



AALBORG UNIVERSITY
DENMARK

Aalborg Universitet

Intra-articular metallic gold micro particles relieve pain and enhance function in patients with knee osteoarthritis

A pilot study

Rasmussen, Sten; Petersen, Kristian Kjær; Arendt-Nielsen, Lars

Publication date:
2018

Document Version
Publisher's PDF, also known as Version of record

[Link to publication from Aalborg University](#)

Citation for published version (APA):

Rasmussen, S., Petersen, K. K., & Arendt-Nielsen, L. (2018). *Intra-articular metallic gold micro particles relieve pain and enhance function in patients with knee osteoarthritis: A pilot study*. Poster presented at IASP 2018, Boston, United States.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- ? Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- ? You may not further distribute the material or use it for any profit-making activity or commercial gain
- ? You may freely distribute the URL identifying the publication in the public portal ?

Take down policy

If you believe that this document breaches copyright please contact us at vbn@aub.aau.dk providing details, and we will remove access to the work immediately and investigate your claim.

Intra-articular metallic gold micro particles relieve pain and enhance function in patients with knee osteoarthritis

A pilot study

Sten Rasmussen^{1,2,3} • Kristian Kjær Petersen¹ • Lars Arendt-Nielsen¹

1. Center for Sensory-Motor Interaction (SMI), School of Medicine, Aalborg University, Aalborg Denmark
2. Department of Clinical Medicine, School of Medicine, Aalborg University, Aalborg Denmark
3. Department of Orthopedic Surgery, Aalborg University Hospital, Aalborg, Denmark

Aim of Investigations

Many patients suffering from osteoarthritis (OA) do not get adequate pain relieve. Current therapies relieve pain to some extent and up to 30 % having an arthroplasty do not achieve sufficient improvement.

Animal studies indicate gold ions have a long-acting effect on OA pain. The immuno-modulatory effect of gold ions have for more than 50 years a known anti-inflammatory effect in the treatment of rheumatic arthritis. Gold ions alter the function of macrophages by inhibiting lysosomal enzymes and lowering production of pro-inflammatory cytokines⁽¹⁻²⁾.

Dissolucytotic metallic gold (DMG) ions have an immune-suppressive effect in laboratory testing⁽³⁻⁵⁾ (Figure 1-3). Animal studies prove the effect of gold implantation in arthritic joints⁽⁶⁻⁹⁾. Injection of DMG in animal models stimulate the immune system⁽¹⁰⁻¹¹⁾. The carrier for injecting the DMG micro particles is hyaluronic acid⁽¹²⁻¹³⁾.

No studies have investigated the effect of intraarticular gold micro particle implants for treatment of knee osteoarthritis in humans. The present open, pilot study aimed to investigate if gold ions have a role in treating knee osteoarthritis⁽¹⁴⁾.

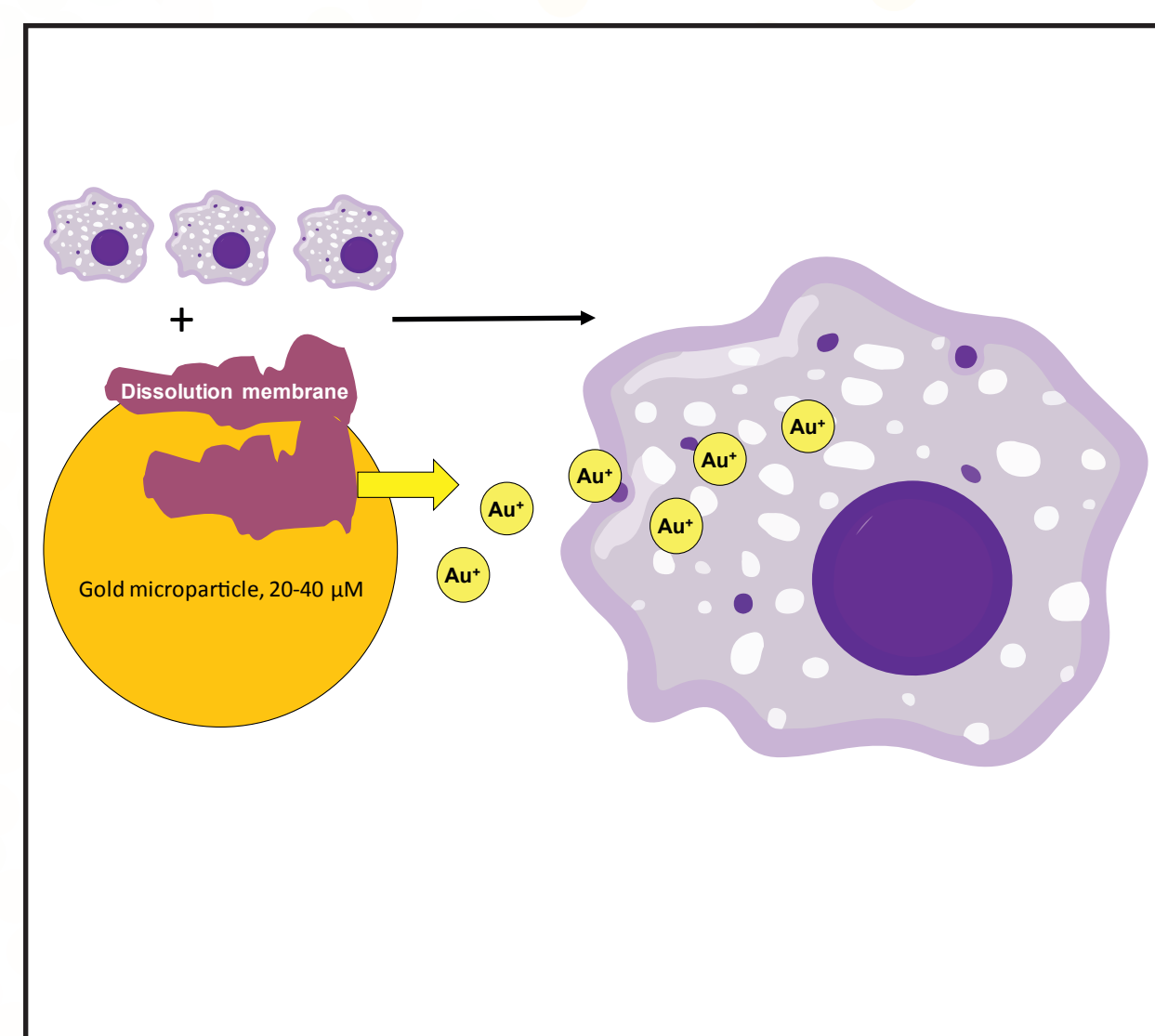


Figure 1: Macrophages controls the dissolution membrane which liberate the gold ions by oxidation of the surface. Once the ions are liberated, most likely as Dicyanogold [Au(CN)₂], they are free to diffuse through the immediate microenvironment. The gold-loaded molecules are taken up into the cells, primarily macrophages, mastcells and histiocytes.

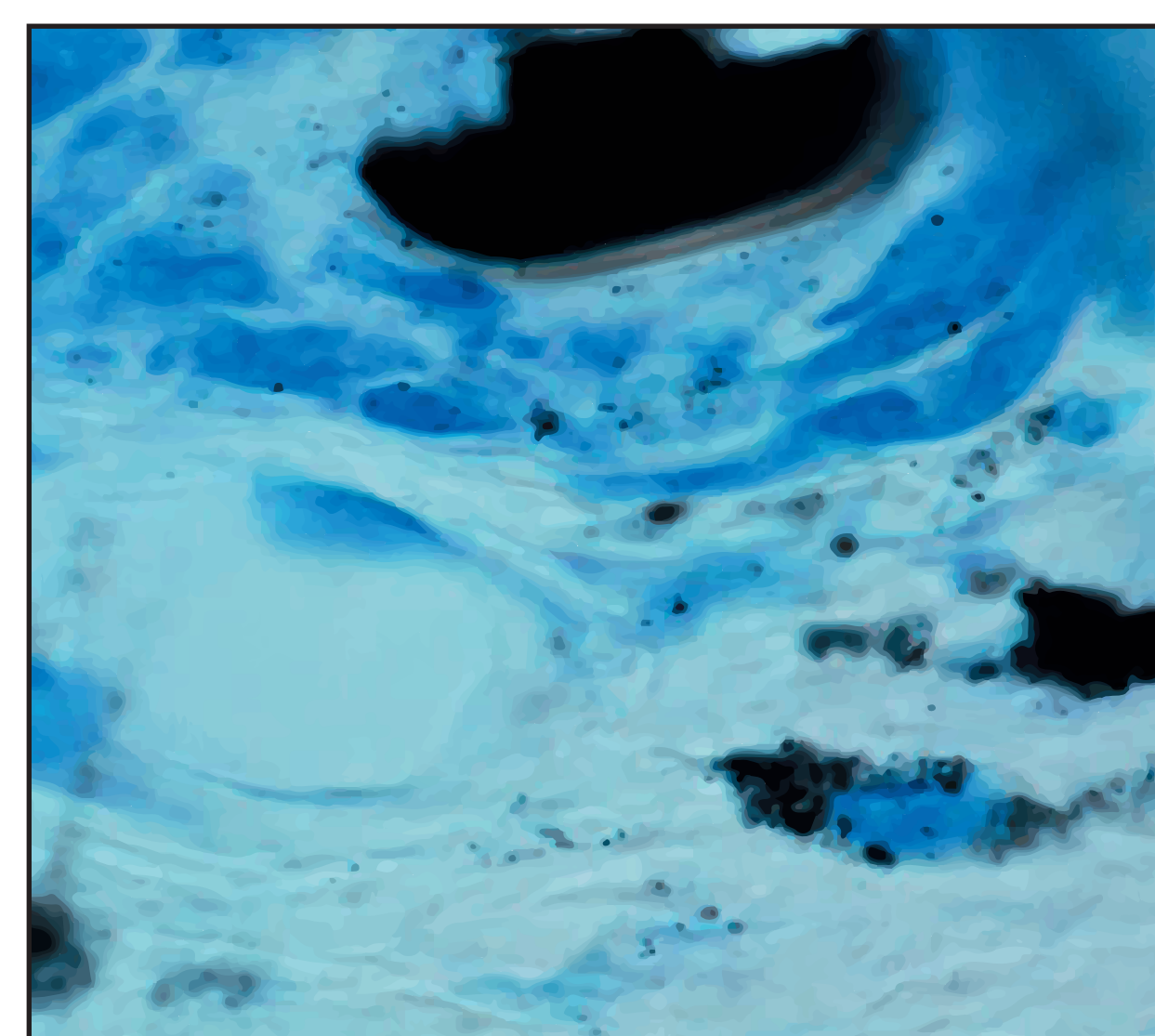


Figure 2: Close to the gold implant gold-loaded molecular clusters are located outside cells. The two loaded cells are believed to be macrophages loaded with gold ions. The gold ions accumulate primarily in the lysosomes. 3. Danscher G. Histochem Cell Biol 2002; 117:447-452

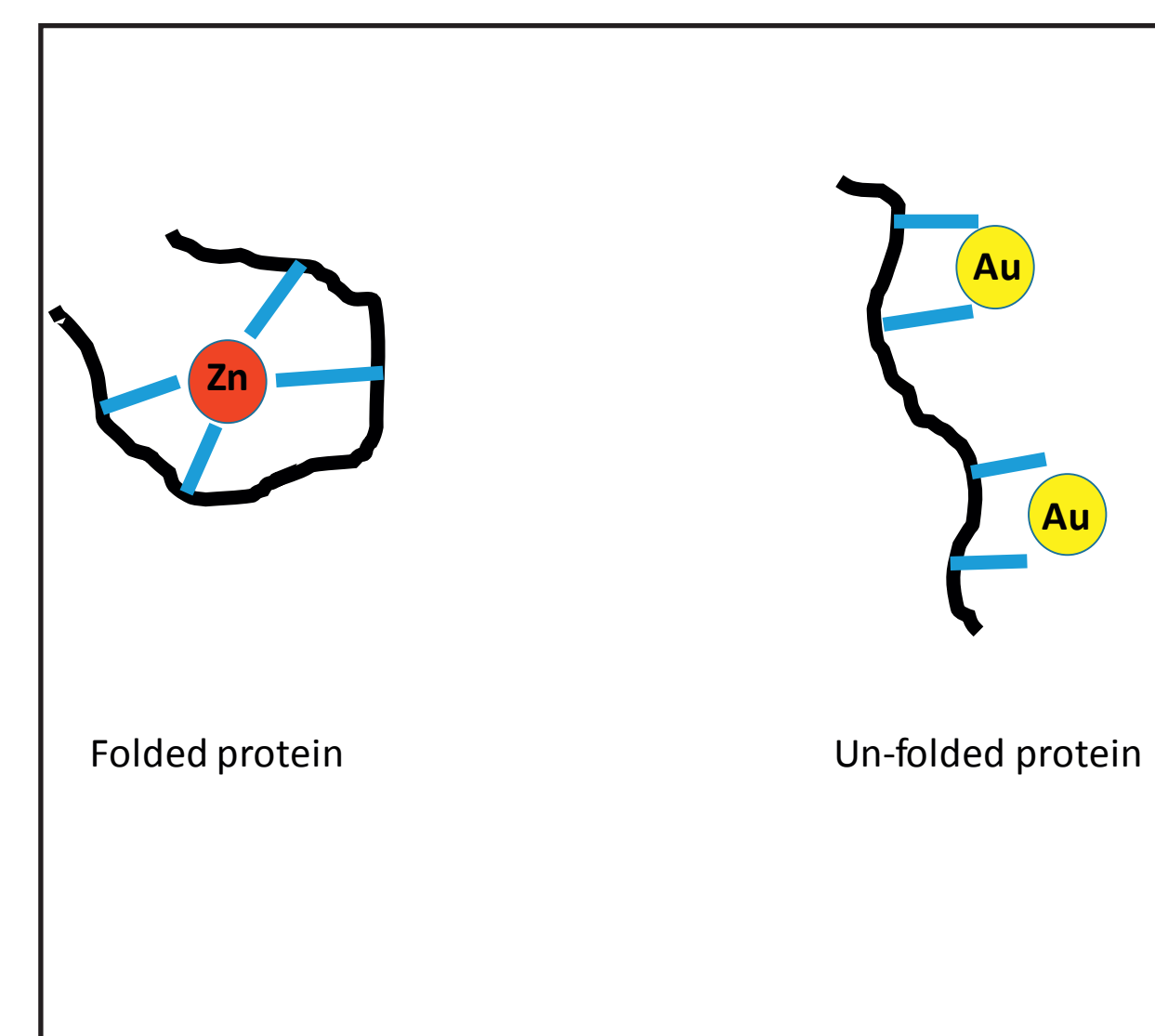


Figure 3: Once in the intercellular fluid and the intracellular compartments, i.e. lysosomes, the gold ions act in the same ways that have been demonstrated for systemically administered gold ions. Gold ions suppress inflammation locally probably partly by affecting certain signalling molecules and binding enzymes essential for the inflammatory process. The reduced production of pro-inflammatory cytokines might relate to the ability of the gold ions to unfold the protein structures.

Methods

A cohort of 30 patients referred for treatment of knee OA, aged ≥18years, pain ≥ 3 months, synovial effusion on MRI, and Kellgren-Lawrence OA grade 3-4 were included. Exclusion criteria were malignancy, active infection and antibiotic treatment, active treatment with steroids, biological or other anti-Rheumatic medication, inability to comply with the protocol, inadequacy in written and spoken national language. Of 38 eligible patients, 32 met the criteria, 1 did not attend and 1 refused. Age was 63 (46-75) year, BMI 28.8 (22.8-41.7), 18 were men 12 women. Metallic gold 20 mg, 72.000 pieces, 20-40 my-meter in

diameter (Berlock-Micro-Implants, BMI, Goldtreat APS)⁽¹²⁻¹³⁾ were injected into the knee joint using the patient's own synovial fluid as the carrier. Outcome measures were WOMAC pain, stiffness and function, PainDetect questionnaire, and Quantitative Sensory Testing (QST) (pressure pain threshold assessed over the knee joint) at inclusion and after 8 weeks.

Results

Pain and function improved in 25 of 30 patients. Womac pain decreased from 9 (6-16) to 3 (0-15), stiffness from 4 (1-8) to 2 (0-8), function from 29 (14-51) to 11 (0-41) (Figure 4), PainDetect decreased from 10 (1-26) to 3 (0-19) (Figure 5). Pain pressure thresholds increased (anti-hyperalgesia) from 598 kPa (276-1043) to 616 kPa (349-1089) (Figure 6). All differences, P < 0.05 (Wilcoxon sign test).

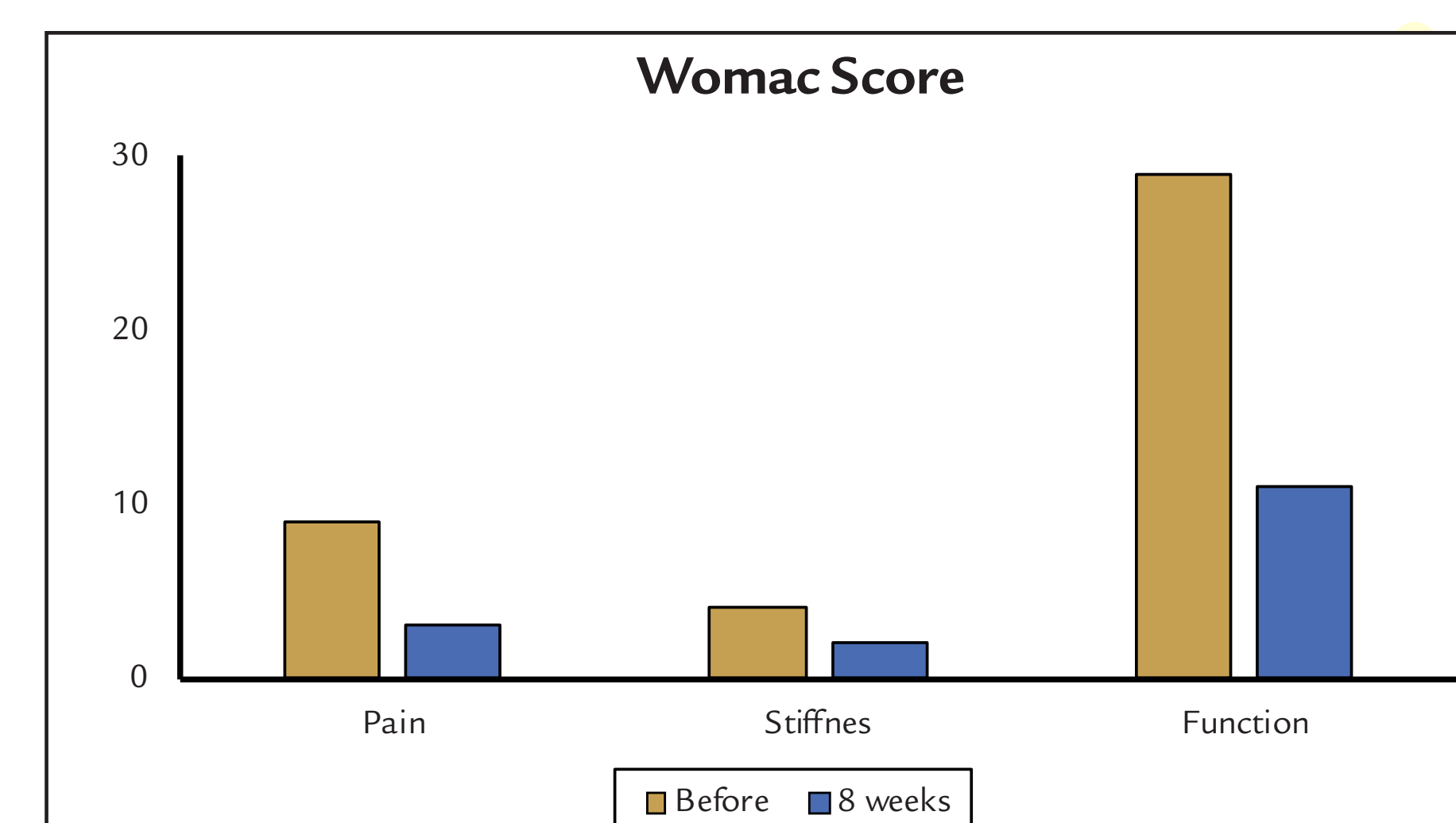


Figure 4

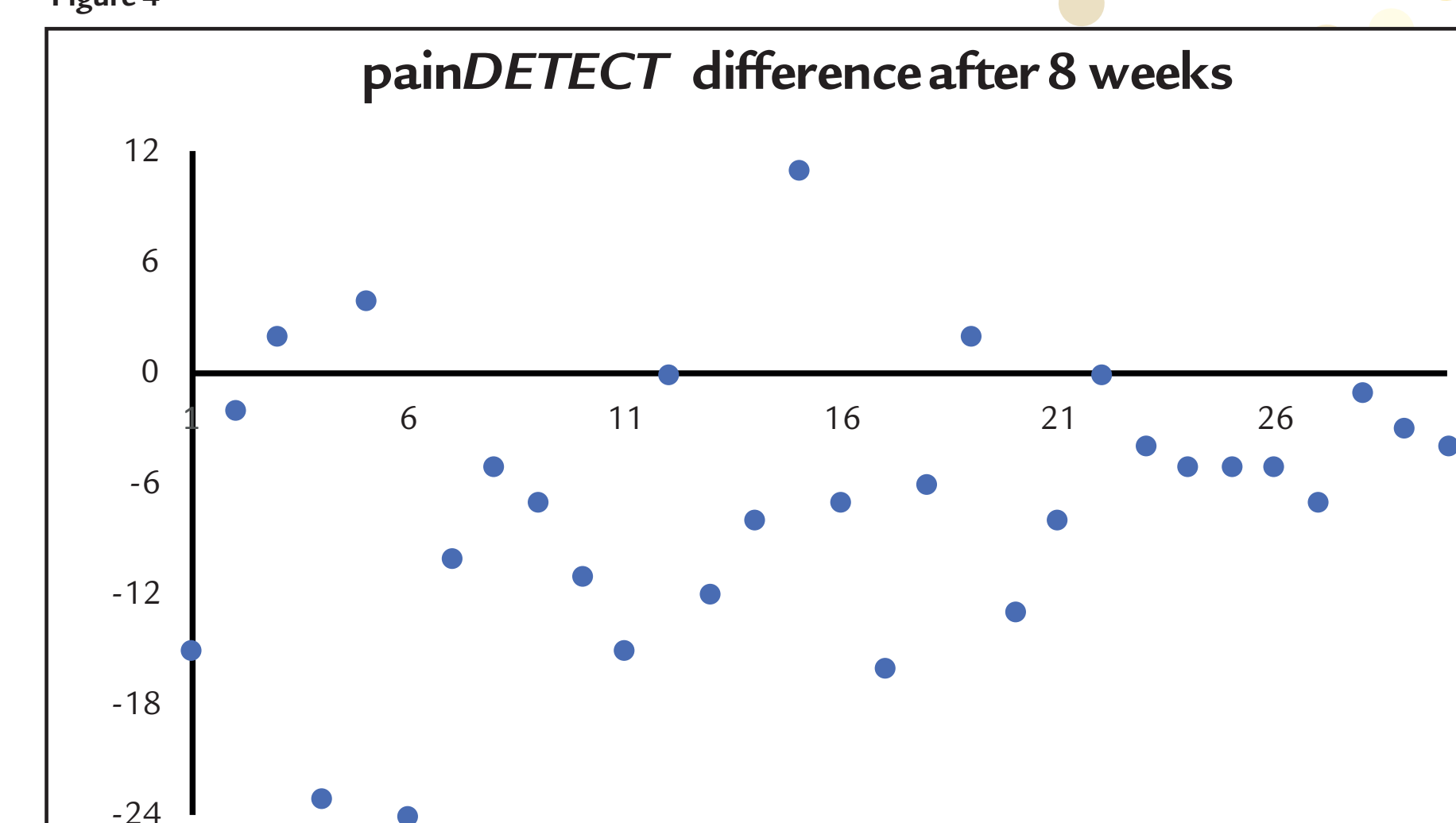


Figure 5

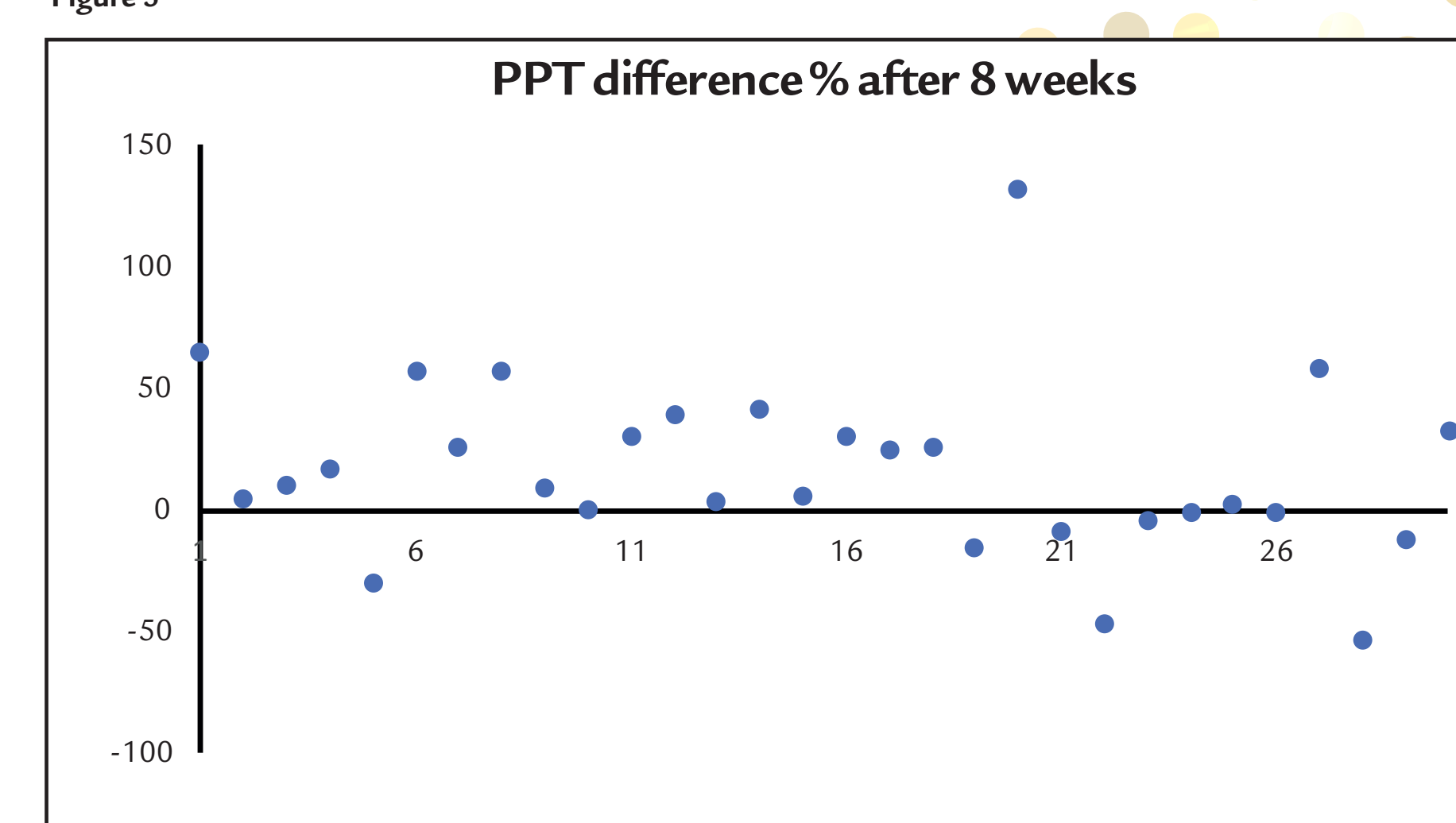


Figure 6

Conclusions

Intra-articular metallic gold improved joint pain, stiffness and function. The increased pressure pain threshold indicate less joint hyperalgesia. Intra articular gold particles may modify the synovial inflammation as a part of the sensitization in knee OA patients. In this cohort of patients with moderate to severe knee osteoarthritis and synovial effusion intra-articular metallic gold relieved pain and enhanced function in more than 80 % of the patients. This study suggests a basis for a future placebo controlled randomized trial in OA patients.

References

- Persellin RH. The effect of gold salt on lysosomal enzymes of the peritoneal macrophage. *Arthritis Rheum* 1966;9:57-65.
- Yanni G. Intramuscular gold decreases cytokine expression and macrophage numbers in the rheumatoid synovial membrane. *Ann Rheum Dis* 1994;53:315-22.
- Danscher G. In vivo liberation of gold ions from gold implants. *Histochem Cell Biol* 2002; 117:447-52.
- Larsen A. Gold ions bio-released from metallic gold particles reduce inflammation and apoptosis and increase the regenerative responses in focal brain injury. *Histochem Cell Biol* 2008;130:681-92.
- Seifert O. Gene expression profiling of macrophages: implications for an immunosuppressive effect of dissolucytotic gold ions. *J Inflamm* 2012;9:43.
- Jaeger GT. Double-blind, placebo-controlled trial of the pain-relieving effects of the implantation of gold beads into dogs with hip dysplasia. *Vet Rec* 2006;158:722-6.
- Jaeger GT. Two years follow-up study of the pain-relieving effect of gold bead implantation in dogs with hip-joint arthritis. *Acta Vet Scand* 2007;49:9.
- Jaeger GT. Gold Bead Implantation in Acupoints for Coxofemoral Arthrosis in Dogs. *Animals* 2012;2:426-36.
- Lie KI. Inflammatory response to therapeutic goldbead implantation in canine hip joint osteoarthritis. *Vet Pathol* 2011;48:1118-24.
- Havarinasab S. Gold causes genetically determined autoimmune and immunostimulatory responses in mice. *Clin Exp Immunol* 2007;150:179-88.
- Hazer DB. Soft tissue response to the presence of polypropylene-G-poly(ethylene glycol) comb-type graft copolymers containing gold nanoparticles. *J Biomed Biotechnol* 2011;2011:956169.
- Danscher G. In: Patent US, editor. Medicament and method of treatment of patients with heavy metals 2010. United States Patent Number US 7,655,261 B2.
- Märki N. Safety of Intra-Articular Gold Microimplants in Horses. *J Equine Vet Res* 2018;60:59-66.
- Rasmussen S. <https://clinicaltrials.gov/ct2/show/NCT03389906>