

Retrospective Review

e High-Voltage Intraarticular Pulsed Radiofrequency for Chronic Knee Pain Treatment: A Single-Center Retrospective Study

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Disclaimer: Financial support was provided by Professor Peng Yao's Funding (No. 20170541032) from the Natural Science Foundation of Liaoning Province.
Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 11-25-2019
Revised manuscript received: 03-17-2020
Accepted for publication: 03-23-2020

Free full manuscript: www.painphysicianjournal.com

Background: Intraarticular pulsed radiofrequency (IAPRF) for the treatment of painful knee osteoarthritis (KOA) is a less invasive treatment method. It has fewer adverse effects and can quickly reduce KOA-related pain and improve knee joint dysfunction.

Objectives: We compared the effectiveness of high- and low-voltage IAPRF for the treatment of chronic knee pain.

Study Design: Retrospective comparative study design.

Setting: This study took place at Shengjing Hospital of China Medical University.

Methods: A total of 57 patients with KOA who were hospitalized between July 2018 and July 2019 were randomly allocated into the high-voltage (n = 29) and low-voltage (n = 28) IAPRF groups. IAPRF was performed under the guidance of computed tomography (CT). Numeric Rating Scale (NRS-11), Oxford Knee Score (OKS), degree of pain relief, global perceived effect, and side effects at baseline and 1 week, 2 weeks, 1 month, 3 months, and 6 months after the procedure were recorded and analyzed.

Results: NRS-11 scores decreased significantly in both groups after the procedure, but gradually increased after the 6-month follow-up period. There was a significant difference in NRS-11 scores between the 2 groups at all follow-up periods postprocedure. OKS were similar between the 2 groups. Patients with pain relief rate 50% or greater at 1, 3, and 6 months after the procedure accounted for 72.41%, 72.41%, and 55.17% in the high-voltage group, and 46.43%, 46.43%, and 28.57% in the low-voltage group, respectively. The difference between the 2 groups was statistically significant. No significant adverse reactions were observed in the 2 groups, however, patient satisfaction in the high-voltage group was significantly higher compared with patients in the low-voltage group.

Limitations: This study was a single-center retrospective study with a relatively small sample cohort and short follow-up period.

Conclusions: CT-guided high-voltage IAPRF is more beneficial in reducing knee pain and improving knee function compared with low-voltage IAPRF. In addition, patients who received high-voltage IAPRF were more satisfied with their treatment.

Key words: Pulsed radiofrequency, knee osteoarthritis, intraarticular, high voltage, Oxford Knee Score, Numeric Rating Scale

Pain Physician 2020; 23:E549-E558

Knee osteoarthritis (KOA) is a common chronic noninflammatory joint disease characterized by joint pain, stiffness, swelling, and movement disorder. Chronic knee pain disease can cause disability, which severely affects the patients' quality of life (1,2). The incidence rates of symptomatic KOA in elderly patients aged older than 65 years is approximately 20% to 30%. With the increase in age and obesity, the incidence of KOA proportionally increases (3). Current treatment methods are limited to relieve pain, delay damage to the articular cartilage, and improve knee function. Patients with poor treatment efficacy after conservative treatment may have to undergo arthroscopic surgery or total knee arthroplasty (TKA) (4). However, the therapeutic efficacy of knee arthroscopy remains controversial (5). Although TKA is the optimal therapy for KOA, it is not suitable for elderly patients with severe complications. In addition, approximately 20% to 53% of patients still suffer from persistent and severe pain after TKA (6-8).

In 1998, Sluijter et al (9) proposed a new radiofrequency treatment method. Pulsed radiofrequency (PRF) is administered typically at a voltage of 45 V with 20-ms bursts followed by 480-ms silent phases. The longer silent phases cause the tissues around the area to be able to dissipate heat, and hence prevent the local temperature from rising above 42°C. Hence the tissues around the treatment area are not damaged (10). Currently, PRF has been widely used for the treatment of neuropathic pain, such as postherpetic neuralgia, trigeminal neuralgia, lumbar radicular pain, lumbosacral radicular pain, and cervical radicular pain. The therapeutic effects of PRF have been widely accepted by clinicians (11). In 2008, Sluijter et al (12) were the first to attempt PRF to treat intractable arthrogenic pain. Patients reported better pain relief and no pain recurrence after 10 months posttreatment (12). In 2011, Karaman et al (13) retrospectively analyzed 31 patients with KOA who were administered intraarticular pulsed radiofrequency (IAPRF). The proportion of patients with 50% or greater decrease in Visual Analog Scale (VAS) score was 35.5% at the 6-month follow-up period (13). In a randomized double-blinded trial performed by Gulec et al (14), the effectiveness of bipolar and unipolar IAPRF for KOA pain control was compared. The proportion of patients with pain relief 50% or greater was 84% for the bipolar IAPRF group, and 50% for the unipolar IAPRF group at the 3-month follow-up period (14). The reason for the difference may be related to the larger electrical field area generated using the bipolar IAPRF. This study aimed to investigate whether increasing the voltage

and electric field intensity of IAPRF could better alleviate knee pain and improve knee function.

METHODS

Patients

Eligible hospitalized patients with KOA were enrolled for this study from the Department of Pain Management Center of Shengjing Hospital affiliated to China Medical University from July 2018 to July 2019. This retrospective randomized controlled trial was approved by the ethics committee of Shengjing Hospital affiliated to China Medical University. All patients were informed of the risks and complications of the procedure and signed informed consent.

The inclusion criteria were as follows: (1) patients who were diagnosed with KOA based on the American College of Rheumatology criteria; (2) age older than 50 years; (3) grade 2 or 3 KOA based on the Kellgren-Lawrence classification; (4) patients who did not respond to conservative treatment (physiotherapy, oral nonsteroidal antiinflammatory drugs [NSAIDs], and/or intraarticular injections of hyaluronic acid and corticosteroid); (5) duration of knee pain 3 months or more; and (6) Numeric Rating Scale (NRS-11) 5 points or more within 24 hours prior to admission.

The exclusion criteria were as follows: (1) grade 1 or 4 KOA based on the Kellgren-Lawrence classification; (2) serious liver, kidney, cardiovascular, and respiratory disease; (3) abnormal blood coagulation; (4) skin infections in the puncture region; (5) patients who previously underwent knee arthroscopy, TKA or intraarticular injections; and (6) mental disorders or inability to complete the follow-up observational form.

All patients were enrolled based on the inclusion or exclusion criteria, and then randomly assigned to the high-voltage group (n = 29) or low-voltage group (n = 28).

Surgical Procedure

Patients were placed in the supine position with a pillow placed underneath the knee. After intravenous access was established, noninvasive blood pressure, electrocardiogram, and peripheral oxygen saturation were monitored. Using strict aseptic techniques, the affected joint space was identified. The clinician placed his thumb on the lateral margin of the patella and pushed it medially. At a midpoint of the medial edge of the patella, local anesthesia was administered with 1 to 2 mL of 0.5% lidocaine. One radiofrequency electrode cannula needle (21-gauge, 10 cm length, and 5 mm ac-

tive tip, PMF-21-100-5; Baylis Medical Inc., Mississauga, ON, Canada) was inserted between the patella and femoral condyles. The needle was gradually inserted into the joint cavity, and then a small amount of saline solution was administered using a syringe. If any resistance was encountered, which indicated that the needle tip was located in a ligament or tendon, the surgeon readjusted the needle tip until the injection proceeded without any significant resistance. If the needle touched the bone during the procedure, the surgeon readjusted the needle into the subcutaneous tissue and repeated the earlier described procedure. After entering the joint cavity, thin-slice computed tomography (CT) scans (1 mm/layer) were performed to confirm that the cannula needle was located in the middle of the joint space. Afterward, sensory stimulation using 50 Hz was performed at a level of greater than 1 V not to induce pain. Voltage set as 2 V means that the tip of the needle is far away from the nerve without causing nerve damage. Patients did not report any discomfort during the procedure. For patients in the high-voltage group, manual PRF mode was used with a temperature no more than 42°C. The output voltage was gradually increased to reach the highest voltage that the patient could tolerate (55–75 V) for 300 seconds. For patients in the low-voltage group, an automatic PRF mode 45 V or less ($\leq 42^\circ\text{C}$, 2 Hz, pulse width of 20 ms) was administered for 300 seconds. After treatment, the cannula needle was removed, and then an aseptic dressing was used to cover the entry point. After 15 minutes of postsurgical observation, the patient was returned to the ward.

Observation and Follow-Up

Presurgical data including age, gender, height, weight, body mass index (BMI), duration of pain, location of pain, NRS-11 and Oxford Knee Scores (OKS), and the Kellgren-Lawrence grade were measured. The output voltage, electric field intensity (output voltage/impedance), tissue resistance, and surgery duration time during the surgical procedure were collected. The follow-up time points were 1 week, 2 weeks, 1 month, 3 months, and 6 months after the procedure. Hospital staff who were blinded to the groups assessed the patients via telephone at the different postsurgical follow-up periods.

NRS-11 was used to measure pain with ranges from 0 (no pain) to 10 (unbearable pain). Degree of pain relief was assessed based on the World Health Organization evaluation criteria for pain relief. This was assessed at 4 levels: (1) complete remission (CR), indicating the complete resolution of pain; (2) partial remission (PR),

indicating significant resolution of pain (50%–75%); (3) mild remission, indicating the partial resolution of pain (<50%); and (4) no response, indicating no resolution of pain (25%–50%). The efficiency rate or 50% or more pain relief rate (%) was calculated based on the following formulae $[(\text{CR} + \text{PR})/n] \times 100\%$. Knee function was assessed using the OKS. The OKS is a valid and reliable self-administered questionnaire. It includes 5 daily activity items related to pain, and 7 daily activity items related to knee function. Each item was scored from 1 to 5 points (1 presenting the best outcome/least symptoms and 5 presenting severe pain/inability of complete movement). The range of total scores for all items was between 12 and 60 points, with 12 points indicating normal knee function. In addition, patient satisfaction surveys were conducted using the global perceived effect (GPE) questionnaire. This questionnaire consisted of a 7-point scale (1 = worst ever, 2 = much worse, 3 = worse, 4 = not improved but not worse, 5 = improved, 6 = much improved, 7 = best ever).

Statistical Analysis

Quantitative data were assessed for normal distribution using the Kolmogorov-Smirnov test and were presented as mean \pm standard deviation ($\bar{x} \pm s$). Two-way repeated-measures analysis of variance with Tukey tests was used for multiple comparisons of VAS and OKS scores for baseline, postprocedure 1 week, 2 weeks, 1 month, 3 months, and 6 months postprocedure. Gender, location of pain, and Kellgren-Lawrence grade were presented as number of cases (percentage) and compared using the chi-square test. Statistical analyses were performed using SPSS 22.0 for Windows (IBM Corporation, Armonk, NY). A P value < 0.05 was considered significantly different.

RESULTS

Patient Characteristics

Of the 73 patients diagnosed with KOA, 3 were lost during follow-up, whereas 10 patients did not meet the study inclusion criteria. Patients who were excluded from the study were due to age younger than 50 years (4 patients), and patients who underwent previous knee arthroscopy, TKA, or intraarticular injections (6 patients). A total of 60 patients were finally included in the study. During the follow-up period, one patient in the high-voltage group and 2 patients in the low-voltage group were lost. The remaining 57 patients were random-

ized into the high- and low-voltage groups. All 29 patients in the high-voltage group and 28 patients in the low-voltage group completed the 6-month follow-up period (Fig. 1).

There were no significant differences in age, gender, height, weight, BMI, duration of pain, location of

pain, presurgical NRS-11 and OKS scores, and Kellgren-Lawrence grade between the 2 groups (Table 1).

Intrasurgical Conditions and Side Effects

Surgery was successfully completed for all the enrolled patients under CT guidance. During the surgery, the needle tip was positioned in the middle of the joint

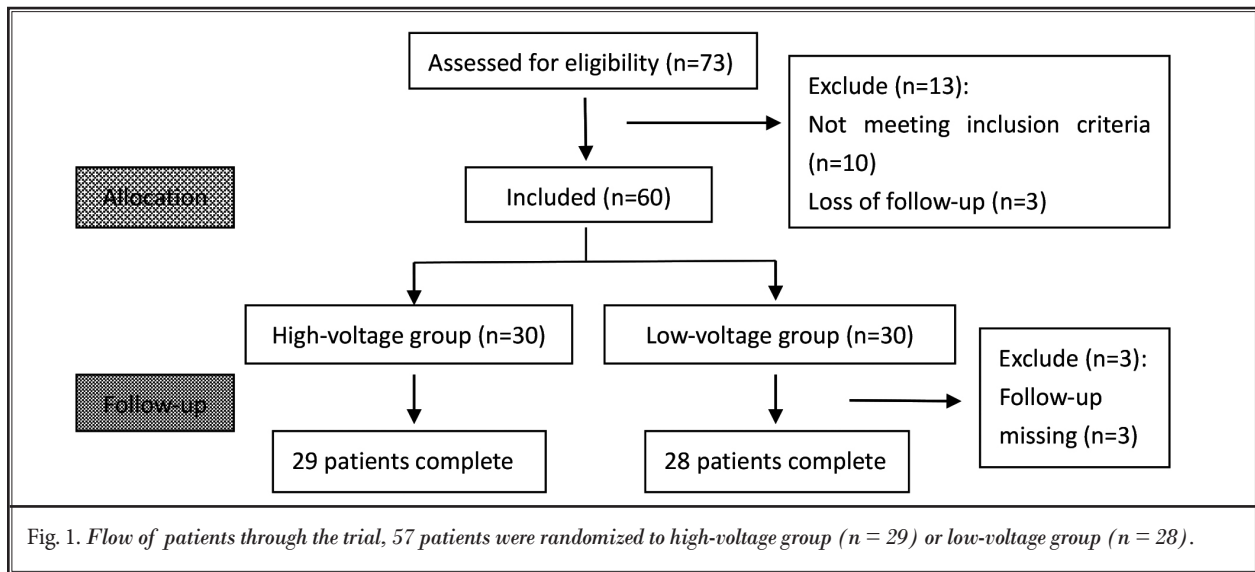


Table 1. Preoperative patient characteristics and intraoperative data.

	High-Voltage Group (n = 29)	Low-Voltage Group (n = 28)	X2/t	P Value
Characteristics				
Age (year, range)	61.51 ± 4.90 (51–71)	60.29 ± 4.99 (52–70)	0.941	0.351
Gender (M/F, %)	14 (48.28) 15 (51.72)	13 (46.43) 15 (53.57)	0.019	0.889
Height (cm)	165.97 ± 8.53	163.21 ± 9.02	1.183	0.242
Weight (kg)	69.83 ± 6.44	66.96 ± 7.02	1.605	0.114
BMI	25.41 ± 2.09	24.96 ± 1.61	0.926	0.359
Pain duration (years)	2.51 ± 0.84	2.72 ± 1.00	0.878	0.384
Left-/right-side (n, %)	12 (41.38)/17 (58.62)	13 (46.43)/15 (53.57)	0.148	0.453
Preoperative NRS-11	6.66 ± 1.17	6.68 ± 0.94	0.083	0.934
Preoperative OKS	41.69 ± 4.83	42.50 ± 6.84	0.518	0.607
Kellgren-Lawrence grade				
2	14	12	0.169	0.681
3	15	16		
Intraoperative parameters				
PRF output voltage (V)	65.10 ± 3.33	36.93 ± 3.73	1.969	<0.001
Electrical field intensity (W)	17.24 ± 2.37	5.71 ± 1.39	3.468	<0.001
Tissue resistance (Ω)	248.66 ± 25.08	244.36 ± 24.63	16.854	0.517
Surgery duration (min)	35.59 ± 5.82	34.46 ± 6.57	0.683	0.498

space and verified using 3-dimensional reconstruction (Fig. 2). There were no significant differences in tissue resistance and surgical duration between the 2 groups ($P > 0.05$). The output voltage and electric field intensity in the high-voltage group were significantly higher compared with the low-voltage group ($P < 0.001$; Table 1). Three patients reported unbearable pain around the knee joint during the procedure, which diminished after adjusting the needle tip position. This may be attributed to the stimulation of the periosteum or ligament. During the peri- and postoperative follow-up period, no patients developed local infections, hematomas, abnormalities in knee movement or sensation.

Comparison of NRS-11 Scores Before and After the Procedure for the 2 Treatment Groups

NRS-11 scores decreased significantly in both groups compared with preprocedural scores ($P < 0.05$). NRS-11 scores were decreased gradually and reached a minimum at 3 months postprocedure, then showed a slightly increasing trend at 6 months postprocedure. However, NRS-11 scores were still lower compared with preprocedural pain intensities. NRS-11 scores in the high-voltage group were significantly lower compared with the low-voltage group for each follow-up time point (from 1 week to 6 months postprocedure) ($P < 0.05$) (Fig. 3).

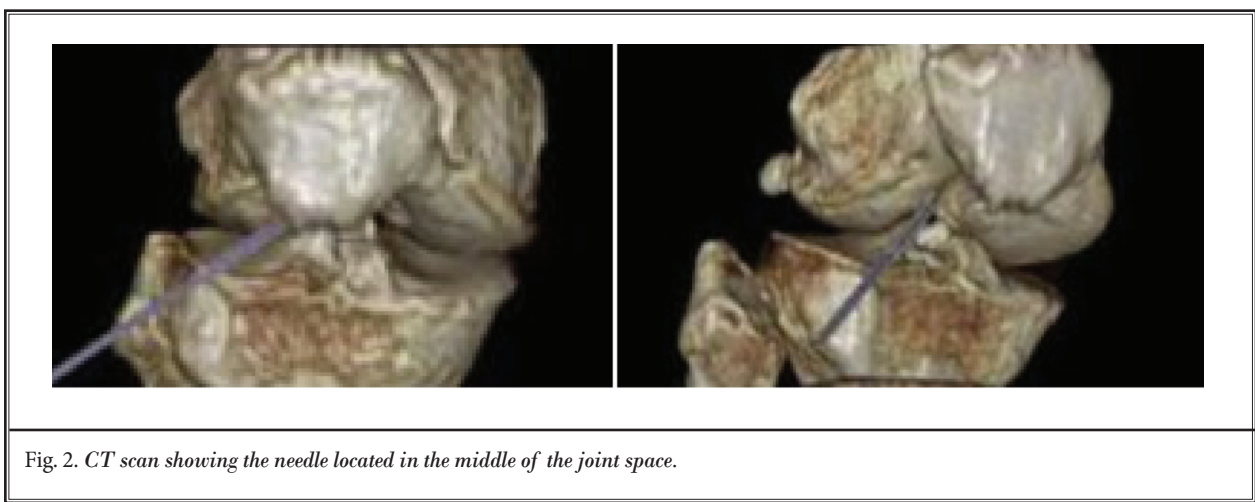


Fig. 2. CT scan showing the needle located in the middle of the joint space.

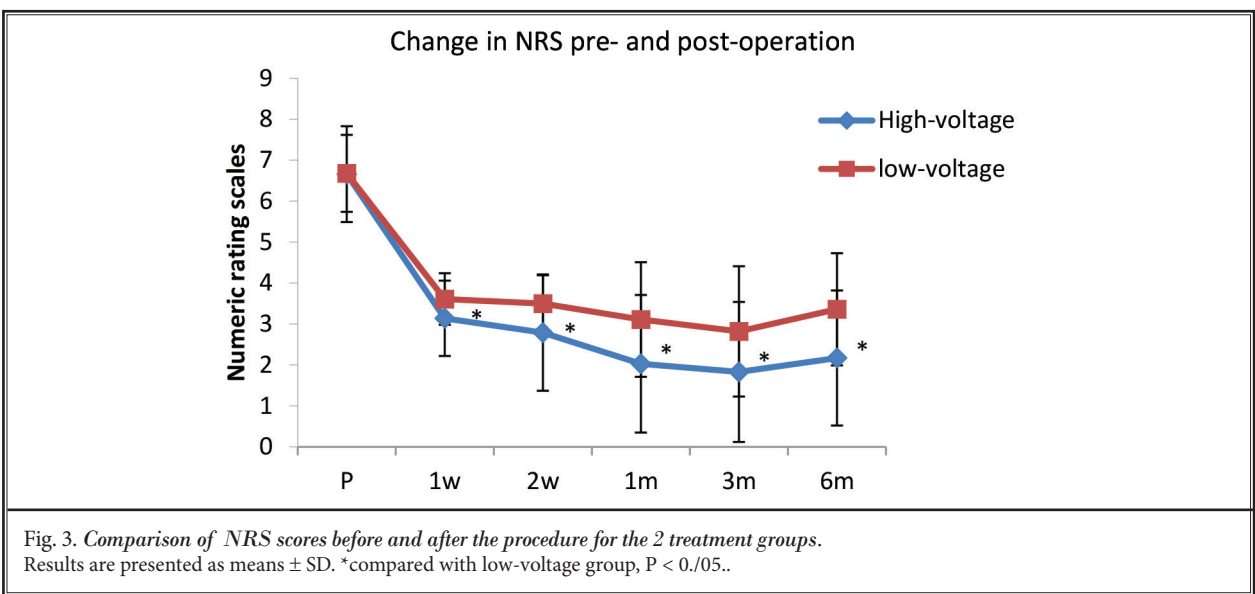


Fig. 3. Comparison of NRS scores before and after the procedure for the 2 treatment groups. Results are presented as means \pm SD. *compared with low-voltage group, $P < 0.05$.

Comparison of OKS Scores Before and After the Procedure for the 2 Treatment Groups

Although a statistically significant decrease in OKS was observed compared with baseline, no statistically significant differences in OKS were observed after the 1-week follow-up period for the 2 treatment groups. The OKS in the low-voltage group gradually returned to baseline levels from 1 week to 6 months postprocedure. Until the 3-month follow-up period, patients in the high-voltage group had at least a 13-point decrease in OKS compared with baseline scores, and a 9-point decrease at the 6-month follow-up period. There were significant differences between the 2 groups at follow-up periods between 2 weeks and 6 months ($P < 0.05$) (Fig. 4).

Efficiency Rate Before and After the Procedure Between the 2 Groups

The effective rate in the high-voltage group was slightly higher compared with the low-voltage group at 1 and 2 weeks postprocedure, however, no statistically significant differences were observed ($P > 0.05$). The effective rates for the high-voltage group were better compared with the low-voltage group at 1, 3, and 6 months posttreatment ($P < 0.05$) (Table 2).

Comparison of GPE After the Procedure in the 2 Treatment Groups

GPE in the high-voltage group was better compared with the low-voltage group at all follow-up time points after the surgery ($P < 0.05$). GPE was the

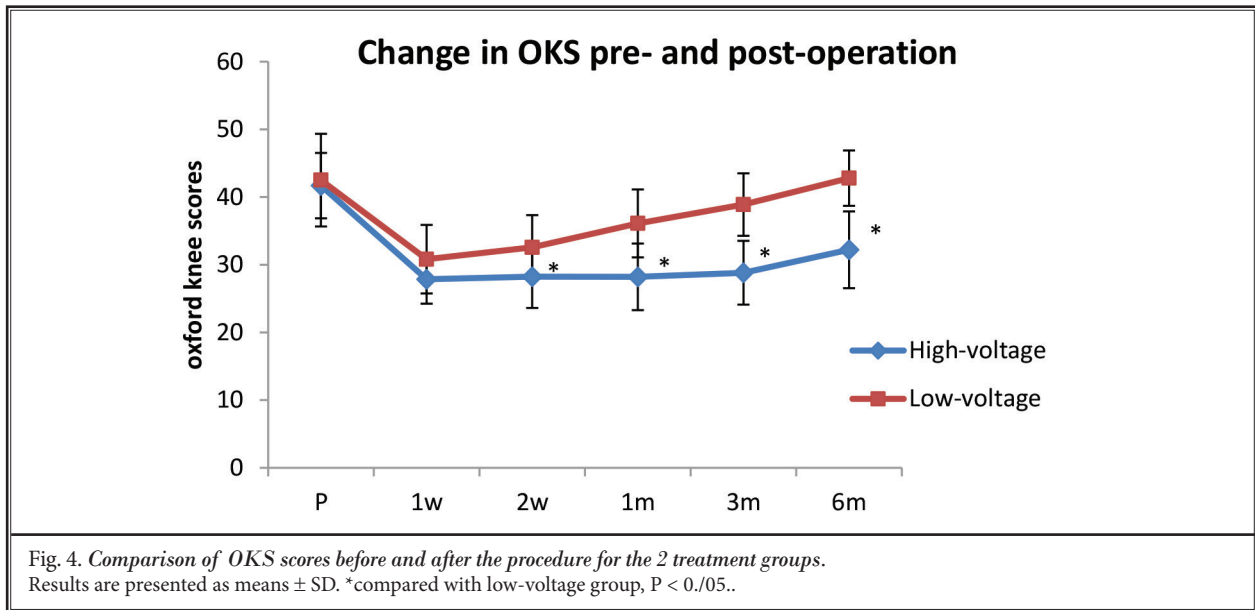


Table 2. Efficiency rate before and after the procedure between the 2 groups.

Time After Surgery	High-Voltage Group (n = 29)			Low-Voltage Group (n = 28)			P Value
	CR (%)	PR (%)	Efficiency rate (%)	CR (%)	PR (%)	Efficiency rate (%)	
1 week	1 (3.45)	13 (44.83)	48.28	0	9 (32.14)	32.14	0.215
2 weeks	4 (13.79)	12 (41.38)	55.17	0	12 (42.86)	42.86	0.352
1 month	10 (34.48)	11 (37.93)	72.41	2 (7.14)	11 (39.29)	46.43	0.046*
3 months	12 (41.38)	9 (31.03)	72.41	4 (14.29)	9 (32.14)	46.43	0.046*
6 months	9 (31.03)	7 (24.14)	55.17	2 (7.14)	6 (21.43)	28.57	0.042*

CR, complete remission; PR, partial remission. Compared with low-voltage group, * $P < 0.05$

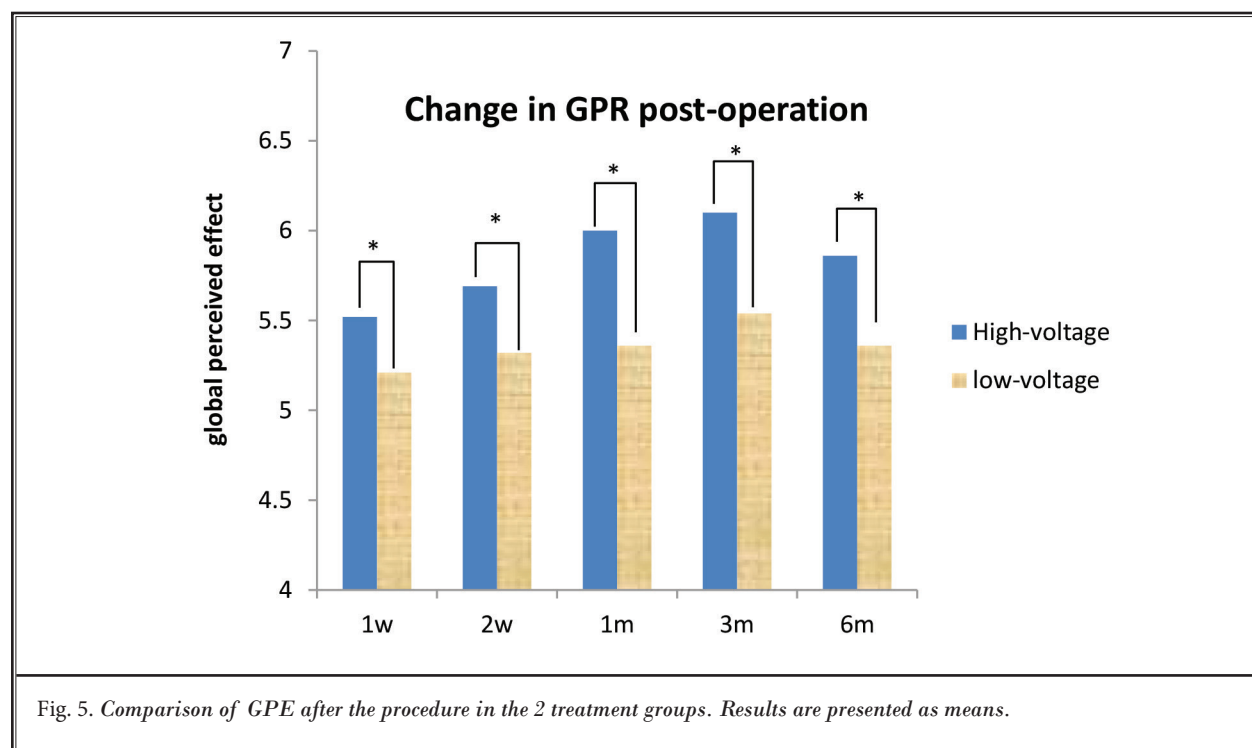
highest at 3 months follow-up for both groups (Fig. 5).

DISCUSSION

To our knowledge, this is the first study that compared the clinical efficacy between high- and low-voltage IAPRF for the treatment of KOA-related pain. In the present study, the output voltage/electrical field intensity in the high-voltage group was 65.10 ± 3.33 V/ 17.24 ± 2.37 W, which was 2 to 4 times greater compared with the low-voltage group. We observed that patients with pain relief 50% or more at 1, 3, and 6 months after the procedure accounted for 72.41%, 72.41%, and 55.17% of patients in the high-voltage group, and 46.43%, 46.43%, and 28.57% of patients in the low-voltage group, respectively. The proportion of patients pain-free in the 2 groups was 31.03% and 7.14% at the 6-month follow-up period. OKS were improved in the high-voltage group compared with patients in the low-voltage group. An average of 27 to 29 points in OKS was maintained until the 3-month follow-up period. In addition, patient satisfaction was higher in the high-voltage group during the long-term follow-up period.

KOA was once thought to be a primary disorder of the articular cartilage caused by long-term load on the

joints due to obesity, or subchondral bone alterations with cartilage damage and loss. However recent studies have demonstrated that synovitis and infrapatellar fat pad (IFP) inflammation are intimately associated with pain and osteoarthritis progression (15). Immune cells, such as macrophages, mast cells, natural killer (NK) cells, NKT cells, T cells, and B cells, reside in adipose tissues (including IFP). Inflammation of the synovial tissue or IFP results in clinical manifestations of knee pain and movement disorders (16). Although there are several peripheral nerves located in the knee joint capsule, including A β , A δ , and C fibers, the analgesic effect of IAPRF does not affect these nerves because the cannula needle tip is positioned in the knee joint cavity and away from these nociceptive nerves. Increased proinflammatory cytokines (such as IL-1b, TNF-a, and IL-6) localized in KOA may have intensive crosstalk to immune cells. The electric field produced by PRF may play a role in interfering with this intercell communication (12,17). After IAPRF, the level of inflammatory mediators decreases, which subsequently results in decreased reflex muscle spasms (relaxation of the sartorius, semitendinosus, and gracilis muscles). In addition, the space between the tibiofemoral and patellofemoral joint increased, thereby partial knee joint function improved (18).



High-voltage PRF was first investigated by Teixeira and Sluifjer (19). Eight patients with discogenic pain were treated with high-voltage PRF with 60 V inside the nucleus pulposus for 20 minutes. All patients had a decrease in NRS-11 scores of greater than 4 points at the 3-month follow-up period, with 5 patients having no pain recurrence at 12.8 months postprocedure. Fang et al (20) performed 2 prospective randomized double-blind trials to investigate the effectiveness of high-voltage PRF for the treatment of trigeminal neuralgia (20,21). The temperature used during the procedure was limited to 42°C or less and 240 seconds. When the therapeutic area was the Gasserian ganglion, the percentage of patients who had 50% pain relief in the high-voltage group (71.52 ± 7.97 V) and low-voltage group (36.30 ± 5.57 V) were 73% and 47% (3–6 month follow-up period) and 73% and 27% (at the 1-year follow-up period), respectively. In another study in which the target area was the infraorbital nerve, the percentage of patients who experienced 50% relief was 90% (at 1-year follow-up period). These patients were administered a higher voltage of 96 ± 9 V during the procedure compared with the previous study. The percent of patients with 50% pain relief in the low-voltage group was 60% at the 1-year follow-up period. Electrical stimulation was performed using 50 Hz, with pain induced at 0.1 to 0.2 V, suggesting that the distance between the needle tip and nerve was comparable. The results suggested that the output voltage used in the procedure was correlated with PRF efficacy.

Although IAPRF for KOA treatment has been rarely reported, the therapeutic efficacy of the procedure is encouraging (12-14,22,23). An output voltage of 40 to 45 V for 10 to 15 minutes during the IAPRF procedure results in 50% pain relief in 50% and 35.5% of patients at the 3- and 6-month follow-up period, respectively (13,14). This is similar to the therapeutic effects observed in patients in the low-voltage group in this study (46.43% and 32.14%). Schianchi et al (23) used a 60 V voltage to perform IAPRF and observed a 50% pain remission rate in 62.5% of patients at the 5-month follow-up period. Gulec et al (14) used bipolar PRF to treat KOA. In their study, the distance between the 2 cannula needle tips was less than 1 cm, which formed an oval electric field, resulting in an enlarged electric field area. They observed a 50% pain relief rate in 84% of the patients at the 3-month follow-up period after surgery. These findings also demonstrate that increasing the voltage and electrical field during IAPRF therapy may increase long-term

pain relief. In the present study, we controlled the treatment temperature to under 42°C. The manual PRF mode was used to gradually increase the output voltage, which indirectly changed the electric field near the needle tip. Follow-up results demonstrated that high-voltage was superior in relieving knee pain, improving knee function, and maintaining a longer analgesic effect.

The patients who we selected have the same treatment target (knee joint), which means that physical conditions of the electrode cannula needles are very similar in all treatments. Under these specific conditions, higher voltage causes larger range of the electric field, and electric field (or thermal lesion caused by electric field) produced by PRF is one of the key factors for the treatment effect of KOA. Based on the method and data proposed in Cosman and Cosman (24), we simulated the process of heating area increasing with time. The result shows that the lesion size under 70 V (191.29 mm²) is 1.97 times than that under 45 V (97.35 mm²) (Fig. 6).

No serious complications were observed in the present study, such as knee movement disorders or abnormal periarticular sensations. This suggested that increasing the voltage and electric field in the manual PRF mode and controlling the temperature to 42°C or less would not increase complications of the procedure. Only 3 patients had pain during the puncture procedure. This may be related to the needle touching the ligament or periosteum. The pain sensation diminished after adjusting the needle position.

The present study had several limitations. (1) This study was a single-center retrospective study with a relatively small sample cohort. Additional multicenter, randomized double-blind trials should be performed to obtain a more objective assessment. (2) Larger randomized controlled trials with appropriate designs are needed to further investigate the effects of the other PRF parameters on its therapeutic effects. These include pulse frequency, pulse width, and pulse duration. (3) The follow-up period was only 6 months. Additional studies should investigate the long-term analgesic effects of PRF. (4) We did not analyze medications and dosages that were administered to patients prior to surgery. A variety of drugs were administered to patients (weak opioids for patients who had stomach ulcers or NSAIDs for other patients). (5) The molecular mechanism of high-voltage PRF remains to be deciphered. Additional in vivo or in vitro studies

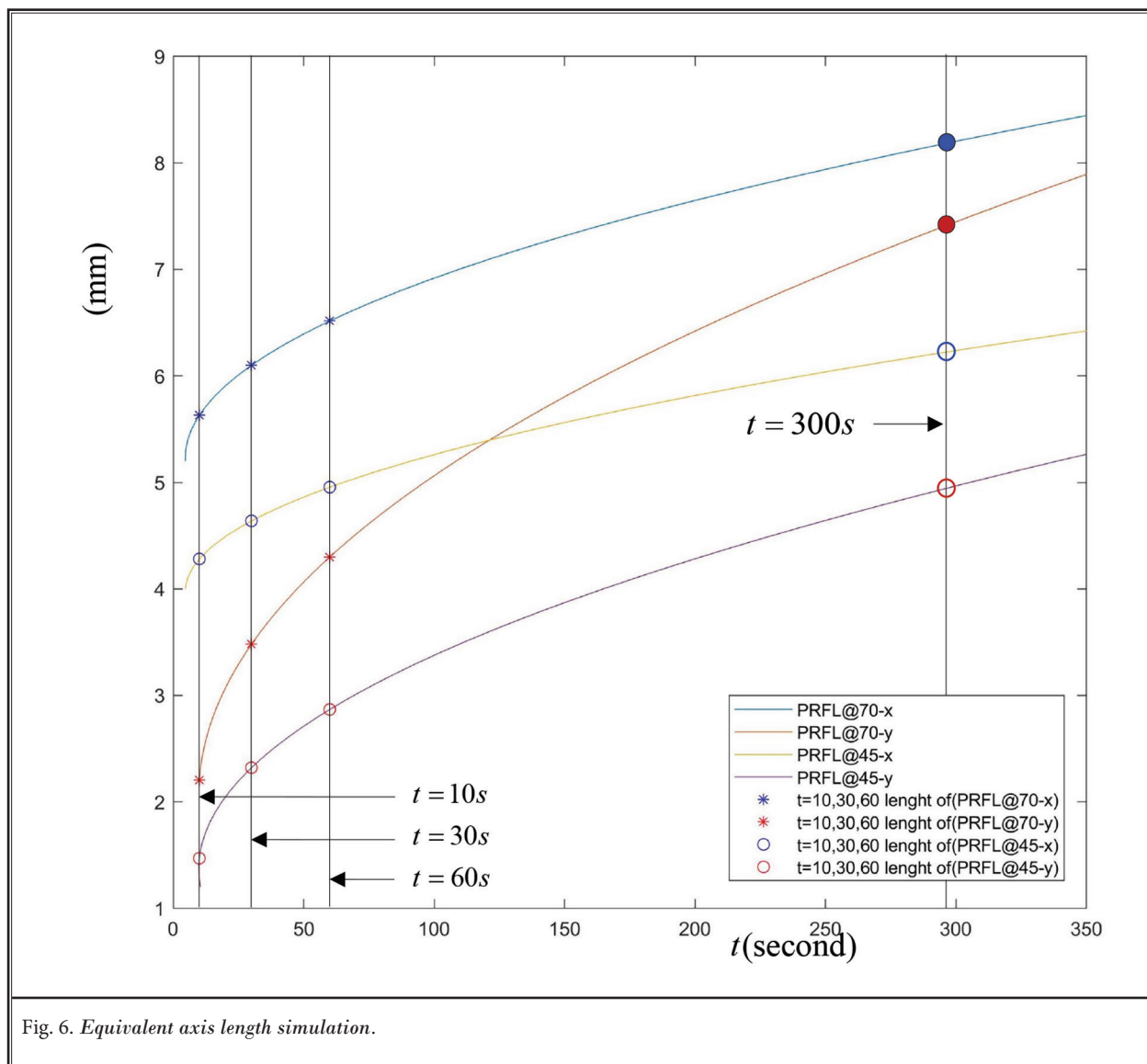


Fig. 6. Equivalent axis length simulation.

should be performed to understand its biological effect. Nonetheless, our findings strongly demonstrate that high-voltage IAPRF is an effective and feasible method for treating KOA-related pain.

CONCLUSIONS

High-voltage IAPRF could significantly relieve

knee pain and improve knee function. This minimally invasive procedure has a longer analgesic effect without significant adverse reactions. In addition, patient satisfaction in the high-voltage group was significantly higher compared with the low-voltage group.

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