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A comparison of intra-articular hyaluronan injection accuracy rates between three approaches based on radiographic severity of knee osteoarthritis

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Summary

Objective: To compare the accuracy rates of intra-articular hyaluronic acid (HA) injections for osteoarthritis (OA) of the knee between the modified Waddell approach (an anteromedial approach with manipulative ankle traction at 30° of knee flexion), an anteromedial approach with the subjects seated (hereinafter the seated anteromedial approach) and a lateral patellar approach based on the Kellgren–Lawrence (K–L) radiographic grade (II, III and IV).

Designs: Fifty patients with knee OA received HA injections through the three approaches. The accuracy rates were confirmed with a single radiograph after injections of a mixture of radiographic contrast medium.

Results: In the K–L grade IV cases ($n = 11$), the accuracy rates through the modified Waddell approach (11 out of 11, 100%) were significantly higher than those through the seated anteromedial approach (six out of 11, 55%) and the lateral patellar approach (six out of 11, 55%) ($P = 0.035$). No significant differences were detected in the accuracy rates of the participants classified as grade II ($n = 21$) or III ($n = 18$) cases between the modified Waddell approach (86% and 78%, respectively), the seated anteromedial approach (71% and 56%, respectively) and the lateral patellar approach (86% and 61%, respectively) ($P > 0.05$).

Conclusion: Although previous studies have been conducted on the accuracy of needle placement into the intra-articular space of the knee, no evaluations were performed with the results categorized by radiographic severity. This study highlighted the need for clinicians to change the approach employed for HA injections, according to the severity of knee OA.

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Key words: Osteoarthritis, Knee, Injection, Hyaluronan, Severity.

Introduction

The use of an intra-articular injection with hyaluronic acid (HA) has recently become more widely accepted as a therapy for pain accompanying osteoarthritis (OA) of the knee¹. However, an incorrect placement of extra-articular HA injection causes discomfort to the patient and declination of the effect of the HA².

Needle placement can be confirmed easily when an effusion is present. During joint aspiration for effusion, the return of synovial fluid clearly indicates intra-articular placement of the needle. However, Luc *et al.*³ suggested that accurate intra-articular placement of the HA was difficult without guidance by real-time fluoroscopic imaging or an ultrasonic method for “dry” knee disease, which was defined as a knee without any clinically detectable effusion. Jones *et al.*⁴ used a single radiograph to evaluate the accuracy of injections of a mixture of radiographic contrast medium without real-time fluoroscopic imaging or the use of an ultrasonic method. They reported that only 39 of 59 knee joint injections (66%) were intra-articular, and almost 33% were extra-articular.

Three routes have been employed for intra-articular knee injections: the medial, lateral, and anterior approaches.

Lussier *et al.*² reported a larger frequency of adverse reactions after injections of HA administered from the medial aspect of the patella than from the lateral side. Iizuka *et al.*⁵ reported patients who developed saphenous neuropathy following knee joint injection *via* the medial approach. Thus, the medial approach was not considered as the first choice for intra-articular injections with HA.

The lateral patellar approach is widely used as the method for intra-articular HA injection. The lateral patellar approach is more appropriate to extra fluid when an effusion is present than anterior technique².

Waddell *et al.*⁶ reported that the contrast material was observed in the synovial space in 100% of injections using the anterolateral approach with the knee flexed between 30 and 40° using a standard dental chair in 11 healthy volunteers and this technique has been utilized successfully in more than 2000 injections of HA for patients with knee OA in their orthopedic practice. However, this study underestimated the potential usefulness encountered when performing injections in patients with severe knee OA.

We modified Waddell's anterolateral approach as a direct approach to the medial tibiofemoral joint space with manipulative ankle traction (the modified Waddell approach). In our previous study, 117 “dry” knee OA patients with Kellgren–Lawrence (K–L) radiographic grade III or IV were treated with HA weekly for 4 weeks through the lateral patellar approach ($n = 58$) or the modified Waddell approach

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($n = 59$)^{8,9}. A significant greater improvement in the remission score shown by the Lequesne index⁹ ($P = 0.031$) was demonstrated in the modified Waddell approach group (3.3 ± 5.5) compared with the lateral patellar approach group (1.5 ± 3.2). We inferred that the greater improvement in the modified Waddell approach group was due to the more accurate placement of the injections, compared with the lateral patellar approach, although the accuracy rates were not confirmed with a radiographic contrast medium.

This study was designed to compare the accuracy rates in our daily outpatient practice between the lateral patellar, anteromedial and modified Waddell approaches using a single radiograph after injections of a mixture of radiographic contrast medium without real-time fluoroscopic imaging. Furthermore, the accuracy rates for the three approaches were compared based on the K–L grade (II, III and IV).

Methods

STUDY DESIGN

This study was accomplished through prospective evaluation of patients with medial compartment knee OA. The setting was an Orthopedic Outpatient Clinic. The principal outcome results considered were as follows:

- The accuracy rate of the intra-articular injection using the contrast material, and
- Algo-functional disability improvement using the Lequesne index^{9,10}.

The procedures employed were conducted in accord with the Declaration of Helsinki¹¹.

INCLUSION/EXCLUSION CRITERIA

Seventy-two new outpatients with medial compartment OA knee seen in our Orthopedic Outcome Clinic from January to March in 2007 were selected according to the American College of Rheumatology criteria and a criteria stipulating a standing femorotibial angle greater than 176° shown by X-ray¹². “Dry” knee disease was defined as a knee without any clinically detectable effusion².

Exclusion criteria following the report by Maillerfert *et al.*¹³ were employed: a greater or similar reduction in the lateral joint space width, compared with the medial femorotibial joint space width (concomitance with lateral knee OA), shown on plain postero-anterior X-rays, bilateral knee OA, secondary knee OA, hip OA, ankle OA, and any intra-articular corticosteroid or HA injection within 1 month.

There were eight patients who were not eligible, according to the exclusion criteria given above, and five patients refused to participate in the study.

At their initial visit, the patients were asked about their drug use history, i.e., use of an analgesic, non-steroidal anti-inflammatory drug (NSAID) and alternative medication, including glucosamine use within the previous week. There were 41 patients who had a positive drug history of the 59 participants who were eligible for inclusion (69.5 %) in the study. It was required that these 41 patients discontinued the use of previous medications during a week employed as a wash-out period between the initial visit and the baseline assessment. During the wash-out period, nine of these 41 patients (22%) could not quit their previous medications.

After providing informed consent, 50 outpatients, including eight males and 42 females with knee OA [mean age: 66.1, standard deviation (SD): 8.9], participated in this study (Table I).

INTERVENTION

The HA used in this study had a molecular weight of 1.9 million Daltons, and it was produced by biological fermentation (Suvenyl[®], Chugai, Tokyo,

Japan). The 2.5 ml HA was injected every 2 weeks (baseline assessment, week 2 and 4). The participants were instructed to return for the final assessment at week 6. The rationale for the 2-week interval between the third injection at week 4 and the final assessment at week 6 was that clinical improvement due to a HA injection begins with a delayed onset between 2 and 5 weeks¹⁴. All participants were given a uniform NSAID (loroxicam 4 mg twice daily) for 6 weeks as an adjunctive therapy.

The injections were performed by one orthopedic surgeon using a 1.25-in (3.2 cm) 23-gauge needle through three approaches: the lateral patellar approach, the anteromedial approach with a knee flexion of 90° (the seated anteromedial approach) and the anteromedial approach with manipulative ankle traction with a knee flexion of 30° (the modified Waddell approach). After the joint space was palpable, the skin was cleansed with a tampon soaked in povidone three times for all of the injections.

The lateral patellar approach involved insertion of a needle 1 cm above and 1 cm lateral to the superior lateral aspect to the patella at a 45° angle according to Zuber¹⁵ [Fig. 1(a)].

Following a report by Jackson *et al.*¹⁶, the seated anteromedial injection was performed with the patients seated with the affected leg hanging over the side of the examination table with the knee flexed to approximately 90°. The patient’s foot was allowed to hang freely without contact with the floor or a stool. The injection site was selected inferior to the patella, one finger breadth proximal to the tibial joint surface, and medial to the patella tendon. The needle was directed obliquely toward the intercondylar notch [Fig. 1(b)].

In the modified Waddell approach, the patients were prone on a bed and the knee was bent to 30° on a plaster shell. The hand opposite to that used for the injection was used for manipulative ankle traction [Fig. 1(d)]. According to Waddell *et al.*⁶, the injection site was proximal to the site of the seated anteromedial approach by approximately 1.0–1.5 cm and the needle was advanced inward to the intra-articular space just at the anterior contact point of the femoral medial condyle.

All three injection techniques were employed on every patient.

The randomization procedure employed for the order of the three approaches was a computer-generated block method using sealed envelopes. The purpose of randomization was decreasing the influence of turn of approaches on the accuracy rates for the intra-articular injections.

In the initial visit, clinicians were given randomly generated treatment allocations within sealed opaque envelopes in a series of blocks of six. Once a patient had entered the trial in the baseline assessment, an envelope was opened and the patient was then offered the allocated intervention regimen.

Those participants whose allocated block number was “one” were sequential injected through the lateral patella, seated anteromedial and modified Waddell’s approaches. If the participants’ allocated number was “two”, the order of injections were the lateral patella, modified Waddell’s and seated anteromedial approaches. Similarly, if the participants’ allocated number was “three”, the turn of injections were the seated anteromedial, lateral patella and modified Waddell’s approaches.

OUTCOME MEASURES

Along with the 2.5 ml HA injection, 2 ml of contrast material (iotrolan) was injected into the knee joint. Once intra-articular positioning of the needle was considered adequate, HA mixed with contrast solution was injected and lateral and anterior–posterior radiographs were taken 10 min later. When the needle was positioned incorrectly, the contrast material pooled as a bolus in either the fat pad or the subsynovial tissues on the radiograph. If the needle was positioned correctly, the contrast material shaped the outlines of suprapatellar pouch and meniscus. The accuracy rates for the intra-articular injections were compared between the three approaches, based on the K–L grade.

In order to assess the effect of incorrect injections on clinical outcomes, the patients were categorized into two groups: patients that received only intra-articular injections (the correct injection group) and patients that received an extra-articular injection at least one time (the incorrect injection group). A research nurse who was blind to the objectives of the study asked the participants to assess the Lequesne index at the baseline and 6-week assessments. The Lequesne indexes at the 6-week assessment were compared with the baseline recordings for both the correct and incorrect injection groups.

Table I
Characteristics of the participants (n = 80)

	Age (years)	Disease duration (years)	Body mass index (kg/m ²)	Femorotibial angle (°)	Lequesne index (score)	Sex (no. of cases)	Radiographic grade (no. of cases)
Mean (SD)	66.1 (8.9)	3.7 (4.1)	24.4 (3.7)	180.1 (4.7)	10.7 (5.4)	Men: 8, women: 42	II: 21
Median	68	2.0	23.7	179	11		III: 18
95% CI	64.7–67.5	3.0–4.3	22.7–25.1	179.3–181	9.2–12.3		IV: 11

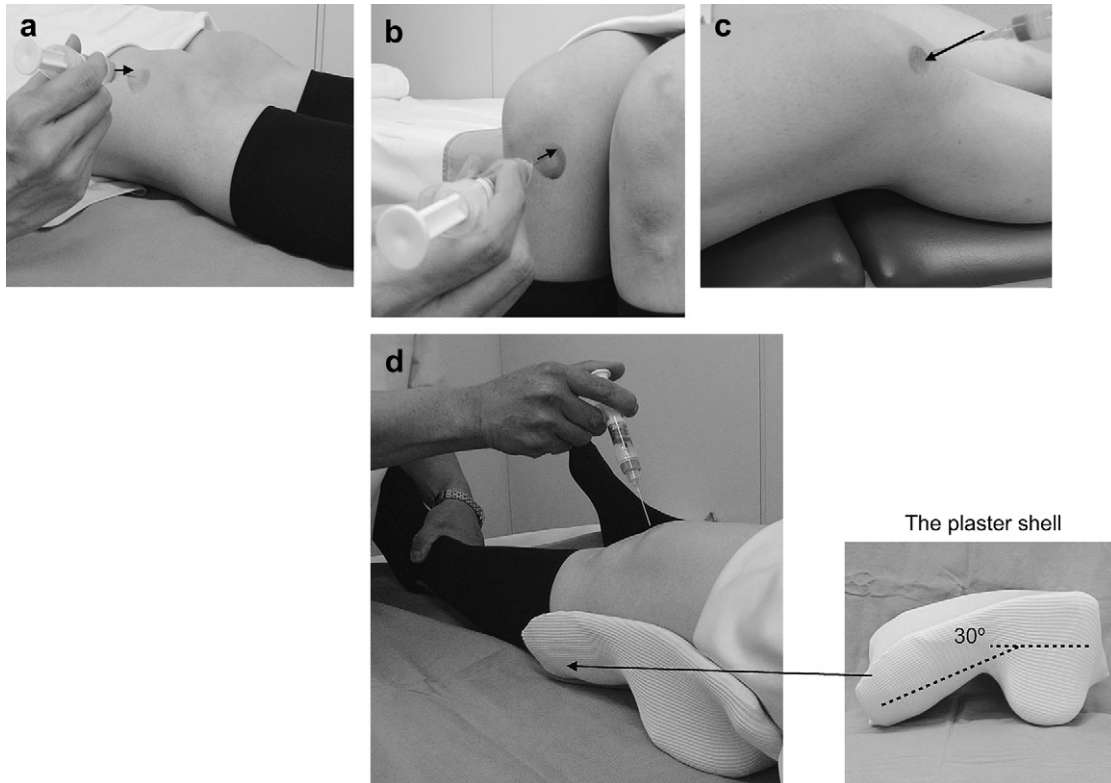


Fig. 1. Approaches for intra-articular knee injections. (a) The lateral patellar approach, (b) the seated anteromedial approach, (c) the original Waddell's approach, and (d) the modified Waddell's approach (the plaster shell).

STATISTICAL ANALYSES

The intra-articular injection accuracy rates were compared between the groups using the χ^2 test. The paired *t* test was used to assess for statistically significant differences in the Lequesne index between the baseline and the 6-week assessments in the correct and incorrect injection groups. Statistical significance levels were considered to be $P < 0.05$.

Results

ACCURACY RATES OF INJECTION BASED ON K–L GRADE

The 50 cases were composed of 21 in the K–L grade II, 18 in grade III and 11 in grade IV. The injection accuracy rates based on the K–L grade for each approach are shown in Fig. 2.

In the grade II cases, 18 of 21 injections through the modified Waddell approach were confirmed to have been placed in the intra-articular space (86% accuracy rate). Fifteen of 21 injections (71%) performed through the seated anteromedial approach were intra-articular. The accuracy rate for the lateral patellar approach was 18 of 21 injections (86%). There were no significant differences in the accuracy rates between any of the approach groups.

No significant differences were detected in the accuracy rate for participants with a grade III ranking between the modified Waddell approach (14 out of 18, 78%), the seated anteromedial approach (10 out of 18, 56%) and the lateral patellar approach (11 out of 18, 61%).

In the grade IV cases, the accuracy rate for the modified Waddell approach (11 out of 11, 100%) was significantly higher than those for the seated anteromedial approach (six out of 11, 55%) and the lateral patellar approach (six out of 11, 55%) ($P = 0.035$).

CLINICAL ASSESSMENT

All participants completed the 6-week study (returned for the final follow-up visit). There were 18 participants in the correct injection group and 32 in the incorrect injection group.

The mean values and SD for changes in the Lequesne index at the final assessment, compared with the baseline assessment, were -4.7 ± 4.1 in the correct injection group and -1.3 ± 4.6 in the incorrect injection group. The patients that received only intra-articular injections demonstrated significantly improved Lequesne index values, in comparison with their baseline assessments ($P < 0.0001$). However, these significant differences were not found in the patients that received even one, or more, extra-articular injections ($P = 0.14$) (Table II).

Discussion

At 30° of knee flexion, the tension of both of the hamstrings and the quadriceps decreases, and the anterior cruciate ligament (ACL) acts as a protagonist to the stability of knee joint¹⁷. However, ACL rupture is frequent among those with radiographic severe knee OA. Hill *et al.*¹⁸ evaluated magnetic resonance imaging in a group of 360 symptomatic knee OA patients. Their results showed complete ACL tears present in 43 of 86 patients (50%) with K–L grade III and 12 of 16 patients (75%) with K–L grade IV. Moul¹⁹ suggested that the function to restrain the widening joint space at 30° of knee flexion is incurred, if ACL strain is decreased.

In a previous study, we assessed the changes in the joint space width in patients with medial compartment knee OA on lateral view radiographs with manipulative ankle traction

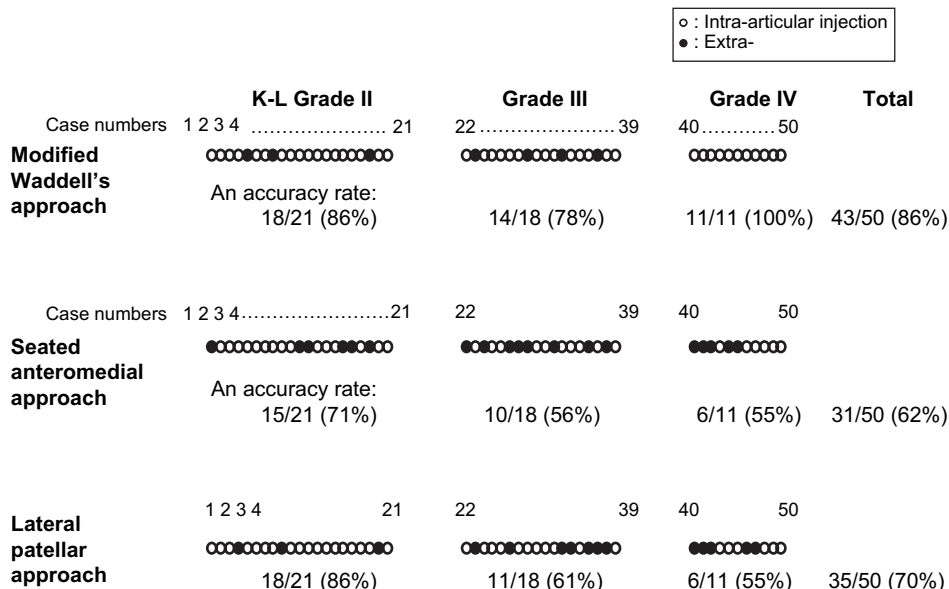


Fig. 2. Accuracy rates for the three approaches. The case number is common in the three approaches.

at 30° of knee flexion based on the K–L grade (II, III and IV)²⁰. According to LaValley *et al.*²¹, the joint space was measured at the points that appeared to be the narrowest visually in the medial compartment. In the grade IV cases ($n = 7$) with manipulative ankle traction, the joint space width was increased by an average of 2.4 ± 1.4 mm, compared with no traction. However, the joint space width with manipulative ankle traction differed by 1.1 ± 0.97 mm and 1.6 ± 1.7 mm compared with no traction in grade II ($n = 22$) and III ($n = 17$) groups, respectively. These changes represented a significant difference between the grade II and IV groups ($P = 0.036$). Therefore, we added manipulative ankle traction to the positioning at 30° of knee flexion to widen the joint space in this study. However, it will be necessary to compare the accuracy rate between groups with the addition of the ankle traction and groups with no traction in a future study.

This study revealed that the accuracy rate for intra-articular HA injections performed with the modified Waddell approach (an anteromedial approach with manipulative ankle traction and a knee flexion of 30°) was significantly higher than that for both the seated anteromedial approach and the lateral patellar approach in patients with a K–L grade IV, but not II or III. An incorrect placement of extra-articular

HA injection caused a declination of the effect of HA in patients that received even one extra-articular injection, or more, but participants that received all intra-articular injections demonstrated significantly improved Lequesne index values at week 6, in comparison with their baseline assessments. From these results, we concluded that clinicians should change the approach employed for an intra-articular injection according to the severity of the knee OA.

In patients with severe knee OA, as shown by radiographic methods, intra-articular surface irregularities and sharpening of the tibial spines have been identified²². Another degenerative process occurs on the anterior surface of the patella and consists of bone proliferation at the site of the osseous attachment of the quadriceps tendon²². These changes would be obstacles for the anteromedial and lateral approaches [Fig. 3(a) and (b)]. However, osteophyte formation at the anterior aspect of the femoral condyle was uncommon even in the patients with K–L grade IV [Fig. 3(c)]. Therefore, we considered that the modified Waddell approach was more accurate than the other two approaches for the patients with K–L grade IV.

We employed injections into the medial joint space of the tibiofemoral joint in this study, although Waddell *et al.*⁶ employed injections into the lateral joint space. The rationale of

Table II
Comparison of the Lequesne index at the baseline and 6-week

	Baseline	4-week	The change for 4 weeks	P value between the baseline and 12-week
Correct injection group ($n = 18$)				
Mean (SD)	11.9 (5.3)	7.4 (6.0)	-4.7 (4.1)	>0.0001*
Median	11	9	-3	
95% CI	9.3–14.5	4.5–10.4	-6.7–-2.7	
Incorrect injection group ($n = 32$)				
Mean (SD)	10.1 (5.4)	8.8 (5.5)	-1.3 (4.6)	0.14
Median	10	8.5	-1.3	
95% CI	8.1–12	6.9–10.8	-3–0.3	

* $P < 0.05$.

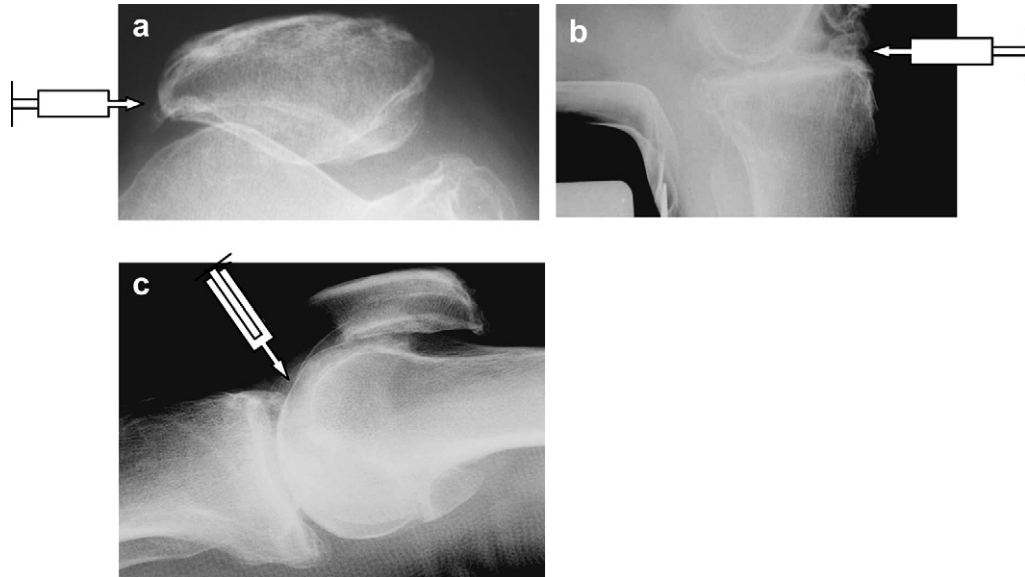


Fig. 3. Schema of the intra-articular approaches for severe knee OA. (a) Lateral patellar approach, (b) seated anteromedial approach, (c) modified Waddell's approach.

this modification was the medial femoral condyle was more prominent as our anatomic landmark than the lateral femoral condyle. However, the accuracy rate of anteromedial approach may be lower than that of anterolateral approach in the patients with medial compartment of knee OA. Esenyel *et al.*²³ evaluated the accuracy rate intra-articular injection using anteromedial, anterolateral, lateral midpatellar, and medial midpatellar portals in 156 knees of 78 fresh cadavers. The accuracy rate in their result was the highest (85%) in the anterolateral injection among the four injections. A future study should be conducted and evaluated using anterolateral approaches at 30° of knee flexion.

A problem encountered in this study was the inability to assess the correlation between the order of approaches and accuracy rates or clinical improvements. We should assess whether modified Waddell's approach is accurate regardless of the approach used as a first, second and third injections in the participants with K–L grade IV. This was secondary to the relative paucity of participants with K–L grade IV ($n = 11$). It will be necessary to study this, including a larger number of participants with K–L grade IV.

The current study was limited to assessment of the relationship between the radiographic K–L grade and the accuracy rate of three approaches. Future research directions also include assessment of other parameters and the accuracy rate of different techniques. Through such studies, we hope to discover a useful parameter to select an approach of intra-articular HA injection for each patient with knee OA.

Conflict of interest

The authors have no conflict of interest.

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