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# Intra-articular gold micro particles relieve pain in knee osteoarthritis -A pilot study

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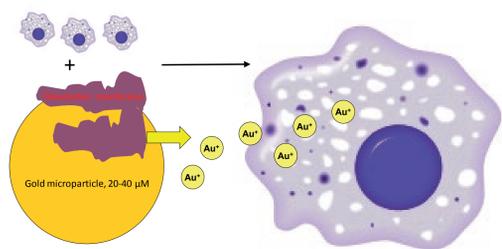
## Background and aims

Many patients suffering from osteoarthritis (OA) do not get adequate pain relieve. Evidence suggest an inflammatory component in OA pain.

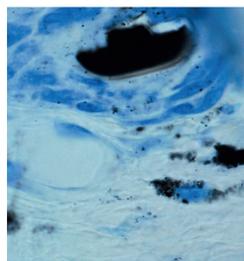
The immuno-modulatory effect of gold ions have for more than 50 years a known anti-inflammatory effect in the treatment of rheumatic arthritis. Gold ions alter the function of macrophages by inhibiting lysosomal enzymes and lowering production of pro-inflammatory cytokines (1-2).

Dissolucytotic metallic gold (DMG) ions have an immune-suppressive effect in laboratory testing (3-6) (Figure 1 - 4). Animal studies prove the effect of gold implantation in arthritic joints (7-10). Injection of DMG in animal models stimulate the immune system (11-12). The carrier for injecting the DMG micro particles is hyaluronic acid (13-14).

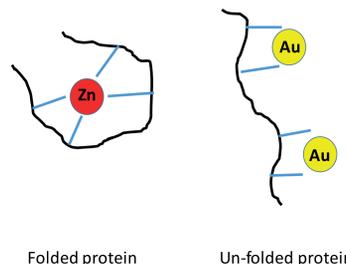
No studies have investigated the effect of intraarticular gold micro particle implants for treatment of knee osteoarthritis in humans. The present open pilot study aimed to investigate if gold ions released from intra-articular gold micro particles have a role in treating knee OA (15).



**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 Au(CN)<sub>2</sub><sup>-</sup>, they are free to diffuse through the immediate microenvironment. The gold-loaded molecules are taken up into the cells, primarily macrophages, mastcells and histocytes.



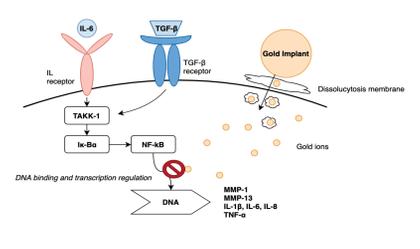
**Figure 2.** Close to the gold implant gold-loaded molecular clusters are located outside cells. The two loaded cells are believed to be macrophages loaded with gold ions. The gold ions accumulate primarily in the lysosomes (3).



Folded protein

Un-folded protein

**Figure 3.** Once in the intercellular fluid and the intracellular compartments, the gold ions act in the same ways that have been demonstrated for systemically administered gold ions. The effect is related to the ability of the gold ions to unfold the protein structures.



**Figure 4.** Gold ions suppress inflammation locally by affecting certain signalling molecules and binding enzymes essential for the inflammatory process. The DNA binding activity and transcription regulation of NF-κB is abolished when Au<sup>+</sup> ions replace Zn<sup>2+</sup> ions. (4)

## Methods

A cohort of 30 patients, aged  $\geq 18$  years, pain  $\geq 3$  months, synovial effusion on MRI, and Kellgren-Lawrence OA grade 3-4 were included. Metallic gold 20 mg, 72.000 pieces, 20-40  $\mu$ -meter (Berlock-Micro-Implants, HumanGoldInject) (13-14) were injected into the knee joint using the patient's own synovial fluid as the carrier. The primary outcome measure was temporal summation of pain (TSP). The secondary outcome measures were Conditioned Pain Modulation (CPM), knee Pressure Pain Threshold (PPT), the PainDetect score, and the Western Ontario and McMaster Universities Arthritis Index (WOMAC).

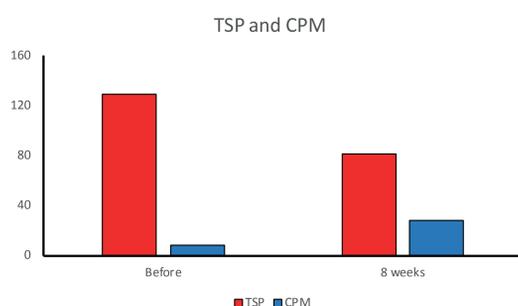


Figure 5

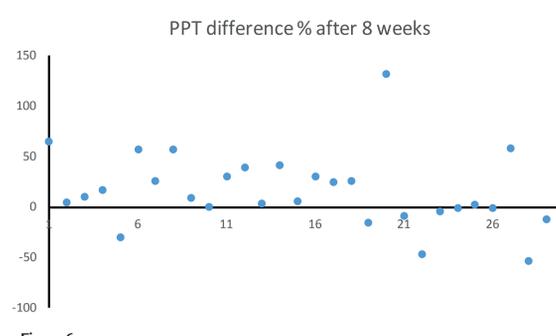


Figure 6



Figure 7

## Results

TSP was reduced 37.5 % ( $P = 0.027$ ) and CPM was improved 22.4 % ( $P = 0.026$ ) (Figure 5). PPT increased 10 % ( $P = 0.0001$ ) (figure 6). PainDetect was reduced from 10 (1-26) to 3 (0-19) ( $P = 0.0005$ ), WOMAC pain decreased from 9 (6-16) to 3 (0-15) ( $P = 0.0001$ ), stiffness from 4 (1-8) to 2 (0-8) ( $P = 0.036$ ) and function improved from 29 (14-51) to 11 (0-41) ( $P = 0.0009$ ) (figure 7).

## Conclusions

The significant improvements in pain caused by the intraarticular gold micro particles indicate an inhibition of inflammation. The significant improvements in qualitative sensory tests indicate less pain hyperalgesia.

## 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.
- Yang JP, Merin JP, Nakano T, Kato T, Kitade Y, Okamoto T. Inhibition of the DNA-binding activity of NF- $\kappa$ B by gold compounds in vitro. *FEBS Lett.* 1995 Mar 13;361(1):89-96.
- 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 nanoparticulates. *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>