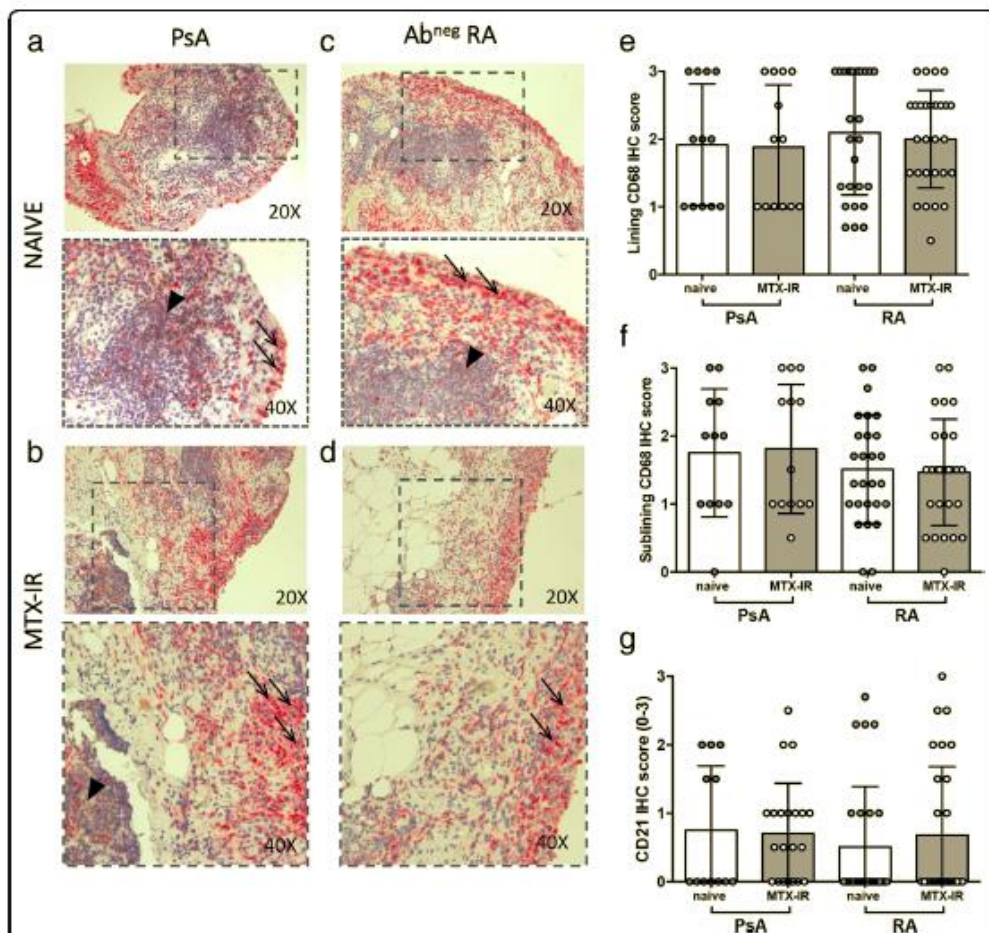


## Synovial Predictors of Differentiation to Definite Arthritis in Patients With Seronegative Undifferentiated Peripheral Inflammatory Arthritis: microRNA Signature, Histological, and Ultrasound Features

### OPEN ACCESS

Edited by:

Stefano Allvemini<sup>1</sup>, Barbara Tolusso<sup>1</sup>, Luca Petricca<sup>1</sup>, Laura Bui<sup>2</sup>, Clara Di Mario<sup>1</sup>, Maria R. Gigante<sup>1</sup>, Gabriele Di Sante<sup>1</sup>, Roberta Benvenuto<sup>2</sup>, Anna L. Fedele<sup>1</sup>, Francesco Federico<sup>2</sup>, Gianfranco Ferraccioli<sup>1\*</sup> and Elisa Gremese<sup>1</sup>



**Fig. 1 a–g** IHC staining for CD68/CD21 on ST of patients with naive or MTX-IR PsA and Ab<sup>neg</sup> RA patients. Example photos of CD68 (RED)/CD21 (BAG) staining of ST biopsies from patients with naive (a) or MTX-IR (b) PsA patients and with naive (c) or MTX-IR (d) Ab<sup>neg</sup> RA (magnification x20 and magnification x40 in the corresponding inset). Black arrows indicate CD68<sup>+</sup> cells (red), and black arrow head indicates CD21<sup>+</sup> cells (brown) in the corresponding inset. **e** Lining IHC score for CD68<sup>+</sup> cells in PsA and Ab<sup>neg</sup> RA patients divided by treatment regimen. **f** Sublining IHC score for CD68<sup>+</sup> cells in PsA and Ab<sup>neg</sup> RA patients divided by treatment regimen. **g** IHC score for CD21<sup>+</sup> cells in PsA and Ab<sup>neg</sup> RA patients divided by treatment regimen. IHC immunohistochemistry, PsA psoriatic arthritis, RA rheumatoid arthritis, Ab antibody, MTX-IR methotrexate inadequately responder, CD cluster designation


Alivernini et al. *Arthritis Research & Therapy* (2019) 21:116  
<https://doi.org/10.1186/s13075-019-1898-7>

Arthritis Research & Therapy

## RESEARCH ARTICLE

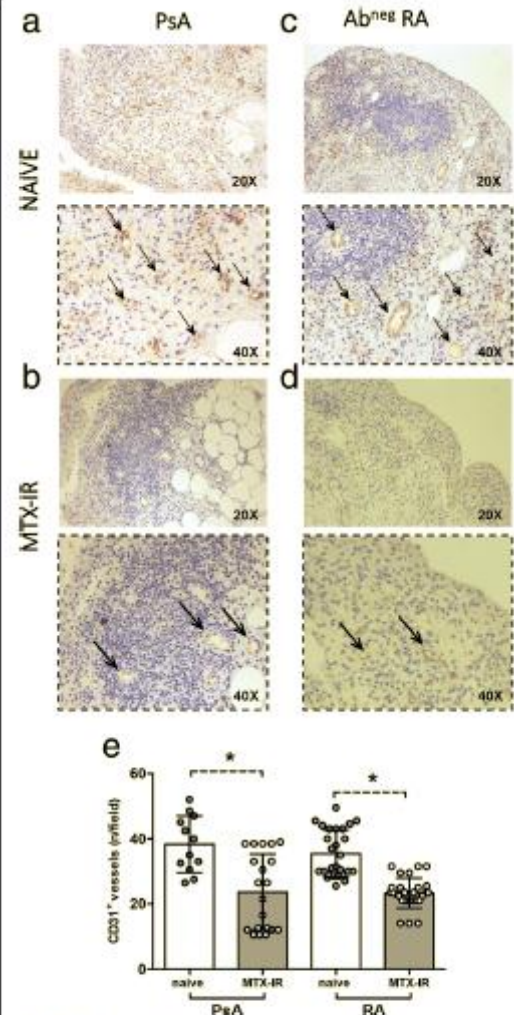
## Open Access

# Differential synovial tissue biomarkers among psoriatic arthritis and rheumatoid factor/anti-citrulline antibody-negative rheumatoid arthritis

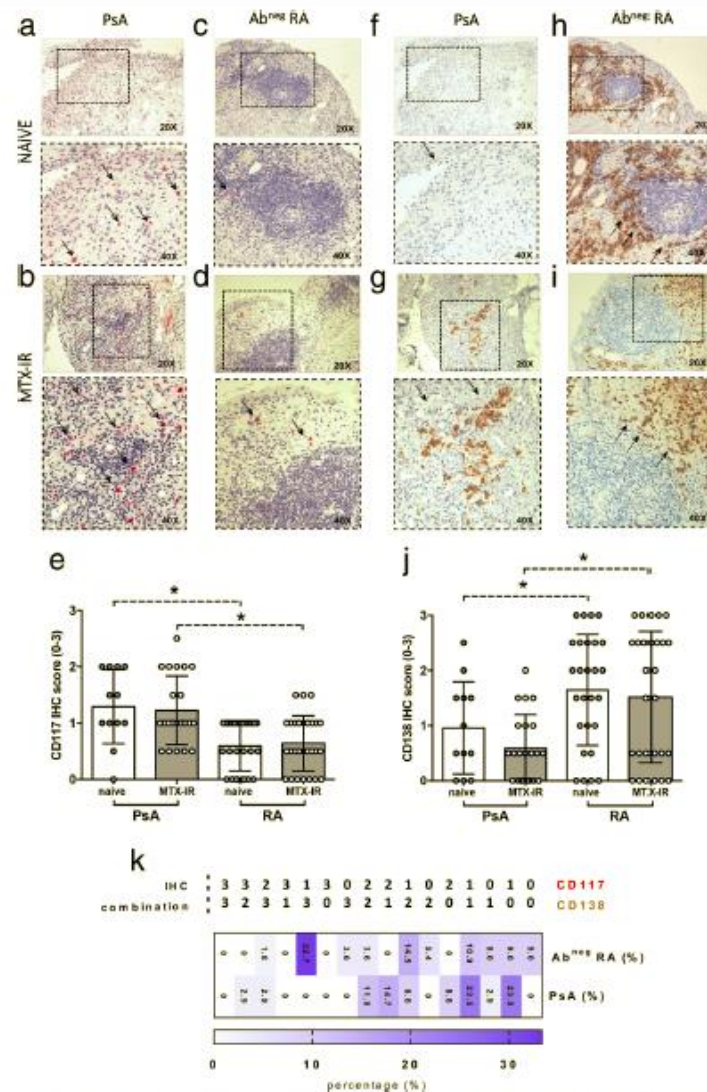
Stefano Alivernini<sup>1,2</sup>, Dario Bruno<sup>2</sup>, Barbara Tolusso<sup>1</sup>, Laura Bui<sup>3</sup>, Luca Petricca<sup>1</sup>, Maria Rita Gigante<sup>1</sup>, Domenico Birra<sup>2</sup>, Anna Laura Fedele<sup>1</sup>, Giusy Peluso<sup>1</sup>, Francesco Federico<sup>3,4</sup>, Gianfranco Ferraccioli<sup>2</sup> and Elisa Gremese<sup>1,2\*</sup> 





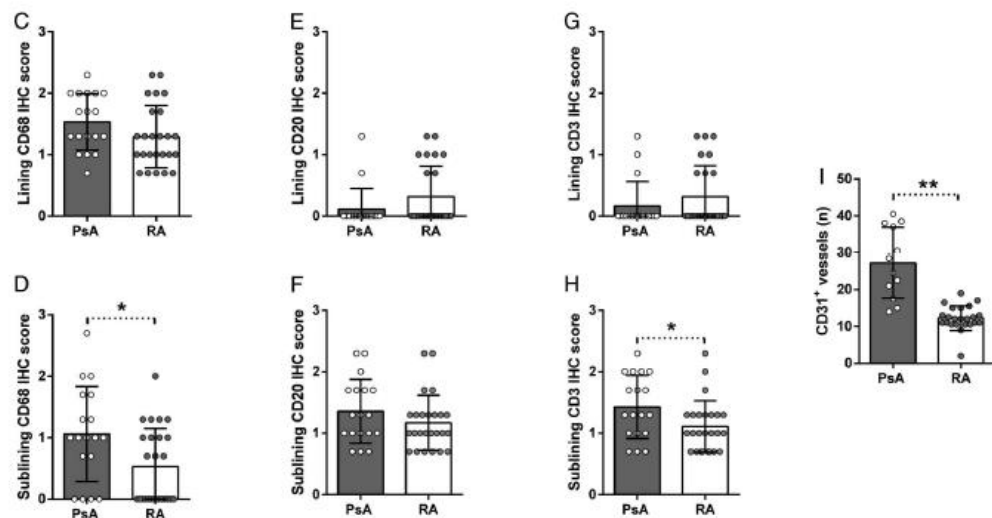
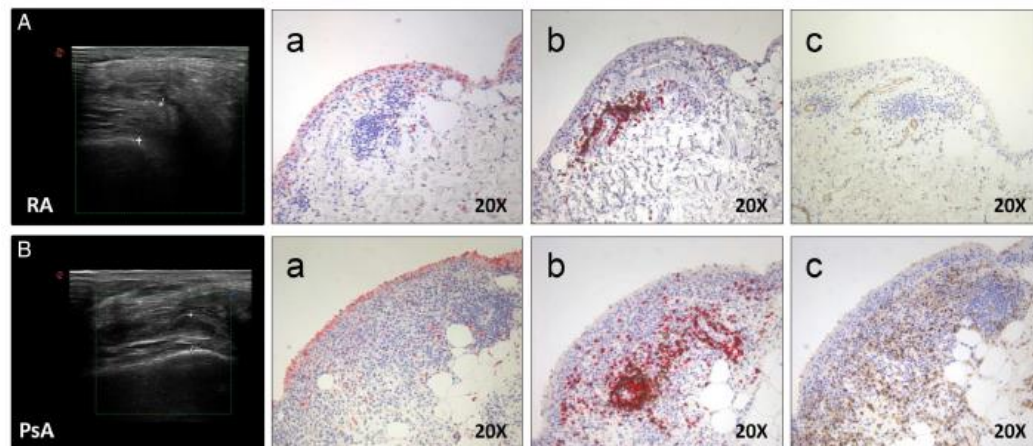


**Fig. 4 a-e** IHC staining for CD31 on ST of patients with naive or MTX-IR PsA and Ab<sup>neg</sup> RA patients. Example photos of CD31 (DAB) staining of ST biopsies from patients with naive (a) or MTX-IR (b) PsA and with naive (c) or MTX-IR (d) Ab<sup>neg</sup> RA (magnification  $\times 20$  and magnification  $\times 40$  in the corresponding inset). Thin black arrows indicate CD31<sup>+</sup> vessels (brown) in the corresponding inset. **e** Synovial CD31<sup>+</sup> vessel count in PsA and Ab<sup>neg</sup> RA patients divided by treatment regimen; \* $p = 0.01$ , naive vs MTX-IR PsA patients; \* $p < 0.001$ , naive vs MTX-IR Ab<sup>neg</sup> RA patients. IHC immunohistochemistry, PsA psoriatic arthritis, RA rheumatoid arthritis, Ab autoantibody, MTX-IR methotrexate inadequately responder, CD cluster designation



**Fig. 3 a-k** IHC staining for CD117 and CD138 on ST of patients with naive or MTX-IR PsA and Ab<sup>neg</sup> RA patients. Example photos of CD117 (RED) staining of ST biopsies from patients with naive (a) or MTX-IR (b) PsA and with naive (c) or MTX-IR (d) Ab<sup>neg</sup> RA (magnification  $\times 20$  and magnification  $\times 40$  in the corresponding inset). Thin black arrows indicate CD117<sup>+</sup> cells (red) in the corresponding inset. **e** IHC scores for CD117<sup>+</sup> cells in PsA and Ab<sup>neg</sup> RA patients divided by treatment regimen; \* $p = 0.0004$ , naive PsA vs naive Ab<sup>neg</sup> RA patients; \* $p = 0.0005$ , MTX-IR PsA vs MTX-IR Ab<sup>neg</sup> RA patients. Example photos of CD138 (DAB) staining of ST biopsies from patients with naive (f) or MTX-IR (g) PsA and with naive (h) or MTX-IR (i) Ab<sup>neg</sup> RA (magnification  $\times 20$  and magnification  $\times 40$  in the corresponding inset). Thin black arrows indicate CD138<sup>+</sup> cells (brown) in the corresponding inset. **j** IHC scores for CD138<sup>+</sup> cells in PsA and Ab<sup>neg</sup> RA patients divided by treatment regimen; \* $p = 0.04$ , naive PsA vs naive Ab<sup>neg</sup> RA patients; \* $p = 0.002$ , MTX-IR PsA vs MTX-IR Ab<sup>neg</sup> RA patients. **k** Rate of distribution of CD117/CD138 IHC combination differentially distributed among PsA and Ab<sup>neg</sup> RA patients. IHC immunohistochemistry, PsA psoriatic arthritis, RA rheumatoid arthritis, Ab autoantibody, MTX-IR methotrexate inadequately responder, CD cluster designation





## Clinical and epidemiological research



### EXTENDED REPORT

Synovial features of patients with rheumatoid arthritis and psoriatic arthritis in clinical and ultrasound remission differ under anti-TNF therapy: a clue to interpret different chances of relapse after clinical remission?

Stefano Alivernini,<sup>1</sup> Barbara Tolusso,<sup>1</sup> Luca Petricca,<sup>1</sup> Laura Bui,<sup>2</sup> Gabriele Di Sante,<sup>1</sup> Giusy Peluso,<sup>1</sup> Roberta Benvenuto,<sup>2</sup> Anna Laura Fedele,<sup>1</sup> Franco Federico,<sup>2</sup> Gianfranco Ferraccioli,<sup>1</sup> Elisa Gremese<sup>1</sup>

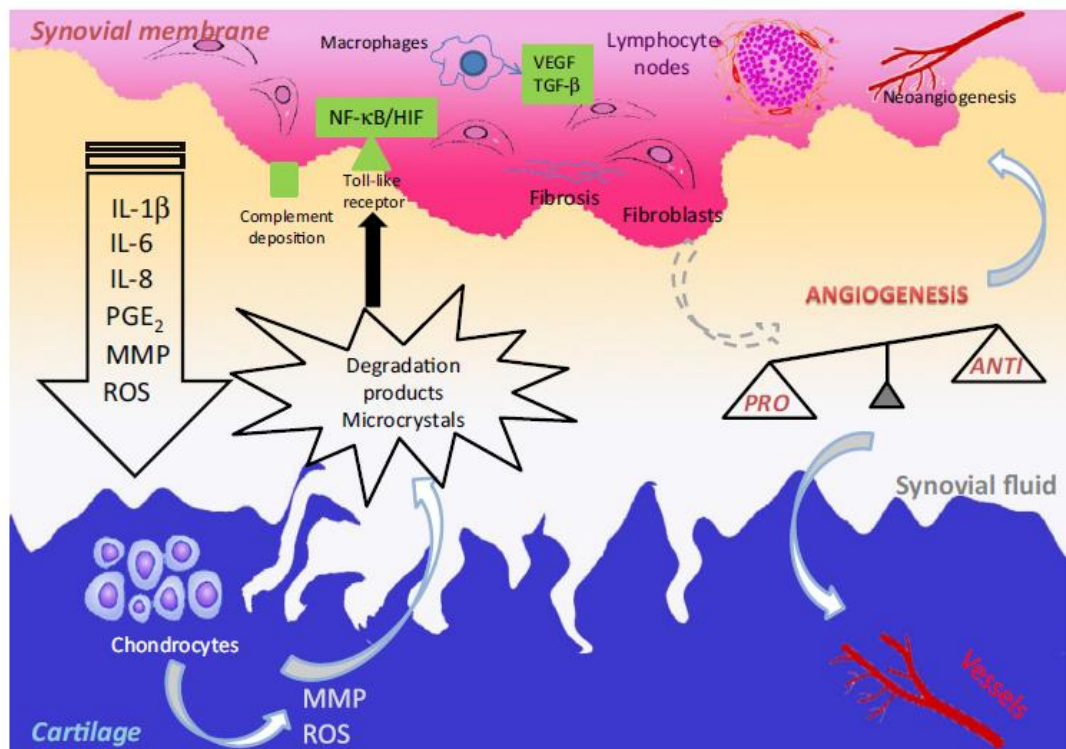
# The Italian Society for Rheumatology clinical practice guidelines for rheumatoid arthritis

**S. Parisi<sup>1,2</sup>, A. Bortoluzzi<sup>1,3</sup>, G.D. Sebastiani<sup>4</sup>, F. Conti<sup>5</sup>, R. Caporali<sup>6</sup>, N. Ughi<sup>1,7</sup>,  
I. Preverte<sup>1,4</sup>, A. Ariani<sup>1,8</sup>, M. Manara<sup>1,7</sup>, G. Carrara<sup>1</sup>, C.A. Scirè<sup>1,3</sup>**

<sup>1</sup>Epidemiology Research Unit, Italian Society for Rheumatology, Milan, Italy; <sup>2</sup>Rheumatology Unit, University Hospital, Turin, Italy; <sup>3</sup>Department of Medical Sciences, Rheumatology Section, University of Ferrara, Italy; <sup>4</sup>Rheumatology Unit, Azienda Ospedaliera San Camillo-Forlanini, Rome, Italy; <sup>5</sup>Rheumatology Division, I Clinica Medica, Policlinico Umberto I, Rome, Italy; <sup>6</sup>Department of Rheumatology, University and IRCCS Foundation Policlinico S. Matteo, Pavia, Italy; <sup>7</sup>Division of Clinical Rheumatology, Centro Specialistico Ortopedico-Traumatologico Gaetano Pini CTO ASST, Milan, Italy; <sup>8</sup>Department of Medicine, Internal Medicine and Rheumatology Unit, Azienda Ospedaliero-Universitaria di Parma, Italy

**Table VI - Final set of Recommendations on treatment strategy in RA (Management).**

No.	The final set of "Management" Recommendations	Category of Evidence	Grade of Recommendation
1	Treatment with csDMARDs should be started as soon as the diagnosis of RA is made.	1	A
2	MTX should be part of the first treatment strategy.	1	A
3	Short-term course of glucocorticoids can be considered to control active RA in combination with csDMARDs. In view of their cumulative side effects, they should be used at the lowest dose necessary and tapered as rapidly as clinically feasible (<6 months). Intra-articular glucocorticoid injections should be considered for the relief of local symptoms of inflammation.	1	A



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Seminars in Arthritis and Rheumatism

journal homepage: [www.elsevier.com/locate/semarthrit](http://www.elsevier.com/locate/semarthrit)



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

Yves Henrotin, PhD<sup>a,\*</sup>, Cécile Lambert, PhD<sup>a</sup>, Pascal Richette, MD, PhD<sup>b,c</sup>

<sup>a</sup> Bone and Cartilage Research Unit, Institute of Pathology, CHU Sart-Tilman, 4000 Liège, Belgium

<sup>b</sup> AP-HP, Hôpital Lariboisière, Pôle appareil locomoteur, fédération de rhumatologie, F-75010, Paris, France; Univ. Paris Diderot, Sorbonne Paris Cité, F-75205, Paris, France

<sup>c</sup> Sorbonne Paris Cité, University Paris Diderot, Paris, France

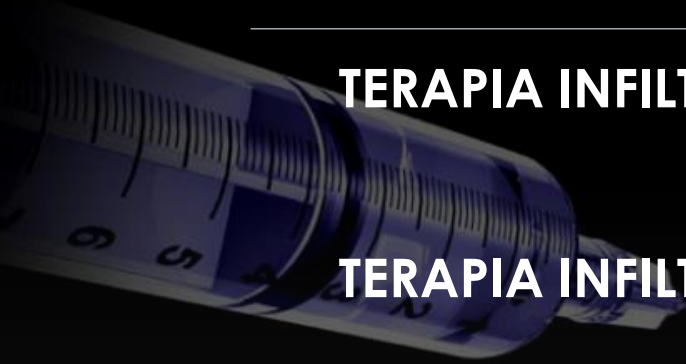


# TERAPIA INTRA-ARTICOLARE NELL' OA

---

TERAPIA INFILTRATIVA CON STEROIDI

TERAPIA INFILTRATIVA CON ACIDO IALURONICO





**Cochrane**  
**Library**

Cochrane Database of Systematic Reviews

## Intra-articular corticosteroid for knee osteoarthritis (Review)

Jüni P, Hari R, Rutjes AWS, Fischer R, Silletta MG, Reichenbach S, da Costa BR

### **Authors' conclusions**

Whether there are clinically important benefits of intra-articular corticosteroids after one to six weeks remains unclear in view of the overall quality of the evidence, considerable heterogeneity between trials, and evidence of small-study effects. A single trial included in this review described adequate measures to minimise biases and did not find any benefit of intra-articular corticosteroids.

In this update of the systematic review and meta-analysis, we found most of the identified trials that compared intra-articular corticosteroids with sham or non-intervention control small and hampered by low methodological quality. An analysis of multiple time points suggested that effects decrease over time, and our analysis provided no evidence that an effect remains six months after a corticosteroid injection.

# Is Local Viscosupplementation Injection Clinically Superior to Other Therapies in the Treatment of Osteoarthritis of the Knee: A Systematic Review of Overlapping Meta-analyses

Kirk A. Campbell, M.D., Brandon J. Erickson, M.D., Bryan M. Saltzman, M.D.,  
Randy Mascarenhas, M.D., F.R.C.S.C., Bernard R. Bach Jr., M.D.,  
Brian J. Cole, M.D., M.B.A., and Nikhil N. Verma, M.D.

## **Intra articular Hyaluronic Acid:**

- is a viable option for patients with knee OA
  - improvements in knee pain and function can persist for up to 26 weeks
    - has been shown to have a good safety profile
      - should be considered in patients with early knee OA



# Studi di confronto terapia HA intra-articolare in OA del ginocchio vs NSAIDs

Relative efficacy of hyaluronic acid in comparison with NSAIDs for knee osteoarthritis: A systematic review and meta-analysis

Raveendhara R. Bannuru, MD, FAGE<sup>a,b,\*</sup>, Elizaveta E. Vaysbrot, MD, MS<sup>a,b</sup>,  
Matthew C. Sullivan, BA<sup>a,b</sup>, Timothy E. McAlindon, MD, MPH<sup>a,b</sup>

<sup>a</sup> Center for Treatment Comparison and Integrative Analysis (CTCIA), Tufts Medical Center, 800 Washington St. #63, Boston, MA 02111

<sup>b</sup> Division of Rheumatology, Tufts Medical Center, Boston, MA

**Table 1**  
Study characteristics

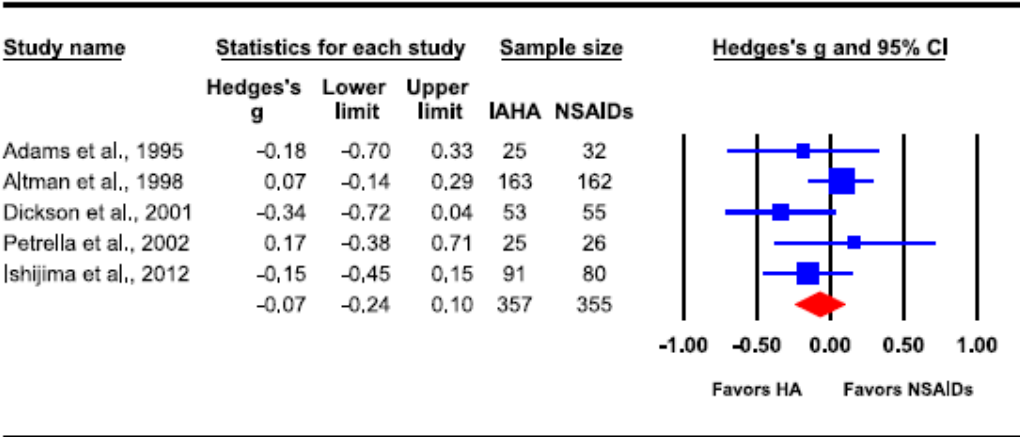
Study	Treatment	Dose	n	Age (yr)	Female (%)	BMI	Duration (wk)	Main outcomes
Adams et al. [26], USA	IAHA	3 weekly IA injections	25	61	68	27.0	12	VAS pain with motion
	Usual NSAID therapy	Usual dose ( × 12 wk) + 3 weekly arthrocenteses	32	63	68	23.7		
Altman and Moskowitz [27], USA	IAHA	5 weekly IAHA injections + oral placebo	163	62	61	31.5	26	VAS pain on walking and WOMAC pain, function, and stiffness
	Naproxen	500 mg orally twice daily ( × 12 wk) + 5 weekly IA saline injections	162	63	57	31.9		
Dickson et al. [28], UK	IAHA	3 weekly IA injections + oral placebo	53	65	57	29.0	12	WOMAC pain, function, and stiffness and Lequesne index
	Diclofenac	100 mg orally once daily ( × 12 wk) +3 weekly arthrocenteses	55	64	55	29.0		
Petrella et al. [29], Canada	IAHA	3 weekly IA injections + oral placebo	25	67	36	29.5	12	WOMAC pain, function, and stiffness and VAS pain on walking
	Diclofenac	75 mg and 100 µg misoprostol orally twice daily ( × 12 wk) + 3 weekly IA saline injections	26	66	42	29.4		
Ishijima et al. [30], Japan	IAHA	5 weekly IA injections	91	nd	nd	nd	5	VAS pain
	Loxoprofen	60 mg orally thrice daily ( × 5 wk)*	80	nd	nd	nd		

Note: IA = intra-articular; IAHA= intra-articular hyaluronic acid; wk = weeks; yr = year; BMI = body mass index; VAS = visual analog scale; WOMAC = Western Ontario & McMaster Universities Osteoarthritis Index; nd = no data.

\* No injection control.

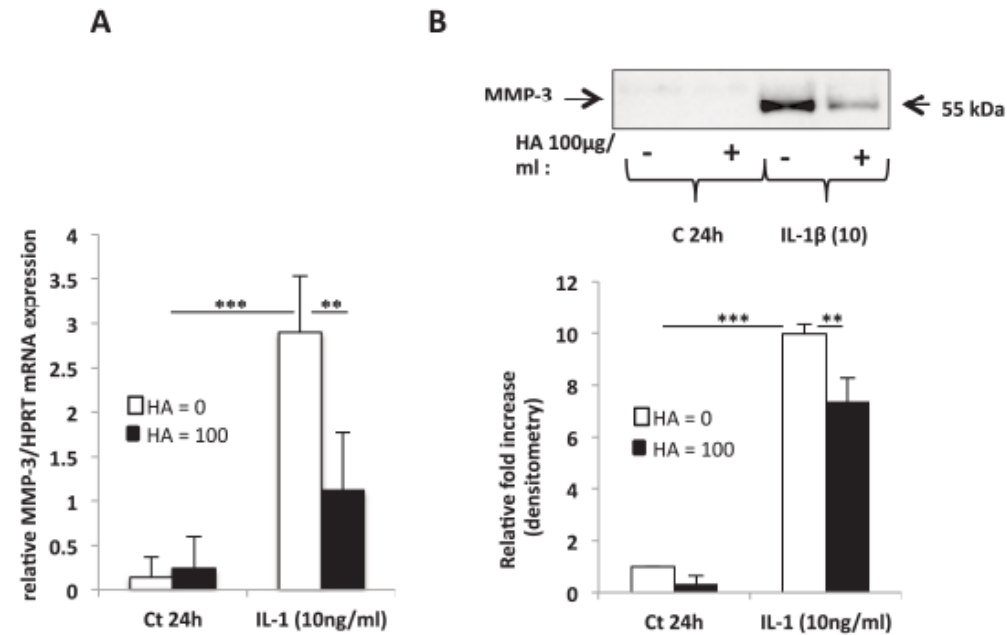
Conclusion

This meta-analysis showed that IAHA injection was not statistically significantly different in terms of efficacy for symptomatic knee OA from continuous oral NSAIDs at 4 weeks, 12 weeks, and end of the trial. Given the favorable safety profile of IAHA over NSAIDs, this result suggests that IAHA may be a viable alternative to NSAIDs in knee OA care, especially for older patients at greater risk for systemic adverse events. Studies evaluating the synergistic effect of the two treatments remain of importance.



Q-value = 4.8; P = 0.31; I<sup>2</sup> = 16%

Fig. 2. Forest plot for pain at the end of trial.



**Figure 1.** Effect of hyaluronan (HA) on interleukin 1 $\beta$  (IL-1 $\beta$ )-induced matrix metalloproteinase 3 (MMP-3) mRNA expression and protein release. Osteoblasts were treated for 7 days with or without HA (100  $\mu$ g/ml). IL-1 $\beta$  (10 ng/ml) was added for the last 24 h. A. Quantitative PCR analysis of mRNA level of MMP-3. B. Western blot analysis of MMP-3 release into medium. Data are mean of 4 independent experiments analyzed in duplicate (corrected p values: \*\* < 0.01; \*\*\* < 0.001). HPRT: hypoxanthine phosphoribosyltransferase.

## The Journal of Rheumatology

The Journal of Rheumatology

Volume 41, no. 5

Potential Role of Hyaluronic Acid on Bone in Osteoarthritis: Matrix Metalloproteinases, Aggrecanases, and RANKL Expression are Partially Prevented by Hyaluronic Acid in Interleukin 1-stimulated Osteoblasts

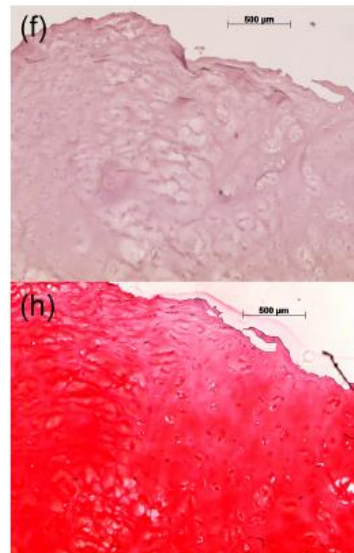
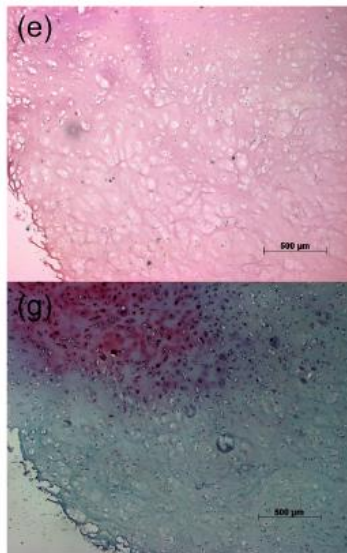
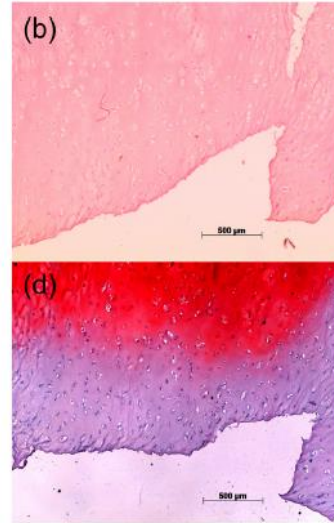
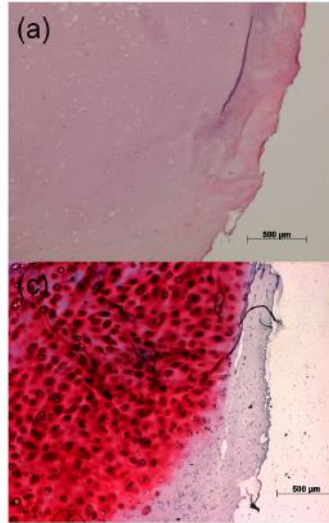
Zvezdana Mladenovic, Anne-Sophie Saurel, Francis Berenbaum and Claire Jacques



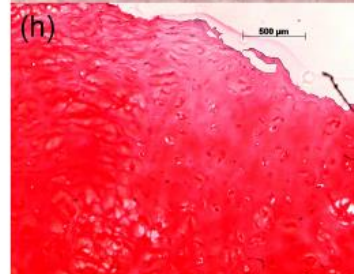
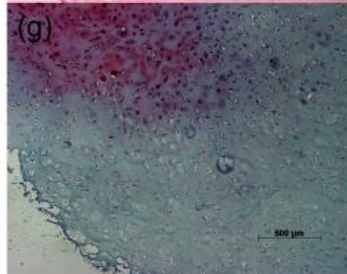
K&L2

K&L4

Mech. Load + IL1 $\beta$



Mech. load + IL1 $\beta$  +  
1 mg/ml HA



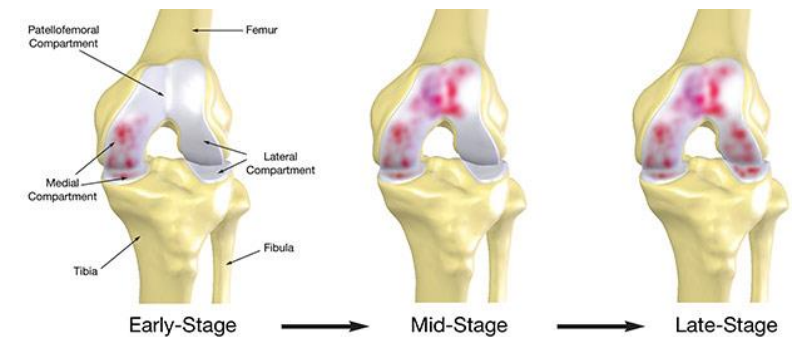
## RESEARCH ARTICLE

# Hyaluronic Acid Suppresses the Expression of Metalloproteinases in Osteoarthritic Cartilage Stimulated Simultaneously by Interleukin 1 $\beta$ and Mechanical Load

Florian Pohlig<sup>1\*</sup>, Florian Guell<sup>1</sup>, Ulrich Lenze<sup>2</sup>, Florian W. Lenze<sup>1</sup>, Heinrich M. L. Mühlhofer<sup>1</sup>, Johannes Schauwecker<sup>1</sup>, Andreas Toepfer<sup>1</sup>, Philipp Mayer-Kuckuk<sup>1</sup>, Rüdiger von Eisenhart-Rothe<sup>1</sup>, Rainer Burgkart<sup>1</sup>, Gian M. Salzmann<sup>3</sup>

**1** Department of Orthopedic Surgery, Klinikum rechts der Isar, Technical University Munich, Ismaninger Str, 22, 81675 Munich, Germany, **2** Department of Traumatology, Universitätsspital Basel, Spitalstr. 21, 4031 Basel, Switzerland, **3** Division of Lower Extremity Surgery, Schulthess Klinik, Lengghalde 2, 8008 Zurich, Switzerland

\* [Florian.Pohlig@mri.tum.de](mailto:Florian.Pohlig@mri.tum.de)



**Table 1** Preparations of intra-articular hyaluronic acid (HA) and hylan available in Europe and/or the USA

Tradename	Concentration (mg/ml)	Generic name	Source (type)	Molecular weight (kDa)
Adant <sup>®</sup>	25 mg/2.5 ml	Sodium hyaluronate	Biofermentation	900
Arthrum <sup>®</sup>	40 mg/2 ml	Sodium hyaluronate	Biofermentation	2,400
Artz <sup>®</sup> /Supartz <sup>®</sup>	25 mg/2.5 ml	Sodium hyaluronate	Rooster combs (avian)	600–1,200
Coxarthrum <sup>®</sup>	75 mg/3 ml	Sodium hyaluronate	Biofermentation	2,400
Durolane <sup>®</sup>	20 mg/3 ml	Sodium hyaluronate	Biofermentation	
Erectus <sup>®</sup>	NA	NA	NA	
Euflexxa <sup>®</sup>	20 mg/2 ml	Sodium hyaluronate	Biofermentation	
Fermathron <sup>®</sup>	20 mg/2 ml	Sodium hyaluronate	Biofermentation	1,000
Go-On <sup>®</sup>	25 mg/2.5 ml	Sodium hyaluronate	Biofermentation	800–1,200
Go-On <sup>®</sup> Mini	10 mg/1 ml			
Hyalart <sup>®</sup>	20 mg/2 ml	Sodium hyaluronate	Rooster combs (avian)	500–730
Hyalgan <sup>®</sup>	20 mg/2 ml	Sodium hyaluronate	Rooster combs (avian)	500–730
Hyalubrix <sup>®</sup>	30 mg/2 ml	Sodium hyaluronate	Biofermentation	1,500
Intragel <sup>®</sup> 0.8%	16 mg/2 ml	Sodium hyaluronate	Biofermentation	1,200
Intragel <sup>®</sup> 1.6%	32 mg/2 ml			
Jointex <sup>®</sup>	16 mg/2 ml	Sodium hyaluronate	Biofermentation	
Jointex <sup>®</sup> Starter	32 mg/2 ml			
MonoVisc <sup>®</sup>	20 mg/ml	Sodium hyaluronate	Biofermentation	NA
NeoVisc <sup>®</sup>	20 mg/2 ml	Sodium hyaluronate	Biofermentation	1,000
Orthovisc <sup>®</sup>	30 mg/2 ml	High molecular weight hyaluronan	Chemical modification	1,100–2,900
Orthovisc <sup>®</sup> mini	15 mg/1 ml			1,450
Ostenil <sup>®</sup>	20 mg/2 ml	Sodium hyaluronate	Biofermentation	1,200
Ostenil <sup>®</sup> mini	10 mg/ml			
RenchaVis <sup>®</sup>	7 mg/0.7 ml + 15.4 mg/0.7 ml	Sodium hyaluronate	Biofermentation	1,000 2,000
Sinovial <sup>®</sup>	16 mg/2 ml	Sodium hyaluronate	Biofermentation	800–1,200
Sinovial <sup>®</sup> Mini	8 mg/1 ml			
Sinovial <sup>®</sup> Forte	32 mg/2 ml			
SportVis <sup>®</sup>	12 mg/1.2 ml +	Sodium hyaluronate	Biofermentation	NA
Suplasyn <sup>®</sup>	20 mg/2 ml	Sodium hyaluronate	Biofermentation	500–730
Suplasyn <sup>®</sup> m.d.	7 mg/0.7 ml			
Synocrom <sup>®</sup>	20 mg/2 ml	Sodium hyaluronate	Biofermentation	1,600
Synocrom <sup>®</sup> mini	10 mg/1 ml			2,100
Synocrom <sup>®</sup> forte	40 mg/2 ml			
Synvisc <sup>®</sup>	16 mg/2 ml	Hylan G-F 20	Rooster combs (avian), cross-linked	6,000
Synvisc <sup>®</sup> One	48 mg/6 ml			
Viscorneal-ortho <sup>®</sup>	20 mg/2 ml	Sodium hyaluronate	Rooster combs (avian)	6,000
Yaral <sup>®</sup>	16 mg/2 ml	Sodium hyaluronate	Biofermentation	800–1,200
Yaral <sup>®</sup> Mini	8 mg/1 ml			
Yaral <sup>®</sup> Forte	32 mg/2 ml			

Antonio Gigante • Leonardo Callegari

---

ORIGINAL ARTICLE

---

# Ultrasound-guided intra-articular injection: efficacy of hyaluronic acid compared to glucocorticoid in the treatment of knee osteoarthritis

Simone PARISI \*, Maria C. DITTO, Marta PRIORA, Richard BORRELLI,  
Angela LAGANÀ, Clara L. PERONI, Enrico FUSARO



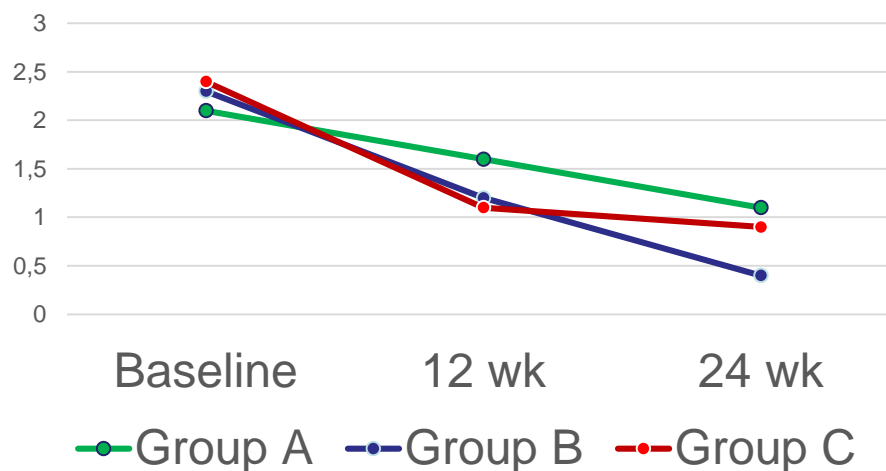




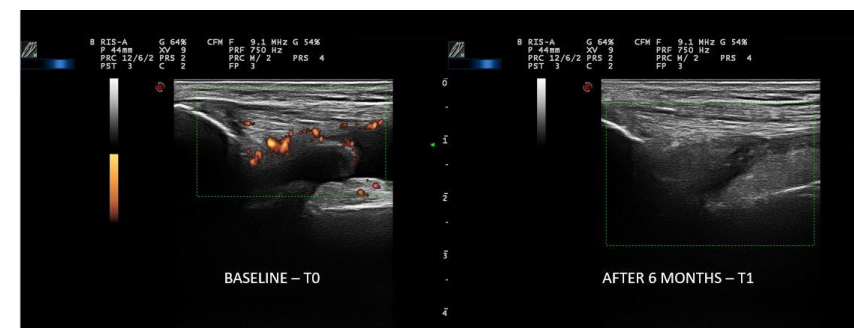
## RESULTS



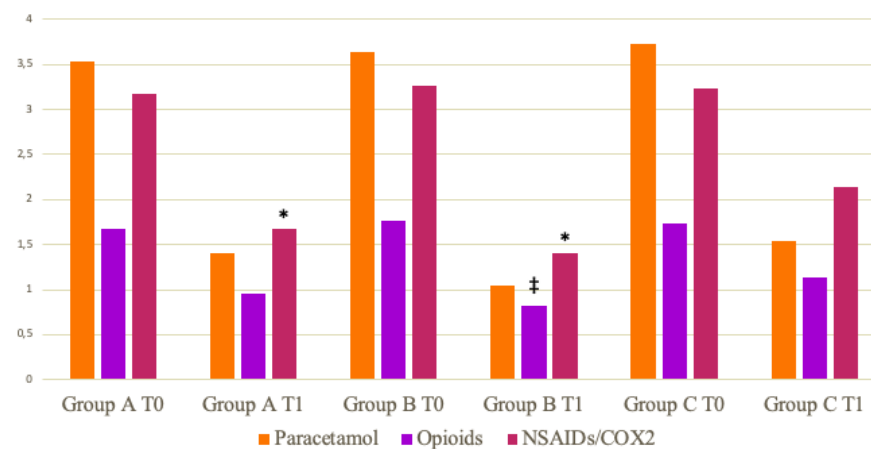
### US PWD



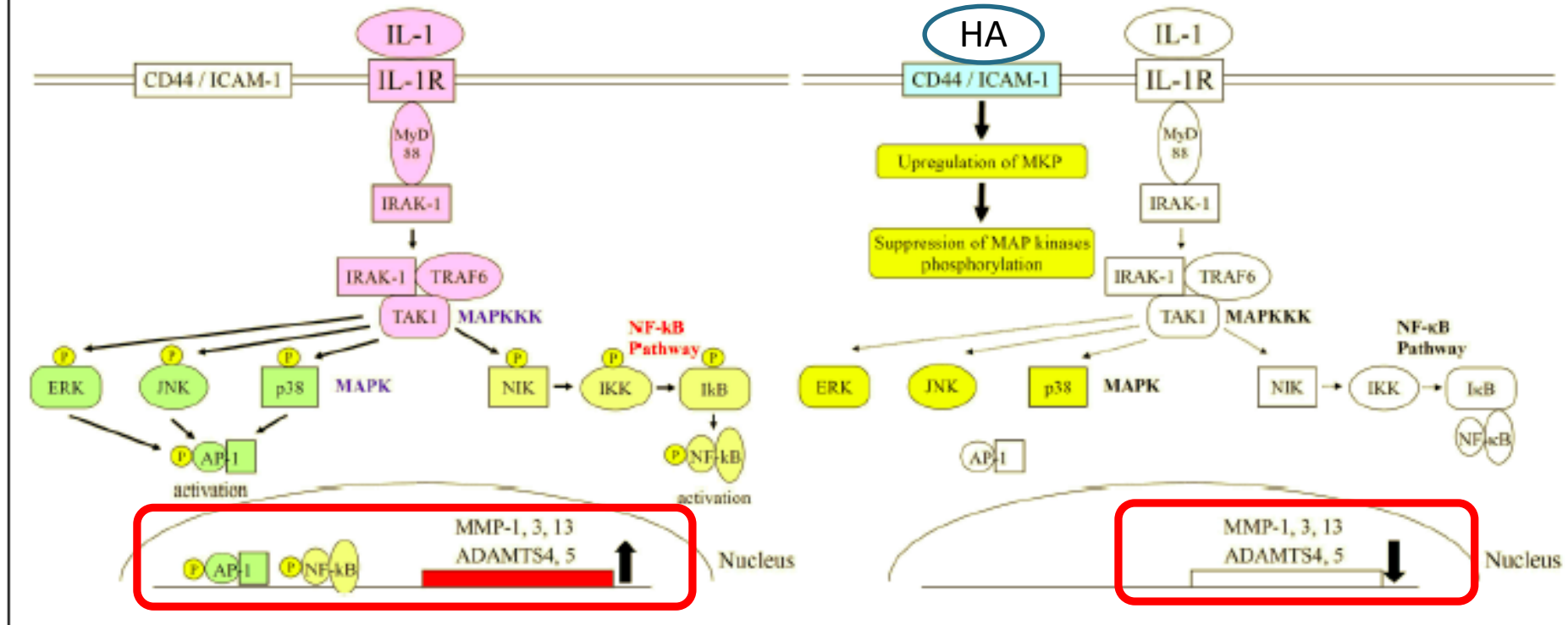
PWD signal got better in group B (p-value 0.001) and C (p-value 0.011) 3 months after the treatment. Furthermore, in group B the PWD signal proved to be statistically significantly decreased after 6 months as well (p= 0.035)



### CONCOMITANT THERAPY IN 3 GROUPS



## Chondrocyte



**Figure 3.** Upregulation of MMP and ADAMTS gene expressions by IL-1 and the molecular mechanism of its downregulation by Supartz FX in chondrocytes. As in synoviocytes, the binding of IL-1 to its receptor activates MAP kinase and NF-κB signal transductions in chondrocytes. These signal transductions induce activation of AP-1 and NF-κB transcription factors, and MMP and ADAMTS gene expressions are upregulated by these transcription factors. The binding of Supartz FX to CD44 or ICAM-1 suppresses phosphorylation of MAP kinases. These molecular changes inactivate AP-1, and MMP and ADAMTS gene expressions are downregulated.

Platelet rich plasma (PRP) è una nuova terapia di natura autologa che sta fortemente emergendo negli ultimi anni per il successo terapeutico riscontrato in alcuni “Super Atleti”

Calciatori, Tiger Woods e Rafael Nadal hanno attribuito , in parte, il loro “recupero miracoloso” all'utilizzo di questo “*enigmatico trattamento*”



**“PRP phenomenon”**



# PRP – LISATO PIASTRINCO – SIERO AUTOLOGO



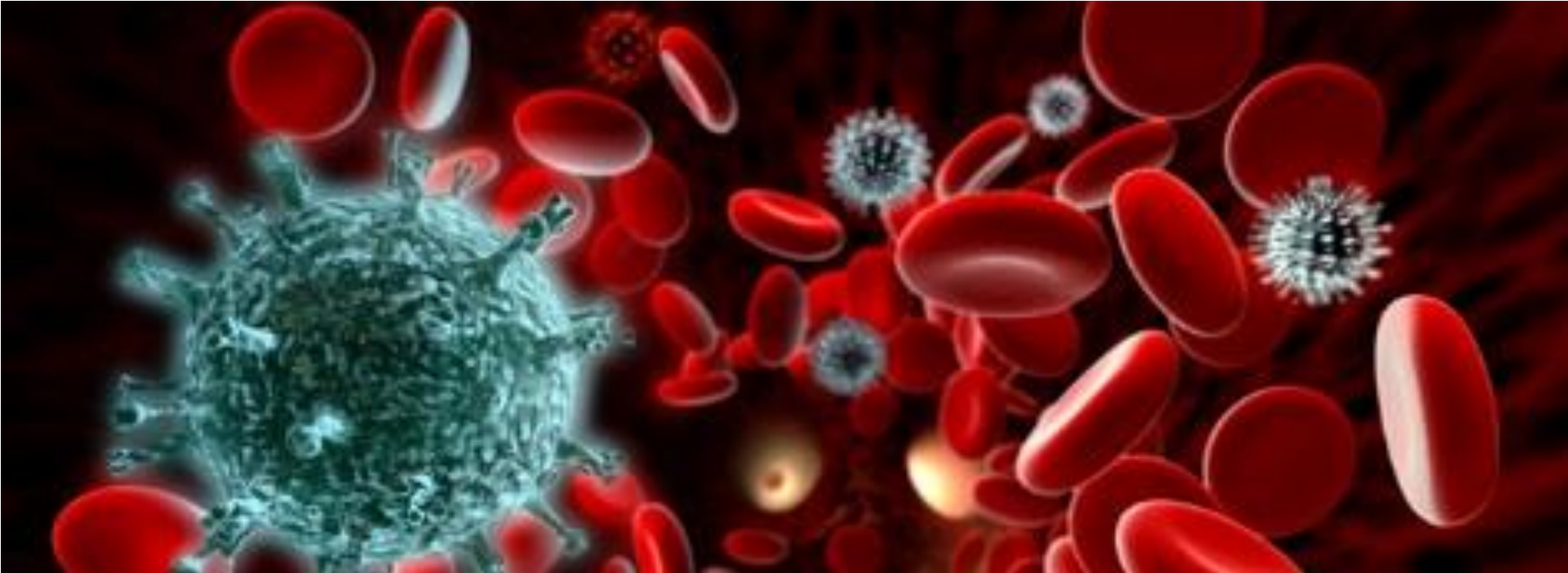


# TARGET DELL' EC

---

- Tendinopatie
- Entesopatie
- Osteoartrosi del ginocchio
- Dry Eye Syndrome
- Ulcere





The scientific base of the PRP treatment is based on factors that contrast the immunity pro inflammatory answer and factors that stimulate muscelskeletal cells.

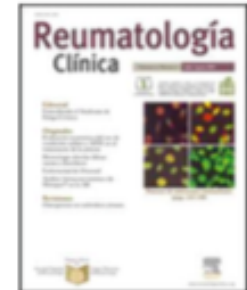
McCarrel T, Fortier L (2009) Temporal growth factor release from platelet-rich plasma, trehalose lyophilized platelets, and bone marrow aspirate and their effect on tendon and ligament gene expression. J Orthop Res 27(8):1033–1042.  
doi:10.1002/jor.20853





# Reumatología Clínica

[www.reumatologiaclinica.org](http://www.reumatologiaclinica.org)



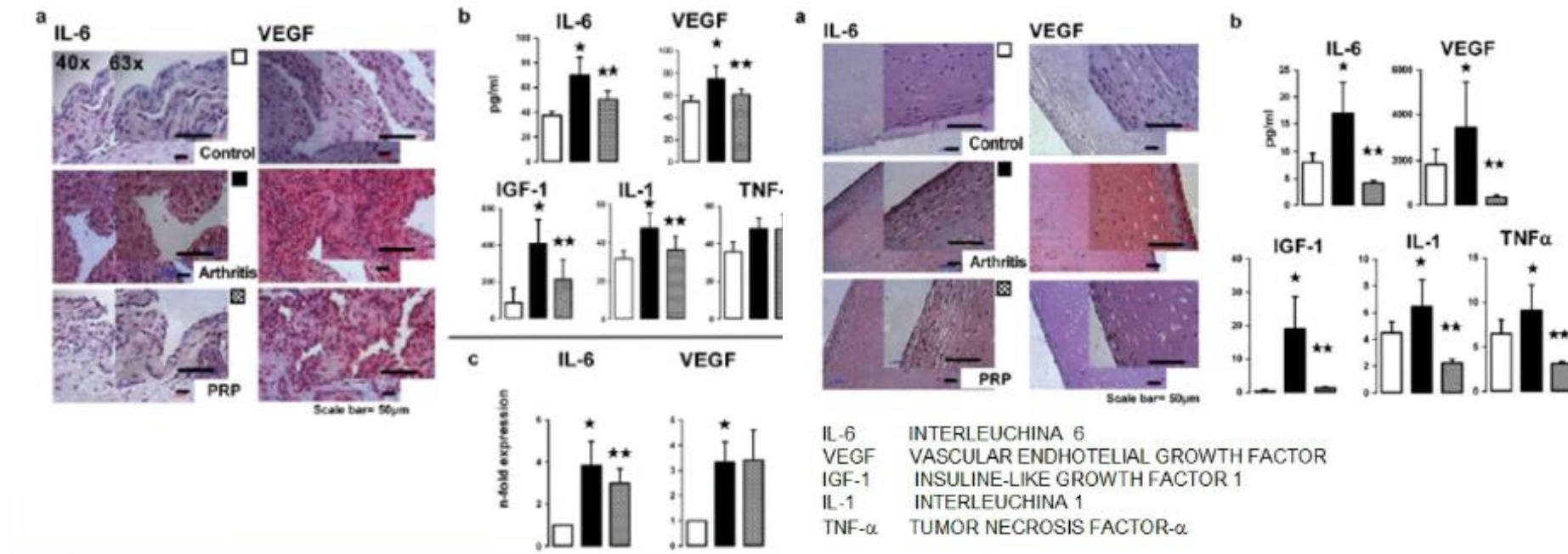
Review Article

## Platelet Rich Plasma. A New Treatment Tool for the Rheumatologist?☆

José De La Mata

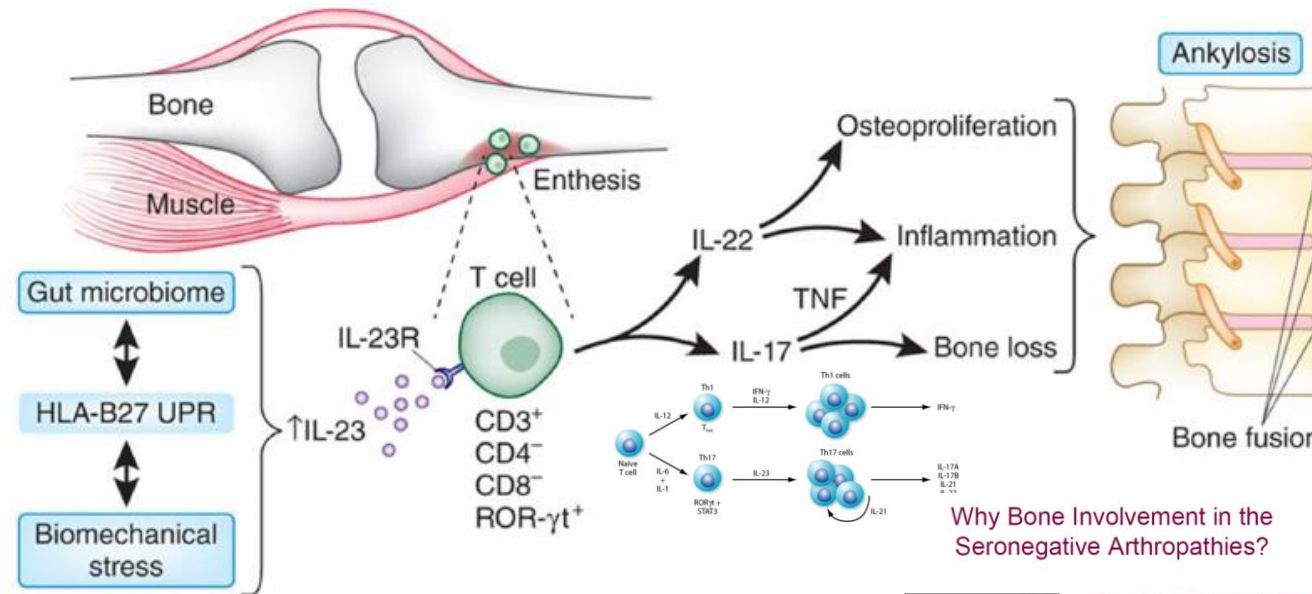
*Servicio de Reumatología, Clínica Nuestra Señora del Valle, Madrid, Spain*

# PRP AND RA



Lippross S et al. Intraarticular Injection of Platelet-Rich Plasma Reduces Inflammation in a Pig Model of Rheumatoid Arthritis of the Knee Joint. ARTHRITIS & RHEUMATISM Vol. 63, No. 11, November 2011, pp 3344–3353 DOI 10.1002/art.30547 © 2011, American College of Rheumatology.

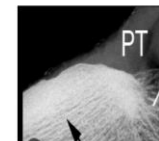
# IL-23 and Enthesal-Resident T Cells Promote Enthesitis and Osteoproliferation in Spondyloarthritis



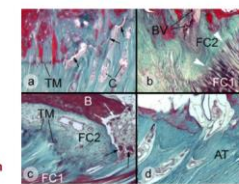
La patogenesi della patologia spondiloartritica vede coinvolte cellule e mediatori del sistema immunitario, come dimostrato sia da studi genetici che immunologici in particolare con riferimento alle cellule T helper Th17

Lories R et al. Nat Med. 2012;18:1018-9 (with permission)

Why Bone Involvement in the Seronegative Arthropathies?

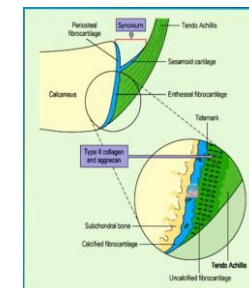


Close functional integration between insertions and bone



Bone Microdamage

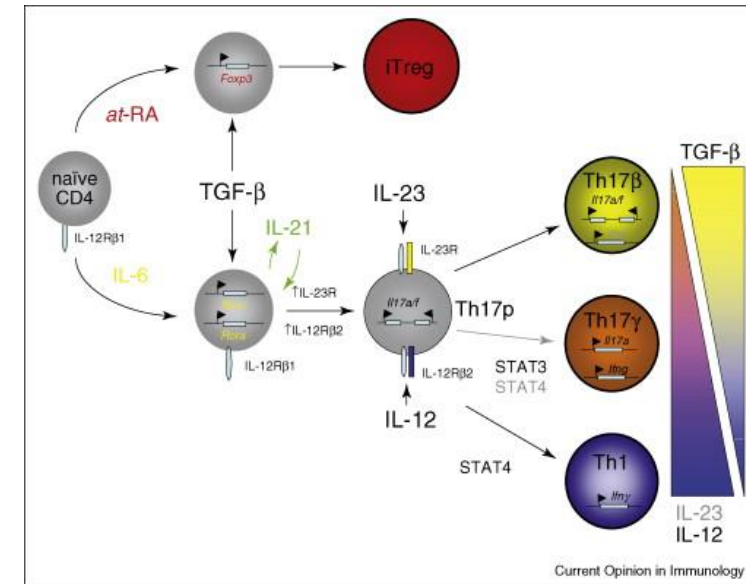
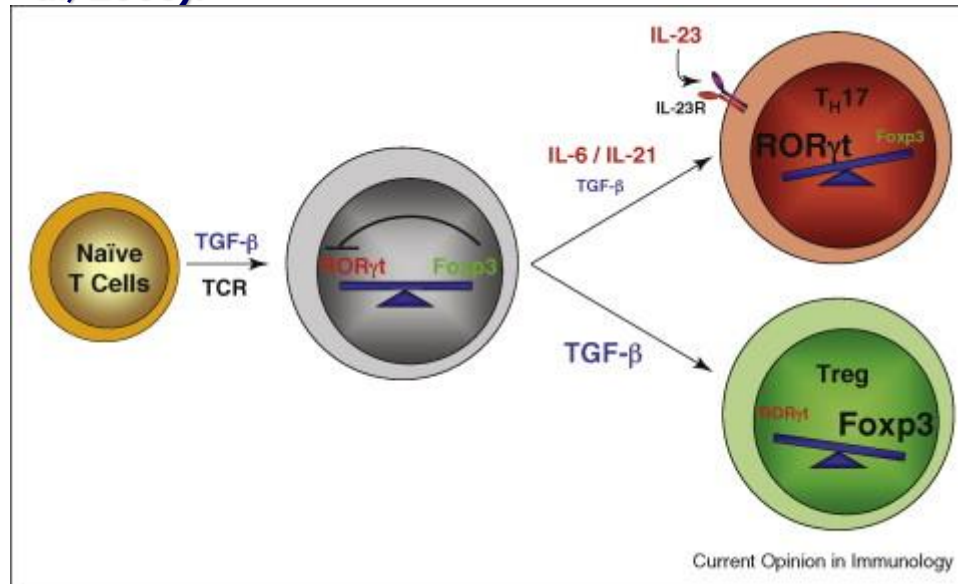
Benjamin et al AR 2007 and Benjamin & McGonagle AR 2007



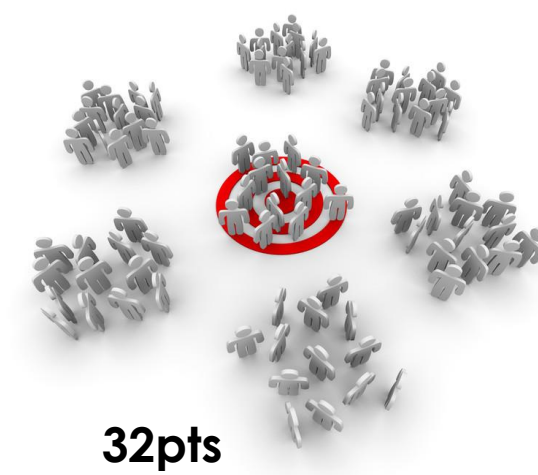
# RAZIONALE

I principi attivi del PRP sono il TGF-beta ed i fattori di crescita quali IGF, il PDGF

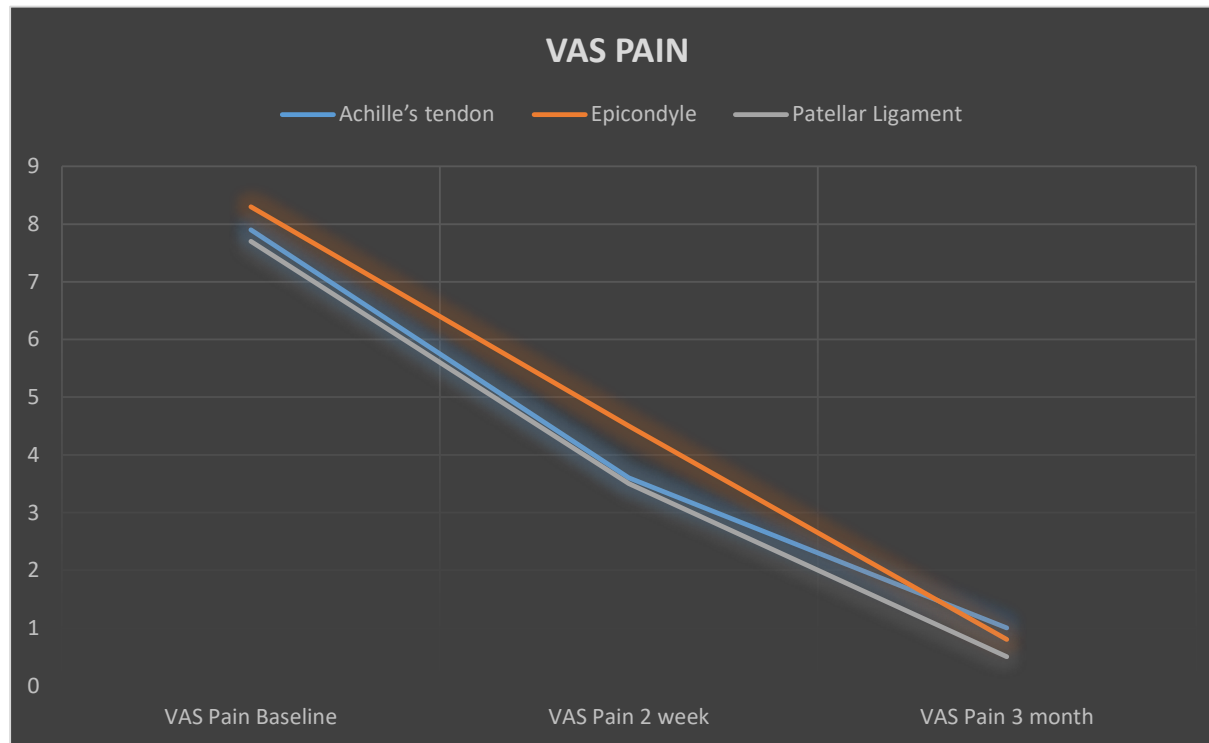
Il TGF-beta a concentrazioni adeguate inibisce la risposta immune mediata da cellule Th17, contrastandone il priming e convertendo i T cell naive in T Reg soppressori (Zhou et al, 2008; Crome et al, 2010); il TGFb ha anche la capacità di inibire altre cellule dell'infiammazione, quali altri fenotipi linfocitari e macrofagi, mentre i fattori di crescita piastrinici, per contro, stimolano i tenociti a produrre collagene riparando le lesioni tendinee già in essere (Everts et al, 2006).



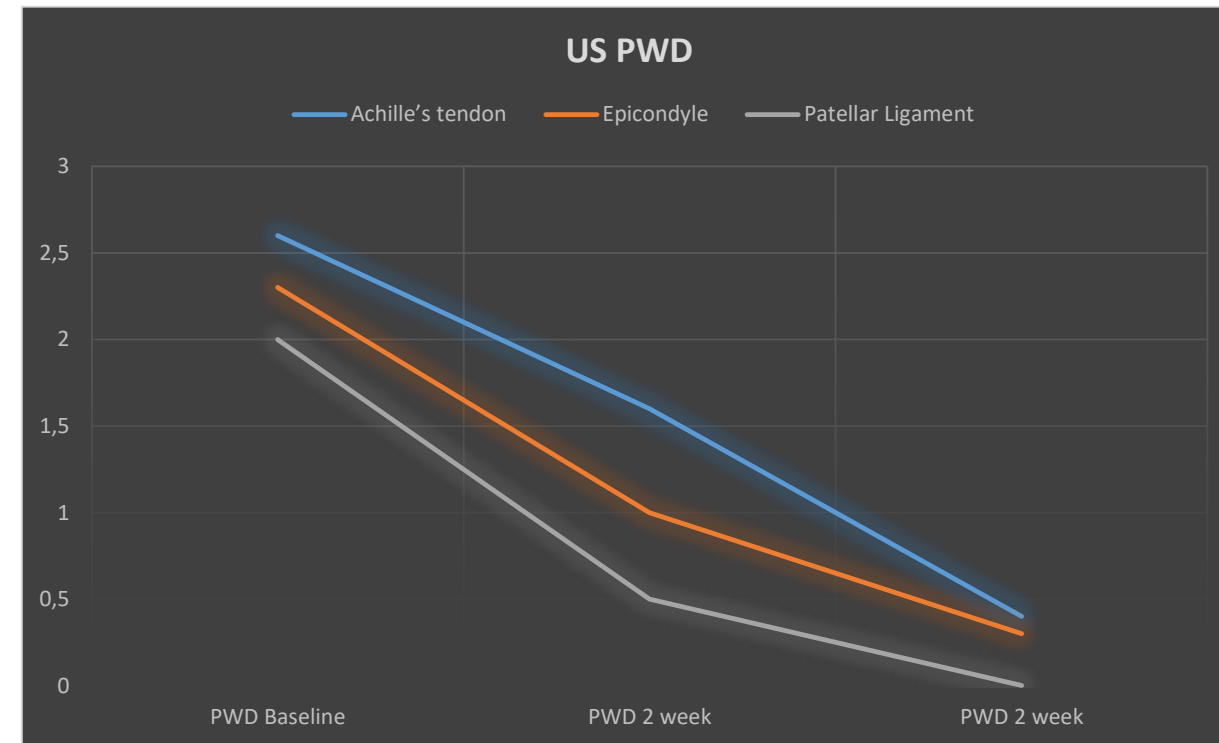




## RISULTATI



**$\Delta$  tot VAS PAIN -7.2 p=0,001**



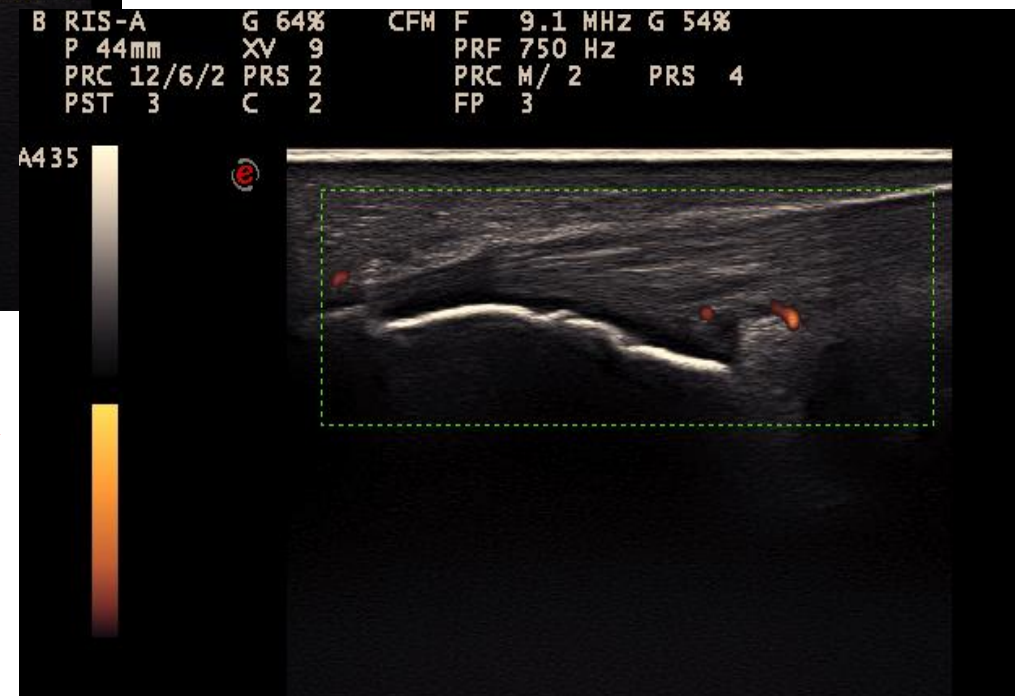
**$\Delta$  PWD tot -2.1 p=0,008**

Unpublished Data



**PRIMA DEL  
TRATTAMENTO CON  
PRP**

**DOPO TRATTAMENTO  
CON PRP**





## TARGET DELL' EC



- Tendinopatie
- Entesopatie
- Osteoartrosi del ginocchio
- Dry Eye Syndrome
- Ulcere

# Platelet-Rich Plasma Intra-Articular Injection Versus Hyaluronic Acid Viscosupplementation as Treatments for Cartilage Pathology: From Early Degeneration to Osteoarthritis

Elizaveta Kon, M.D., Bert Mandelbaum, M.D., Roberto Buda, M.D., Giuseppe Filardo, M.D., Marco Delcogliano, M.D., Antonio Timoncini, M.D., Pier Maria Fornasari, M.D., Sandro Giannini, M.D., and Maurilio Marcacci, M.D.

*Arthroscopy: The Journal of Arthroscopic and Related Surgery, Vol 27, No 11 (November), 2011: pp 1490-1501*

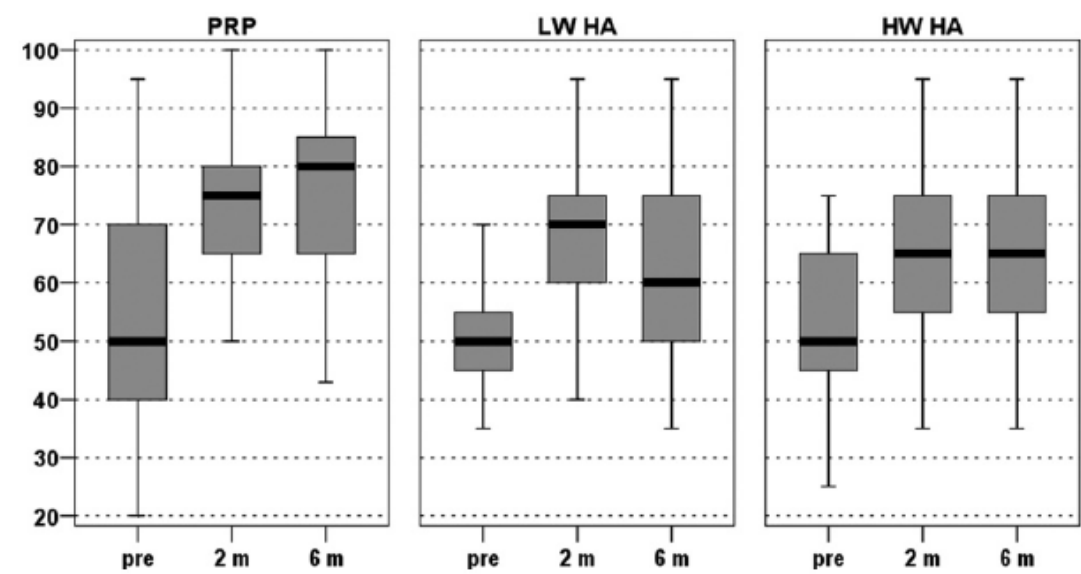
**TABLE 1.** *Comparison of Patient Characteristics of 3 Treatment Groups*

	PRP	LW HA	HW HA	
Age (yr)	50.6 ± 13.8 (30-81)	53.2 ± 13.0 (26-75)	54.9 ± 12.6 (29-76)	NS
Sex	30 M, 20 F	27 M, 23 F	25 M, 25 F	NS
Body mass index (kg/m <sup>2</sup> )	24.6 ± 3.2 (18-32)	26.2 ± 2.2 (20-31)	24.8 ± 3.5 (20-35)	<i>P</i> = .004
Pathology				NS
Cartilage degeneration	22	19	21	
Early OA	20	22	19	
Advanced OA	8	9	10	
Previous surgery	18 (7 meniscectomies, 6 ACL, 1 PCL, 1 patellar osteosynthesis, 4 shavings, 1 microfracture, 1 mosaicplasty, 3 second-generation ACI)	13 (12 meniscectomies, 2 ACL, 1 tibial plateau fracture osteosynthesis, 5 shavings)	17 (7 meniscectomies, 9 ACL, 2 microfracture, 5 shavings)	NS

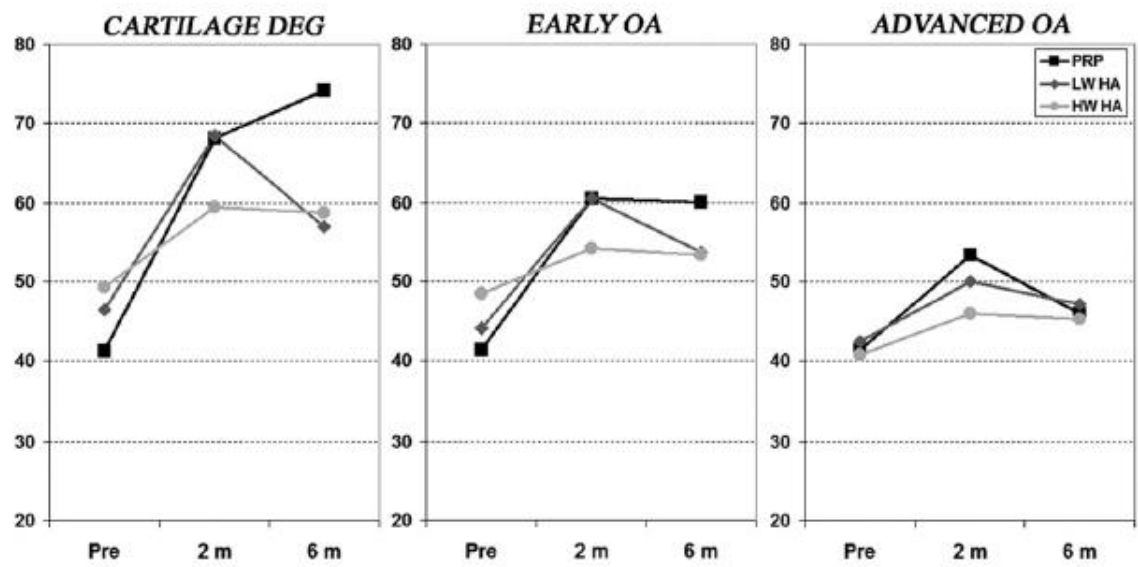
NOTE. The groups were homogeneous except for body mass index, which was higher in the LW HA group.  
Abbreviations: ACI, autologous chondrocyte implantation; ACL, anterior cruciate ligament; PCL, posterior cruciate ligament.



EQ VAS score (0-



IKDC score (0-100)



## Mechanistic insight into hyaluronic acid and platelet-rich plasma-mediated anti-inflammatory and anti-apoptotic activities in osteoarthritic mice

Chi-Sheng Chiou<sup>1,2</sup>, Chi-Ming Wu<sup>3</sup>, Navneet Kumar Dubey<sup>4,5</sup>, Wen-Cheng Lo<sup>6,7</sup>, Feng-Chou Tsai<sup>8</sup>, Tran Dang Xuan Tung<sup>1,9</sup>, Wei-Ching Hung<sup>10</sup>, Wei-Che Hsu<sup>10</sup>, Wei-Hong Chen<sup>10</sup>, Win-Ping Deng<sup>1,10,11</sup>

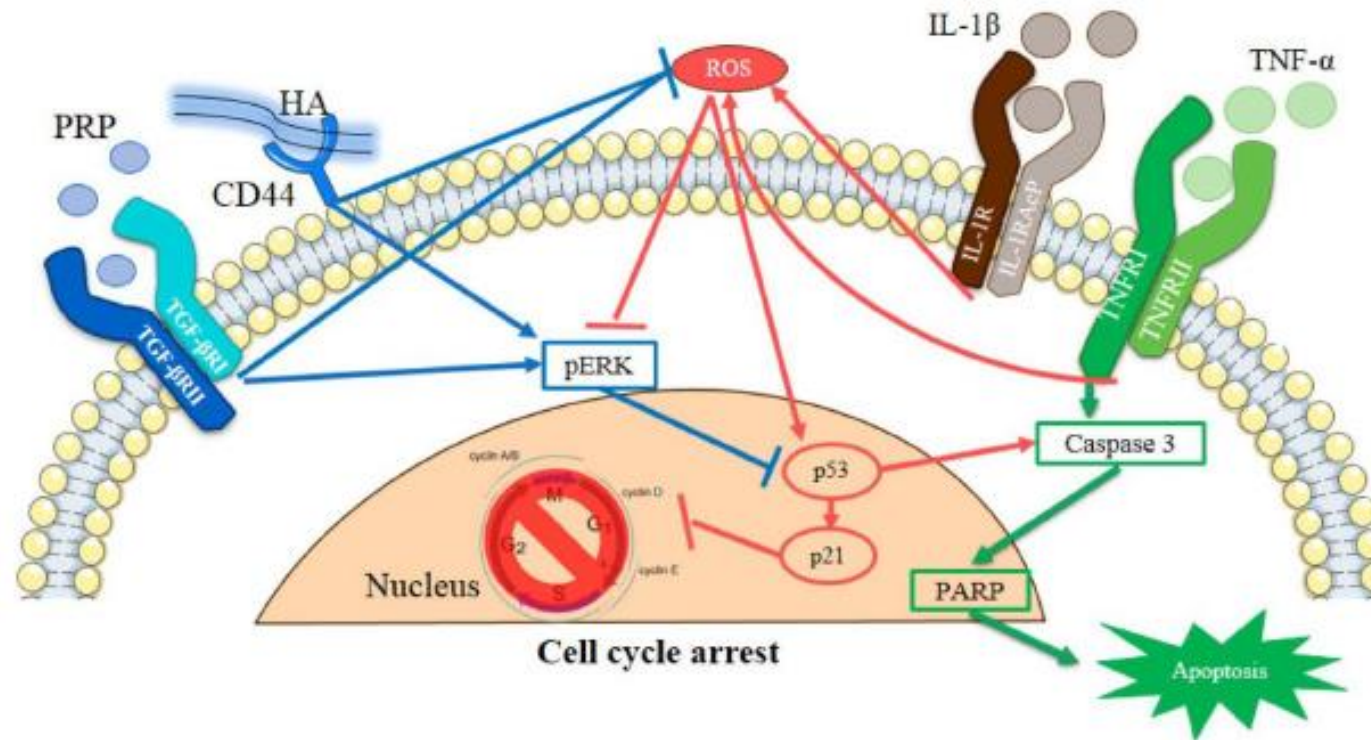


Figure 7. Schematic representation of HA and PRP-mediated cellular apoptosis in osteoarthritic chondrocytes.

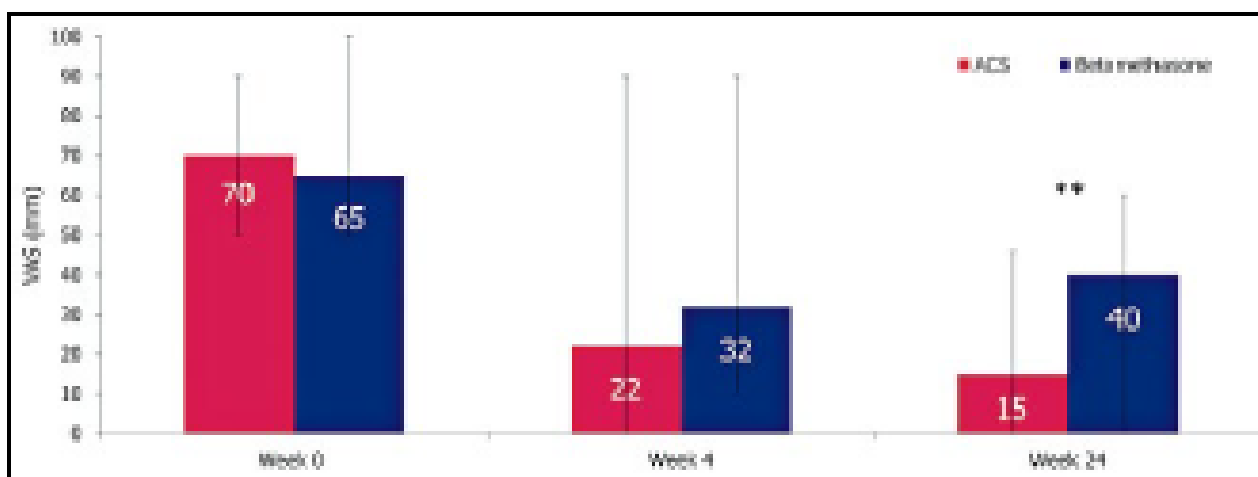
# SIERO AUTOLOGO CONDIZIONATO

## Original papers

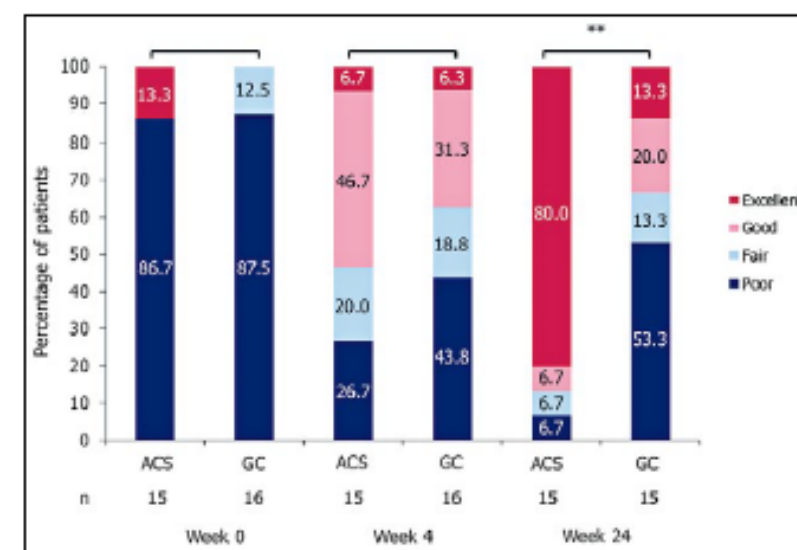
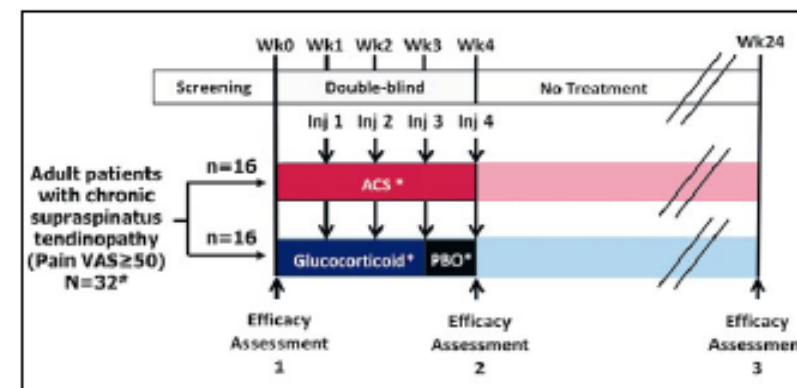
Med Ultrason 2018, Vol. 20, no. 3, 335-341  
DOI: 10.11152/nu-1495

The efficacy and safety of autologous conditioned serum (ACS) injections compared with betamethasone and placebo injections in the treatment of chronic shoulder joint pain due to supraspinatus tendinopathy: a prospective, randomized, double-blind, controlled study

Nemanja Damjanov<sup>1</sup>, Branko Barać<sup>1</sup>, Jelena Čolić<sup>1</sup>, Vladan Stevanović<sup>2</sup>, Ana Zeković<sup>1</sup>, Goran Tulić<sup>3</sup>



**Fig 3.** Shoulder pain (VAS) data at weeks 0, 4 and 24. \*\* Highly significant:  $p=0.002$ . VAS: visual analog scale for pain. Median values depicted. Error bars denote minimum and maximum values.



**Fig 4.** Shoulder function (CSS) data at weeks 0, 4 and 24 of ACS and glucocorticoid-treated patients. \*\* Highly significant:  $p<0.002$ . Full analysis set. CSS: Constant shoulder score. GC: glucocorticoid. CSS scores: <11 is Excellent, 11-20 is Good, 21-30 is Fair and >30 is Poor.

**Table 1.** Summary of IA therapies.

	Corticosteroids	HA	Platelet-rich plasma	Autologous conditioned serum	Mesenchymal stem cells
<b>Components</b>	Glucocorticoid (usually triamcinolone), in suspension	Hyaluronic acid or its sodium salt (sodium hyaluronate)	Plasma containing cells and coagulation factors, plus additives [anticoagulants, fibrinogen, activator (Ca <sup>2+</sup> )]. Cell concentration varies depending on manufacturers' processing recommendations	Cell-free serum without platelets, white or red blood cells or additives. Standardized manufacturing process	Suspension of multipotent adult stem cells
<b>Mechanism of action</b>	Anti-inflammatory agent	Lubricating component of synovial fluid	Growth factor release, including TGF- $\beta$ , PDGF, IGF, VEGFs, EGF and FGF-2	Elevated concentration of anti-inflammatory cytokines (including IL-1Ra, IL-4 and IL-10) and regenerative growth factors	Stem cell-secreted factors including cytokines and growth factors
<b>Preparation and administration</b>	Product injection directly into the joint	Product injection directly into the joint	Platelet enrichment in device from anticoagulated blood by centrifugation and elimination of superfluous plasma. Platelet yield is usually 50–75%. PRP may be activated with Ca <sup>2+</sup> , and then injected directly (single injection). Sterile filtration not possible	Serum conditioning by incubation of whole blood in a pyrogen-free device at 37°C. Conditioning stimulates production of cytokines including IL-1Ra. Serum is separated by centrifugation and extracted/stored at –18°C for $\leq$ 7 months. Injection 3–6 times per visit, given twice a week for 3 weeks, 1–3 times, sterile filtration possible	MSCs can be isolated from several organs and tissues (e.g. bone marrow) and grown using various cell culture techniques
<b>Efficacy</b>	Evidence for short-term efficacy over placebo. Long-term benefits less well substantiated <sup>11,22</sup>	Incongruous literature regarding efficacy and safety: some indicating a good efficacy, <sup>24</sup> others suggesting HA provides little or no benefit over placebo. <sup>25,26</sup>	Most reviews provide evidence of clinical benefits, <sup>27,28</sup> some remain equivocal. <sup>29</sup>	Limited data due to less expanded use and nonconsideration in guidelines. Clinical studies indicate significant improvements over placebo and saline. <sup>30</sup>	Efficacy data are very limited, albeit encouraging. <sup>31–37</sup> Further studies are ongoing.
<b>Safety</b>	Prolonged exposure may adversely affect articular cartilage or be associated with chondrotoxicity	Incongruous literature, some meta-analyses concluding HA to have a low risk of harm, <sup>26</sup> others identifying concerning safety signals, albeit with unclear causal mechanisms. <sup>25</sup>	Perceived favorable safety profile due to autologous nature. Limited evidence available from long-term safety studies. Some evidence that PRP injections may lead to an increase in adverse events. <sup>28,38</sup>	Perceived favorable safety profile due to autologous nature. Limited data are available, but no serious side effects have been observed in published trials. <sup>30,39</sup>	Based on limited data available to date, IA MSC therapy appears to be relatively safe. <sup>40,41</sup>
<b>Treatment recommendations</b>	OARSI recommend corticosteroids, but recognize that other treatments may be more appropriate for long-term analgesia. <sup>10</sup>	OARSI do not recommend HA in multi-joint OA and cite uncertainty in the use of HA to treat knee OA. <sup>10</sup>	Not considered by OARSI in OA treatment recommendations	Not considered by OARSI in OA treatment recommendations	Not considered by OARSI in OA treatment recommendations
ACS, autologous conditioned serum; CS, corticosteroid; EGF, epidermal growth factor; FGF-2, basic fibroblast growth factor; HA, hyaluronic acid; IA, intra-articular; IGF, insulin-like growth factor; IL-1Ra, interleukin-1 receptor antagonist; IL-4, interleukin-4; IL-10, interleukin-10; MSC, mesenchymal stem cell; OA, osteoarthritis; OARSI, Osteoarthritis Research Society International; PDGF, platelet-derived growth factor; PRP, platelet-rich plasma; TGF- $\beta$ , transforming growth factor beta; VEGF, vascular endothelial growth factor.					





# DRY EYE...

Hindawi Publishing Corporation  
BioMed Research International  
Volume 2016, Article ID 8406832, 10 pages  
<http://dx.doi.org/10.1155/2016/8406832>



## Research Article

### The Effect of Autologous Platelet Lysate Eye Drops: An In Vivo Confocal Microscopy Study

Antonio M. Fea,<sup>1</sup> Vittoria Aragno,<sup>1</sup> Valeria Testa,<sup>1</sup> Federica Machetta,<sup>1</sup> Simone Parisi,<sup>2</sup>  
Sergio D'Antico,<sup>3</sup> Roberta Spinetta,<sup>1</sup> Enrico Fusaro,<sup>2</sup> and Federico M. Grignolo<sup>1</sup>

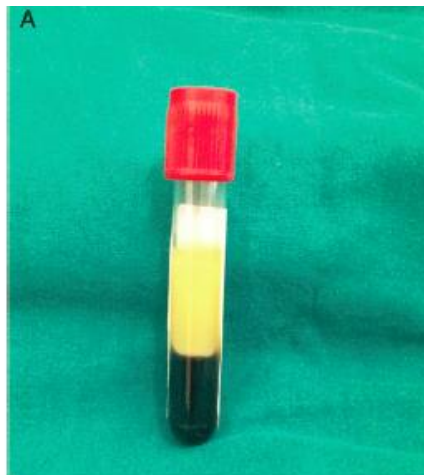
<sup>1</sup>Department of Clinical Sciences, Ophthalmology Institute, University of Turin, 10122 Turin, Italy  
<sup>2</sup>Ophthalmology Department, AOU Città della Salute e della Scienza di Torino, 10134 Turin, Italy  
<sup>3</sup>Department of Clinical Sciences, AOU Città della Salute e della Scienza di Torino, 10134 Turin, Italy

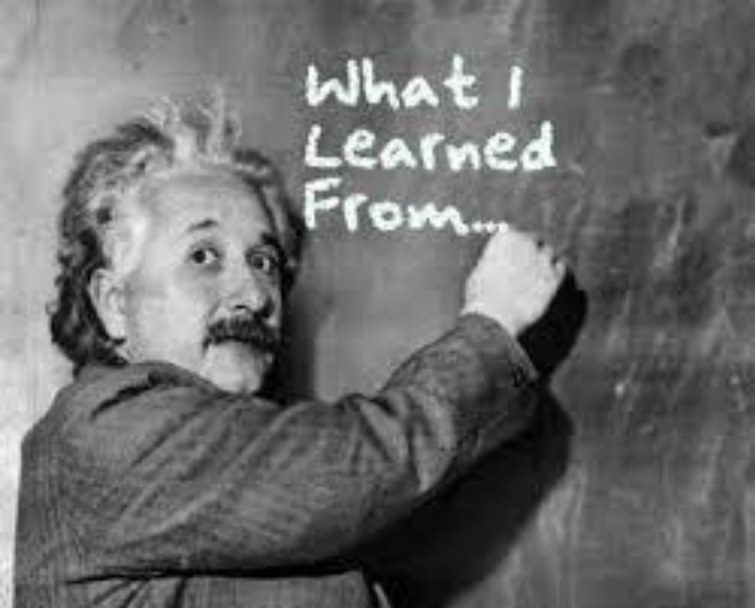
IWJ International Wound Journal

International Wound Journal ISSN 1742-4801

## LETTER TO THE EDITOR

### Autologous platelet-rich fibrin in treatment of scleroderma ulcer





# CONCLUSIONI

## Pro

- Possono avere duplice funzione: diagnostica e terapeutica
- Aiutano nel perseguire l'obiettivo delle «medicina di precisione»
- Diversi approcci secondo le patologie
- Buona Sicurezza

## Contro

- Operatore
- Marginalizza l'esame obiettivo

# REUMA SPORT

## PATOLOGIE REUMATICHE E ATTIVITA' SPORTIVA

La profilazione della terapia  
anti-reumatica in accordo  
con l'attività sportiva:  
le prospettive di prevenzione  
e di cura alla luce dei  
trattamenti disponibili

**TORINO**  
**7 FEBBRAIO**  
**2020**

Hotel NH Collection  
Piazza Carlina



# GRAZIE PER L'ATTENZIONE...

---