

# 통증 물리치료학 및 실습

## CH 9. 관절염 재활

**Gachon University**

**Department of Physical Therapy**

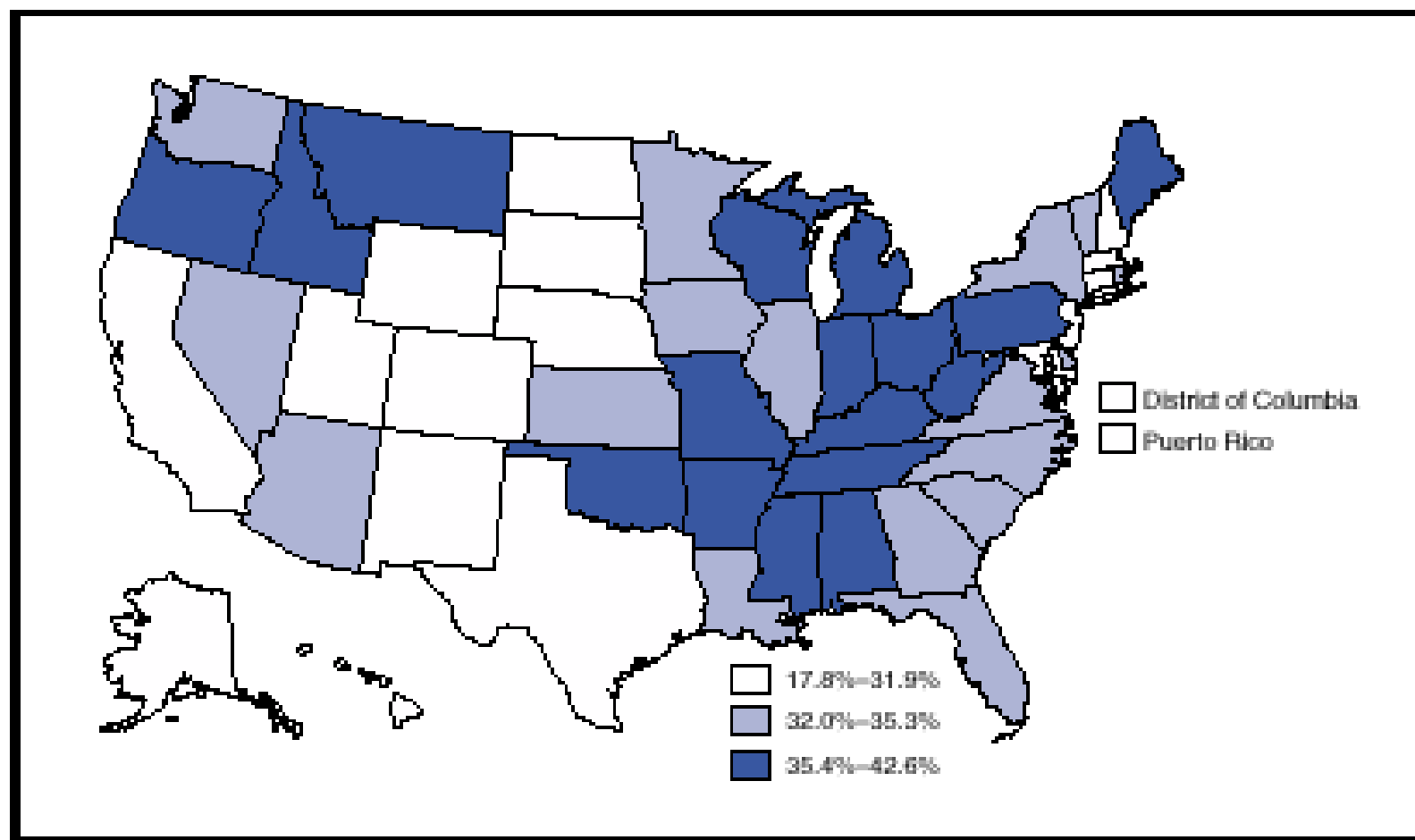
**Hwi-young Cho, PT, PhD**



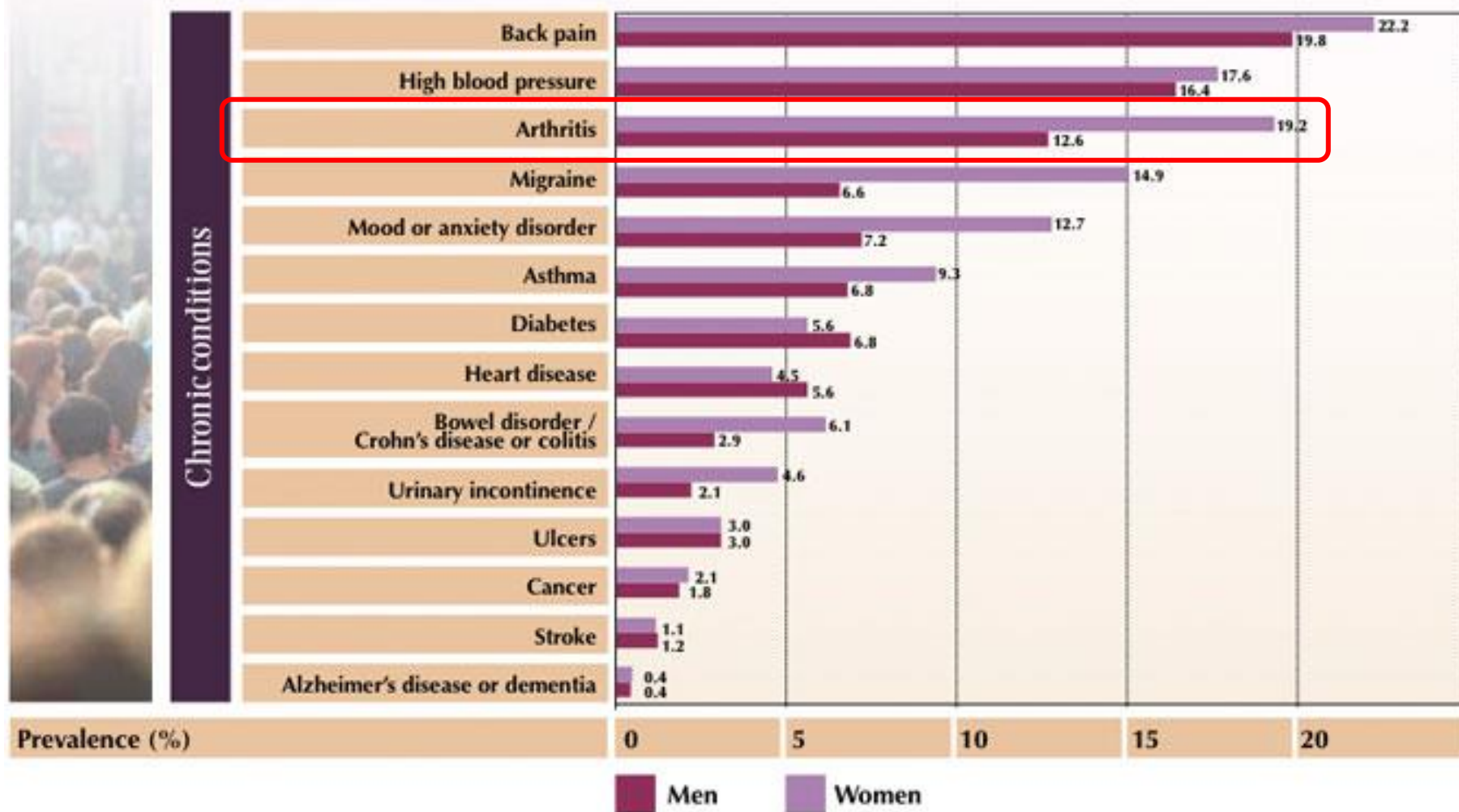
# Arthritis

- Arthritis (*Ashburn, 2002*)
  - One of the most prevalent **chronic health problems**
  - A **leading cause of disability**
- Incidence
  - 90% of people (60 years of age) will suffer from some form of arthritis
  - The 400 thousand day-patient / year
- The social side
  - 1000 hundred million for medical expenses / year

**FIGURE. Percentage of adults aged  $\geq 18$  years with arthritis/chronic joint symptoms, by state/area —United States, Behavioral Risk Factor Surveillance System, 2001**

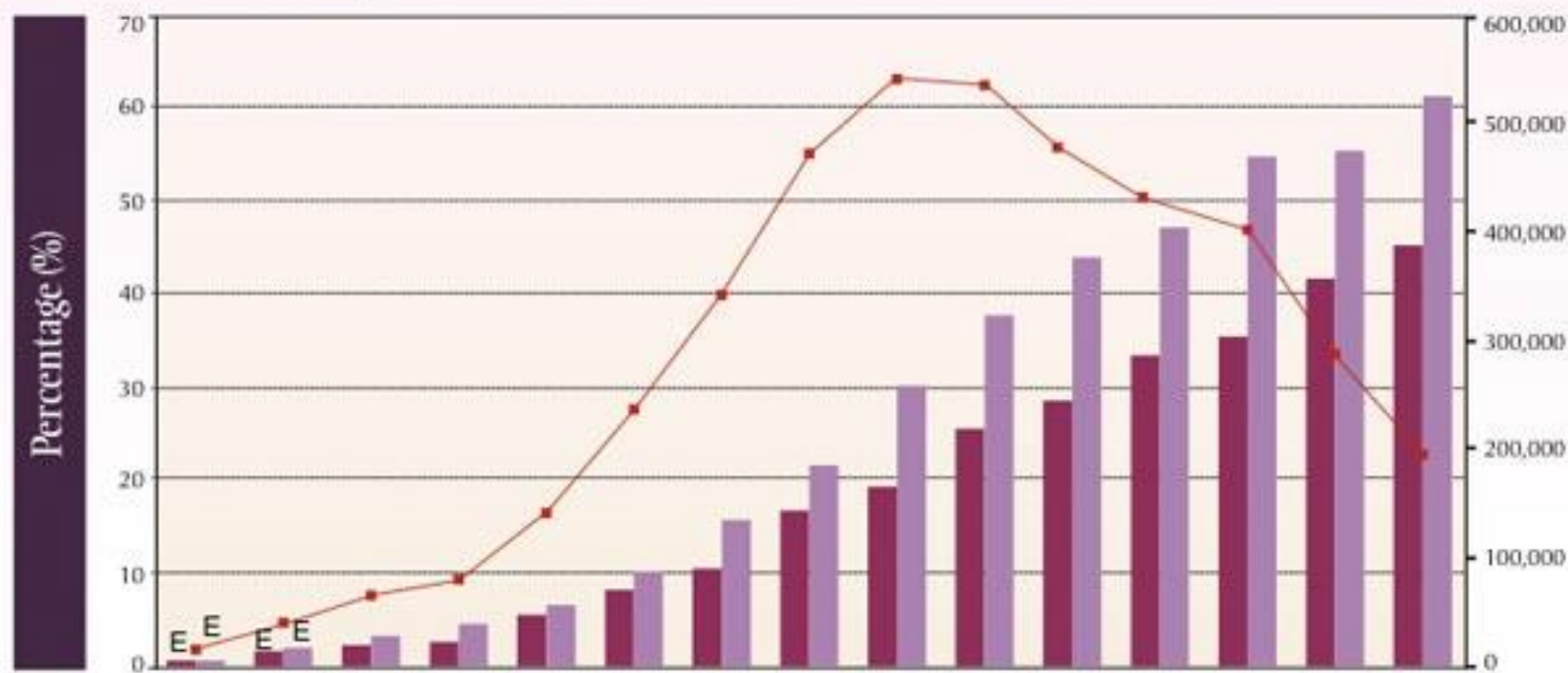


**Figure 1-1** *Self-reported prevalence of specific chronic conditions by sex, household population aged 15 years and older, Canada 2007-2008*



◆ Source: Public Health Agency of Canada, using Canadian Community Health Survey, 2007-2008, Statistics Canada.

**Figure 1-2** *Self-reported prevalence and number of individuals with arthritis by age and sex, household population aged 15 years and older, Canada, 2007-2008*



Age Group	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Men	0.7	1.7	2.4	2.7	5.6	8.4	10.5	16.8	19.5	25.4	28.6	33.2	35.4	41.6	45.2
Women	0.8	2.0	3.4	4.8	6.8	10.1	15.6	21.6	30.1	37.5	43.7	47.0	54.7	55.3	61.0
Number of men and women	15,476	40,301	65,772	81,570	141,762	235,798	341,549	471,367	537,992	534,737	478,442	431,613	401,337	287,528	194,450

♦ Source: Public Health Agency of Canada, using Canadian Community Health Survey, 2007-2008, Statistics Canada. ♦ E – Interpret with caution.

# Symptom of Arthritis

## 1. Arthritic Pain

- The **major symptom**
- The main reason : seek medical care
- A major determinant of **functional loss**
- Despite its importance, there is much about arthritic pain that remains unclear

## 2. Disability (motor function)

- Limitation of functional activity

# Mechanism of Arthritic pain

## 1. Peripheral mechanism

- ↑ Activity in afferent fibers of joint structures

## 2. Central mechanism

- ↑ Nociceptive information to **dorsal horn neurons** : central sensitization
  - 2-1. ↑ Peripheral receptive field
  - 2-2. ↑ Background firing
  - 2-3. ↑ Responsiveness to cutaneous and joint mechanical stimuli

# Types of articular pain

- Primary pain
  - Movement-related pain
- Secondary pain
  - Referred pain
  - Secondary mechanical allodynia & hyperalgesia
  - Secondary thermal allodynia & hyperalgesia
- Spontaneous pain



# Pain mechanism of arthritis

- Peripheral mechanisms
- Central mechanisms
- Changed plasticity

# Arthritic pain is associated with plastic changes in Brain.

Neurobiology of Disease

## Abnormalities in Hippocampal Functioning with Persistent Pain

Amelia A. Mutso,<sup>1</sup> Daniel Radzicki,<sup>1</sup> Marwan N. Baliki,<sup>1</sup> Lejian Huang,<sup>1</sup> Ghazal Banisadr,<sup>2</sup> Maria V. Centeno,<sup>1</sup> Jelena Radulovic,<sup>3</sup> Marco Martina,<sup>1</sup> Richard J. Miller,<sup>2</sup> and A. Vania Apkarian<sup>1,4</sup>

Departments of <sup>1</sup>Physiology, <sup>2</sup>Molecular Pharmacology and Biological Chemistry, <sup>3</sup>Psychiatry and Behavioral Sciences, and <sup>4</sup>Anesthesia and Surgery, Feinberg School of Medicine, Northwestern University, Chicago, Illinois 60611

Chronic pain patients exhibit increased anxiety, depression, and deficits in learning. The brain area regulating these behaviors, the hippocampus, has remained minimally spared in nerve injury (SNI) neuropathic pain in mice on hippocampal-dependent behavior. In parallel, we measured the hippocampal volume of three groups of chronic pain patients. Pain patients who could not extinguish contextual fear and showed increased anxiety-like behavior. Addition of hippocampal (1) reduced extracellular signal-regulated kinase expression and altered short-term synaptic plasticity. To relate the observed hippocampal abnormalities to the volume of human hippocampus in chronic back pain (CBP), complex regional pain syndrome (CRPS), and osteoarthritis (OA), we compared CBP and CRPS, but not OA, with controls. CBP and CRPS, but not OA, had significantly less bilateral hippocampal volume. Hippocampal volume, synaptic plasticity, and neurogenesis are all related to the reduction in hippocampal volume we see in chronic pain patients. Emotional deficits commonly observed in such patients.



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Neuropharmacology 46 (2004) 918–926

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## Enhanced group III mGluR-mediated inhibition of pain-related synaptic plasticity in the amygdala

Jeong S. Han, Gary C. Bird, Volker Neugebauer\*

Department of Anatomy and Neurosciences and Marine Biomedical Institute, The University of Texas Medical Branch, 301 University Boulevard, Galveston, TX 77555-1069, USA

Received 19 August 2003; received in revised form 25 October 2003; accepted 7 January 2004

### Abstract

Pain has a strong emotional component. A key player in emotionality, the amygdala is also involved in pain processing. Our previous studies showed synaptic plasticity in the central nucleus of the amygdala (CeA) in a model of arthritic pain. Here, we address the role of group III metabotropic glutamate receptors (mGluRs) in the regulation of synaptic transmission in CeA neurons. Whole-cell current- and voltage-clamp recordings were made from neurons in the latero-capsular part of the CeA in brain slices from control rats and arthritic rats (>6 h postinduction). The latero-capsular part of the CeA is the target of the spino-parabrachio-amygdaloid pain pathway and is now designated as the “nociceptive amygdala”. Monosynaptic excitatory postsynaptic currents (EPSCs) were evoked by electrical stimulation of afferents from the pontine parabrachial (PB) area. LAP4 decreased the amplitude of EPSCs more potently in CeA neurons from arthritic rats ( $EC_{50} = 1.2$  nM) than in control animals ( $EC_{50} = 11.5$  nM). The inhibitory effect of LAP4 was reversed by a selective group III mGluR antagonist (UBP1112). During the application of LAP4, paired-pulse facilitation was increased, while no significant changes in slope conductance and action potential firing rate of CeA neurons were observed. These data suggest that presynaptic group III mGluRs are involved in the regulation of synaptic plasticity in the amygdala in an arthritis pain model.

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# Classification of arthritis

- There are over 100 different forms of arthritis.
- Osteoarthritis (OA)
- Rheumatoid arthritis (RA)
- Gout and pseudo-gout
- Septic arthritis
- Ankylosing spondylitis
- Juvenile idiopathic arthritis
- Still's disease

# Arthritis

- **Rheumatoid Arthritis (RA)**

- Autoimmune
- Symmetrical
- Joint pain, swelling, stiffness, fatigue
- Synovial inflammation → Cartilage

- **Osteoarthritis (OA)**

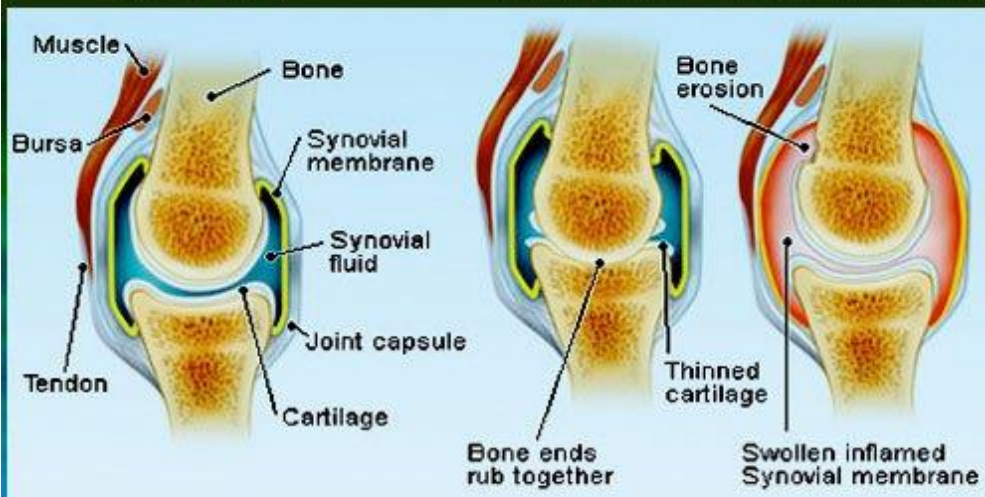
- Degenerative
- Asymmetrical
- Joint pain, stiffness
- Pain is worse with use
- Weight bearing joints
- Joint space narrowing
- Cartilage → Synovial inflammation

RHEUMATOID ARTHRITIS		OSTEOARTHRITIS
More severe than OA	➞	Generally less severe than RA
Caused by immune system attacking the body	➞	Caused by wear and tear on the body
Can affect people of any age, but most commonly affects those between ages 20 and 60	➞	Generally affects people over age 40
Symptoms can be felt throughout the entire body	➞	Usually only affects the joints
Affects more women than men	➞	Commonly found in both men and women

Normal Joint

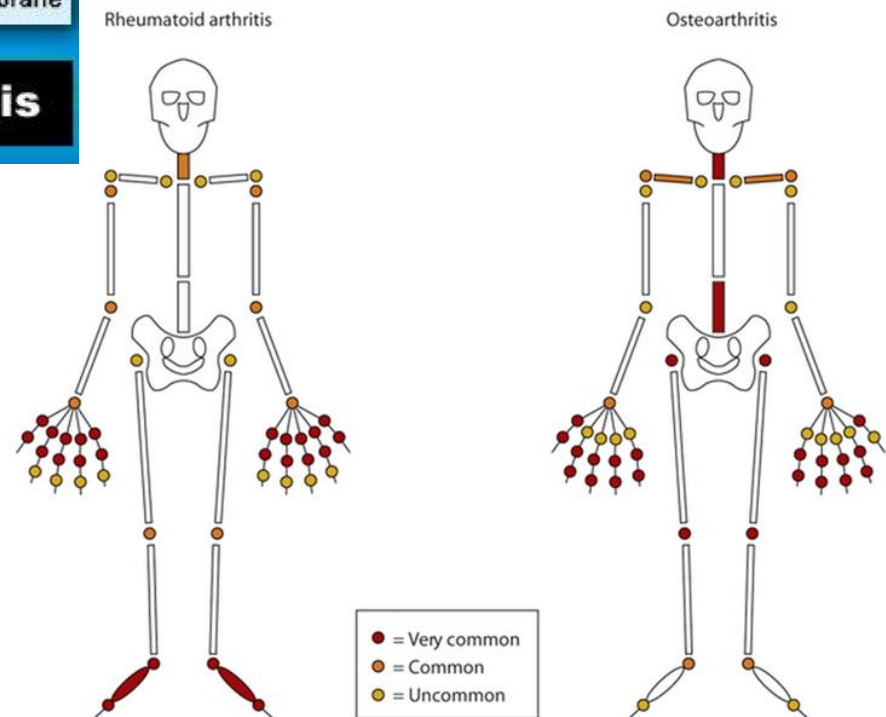
Osteoarthritis

Rheumatoid Arthritis



<http://jarrettmorrow.com/2013/05/03/natural-remedies-arthritis-pain/>

## Osteoarthritis vs. Rheumatoid Arthritis

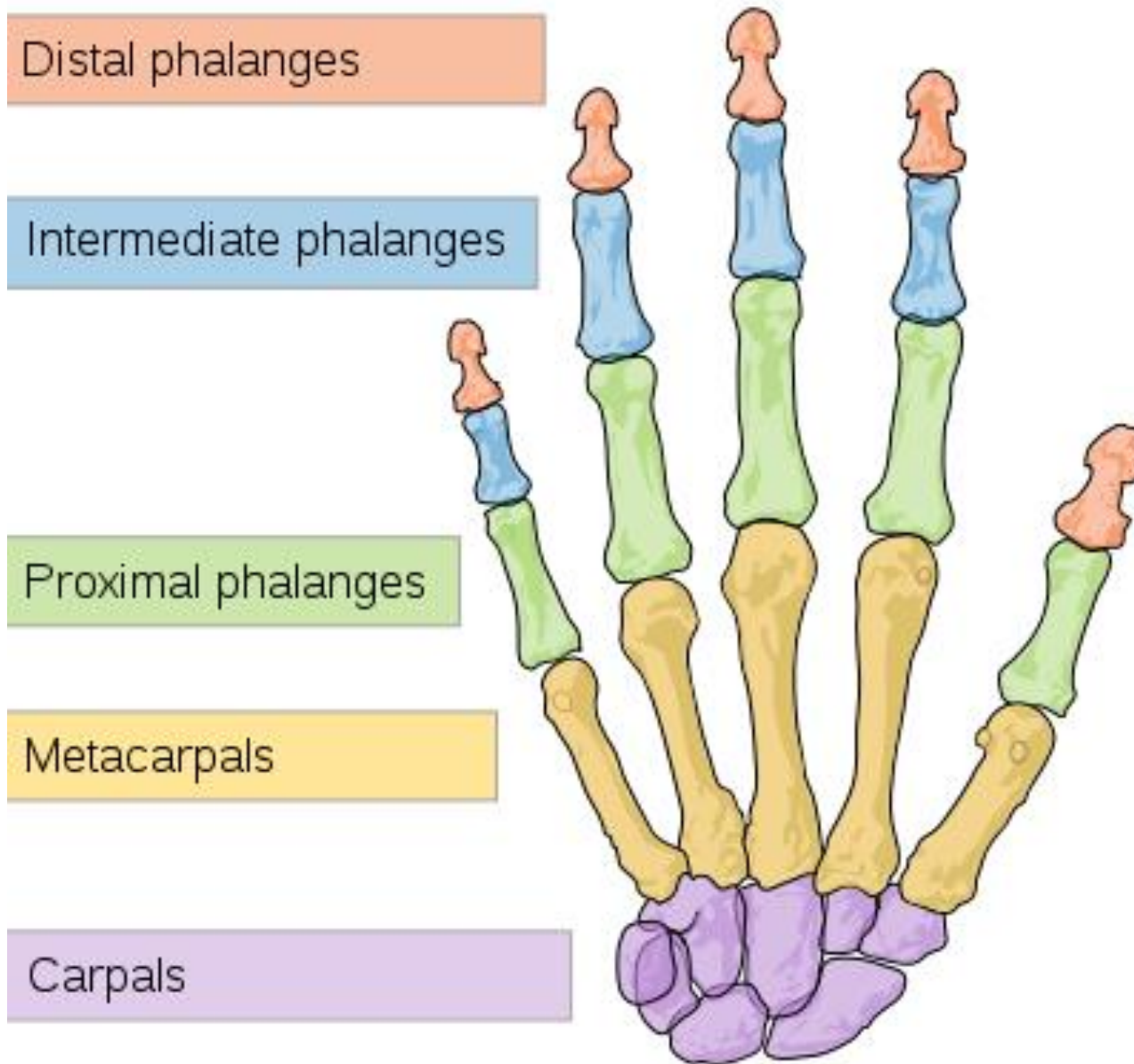


<http://diplomat.is/blogging/weather-can-weather-affect-rheumatoid-arthritis-osteoarthritis/>

Source: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM: *Pharmacotherapy: A Pathophysiologic Approach*, 8th Edition: [www.accesspharmacy.com](http://www.accesspharmacy.com)  
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OA

RA



# Signs & Symptoms

## Direct influences

- Inability to use the hand or walk (손사용 및 보행 저하)
- Morning stiffness (조조강직)
- Malaise and a feeling of tiredness (불만감 & 피로)
- Weight loss (체중 소실)
- Poor sleep (수면 부족)
- Muscle aches and pains
- Tenderness (압통)
- Difficulty moving the joint

## Secondary changes

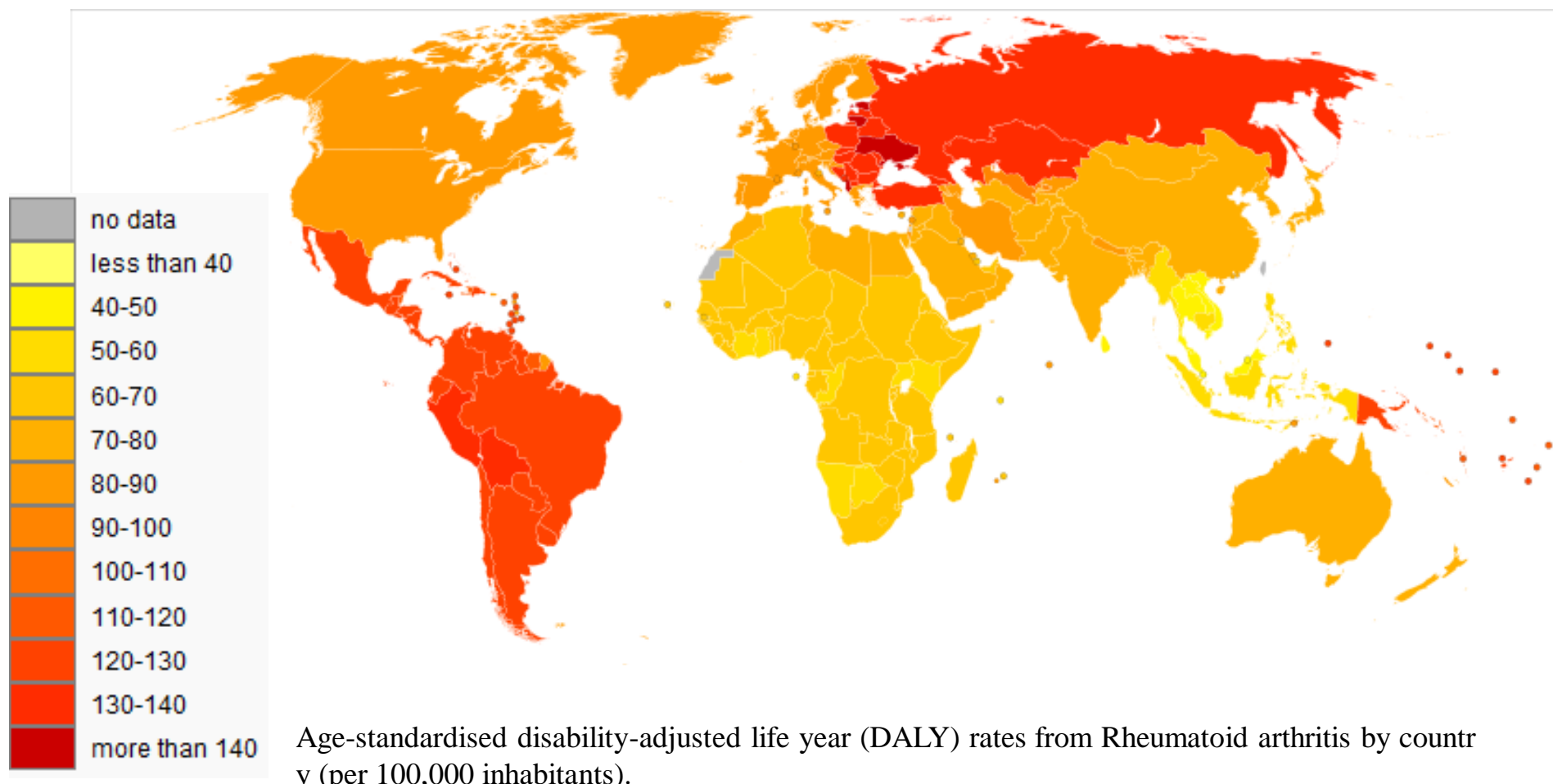
- Muscle weakness
- Loss of flexibility
- Decreased aerobic fitness



# **Rheumatoid arthritis**



## Rheumatoid arthritis world map - DALY - WHO2004



# Introduction for RA

- Gross explanation
  - <http://www.youtube.com/watch?v=Yc-9dfem3lM>
- Cell approach
  - <http://www.youtube.com/watch?v=imR4hCwrGmQ>

# Rheumatoid Arthritis (RA)

- Chronic multi-system disease
- 말초 관절에 대칭적으로 침범
- Autoimmune disease
- Persistent inflammatory synovitis
  - 활액막의 염증 : 연골파괴와 골미란 → 관절의 변형  
(*erosion*)
- 역학
  - Prevalence : Approximately 0.8%
  - Male : Female = 1 : 3 (F>M)
  - 발병: 30-40대에 가장 흔하며, 80%가 35-50세 사이에 시작

# RA (2)

- **Pathogenesis**

1. Genetic factors

- Rheumatoid factor를 동반한 환자 : 발생율이 정상보다 약 4배 높다.
- 일란성 쌍생아의 RA에 대한 합치율 (concordance)이 이란성 쌍생아에 비해 적어도 4배 높다.

2. Environmental factors

- Bacterial & Viral infections

# RA (3)

## ● 병리학 및 병리 기전

- 미세혈관 손상 & synovial lining cell 수의 증가
- 단핵구들이 혈관 주위로 집중되면서 활액막의 부종
- 과증식된 활액막이 관절강으로 villi(융모) 형성 = pannus
- 현미경적 소견
  - Synovial lining cell의 과증식
  - 부분적인 혈관 변화 (미세혈관 손상, 혈전, 혈관 신생 등)
  - 부종, 단핵구의 침윤

<http://www.youtube.com/watch?v=imR4hCwrGmQ>

# Arthritis process

- Arthritis (*Bendele et al., 1999*)
  1. Inflammation of a joint
  2. Infiltration of inflammatory cells (monocytes)
  3. Synovial hyperplasia
  4. Bone erosion
  5. New bone formation
  6. Narrowing of the joint space
  7. Ankylosis of the joint

# Criteria for classification of RA (4)

## 1. Morning stiffness

- more than 1 hour

## 2. Arthritis of three or more joint areas

- At least 3 joint areas simultaneously have had soft tissue swelling or fluid

## 3. Arthritis of hand joints

- At least one area swollen in wrist, MCP, or PIP joints
- DIP (원위지절관절): 보통 침범이 되지 않음

## 4. Symmetric arthritis

- Simultaneous involvement of the same joint areas on the both sides of the body

## 5. Rheumatoid nodules

- Subcutaneous nodules

## 6. Serum rheumatoid factor

- Abnormal amounts of serum rheumatoid factor (Normal : <5%)

## 7. Radiographic changes

- Erosions and/or periarticular osteopenia, in hand or wrist joints (**초기: 잘 나타나지 않음 / 후기: 소견 O**)
  - \* Criteria 1-4 must be present for at least 6 weeks
  - \* Criteria 2-5 must be observed by a physician
- 미국 : 진단기준에 의하면 검사항목 **7개중 4개** 이상의 증상이 있고, 관절이 적어도 **6주 이상** 지속되는 경우 RA라고 한다.



# Radiographic finding



# Clinical manifestations of RA

## ○ Arthritis

- Pain, swelling and tenderness
- Morning stiffness greater than 1hr
- Joint swelling : accumulation of joint fluid
- Hypertrophy of synovium
- Thickening of joint capsule
- Tenderness, LOM, warmth, erythema (infrequent)
- Flexion contracture of joint

## ○ Deformity

- Swan neck deformity
- Boutonniere deformity

# Symptoms of RA

A photograph of a man with dark hair, shirtless, holding his right shoulder with his left hand, appearing to be in pain. The background is a light blue gradient.

**Symptoms Of Shoulder Joint Rheumatoid Arthritis**

- Weight Loss
- Fatigue
- Fever
- Painful Shoulder Joint Movements
- History of Muscle Spasm
- History of Shoulder Joint Stiffness

ePainAssist.com

# RA deformities

- 건관절 : 내전, 내회선
- 주관절 : 굴곡, 전완의 회내선
- 수근관절 : 굴곡, 척골편위
- 수지관절 : 백조목변형, 단춧구멍 변형
- 모지 : Game keeper thumb
- 척추 : 경,흉추 상부 침범
- 고관절 : 굴곡, 외전, 내회전의 운동장애
- 슬관절 : 굴곡, 관절의 내외측 침범
- 족부 : 갈퀴족변형, 후족분 침내반

# Game keeper thumb



- A type of injury to the ulnar collateral ligament (UCL) of the thumb.
- Symptom
  - Instability of the MCP joint of the thumb, accompanied by pain and weakness of the pinch grasp
  - Sign: pain, swelling, and ecchymosis (얼룩출혈) around the thenar eminence, and especially over the MCP joint of the thumb

# Game keeper thumb

## Special test



## Orthosis



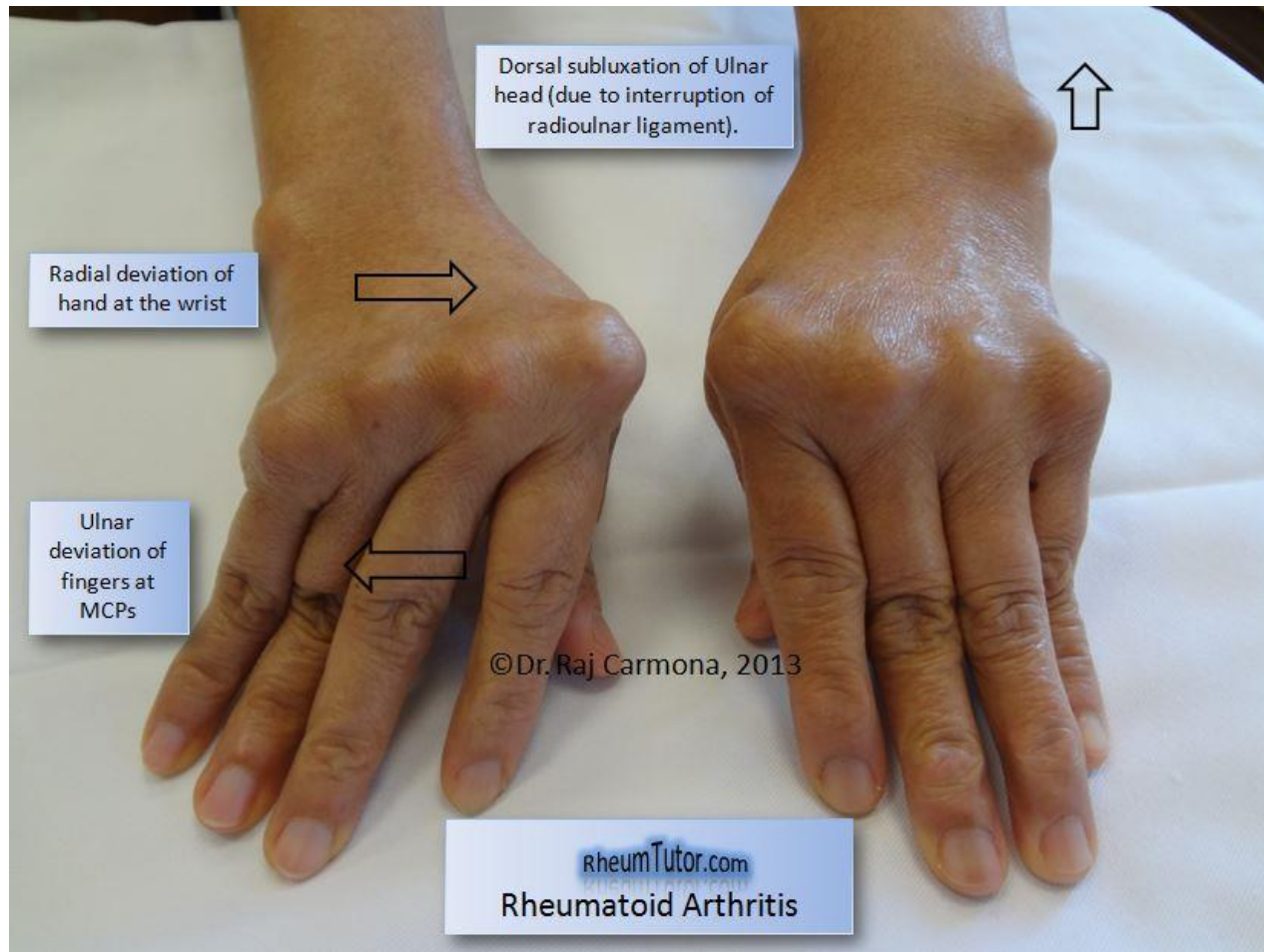
<http://www.supports4u.com/brdthumb.htm>

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<http://www.netterimages.com/image/8336.htm>



# Deformation following RA



# Swan neck deformity

- PIP : hyperextension
- DIP : flexion

Normal joint

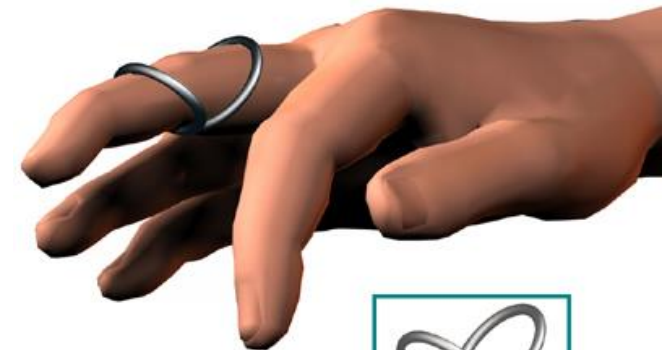


Swan neck deformity



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[http://www.google.co.kr/url?sa=i&rct=j&q=&esrc=s&source=images&cd=&ved=0CAUQjhw&url=http%3A%2F%2Fwww.methodistorthopedics.com%2Fswan-neck-deformity-of-the-finger&ei=esW7VNjnLMG7mgW5h4CQDw&bvm=bv.83829542,d.dGY&psig=AFQjCNGcXLok6QE2xsnEgmhLDxW\\_N75JwA&ust=1421678301922326&cad=rjt](http://www.google.co.kr/url?sa=i&rct=j&q=&esrc=s&source=images&cd=&ved=0CAUQjhw&url=http%3A%2F%2Fwww.methodistorthopedics.com%2Fswan-neck-deformity-of-the-finger&ei=esW7VNjnLMG7mgW5h4CQDw&bvm=bv.83829542,d.dGY&psig=AFQjCNGcXLok6QE2xsnEgmhLDxW_N75JwA&ust=1421678301922326&cad=rjt)



Tripoint splint

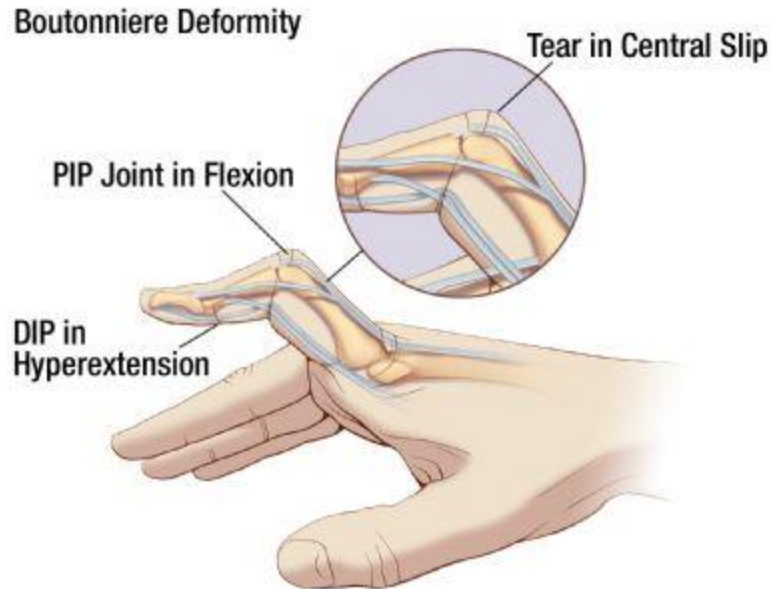


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# Boutonniere deformity

- PIP : flexion
- DIP : extension



- TX
  - <http://www.3pointproducts.com/boutonniere-deformity>

# Treatment

## 1. Surgery:

- Removal of inflamed synovium
- Arthroplasty

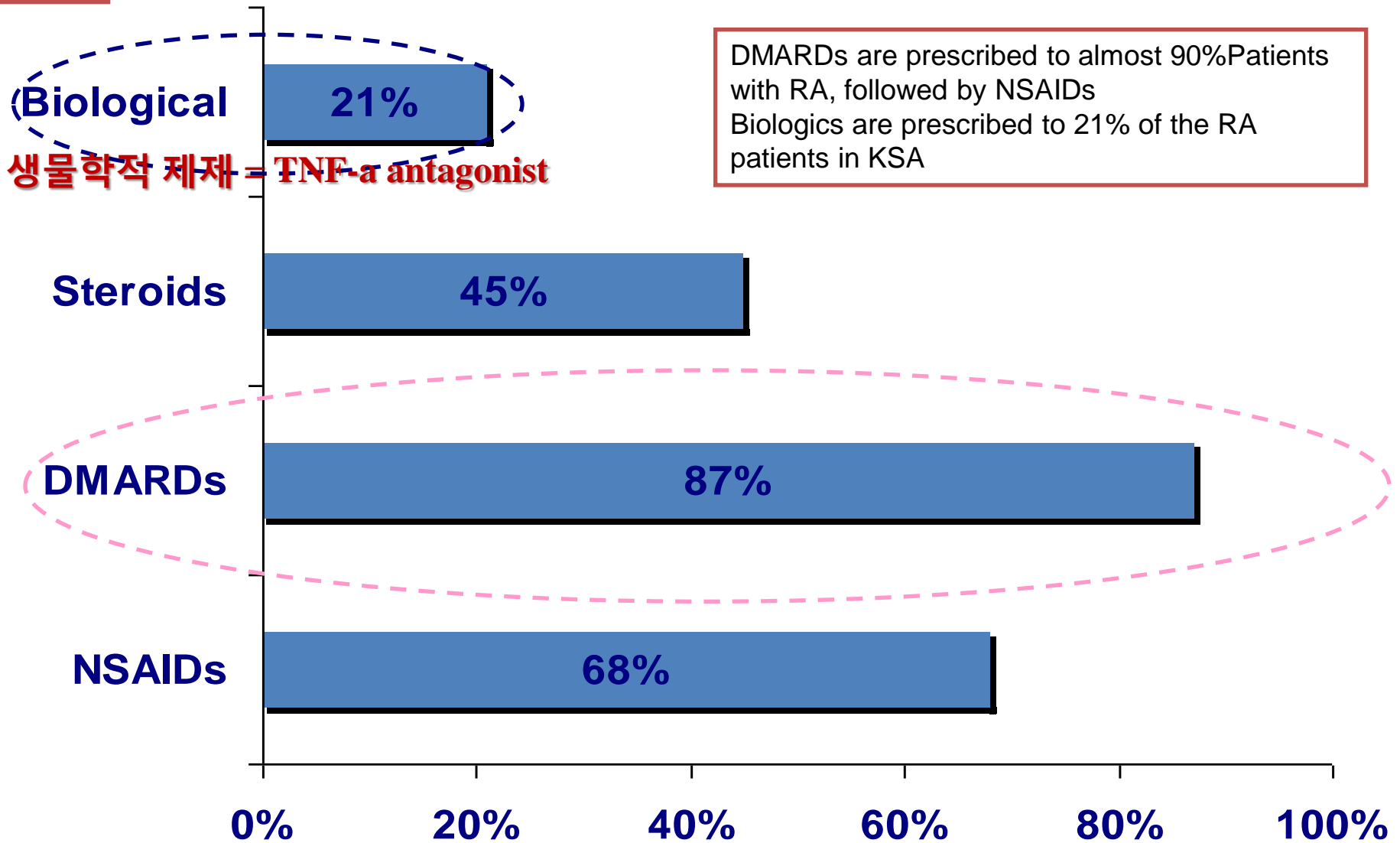
## 2. Medication

## 3. Physical therapy



Overall Prescription Shares of different therapeutic classes used in the  
treatment of Rheumatoid Arthritis (KSA)

(n=30)



# ● Treatment -1

- 치료목적
  - 통증의 완화, 염증의 감소
  - 관절구조의 보호, 기능 유지
  - 전신 침범의 조절
  
- 물리치료의 치료원칙
  1. 정상 관절 가동범위 유지
  2. 근력유지와 증강
  3. 변형 발생 방지와 교정
  4. 지속적인 안정치료
  5. 병의 진행을 정지, 감소
  
- Treatment materials
  1. Paraffin Bath : 국소부 적용 용이
  2. Hubbard Tank : RA가 전신으로 유발 시
  3. 침상 안정 : 딱딱한 침대

**안타깝게도 현재까지 RA 중재에 관련된 Physical therapy 보고는 현저하게 부족한 실정임.**

## ● Treatment -2

### ○ Exercise therapy (Tai chi)

First author (year)	Design, quality score, allocation concealment sample size (randomized or allocated/analysed)	Intervention (regimen)	Control	Main outcomes	Intergroup difference	Authors' conclusion
Wang (2005) [14]	RCT, 2, NR (20/20)	Tai chi (60min, twice weekly for 12 weeks, $n=10$ )	Education on nutrition and RA (40min), plus stretching exercise (20min) (twice weekly for 12 weeks, $n=10$ )	Pain (VAS) Disability Index Quality of life	NS $P=0.01$ Vitality, $P=0.01$	'Tai chi is a safe and potentially promising complementary therapy for adults with functional class I or II RA.'
Lee (2005) [17]	RCT, 2, NR (42/31)	Tai chi (60min, once weekly for 6 weeks, $n=21$ )	Usual activity ( $n=21$ )	Pain (VAS) Mood (Profile of Mood State) Fatigue	N.S. $P=0.02$ N.S.	'Six week tai chi program can be utilized as a safe and effective nursing program to improve mood and sleep disturbance in patients with RA.'
Kirsteins (1991) [19]*	CCT, 1, NR (47/31)	Tai chi (60min, once weekly for 10 weeks, $n=25$ ), plus home practice (20 min daily)	Usual activity ( $n=22$ )	Joint tenderness Functional assessment No. swollen joints 50-foot walk	NS NS NS NS	'Tai chi appears to be safe for RA patients and may serve as an alternative for their exercise therapy and part of their rehabilitation program.'
Kirsteins (1991) [19]*	CCT, 1, NR (28/22)	Tai chi (60min, twice weekly for 10 weeks, $n=18$ ), plus home practice (20 min daily)	Usual activity ( $n=10$ )	Joint tenderness Functional assessment No. swollen joints 50-foot walk	NS NS NS $P=0.01$	'Same as above'
Lee (2006) [18]	CCT, 0, NR (80/61)	Tai chi (50min, once weekly for 12 weeks, $n=40$ )	Usual activity ( $n=40$ )	Pain (VAS) Fatigue	$P<0.01$ $P=0.002$	'Both hydrotherapy and tai chi classes provide symptomatic benefit for older people with chronic hip or knee osteoarthritis.'

## **The fluence effects of low-level laser therapy on inflammation, fibroblast-like synoviocytes, and synovial apoptosis in rats with adjuvant-induced arthritis.**

Hsieh YL<sup>1</sup>, Cheng YJ, Huang FC, Yang CC.

### **Author information**

### **Abstract**

**Abstract Objective:** The aim of this study was to evaluate the effect of low-level laser therapy (LLLT) operating at low and high fluences on joint inflammation, fibroblast-like synoviocytes (FLS), and synovial apoptosis in rats with adjuvant-induced arthritis.

**BACKGROUND DATA:** Rheumatoid arthritis (RA) is characterized by pronounced inflammation and FLS proliferation within affected joints. Certain data indicate that LLLT is effective in patients with inflammation caused by RA; however, the fluence effects of LLLT on synovium are unclear.

**METHODS:** Monoarthritis was induced in adult male Sprague-Dawley rats (250-300 g) via intraarticular injection of complete Freund's adjuvant (CFA) into the tibiotarsal joint. Animals were irradiated 72 h after CFA administration with a 780 nm GaAlAs laser at 4.5 J/cm<sup>2</sup> (30 mW, 30 sec/spot) and 72 J/cm<sup>2</sup> (80 mW, 180 sec/spot) daily for 10 days. After LLLT, the animals were euthanized and their arthritic ankles were collected for histopathological analysis, immunoassays of tumor necrosis factor (TNF)- $\alpha$ , matrix metalloproteinase (MMP)3 and 5B5, and terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assays.

**RESULTS:** LLLT at a fluence of 4.5 J/cm<sup>2</sup> significantly reduced infiltration of inflammatory cells and expressions of TNF- $\alpha$ , MMP3- and 5B5-like immunoreactivities, as well as resulting in more TUNEL-positive apoptotic cells in the synovium. No significant changes were observed in these biochemicals and inflammation in arthritic animals treated with 72 J/cm<sup>2</sup>.

**CONCLUSIONS:** LLLT with low fluence is highly effective in reducing inflammation to sites of injury by decreasing the numbers of FLS, inflammatory cells, and mediators in the CFA-induced arthritic model. These data will be of value in designing clinical trials of LLLT for RA.

# PT for managing RA in the Clinics

- Paraffin bath
  - <http://www.youtube.com/watch?v=8tXrNB6pyAw>
- Pain management
  - TENS
  - Therapeutic ultrasound
  - Laser therapy
- Exercise for increasing muscle strength

# RA 관련 사진들



# Stages of RA

Early RA

Intermediate RA

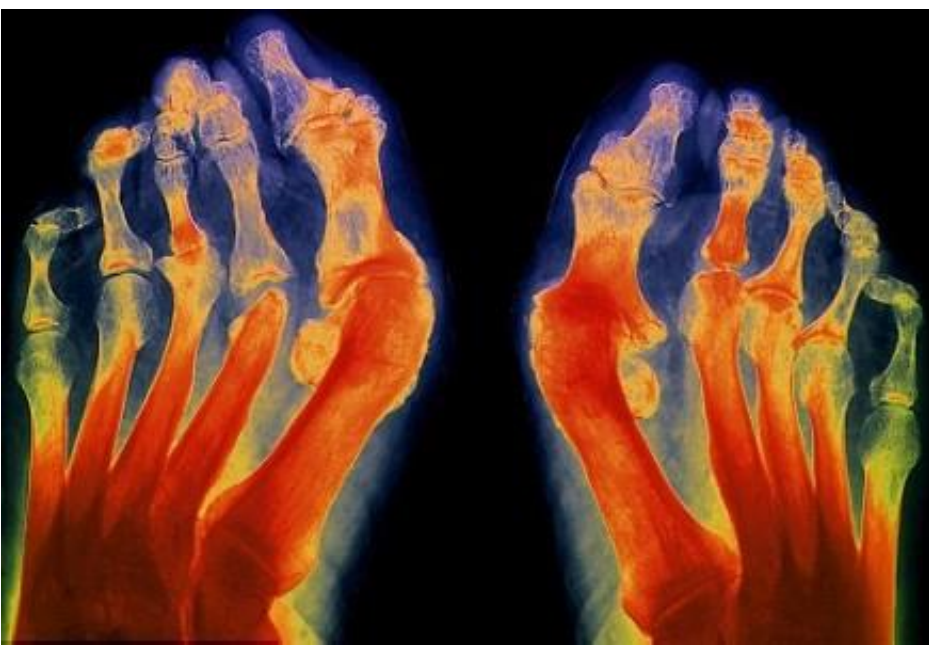
Late RA



[http://www.bodybuilding.com/fun/images/2009/manage\\_rheumatoid\\_arthritis\\_b.jpg](http://www.bodybuilding.com/fun/images/2009/manage_rheumatoid_arthritis_b.jpg)

<http://www.paleoterran.com/journal/2012/5/1/rheumatoid-arthritis-is-associated-with-obesity.html>





<http://www.scenartherapist.co.uk/CONDITIONS-+-CASES/CONDITIONS/Rheumatoid-Arthritis-Scenar-Brighton-Lewes-London-Kent-Sussex.html>

[http://www.medicinenet.com/rheumatoid\\_arthritis\\_pictures\\_slideshow/article.htm](http://www.medicinenet.com/rheumatoid_arthritis_pictures_slideshow/article.htm)



# **Osteoarthritis**

# OA symptoms of our living

- Your mother, who is **overweight**, has **pain** in both knees whenever she walks too far. Her knees are **stiff in the morning** and **hurt before it rains**. The pain gets better when she rests or takes acetaminophen, ibuprofen, or naprosyn over the counter. Her knees are **big, bony**, and sometimes **swollen**, but don't get red or warm.

# Osteoarthritis (OA)

- Osteoarthrosis or degenerative joint disease (DJD)

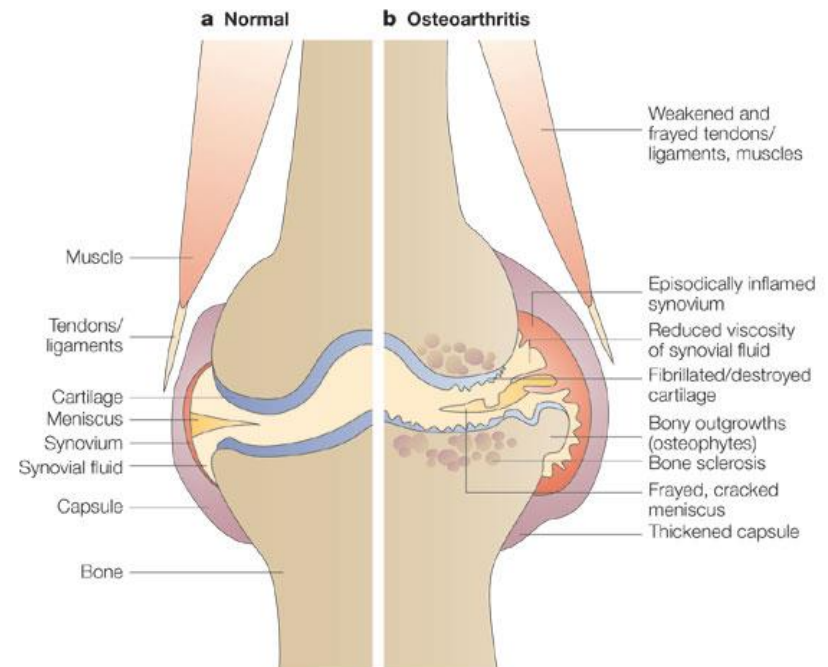
- Progressive disorder of the joints caused by gradual loss of cartilage
- Development of bony spurs and cysts at the margins of the joints

- Osteoarthritis = degenerative joint disease = hypertrophic arthritis = 노인성 관절염

- OA : Ankylosis (초기, 후기 모두 나타남)

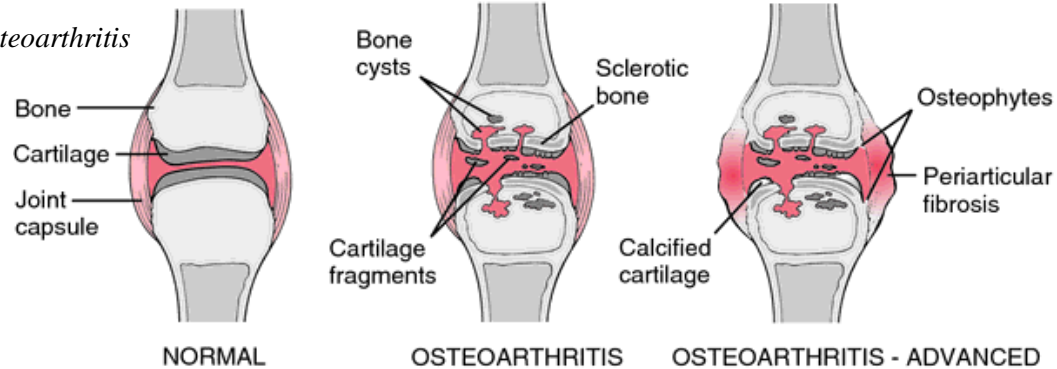
- Asymmetrical features

- <http://www.youtube.com/watch?v=IKC52uY>



# Risk factors for OA. (Kraus, 1997)

1. Age older than 50
2. Crystals in joint fluid or cartilage
3. High bone mineral density
4. History of immobilistaion
5. Injury to the joint
6. Joint hypermobility or instability
7. Obesity (weight-bearing joints)
8. Peripheral neuropathy
9. Prolonged occupational or sports stress



## ● 병리소견

- OA는 보통 관절연골의 체중부하를 많이 받는 곳
- 초기에는 연골이 정상보다 두꺼워지지만 진행될수록 관절면이 얇아지고 연골이 부드러워지며, 갈라지면서 수직의 틈이 발생 (fibrillation)
- 뼈까지 확장되는 심부연골 궤양이 발생할 수 있음
- 뼈의 remodeling과 hypertrophy
  - 연골 하 지역에서 뼈의 성장 → 방사선적으로 bony "sclerosis" 유발
  - 연골궤양 아래의 박리된 뼈 → ivory (상아) 모양
  - 관절 경계부위에서 연골과 뼈의 성장 → osteophytes (spurs) 형성 → 관절운동 제한
- 관절주위 근육의 위축
  - 흔하고 증상을 유발하는데 중요한 역할

# Classification

- Grade 0 : normal radiograph
- Grade 1 : doubtful narrowing of the joint space & possible osteophyte
- Grade 2 : definite osteophytes & joint space narrowing of the joint space
- Grade 3 : moderate osteophytes & joint narrowing, some sclerosis, and possible deformities
- Grade 4 : large osteophytes & joint narrowing, some sclerosis, and definite deformities



Figure 1



Figure 2



## ● 임상증상

### ○ 관절통

- 흔히 침범된 관절에 국한된 심부통증으로 묘사
- 전형적으로 관절을 움직이면 악화되고 쉬면 완화
- 관절 연골은 신경이 없어 관절통은 다른 구조물들에 의해 발생

### ○ 침범된 관절의 **stiffness**

- 아침에 일어나거나 오랫동안 움직이지 않은 후에 발생

### ○ 이학적 소견

- 침범된 부위의 압통과 뼈의 연부조직의 종창
- **Bony crepitus** (마찰음)
  - ❖ 관절을 움직일 때 유발되는 뼈가 비벼지는 느낌
- 촉진 시 침범된 관절 위로 온기가 느껴진다.
- 관절주위의 근육위축
- 많이 진행된 경우
  - ❖ 육안적 기형, 뼈의 비대, **Subluxation** (아탈구)
  - ❖ 관절운동의 심한 제한

- Interphalangeal joint의 OA

- Heberden's node
- Gelatinous dorsal cysts
- Bouchard's node

- Erosive (미란성) OA

- 미란성 OA는 **DIP** 또는 PIP joints 에서 가장 많이 발생
- Bony ankylosis가 발생할 수 있다.
- 관절 기형과 기능 장애

- 전신성 OA

- 3개 이상의 관절이나 관절군 침범
- 증상은 산발적이고 연부조직의 종창, 발적

- Thumb base

- OA에서 두번째로 가장 흔히 침범되는 부위
- 종창, 압통, 그리고 관절 운동시 crepitus가 전형적

- Common spots of osteoarthritis

- ✓남자 : hip > knee > spine > ankle joint > shoulder

- ✓여자 : knee > phalynger joint > spine > hip > ankle > shoulder

- ✓하지 : 슬관절, 고관절

- ✓상지 : 견관절, 원위지절관절

- ✓척추 : 요추, 경추

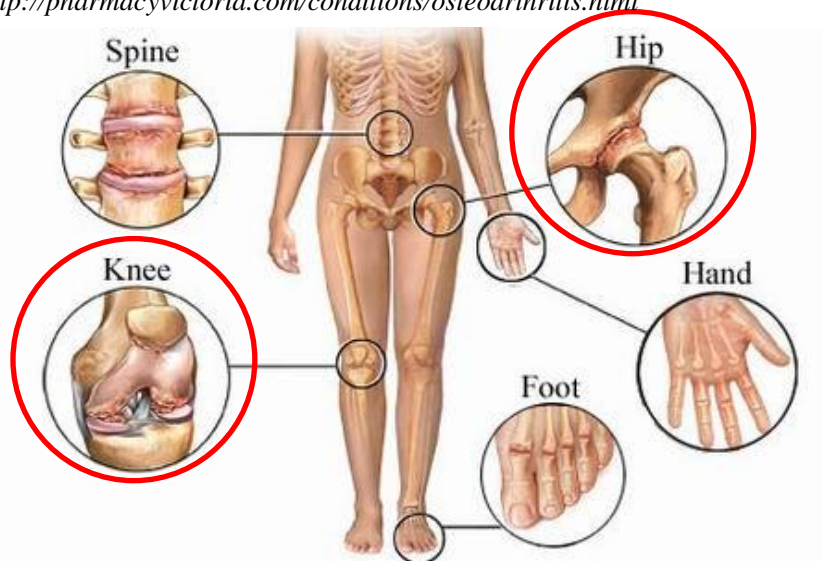


# Degeneration

- Metabolism imbalance [Main]
  - Catabolism > anabolism
- Muscle imbalance
- Overuse
- Et al..

# • Site and causes of OA

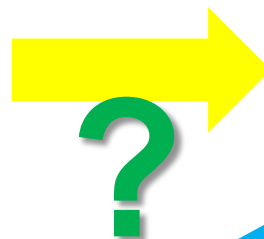
<http://pharmacyvictoria.com/conditions/osteoarthritis.html>



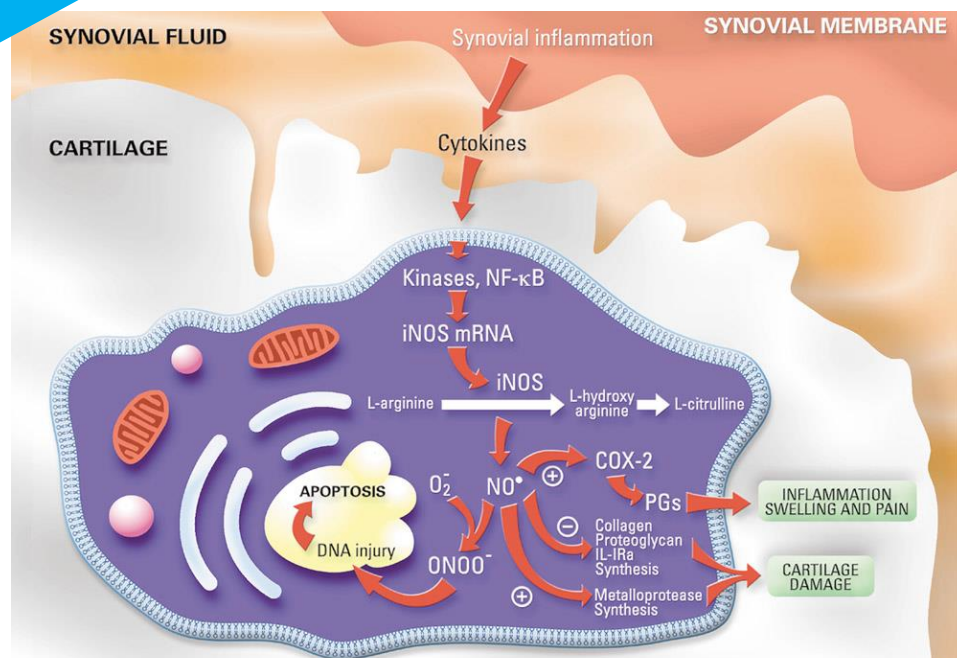
## Weight-bearing joints



## Inducible Nitric Oxide Synthase



**Metabolic imbalance in extracellular matrix of cartilage**  
- **Catabolism** > **anabolism**



## Altered Cortical Processing

- Affective, cognitive integration

## Pain generation

- ✓ Central neuropathic pain
- ✓ Referred pain

- ✓ Dysfunction of descending noxious inhibitory control

## Altered Spinal Cord Gating

- ✓ iNOS, COX, mGluR, NR2B, Opioids, CCR

## Peripheral Nervous System

- ↑ innervation density
- ↑ receptor & neuropeptide expression

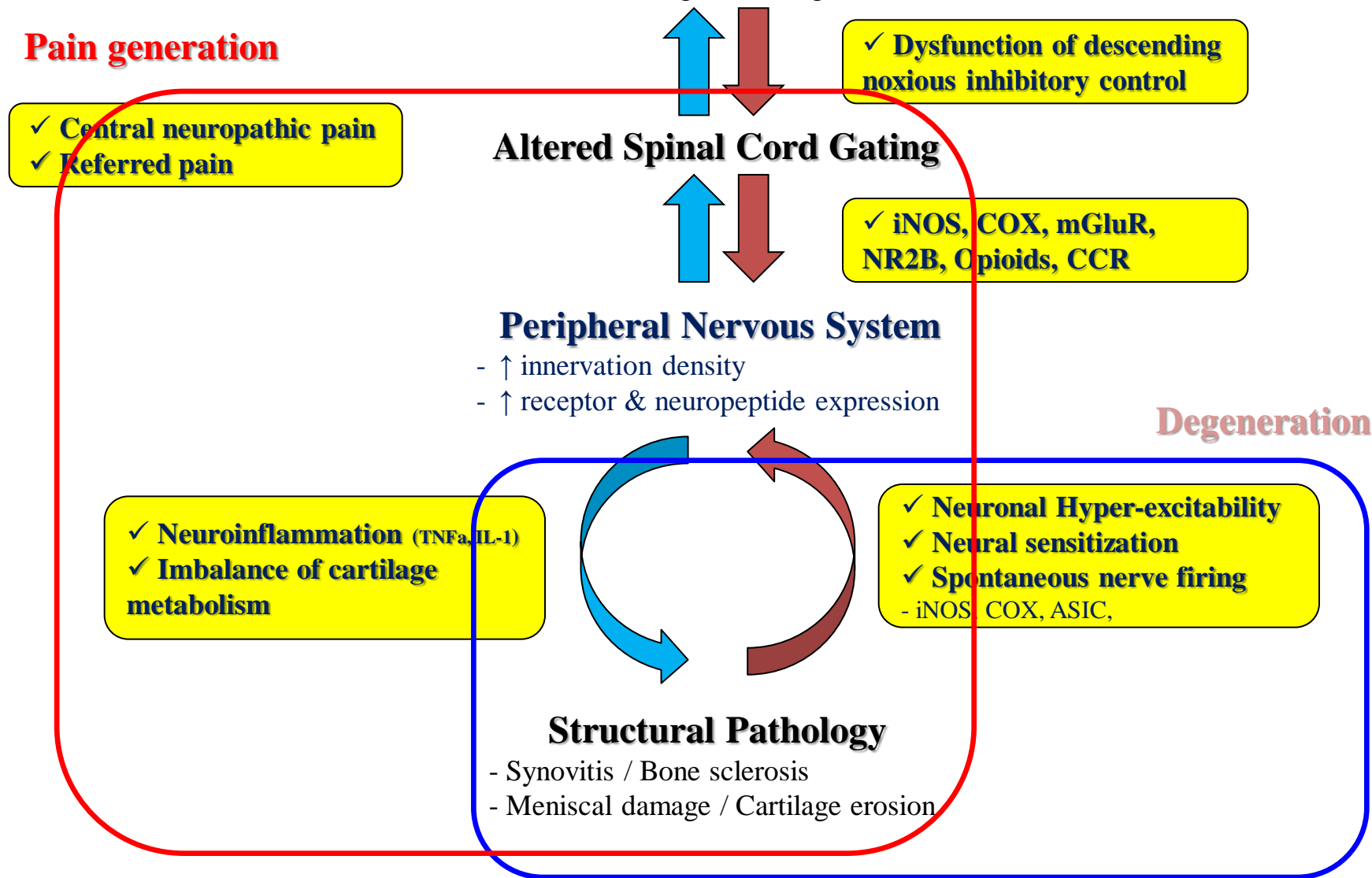
## Degeneration

- ✓ Neuroinflammation (TNF $\alpha$ , IL-1)
- ✓ Imbalance of cartilage metabolism

- ✓ Neuronal Hyper-excitability
- ✓ Neural sensitization
- ✓ Spontaneous nerve firing
- iNOS, COX, ASIC,

## Structural Pathology

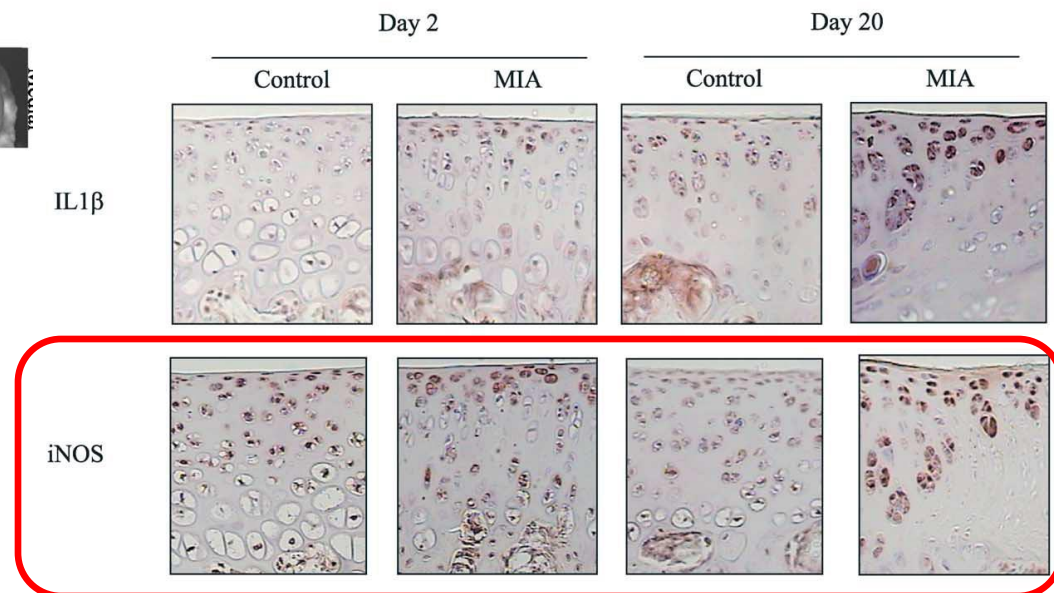
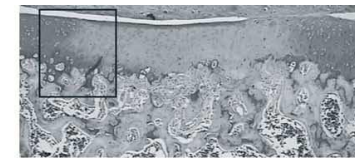
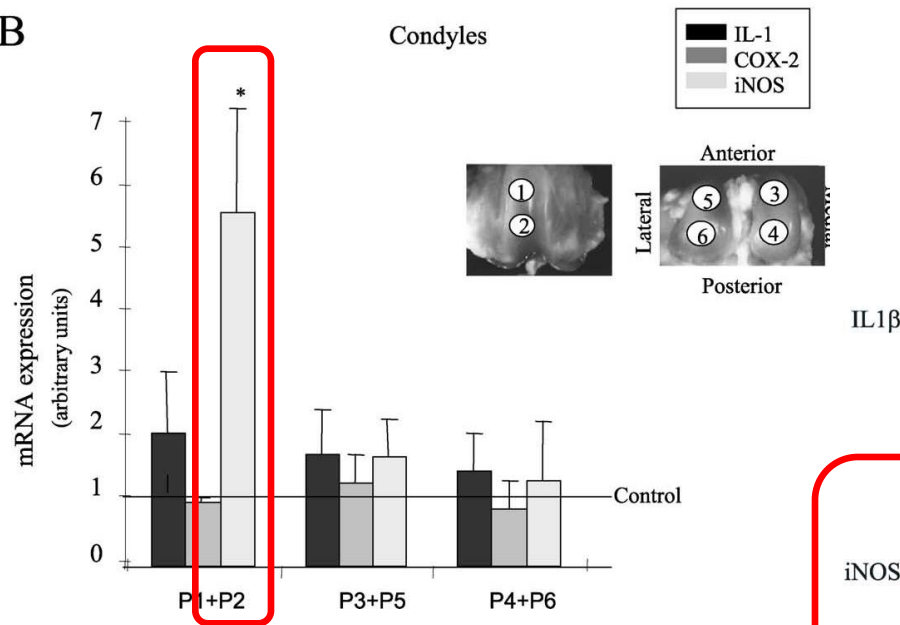
- Synovitis / Bone sclerosis
- Meniscal damage / Cartilage erosion



# Interrelation between iNOS and OA

- Dumond H (2004) Osteoarthritis and cartilage, 12:284-295.
  - MIA 0.03 mg i.a. in rats
  - iNOS expression  $\uparrow$  in cartilage at post-injection day 2 and 20. = cartilage degeneration

B





# Muscle imbalance related with Arthritis

## Altered hamstring-quadiceps muscle balance in patients with knee osteoarthritis

Tibor Hortobágyi <sup>a,\*</sup>, Lenna Westerkamp <sup>a</sup>, Stacey Beam <sup>a</sup>, Jill Moody <sup>a</sup>, Joseph Garry <sup>b</sup>,  
Donald Holbert <sup>c</sup>, Paul DeVita <sup>a</sup>

<sup>a</sup> Biomechanics Laboratory, East Carolina University, 332A Ward Sports Medicine Building, Greenville, NC 27858, USA

<sup>b</sup> Departments of Family Medicine, East Carolina University, Greenville, NC 27858, USA

<sup>c</sup> Departments of Biostatistics, East Carolina University, Greenville, NC 27858, USA

Received 19 March 2004; accepted 18 August 2004

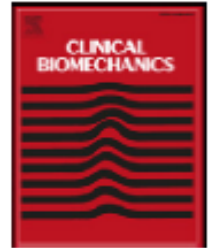
- Two ms coactivity : OA > healthy subjects
- Muscle activation in OA
  - Biceps femoris > quadriceps
- Biceps femoris activation in OA pts.
  - 92 % (healthy persons : 47~57%)



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## Muscle activations to stabilize the knee following arthroscopic partial meniscectomy<sup>☆</sup>

Daina L. Sturnieks<sup>a,b,\*</sup>, Thor F. Besier<sup>c</sup>, David G. Lloyd<sup>a</sup>

<sup>a</sup> School of Sports Science, Exercise and Health, The University of Western Australia, Perth, Australia

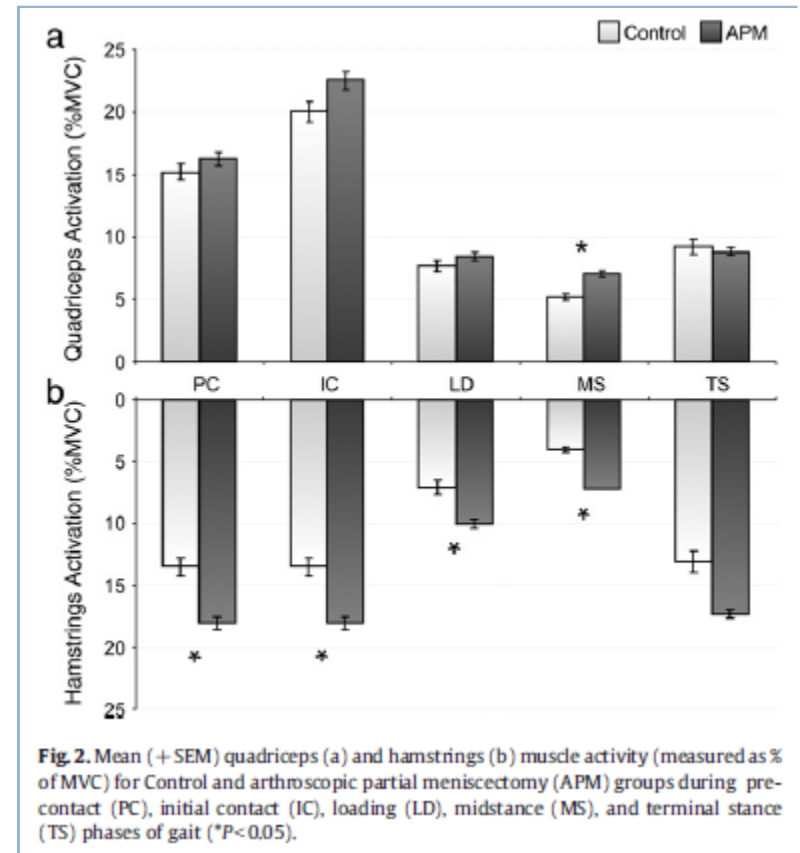
<sup>b</sup> Neuroscience Research Australia, Sydney, Australia

<sup>c</sup> Department of Orthopaedics, Stanford University, Stanford, USA

- Partial meniscectomy (PM)
  - High risk of developing knee OA
  - Weak quadriceps, larger than normal knee adduction moments = tend to load the medial tibiofemoral joint

# Sturnieks et al. (2011)

- Increased hamstrings activation while walking.
- No difference in direct co-contraction.



# Osteoarthritis Measurement Scales

- Western Ontario and McMaster Osteoarthritis Index (WOMAC)
  - Questionnaire with twenty four questions about pain, function, and stiffness
- Visual Analogue Scale
  - 100 mm long line with descriptive words (no pain / worst pain ever felt) on either side
- Lequesne Index
  - Questionnaire 11 questions that ask about the patient's symptoms and functional ability

# Review of Literature

- Exercise Related Therapy
- Pharmaceutical therapy
- Various procedures performed to relieve symptoms

# Exercise Therapy

- Indicated for mild to moderate osteoarthritis
- Water therapy – Very effective
  - Good for elderly patients
- Exercise training – Effective
  - Improvements in both knee and hip patients
- Weight loss – Effective
  - Weight loss groups improved over weight stable group

(All studies had statistically significant results on the scales discussed earlier)

# Pharmaceutical therapy

- Indicated for mild, moderate, and severe
- NSAIDS – Very common
- Transdermal Fentanyl
  - Indicated when NSAIDS, weak opioids don't work
- Glucosamine
  - Improves repair process and formation of cartilage

(All studies had statistically significant results on the scales discussed earlier)

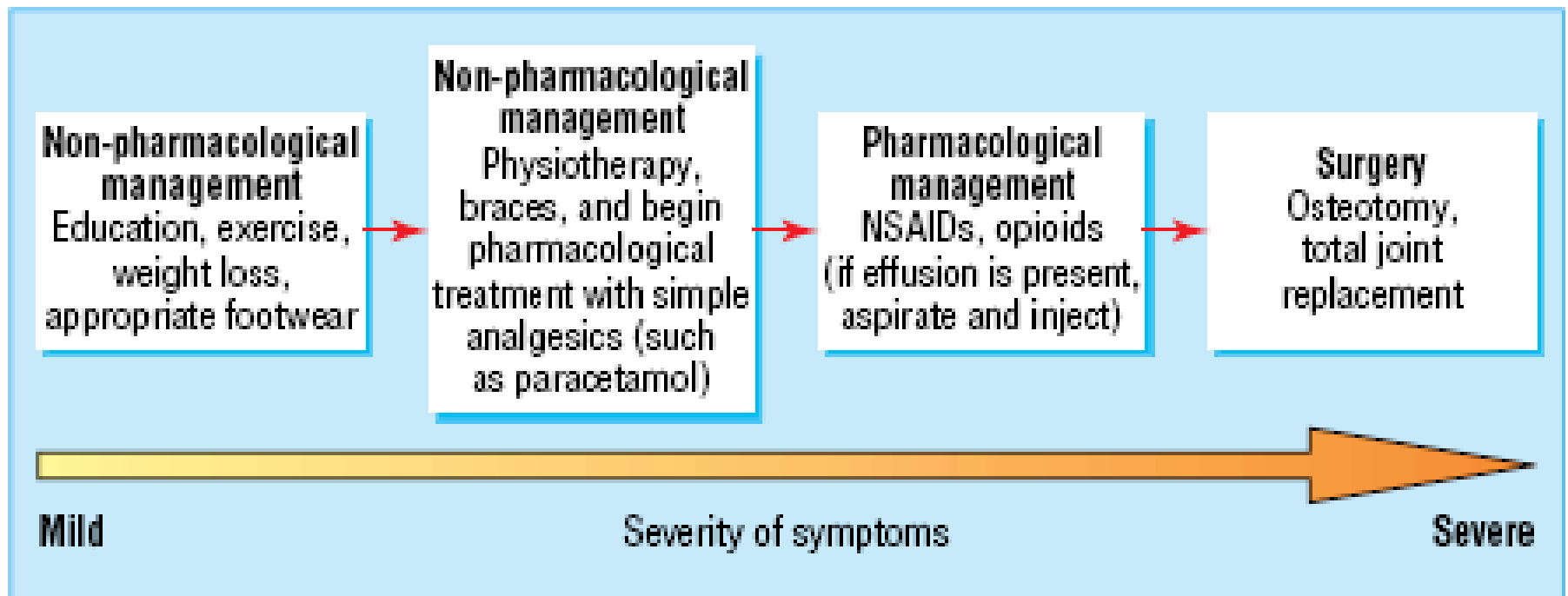


# Various Procedures

- Joint Replacement Surgery
  - Improved pain and overall patient well being



# Treatment Overview



**Fig 3** Stepwise algorithm for the management of patients with osteoarthritis. This is an example of a treatment algorithm that is modified according to patient's response and clinician's preference. It highlights the encompassing need to consider non-pharmacological management as first line for all patients

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- Google images

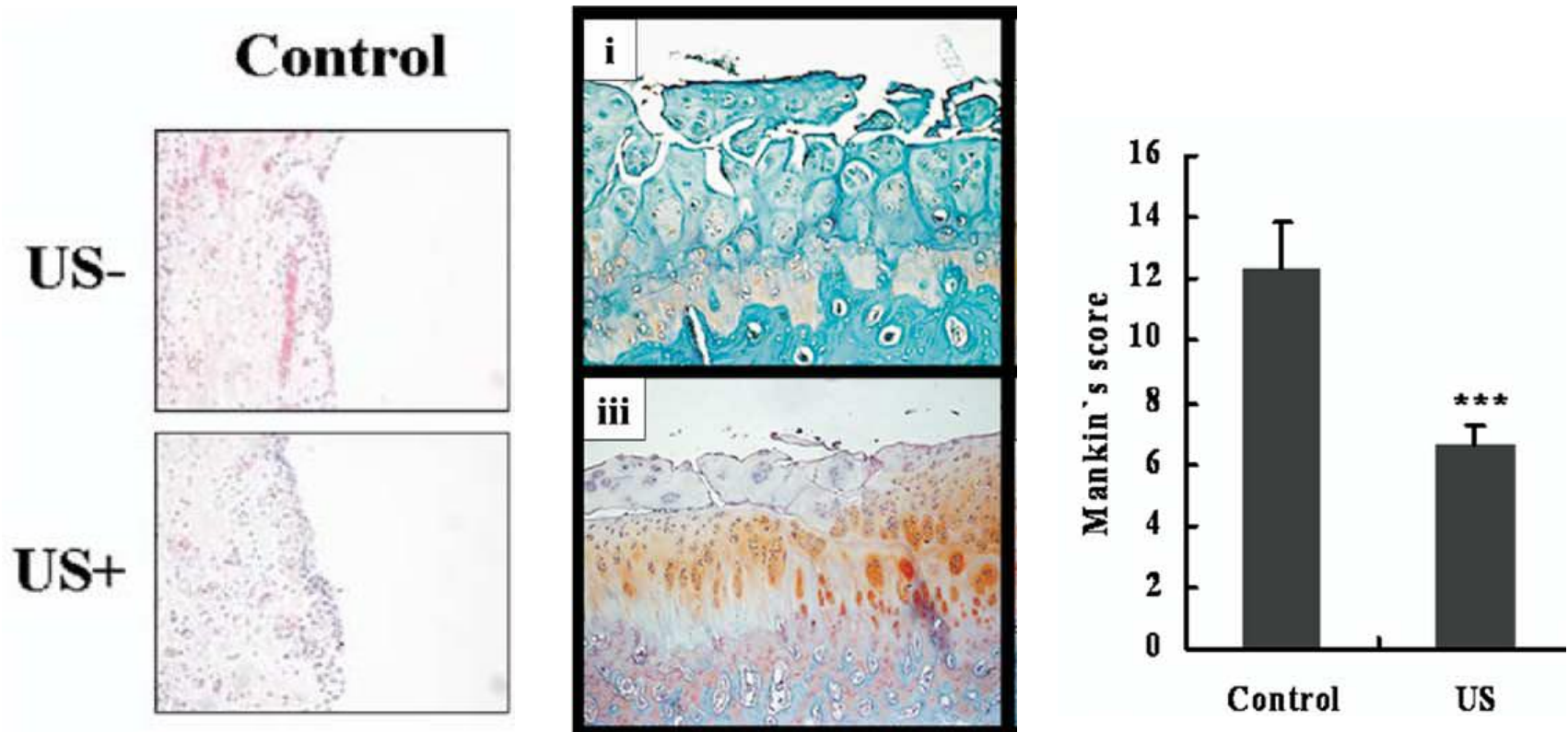
# Treatment of OA

- Muscle strengthening exercise
  - Quadriceps
    - Treadmill Ex, N-K table, Stair board
  - Q-setting exercise
    - Vastus medialis
    - Cast status: can
- <http://www.youtube.com/watch?v=sN6wwkT7qxs>

PT materials to  
treat OA

# Therapeutic effects of LIPUS on articular cartilage damage

- Park (2005) Ultrasound in Med. & Biol., 31(11):1559-1566.
  - Anterior-cruciate ligament and menisectomy transection (ACLMT)-induced OA rabbit
  - 1 MHz, 400 mW/cm<sup>2</sup>, for 10 min bid. During 4 weeks.



**Authors:**

Nuri Cetin, MD  
Aydan Aytar, PT, MSc  
Ayce Atalay, MD  
Mahmut Nafiz Akman, MD

*Knee Osteoarthritis*

**Affiliations:**

From the Department of Physical Medicine and Rehabilitation, Baskent University Faculty of Medicine, Ankara, Turkey (NC, A Atalay, MNA); and Department of Physical Therapy and Rehabilitation, Baskent University Faculty of Health Sciences, Ankara, Turkey (A Aytar).

**Correspondence:**

All correspondence and requests for reprints should be addressed to Nuri Cetin, MD, Bahcelievler 5. sok no: 48, 06490, Cankaya, Ankara, Turkey.

0894-9115/08/8706-0443/0

**ORIGINAL RESEARCH ARTICLE**

# Comparing Hot Pack, Short-Wave Diathermy, Ultrasound, and TENS on Isokinetic Strength, Pain, and Functional Status of Women with Osteoarthritic Knees

A Single-Blind, Randomized, Controlled Trial

- Group 1 : SWD + HP + isokinetic exercise
- Group 2 : TENS + HP + isokinetic exercises
- Group 3 : US + HP + isokinetic exercises
- Group 4 : HP + isokinetic exercises
- Group 5 : only isokinetic exercises

**TABLE 2** VAS, WT, and LI scores at baseline and at the end of the study period, and the group differences

	Group 1	Group 2	Group 3	Group 4	Group 5	<i>P</i>
Baseline VAS	5.69 ± 1.55	5.85 ± 1.34	5.90 ± 1.45	5.76 ± 1.48	5.93 ± 1.15	0.888
Final VAS	3.36 ± 1.33	3.52 ± 1.18	3.55 ± 1.41	3.49 ± 1.28	4.10 ± 1.32	0.325
Δ VAS	2.33 ± 0.77	2.32 ± 0.60	2.34 ± 0.94	2.27 ± 0.88	1.83 ± 1.32	0.019*
<i>P</i>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	
Baseline WT	51.35 ± 6.49	52.95 ± 10.77	53.10 ± 9.84	49.65 ± 6.93	49.70 ± 10.17	0.727
Final WT	39.90 ± 6.47	42.40 ± 8.40	42.60 ± 11.50	40.60 ± 6.04	39.95 ± 8.89	0.812
Δ WT	11.45 ± 5.78	10.55 ± 4.70	10.50 ± 3.85	9.05 ± 4.48	9.75 ± 3.86	0.589
<i>P</i>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	
Baseline LI	10.95 ± 2.73	11.70 ± 1.93	11.40 ± 2.45	10.77 ± 3.12	10.80 ± 1.56	0.582
Final LI	6.81 ± 2.69	7.22 ± 2.06	7.67 ± 2.30	6.87 ± 2.58	7.72 ± 2.06	0.562
Δ LI	4.14 ± 1.24	4.47 ± 1.11	3.72 ± 1.08	3.90 ± 1.15	3.07 ± 1.38	0.018*
<i>P</i>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	

VAS, visual analog scale; WT, walking time; LI, Lequesne index.

Values are expressed as means ± standard deviations.

<sup>‡</sup> Significant differences in VAS, WT, and LI in each group after treatment ( $P < 0.05$ ). *P* values are computed using the Wilcoxon test.

\* Significant differences in VAS and LI in each group when compared with group 5 ( $P < 0.05$ ). *P* values are computed using the Kruskal-Wallis test.

**TABLE 4** Mean peak torque values for right knee flexion in each group before and after treatment (N·m)

Angular Velocity	Time	Group 1	Group 2	Group 3	Group 4	Group 5	<i>P</i>
60 degrees	Baseline	16.80 ± 3.69	17.35 ± 6.32	17.15 ± 7.02	17.00 ± 7.92	16.55 ± 4.88	0.001*
	Final	27.30 ± 7.80	25.50 ± 6.43	25.75 ± 8.03	27.95 ± 9.28	18.80 ± 6.31	
	Δ	10.50 ± 8.56	8.15 ± 6.08	8.60 ± 4.90	10.95 ± 6.78	2.25 ± 6.85	
	<i>P</i>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.178	
120 degrees	Baseline	13.70 ± 4.41	13.95 ± 3.85	13.50 ± 6.17	14.00 ± 6.75	12.70 ± 4.74	0.0001*
	Final	23.60 ± 7.42	23.75 ± 4.39	21.35 ± 7.09	23.60 ± 9.51	14.85 ± 6.37	
	Δ	9.90 ± 6.72	9.80 ± 4.46	7.85 ± 4.42	9.60 ± 6.89	2.15 ± 6.39	
	<i>P</i>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.107	
180 degrees	Baseline	11.30 ± 5.03	12.05 ± 5.44	11.95 ± 6.03	12.05 ± 4.25	11.40 ± 4.50	0.022*
	Final	19.50 ± 8.12	18.45 ± 5.77	18.35 ± 5.41	19.75 ± 9.28	13.60 ± 7.07	
	Δ	8.20 ± 7.97	6.40 ± 6.73	6.40 ± 5.37	7.70 ± 7.42	2.20 ± 5.89	
	<i>P</i>	0.0001 <sup>‡</sup>	0.001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.001 <sup>‡</sup>	0.097	

<sup>‡</sup> Significant differences in mean peak torque values for right knee flexion in groups 1–4 after treatment ( $P < 0.05$ ). *P* values are computed using the Wilcoxon test.

\* Significant differences of change in mean peak torque values for right knee flexion between groups ( $P < 0.05$ ). *P* values are computed using the Kruskal-Wallis test.

**TABLE 5** Mean peak torque values for left knee extension in each group before and after treatment (N·m)

Angular Velocity	Time	Group 1	Group 2	Group 3	Group 4	Group 5	<i>P</i>
60 degrees	Baseline	32.50 ± 7.81	35.30 ± 12.11	31.10 ± 11.50	33.25 ± 11.09	35.65 ± 10.82	0.0001*
	Final	53.65 ± 12.95	54.05 ± 14.36	50.60 ± 12.98	44.20 ± 13.97	44.90 ± 12.65	
	Δ	21.15 ± 11.83	18.75 ± 11.36	19.50 ± 10.63	10.95 ± 10.78	5.25 ± 5.19	
	<i>P</i>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.001 <sup>‡</sup>	
120 degrees	Baseline	26.55 ± 9.49	28.35 ± 9.54	25.60 ± 9.88	26.05 ± 8.12	27.15 ± 11.45	0.0001*
	Final	47.25 ± 12.52	44.85 ± 11.40	42.65 ± 12.04	36.50 ± 12.20	32.65 ± 12.36	
	Δ	20.70 ± 11.84	16.50 ± 11.50	17.05 ± 9.91	10.45 ± 9.33	5.50 ± 5.79	
	<i>P</i>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.001 <sup>‡</sup>	0.003 <sup>‡</sup>	
180 degrees	Baseline	24.10 ± 9.87	24.85 ± 10.54	22.80 ± 9.30	22.75 ± 9.02	23.95 ± 10.21	0.002*
	Final	42.25 ± 12.18	38.70 ± 14.25	35.70 ± 11.81	32.95 ± 13.04	28.35 ± 9.28	
	Δ	18.15 ± 13.27	13.85 ± 11.05	12.90 ± 9.92	10.20 ± 10.88	4.40 ± 5.44	
	<i>P</i>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.0001 <sup>‡</sup>	0.002 <sup>‡</sup>	0.005 <sup>‡</sup>	

<sup>‡</sup> Significant differences in mean peak torque values for left knee extension in each group after treatment ( $P < 0.05$ ). *P* values are computed using the Wilcoxon test.

\* Significant differences of change in mean peak torque values for left knee extension between groups ( $P < 0.05$ ).



## TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION AT BOTH HIGH AND LOW FREQUENCIES ACTIVATES VENTROLATERAL PERIAQUEDUCTAL GREY TO DECREASE MECHANICAL HYPERALGESIA IN ARTHRITIC RATS

J. M. DESANTANA,<sup>a\*</sup> L. F. S. DA SILVA,<sup>b</sup>  
M. A. DE RESENDE<sup>c</sup> AND K. A. SLUKA<sup>b</sup>

<sup>a</sup>*Department of Physical Therapy, Federal University of Sergipe, Cidade Universitária Professor José Aloísio de Campos, Av. Marechal Rondon, s/n, Jardim Rosa Elze, São Cristóvão/Sergipe, Brazil*

<sup>b</sup>*Physical Therapy and Rehabilitation Science Graduate Program, Pain Research Program, University of Iowa, Iowa City, IA, USA*

<sup>c</sup>*Department of Physical Therapy, Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil*

The midbrain periaqueductal grey (PAG) surrounds the midbrain aqueduct (Osborne et al., 1996) and is implicated in a wide variety of functions including opioid-mediated analgesia (Gebhart et al., 1988; Fields et al., 1991; Osborne et al., 1996; Vaughan and Christie, 1997). Two separate, and distinct, nociceptive modulatory systems operate in the caudal PAG: a dorsal system which encompasses the dorsomedial, dorsolateral and lateral subdivisions of the PAG; and a ventral system which includes the

Abstract—Transcutaneous electric nerve stimulation (TENS) is widely used for the treatment of pain. TENS produces an opioid-mediated antinociception that utilizes the rostroventromedial medulla (RVM). Similarly, antinociception evoked from the periaqueductal grey (PAG) is opioid-mediated and includes a relay in the RVM. Therefore, we investigated whether the ventrolateral or dorsolateral PAG mediates antinociception produced by TENS in rats. Paw and knee joint mechanical withdrawal thresholds were assessed before and after knee joint inflammation (3% kaolin/carrageenan), and after TENS stimulation (active or sham). Cobalt chloride ( $\text{CoCl}_2$ ; 5 mM) or vehicle was microinjected into the ventrolateral periaqueductal grey (vlPAG) or dorsolateral periaqueductal grey (dlPAG) prior to treatment with TENS. Either high (100 Hz) or low (4 Hz) frequency TENS was then applied to the inflamed knee for 20 min. Active TENS significantly increased withdrawal thresholds of the paw and knee joint in the group microinjected with vehicle when compared to thresholds prior to TENS ( $P < 0.001$ ) or to sham TENS ( $P < 0.001$ ). The increases in withdrawal thresholds normally observed after TENS were prevented by microinjection of  $\text{CoCl}_2$  into the vlPAG, but not the dlPAG prior to TENS and were significantly lower than controls treated with TENS ( $P < 0.001$ ). In a separate group of animals, microinjection of  $\text{CoCl}_2$  into the vlPAG temporarily reversed the decreased mechanical withdrawal threshold suggesting a role for the vlPAG in the facilitation of joint pain. No significant difference was observed for dlPAG. We hypothesize that the effects of TENS are mediated through the vlPAG that sends projections through the RVM to the spinal cord to produce an opioid-mediated analgesia.

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# Physiological effects of COLD

- General effects
  - ↓ Temperature of skin, muscle & joint
  - Blood flow : ↓, ↑
  - ↓ Inflammatory symptoms (Bugaj, 1995; Melzack, 1980; Farry, 1980)
  - ↑ Swelling (Farry, 1980)
  - ↓ Synovial fluid (Dorwart, 1974)

# Physiological effects of COLD

- Motor function
  - ↑ Joint function (Wright, 1960)
  - ↑ Grip strength (Heijde, 1989)
- Pain
  - Analgesia (Ernst, 1994; Bugaj, 1995)
  - Slow the conduction velocity of peripheral nerves (Lee JM, 1978; Abramson, 1966)
  - ↓ Pain (Melzack, 1980; Williams, 1986; Bulgen, 1984)

# Physiological effects of HEAT

- General effects
  - ↑ Temperature of skin & joint (Borrell, 1980)
  - ↑ Blood flow
  - ↓ Joint stiffness (Wright, 1960) or Not (Yung, 1986)
- Motor function
  - ↑ Grip strength (Heijde, 1989)
  - ↑ Joint function (Quirk, 1985)

# Physiological effects of HEAT

- Pain
  - ↓ (Quirk, 1985; Clarke, 1974)
  - ↑ or no change (Oosteveld, 1994; Nichols, 1994; Sambroski, 1992)
- Heat effects are more controversy than Cold effects... Why?
  - The temperature range of heat application are diverse
    - Warm bath : 35 - 40 °C
    - Paraffin bath : 126 F (50 °C)
    - Hot Pack : 55 – 60 °C (Post 20 min : 30 - 37 °C)

# Arthritis condition

- Intra-articular temperature
  - Healthy human knee : 32.8 °C (Haimovici, 1982)
  - In synovitis & inflammatory Dz : 35 ~36 °C (Oosterveld, 1994)
- Cartilage degrading enzyme activity
  - IL-1, IL-6, IL-8, metalloproteinases
  - ↓ 30 °C : ↓ activity (Oosterveld, 1992; Wolley, 1977; Harris, 1974)
  - 30 ~ 40 °C : ↑ activity (Castor, 1976)
  - ↑ 40 °C : ↓ activity (Castor, 1976; Harris, 1974)

# Interrelation between **LIPUS** and pain

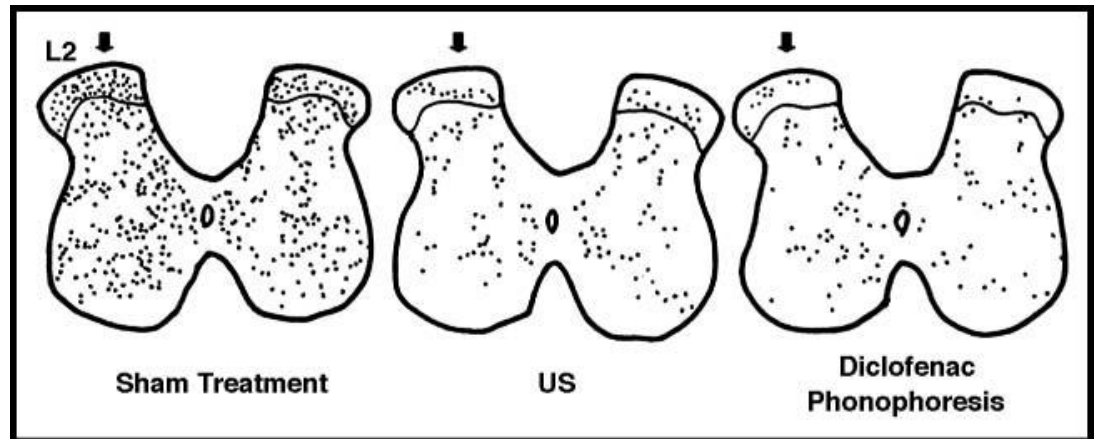
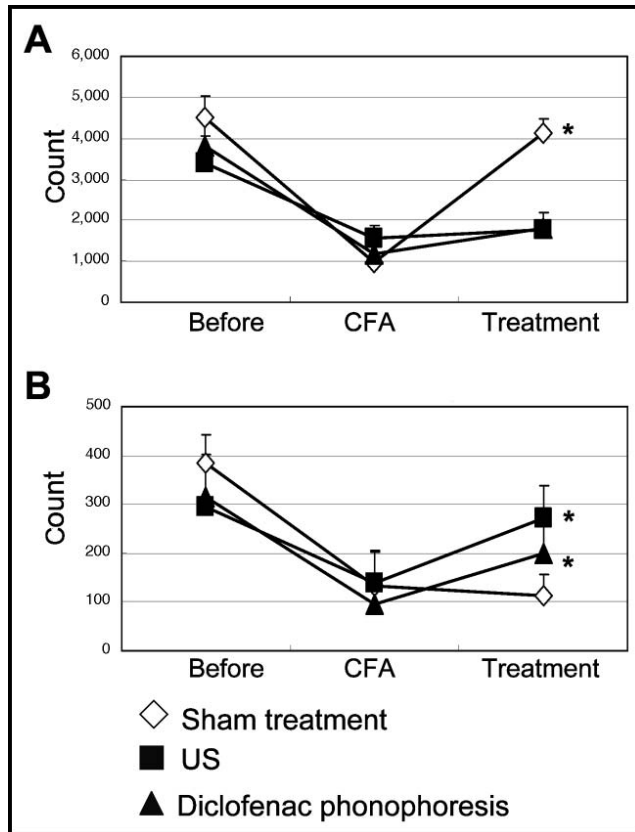
## •In animals

–Hsieh (2006) Phys Ther. 86:39-49.

➤ RA rats by CFA : once treated by LIUS

✓ 1 MHz, 0.5 W/cm<sup>2</sup>, 50% duty cycle for 5 minutes.

✓ At post-CFA injection 4h





- **Tai Chi exercise**

- **Effects of a Sun-style Tai Chi exercise on arthritic symptoms, motivation and the performance of health behaviors in women with osteoarthritis**

Taehan Kanho Hakhoe Chi. 2007 Mar;37(2):249-56

# Cardiovascular Response During Aquatic Exercise in Patients with Osteoarthritis

## ABSTRACT

Asahina M, Asahina MK, Yamanaka Y, Mitsui K, Kitahara A, Murata A: Cardiovascular response during aquatic exercise in patients with osteoarthritis. *Am J Phys Med Rehabil* 2010;89:731–735.

**Objective:** To assess the acute cardiovascular response to aquatic exercise in patients with osteoarthritis.

**Design:** Blood pressure (BP) and heart rate (HR) were measured in 13 female patients with osteoarthritis ( $63.3 \pm 8.4$  yrs) during aquatic walking for 40 mins. A double product (DP) value was calculated by multiplying systolic BP by HR to evaluate the workload of the heart.

**Results:** BP and DP increased transiently with a decrease in HR after water immersion. Aquatic walking induced increases in BP, DP, and HR. Furthermore, BP and DP increased sharply with an increase in HR on leaving the water. The mean maximum increases in systolic BP and DP during each process were  $23.5 \pm 18.2$  mm Hg and  $2931.1 \pm 2758.5$  mm Hg/min when entering the water,  $36.5 \pm 16.5$  mm Hg and  $4557.2 \pm 3435.1$  mm Hg/min during aquatic walking, and  $38.5 \pm 18.9$  mm Hg and  $5132.3 \pm 3228.8$  mm Hg/min on leaving the water.

**Conclusions:** Water immersion, aquatic walking, and the process of leaving the water induced marked increases in BP in patients with osteoarthritis.

**Key Words:** Blood Pressure, Heart Rate, Autonomic Nervous System, Osteoarthritis, Aging

# Arthritis care : around tissues

Arthritis Care & Research  
Vol. 62, No. 8, August 2010, pp 1190–1193  
DOI 10.1002/acr.20199  
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## CONTRIBUTIONS FROM THE FIELD

# Hip Muscle Weakness in Individuals With Medial Knee Osteoarthritis

RANA S. HINMAN, MICHAEL A. HUNT, MARK W. CREABY, TIM V. WRIGLEY, FIONA J. McMANUS,  
AND KIM L. BENNELL

**Objective.** To compare the strength of the hip musculature in people with symptomatic medial knee osteoarthritis (OA) with asymptomatic controls.

**Methods.** Eighty-nine people with knee OA and 23 controls age >50 years were recruited from the community. The maximal isometric strength (torque relative to body mass) of the hip abductors, adductors, flexors, extensors, and internal and external rotators was evaluated using hand-held dynamometry or a customized force transducer apparatus. Univariate linear models with age and sex included as covariates were used to compare muscle strength between groups.

**Results.** In people with knee OA, significant strength deficits were evident for all hip muscle groups evaluated ( $P < 0.05$ ). Compared with controls, strength deficits ranged from 16% (hip extensors) to 27% (hip external rotators) after accounting for differences in sex and age between groups.

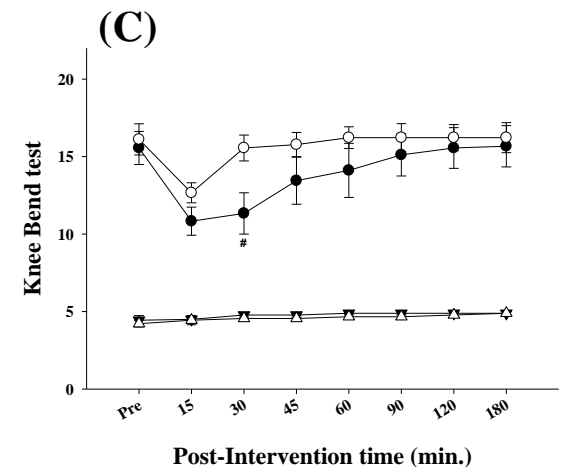
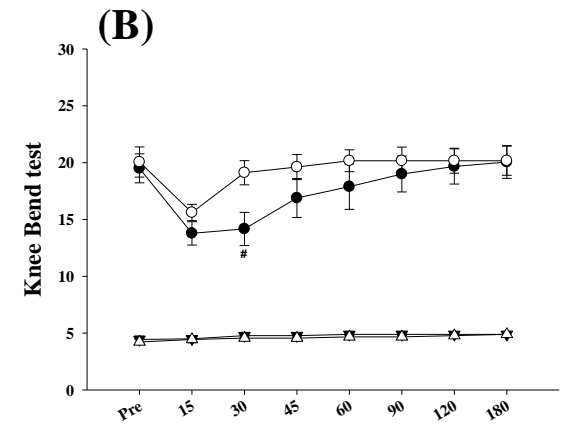
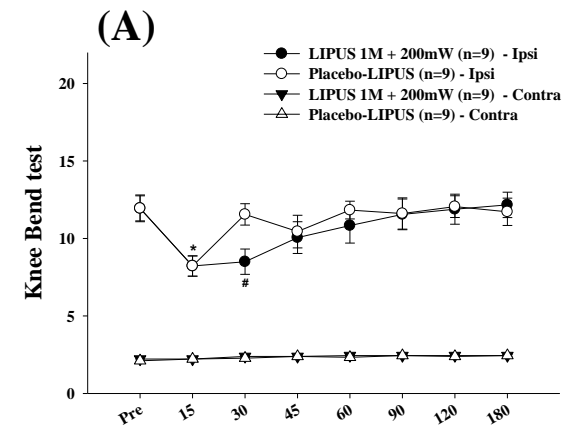
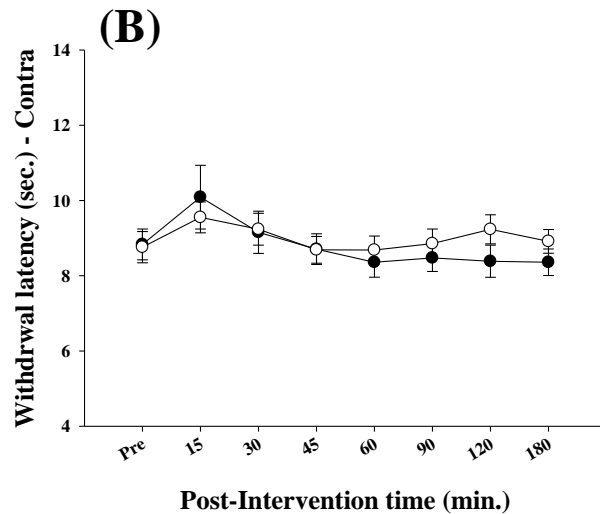
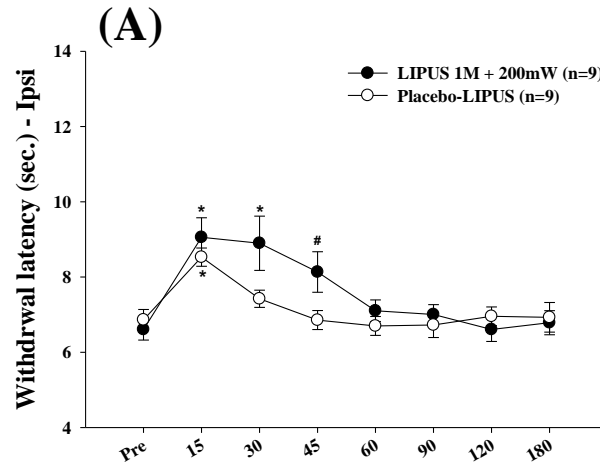
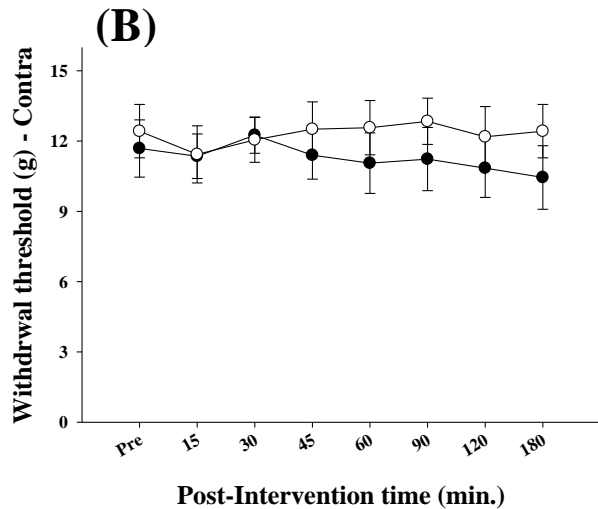
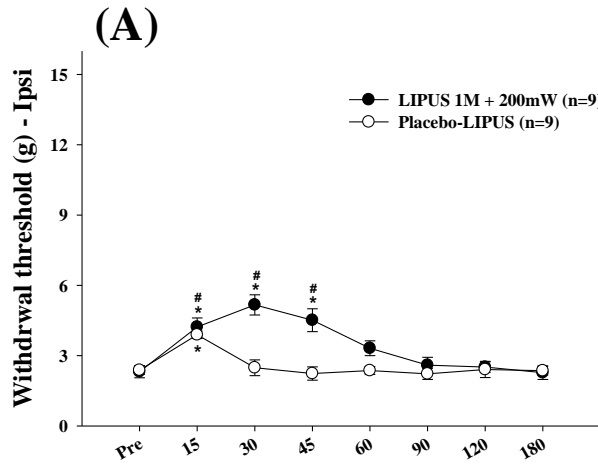
**Conclusion.** People with knee OA demonstrate significant weakness of the hip musculature compared with asymptomatic controls. It is not clear if hip muscle weakness precedes the onset of knee OA or occurs as a consequence of disease. Findings from this study support the inclusion of hip strengthening exercises in rehabilitation programs.

According to my study

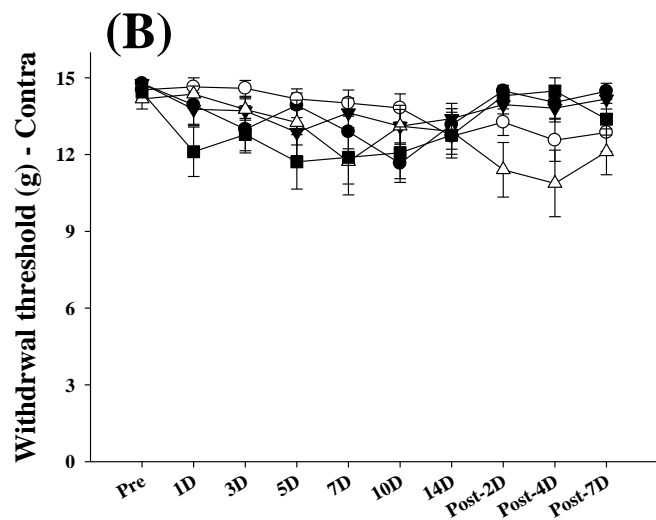
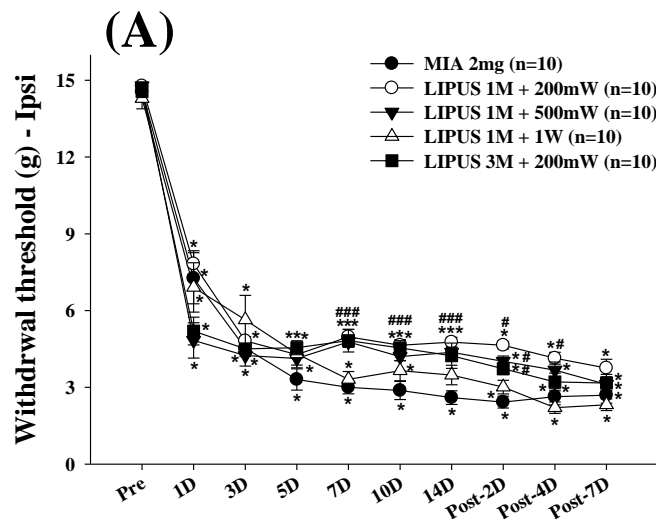
Low-intensity pulsed ultrasound

Osteoarthritic rats

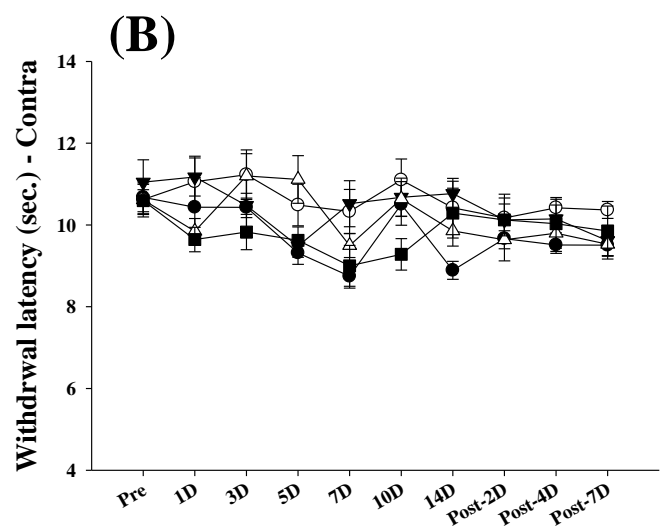
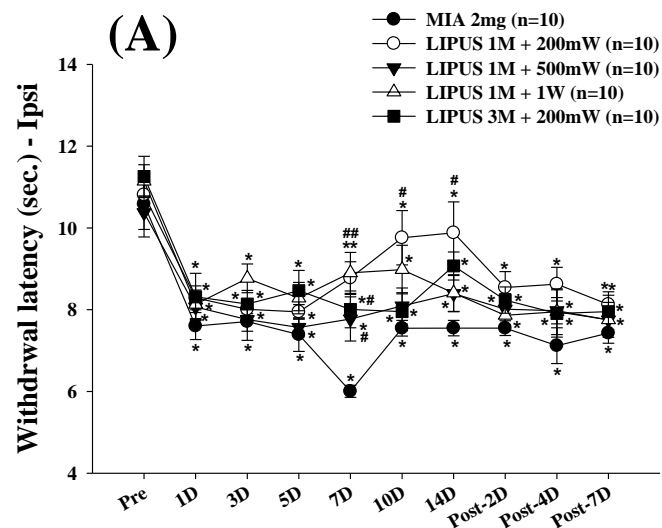
# The short-term effects of LIPUS



# The long-term effects of LIPUS

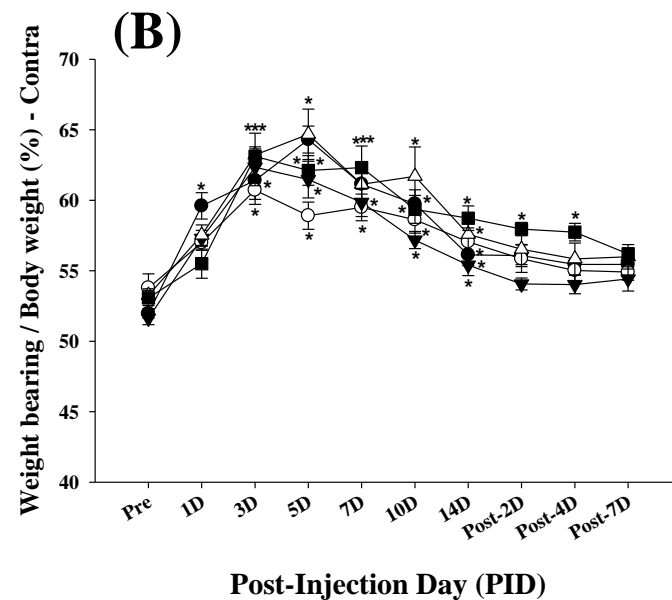
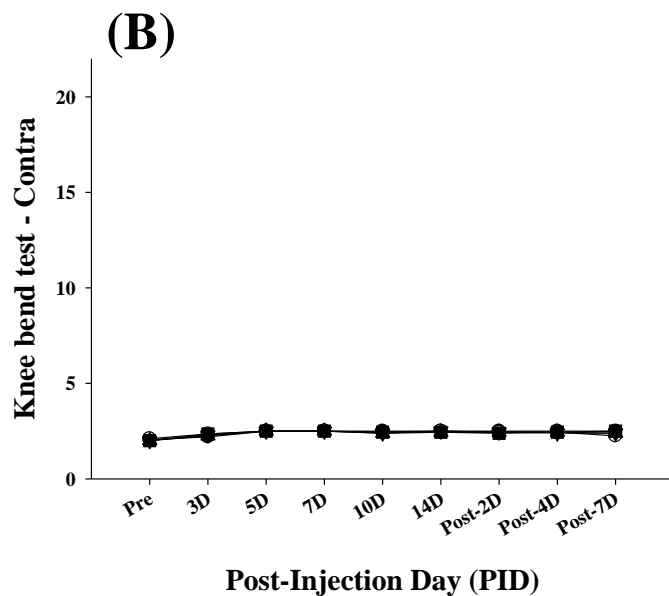
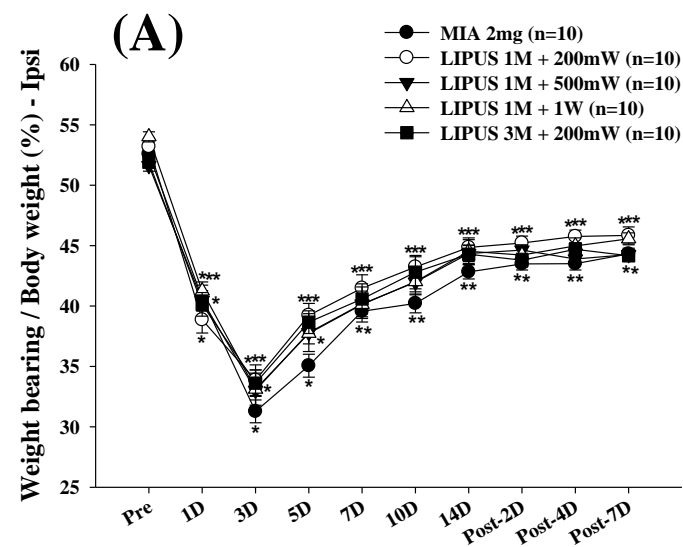
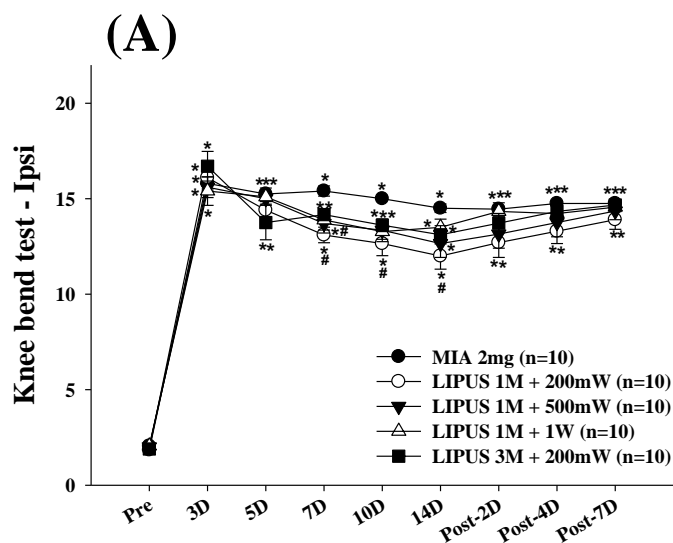


Post-Injection Day (PID)

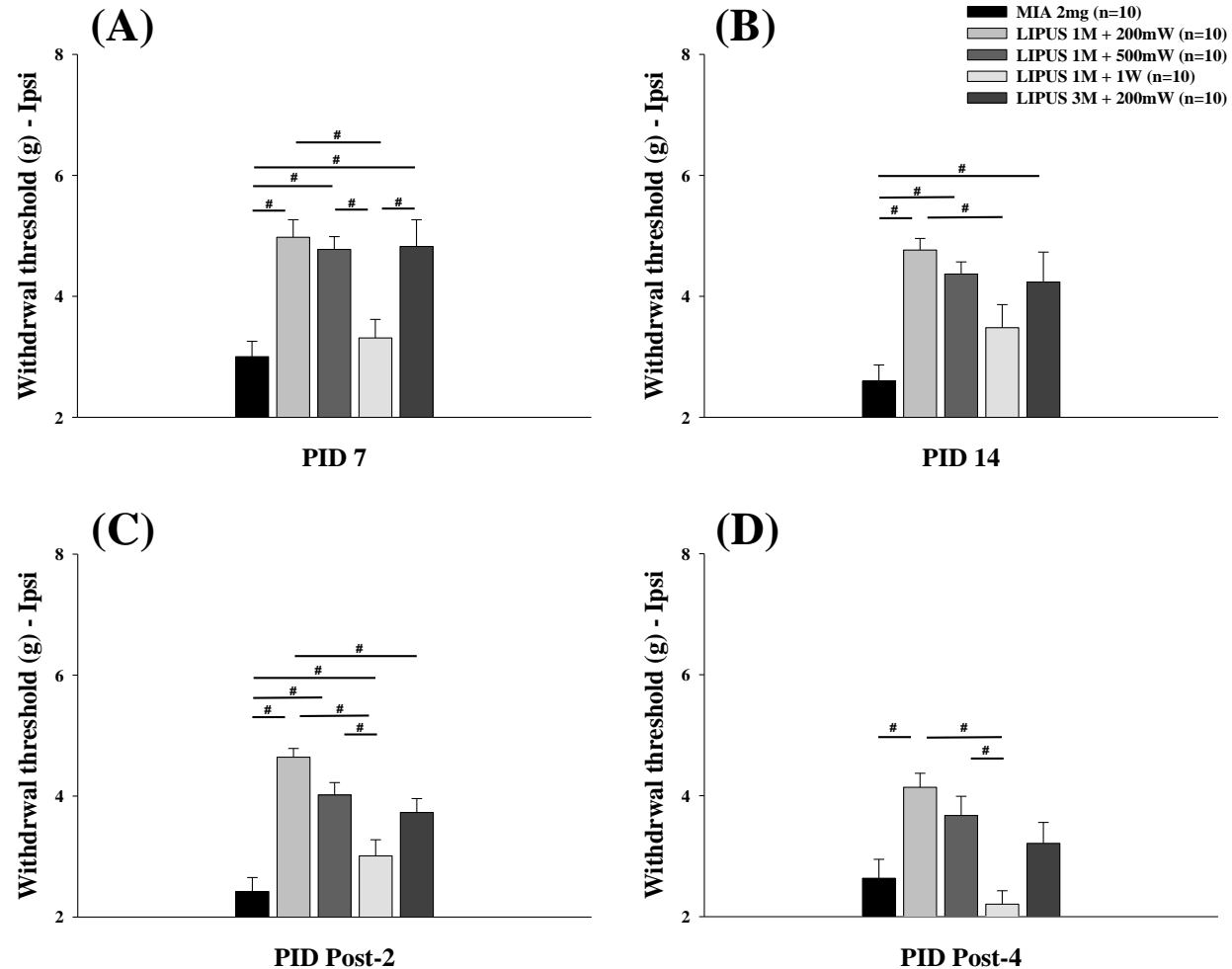


Post-Injection Day (PID)

# The long-term effects of LIPUS

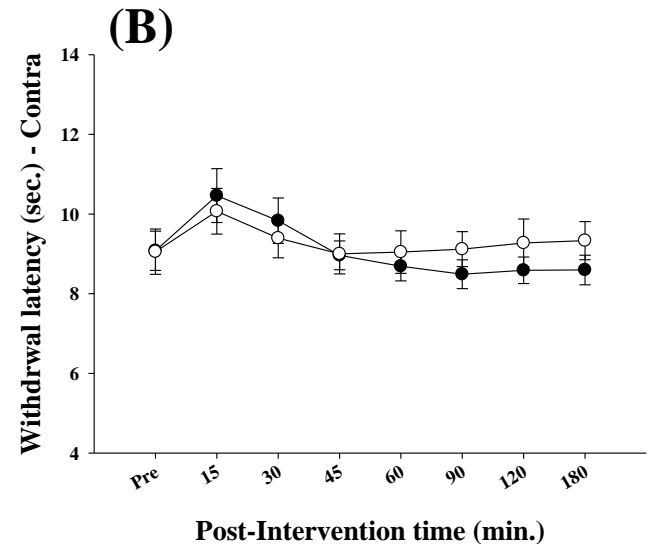
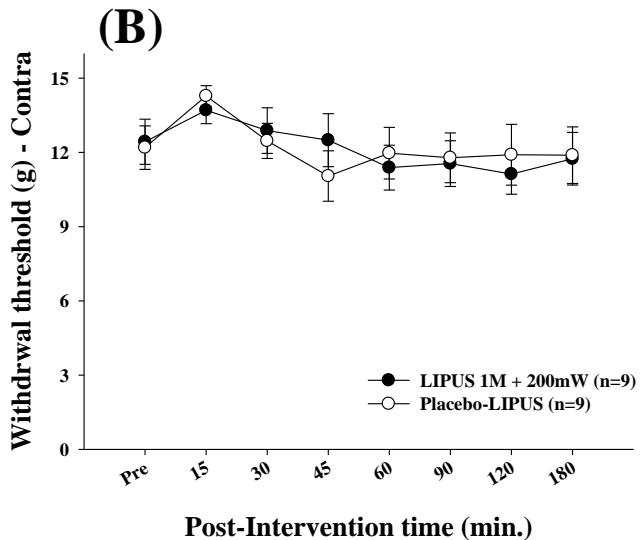
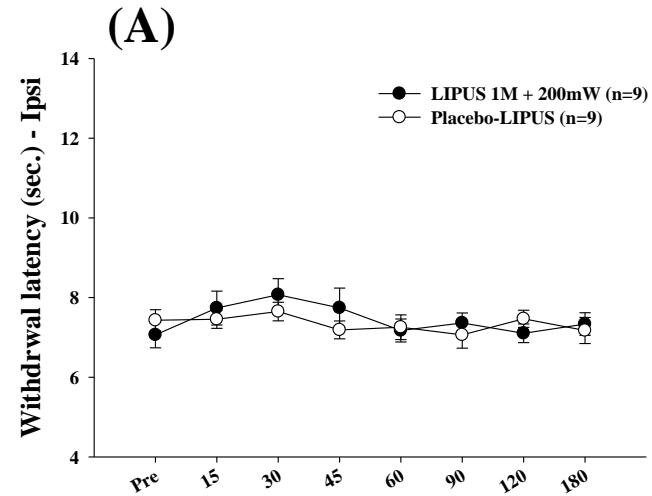
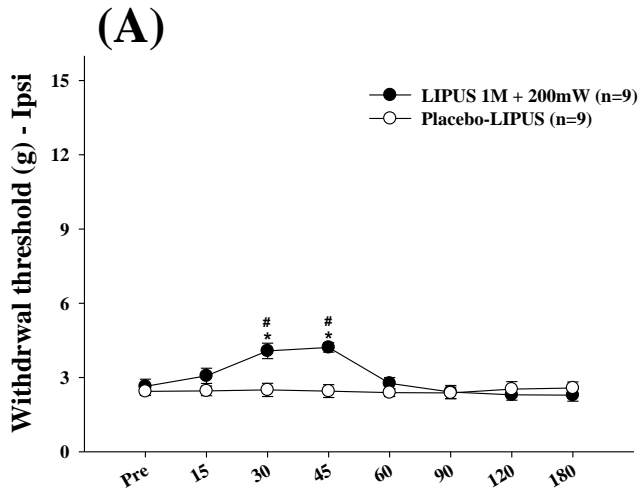


# The long-term effects of LIPUS

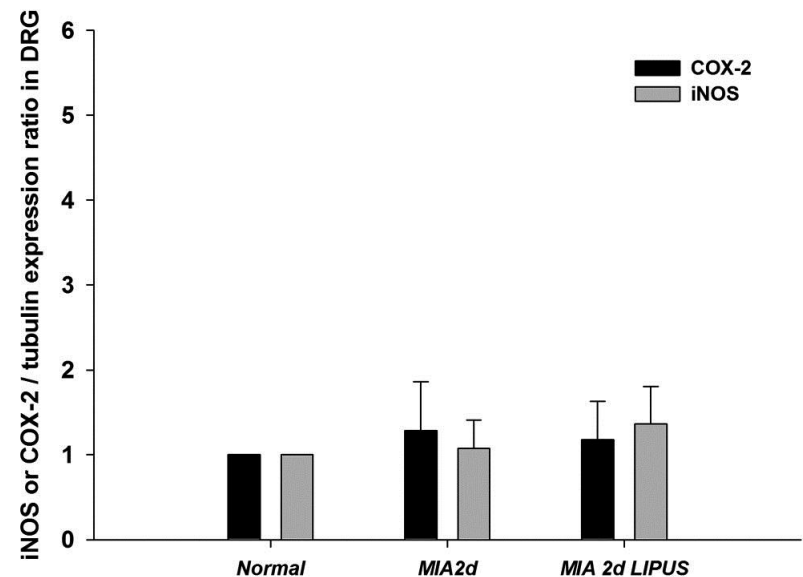
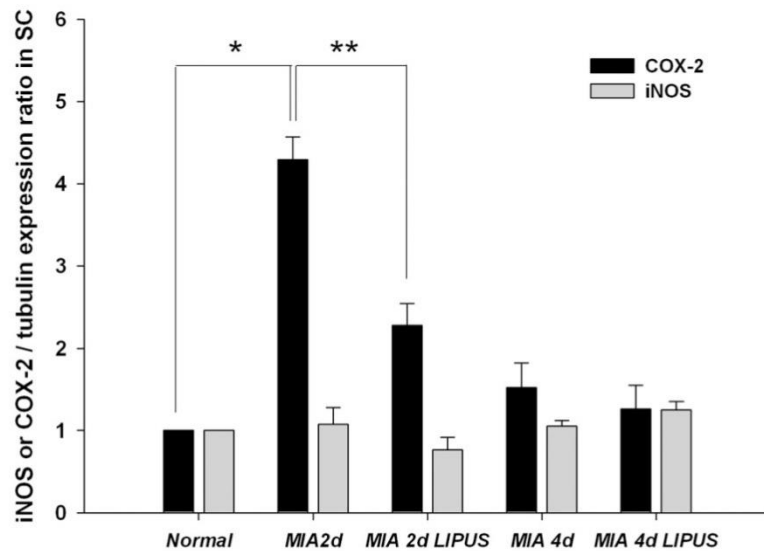
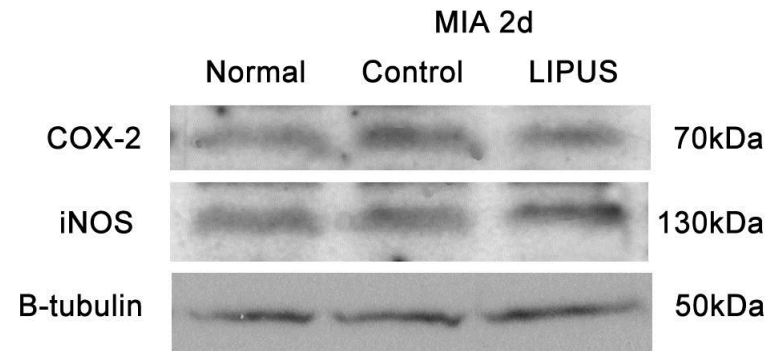
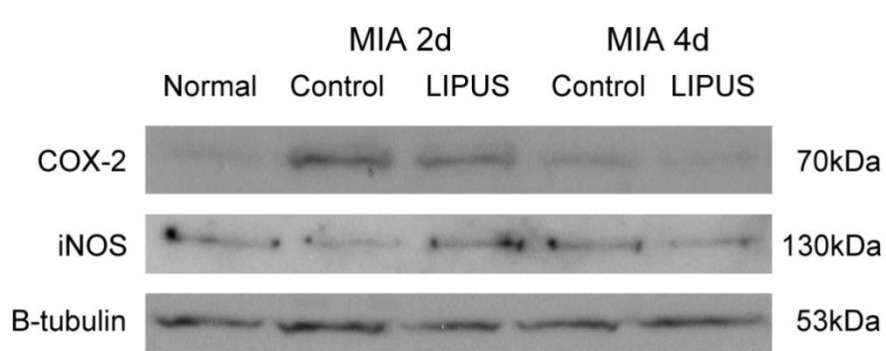


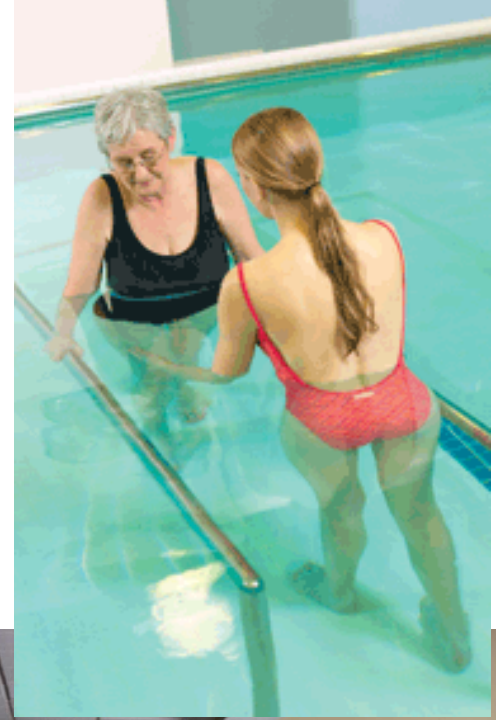


# The effects of LIPUS applied to the contra-lateral knee joint



# iNOS & COX-2 expression





# Animal Models of Arthritis

- Object

- Monkeys, guinea pigs, sheep, dogs, cats, rabbits, rats and mice

- A merit for using animal models

- Provided useful tools for investigating pain arising from other conditions, such as peripheral neuropathies
- To study the neurobiological basis of arthritic pain
- To study the involvement of neurogenic mechanisms in the pathogenesis of inflammatory lesions

## ● Joint swelling

- Measurement of diameter
  - Distance between the lateral and medial collateral ligament regions
- Vernier caliper

## ● Behavioral test

- Weight bearing
- Mechanical hyperalgesia
  - Mechanical hyperalgesia is assessed by measuring PWT to an increasing pressure stimulus placed on the dorsal surface of the hind paw using an analgesymeter (7200, Ugo-Basile, Milan, Italy), employing a wedge-shaped probe (area 1.75 mm<sup>2</sup>) and a cut-off of 250 g
- Tactile allodynia (Von Frey hairs)
  - Tactile allodynia is assessed by measuring withdrawal thresholds to calibrated von Frey hairs