Prospective Evaluation

Intradiscal Pulsed Radiofrequency for Chronic Lumbar Discogenic Low Back Pain: A One Year Prospective Outcome Study Using Discoblock for Diagnosis

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Background: Discogenic pain is an important cause of low back pain (LBP). We have developed a pulsed radiofrequency (PRF) technique, using Diskit II® needles (NeuroTherm, Middleton, MA, USA) placed centrally in the disk, for applying radiofrequency current in the disc (Intradiscal PRF method).

Objective: The purpose of this study was to investigate the effect of this intradiscal pulsed radiofrequency method in patients with chronic discogenic LBP diagnosed by discoblock, in terms of pain relief and reduction of disability.

Study Design: Prospective case series clinical outcome study.

Methods: The participants consisted of 23 patients with a mean age of 35.3 ± 9.86 years with chronic discogenic LBP that was not responsive to aggressive nonoperative care. A Diskit II needle (15-cm length, 20G needle with a 20-mm active tip) was placed centrally in the disc. PRF was applied for 15 minutes at a setting of 5 × 5 ms/s and 60 V. Outcome measures included the pain intensity score on a 0-10 numeric rating scale (NRS) and the Roland-Morris Disability Questionnaire (RMDQ) at pre-treatment, one, 3, 6, and 12 months post-treatment.

Results: The mean pain severity scores (NRS) improved significantly from 7.47 ± 0.85 pre-treatment to 3.13 ± 2.58 at the 12 month follow-up ($P < 0.01$). The RMDQ showed significant ($P < 0.01$) improvement from 11.4 ± 1.57 pre-treatment to 2.90 ± 2.97 at the 12 month follow-up ($P < 0.01$). Nineteen of 23 (82.6%) of the patients demonstrated NRS improvements of greater than 2, and 15 of 23 (65.2%) had > 50% pain reduction, 12 months after treatment.

Limitations: The number of patients was relatively low and secondary outcomes such as medication requirement or psychological effects were not addressed.

Conclusions: This intradiscal PRF method with consecutive PRF 5/5/60V, 15 min (with Diskit needle) appears to be a safe, minimally invasive treatment option for patients with chronic discogenic LBP.

Key words: Pulsed radiofrequency, discogenic pain, intradiscal procedures, chronic low back pain, Roland-Morris Disability Questionnaire

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Low back pain (LBP) is one of the most common causes of disability (1). Although there are a variety of etiologies, it has been estimated that discogenic LBP occurs in approximately 28 – 40% of all patients with low back pain (LBP) (2,3). Clinically the patients complain of chronic LBP often radiating into the buttock and the leg, uni- or bilaterally but without significant radicular pain. The pain is often provoked by cumulative loading. Patients also experience sitting intolerance. Neurological examination does not show severe neurological deficit, and the straight leg raising (SLR) test often gives equivocal results (2,3).

Discogenic pain is attributed to degenerative changes in the intervertebral disc due to aging or to traumatic events. The healthy adult disc has few nerves, and these are mainly restricted to the outer lamellae. In degenerated discs, nerves, containing nociceptive neurotransmitters and introdicing cytokines, have been found to penetrate into deeper intradiscal structures as far as the inner third of the annulus and the nucleus pulposus (4,5), creating nociceptive information from within the disc (4,5). The high levels of proinflammatory mediator has been found in disc tissue from LBP patients undergoing fusion (6). The production of proinflammatory mediators within the nucleus pulposus is assumed to be a major factor in the genesis of a painful lumbar disc (6-8).

Provocative discography has been considered a reference technique for confirming the intervertebral disc as a cause of the disogenic LBP (2,3). However, the reliability of discography is considered controversial (9). Ohtori et al (9) reported that pain relief after injection of a small amount of local anesthetic into the painful disc is a useful tool for the diagnosis of discogenic LBP compared with provocative discography. We have been considering whether it is important for the diagnosis of discogenic pain that discography blocks pain by more than 70% when injected with a small amount of local anesthetic(9).

Intradiscal electrothermal therapy (IDET), in which the annulus is coagulated using flexible catheters, has been used as a minimally invasive procedure for managing chronic discogenic LBP in patients failing conservative treatments (10-13). However, meta-analyses of the available documented evidence of the efficacy of IDET yields controversial conclusions (14-16).

In recent years, there has been a general trend in interventional treatment away from radiofrequency thermocoagulation toward pulsed radiofrequency (PRF) as a less invasive treatment. The use of PRF in the disc relies on the electric field generated, and the electric field is assumed to induce changes in the tissue that may explain changes in pain conduction and possibly induce a healing process (17,18). Degenerated discs producing discogenic back pain had nerves reportedly to be present in the inner third of the annulus fibrosis and nucleus pulposus (4,5). The electromagnetic field of the intradiscal PRF method was focused at the center of the target disc rather than on the outer one third, a more sensitive and essential area, in order to produce discogenic pain.

Teixeira and Sluijter (19) reported that high-voltage, long-duration intradiscal PRF, achieved by means of an electrode placed in the center of the nucleus pulposus, in patients with discogenic LBP produced excellent to good outcomes in 8 cases. Recently, minimally invasive intradiscal Diskit II® needles (NeuroTherm, Middleton, MA; USA), which are able to provide PRF to the disc with the 20mm active tip, have been developed (20). In the application of PRF, the length of the active tip has been shown to be an important element and the magnitude of the electric field parallel to the uninsulated part of the needle has been shown to be largest area (21).

We have developed a PRF technique, using one electrode placed centrally in the disc, for applying radiofrequency current in the disc (intradiscal PRF method).

The purpose of this study was to evaluate the efficacy of the intradiscal PRF of the intervertebral disc in a procedure with Diskit II® needles (NeuroTherm) in terms of pain relief and reduction of disability.

Table 1. *Patient demographics, levels treated and overall results*

Total Patients	n=23
Males	n=15
Females	n=8
Mean Age	35.3±9.86 years (Range 18-60)
Mean Symptom Duration	8 Months (Range 6-180)
Levels treated Frequency % total	
L4–5	9/23 (39.1%)
L5-S1	10/23 (43.4%)
L5–6	1/23 (4.3%)
L4–5, L5-S1	2/23 (8.6%)
L2–3, L4–5	1/23 (4.3%)

Methods

Study Design

Twenty-three patients who were diagnosed with disogenic LBP by analgesic discblock were enrolled in the study and underwent intradiscal PRF between October 2009 and January 2012.

All patients who met the criteria for the intradiscal PRF had presented to the Pain Management Clinic of Shiga University of Medical Science Hospital between 2009 and 2012. There were 23 patients (15 men, 8 women, 3 had 2 discs treated) and a total of 26 procedures were performed. The mean age was 35.3 ± 9.86 years (age 21 to 55 years). Of the total 23 discs treated, 9 were at L4-5, 10 were at L5-S1, one was at L5-6, 2 were at L4-5, L5-S1, and one was at L2-3, L4-5 (Table 1).

All patients had continuous back pain without

referral to the legs for a minimum of 6 months. All patients had been taking a variety of medications, including various nonsteroidal anti-inflammatory drugs (NSAIDS) and cyclooxygenase (COX)-inhibitors.

No patients had been taking opioids.

The criteria for inclusion in our study of intradiscal PRF were the following:

1. Chronic low back pain of at least 6 months continuous duration.
2. Lack of satisfactory improvement with a comprehensively applied non-operative care program including the following: epidural corticosteroid injection, a trial of physical therapy, and oral anti-inflammatory medication.
3. Normal neurologic examination findings.
4. Negative SLR results.
5. A magnetic resonance scan that did not demonstrate a neural compression lesion.
6. Concordant pain at low pressurization (low volume ≤ 1.25 mL contrast medium) during discography of the concerned disc. Intradiscal administration of 1 mL of lidocaine 2% diminished pain more than 70% (9).

The criteria of exclusion were

1. Disc extrusion or a sequestered fragment.
2. Severe spinal canal narrowing.
3. Segmental instability or psychological issues.
4. Systemic infection or localized infection at the anticipated needle entry sites.
5. Previous lumbar surgery.
6. Chronic lower extremity radiculopathy.
7. History of opioid abuse (22).

The study protocol was approved by the Human Ethics Committee of Shiga University of Medical Science Hospital. The procedure and associated potential complications such as nerve root injuries, epidural space bleeding, and discitis were explained to the patients, and informed consent was obtained before treatment.

The intradiscal PRF technique was performed with the patients who were lying on a fluoroscopy table in the prone position. The discs treated were selected on clinical grounds according to the level of provocative discography and discoblock.

Under fluoroscopic guidance, by a posterior oblique approach, the Diskit II® needle (NeuroTherm,20G, 15cm length, 20mm active tip, with radiopaque marker active tip) was percutaneously advanced and placed central of the disc that was responsible for the symptoms (Fig. 1).

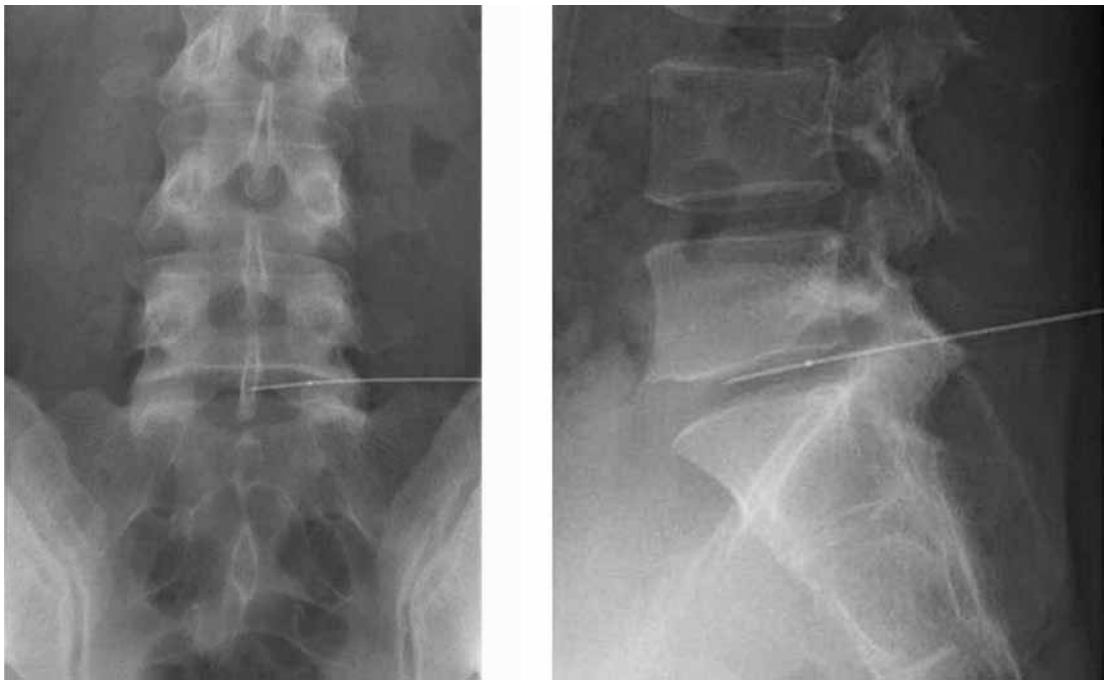

Fig. 1. *Intradiscal pulsed radiofrequency (PRF) procedures. Lateral view and anteroposterior (AP) view showing that the* Diskit II® needle *is positioned in the L4/5 and the active part of the Diskit needle is totally inside the disc*

Proper placement of the introducer needle was confirmed with anteroposterior, oblique, and lateral fluoroscopic projections. The proximal end of the tip was equipped with a radiopaque marker, the active tip was advanced to a position that was totally placed within the disc.

We applied intradiscal PRF at a frequency of 5Hz, pulse width of 5 ms, amplitude of 60V, and a maximum temperature of 40°C, for a duration of 15 minutes, by the NT1100 generator (NeuroTherm, Middleton, MA, USA).

Intradiscal PRF was performed on an outpatient basis. Prophylactic intravenous antibiotics were administered 15 – 40 minutes prior to beginning the procedure. After an hour of bed rest, patients were allowed to leave the outpatient room.

Outcome Measures

The intensity of the pain was assessed using the pain intensity score on a 0 – 10 numeric rating scale (NRS) at pre-procedure, after one, 3, 6, and 12 months.

In addition, the Roland-Morris Disability Questionnaire (RMDQ) score (23) was measured pre-procedure, and at one, 3, 6, and 12 months.

A successful clinical outcome was described as moderate when there was over a 2 point reduction in NRS to below 50% pain reduction, and good when 50% or more pain reduction was reported.

Stastical Analysis

Wilcoxon signed-rank test was applied to evaluate the improvement in NRS and RMDQ scores before and after the procedure. *P* values < 0.01 were considered statistically significant.

Results

The mean pre-operative NRS score was 7.47 ± 0.85 (range 6 – 9). Mean NRS decreased significantly, from 7.47 at pre-treatment to 3.87 ± 2.23 (range 0 – 8) at one month post-treatment, 3.47 ± 2.52 (range 0 – 8) at 3 months post-treatment, 3.21 ± 2.48 (range 0 – 8) at 6 months post-treatment, and 3.13 ± 2.58 (range 0 – 7) at 12 months post-treatment (Fig. 2). There were statistically significant decreases in NRS scores ($P < 0.01$, Wilcoxon signed-rank test) when compared to the pre-operative values (Fig. 2).

Mean RMDQ score improved from 11.4 ± 1.57 (range 8 – 14) to 5.00 ± 2.73 (range 1 – 12) at one month

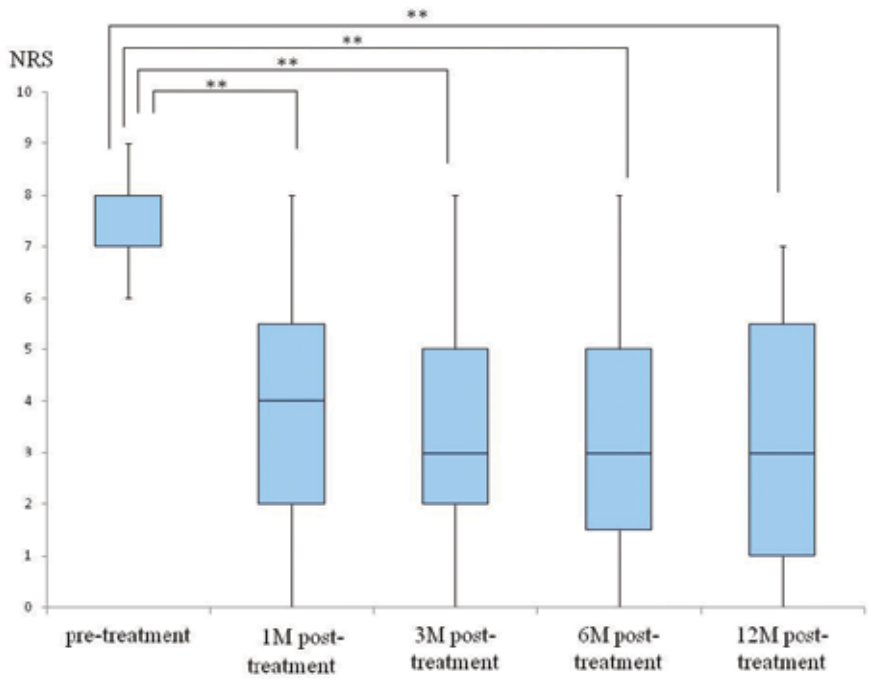

Fig. 2. *Mean numeric rating scale (NRS) scores at pre-procedure, one, 3, 6, and 12 months post-procedure. Data are presented as median and lower limit, 25th, 75th and upper limit percentiles. Wilcoxon signed-rank test **P < 0.01.*

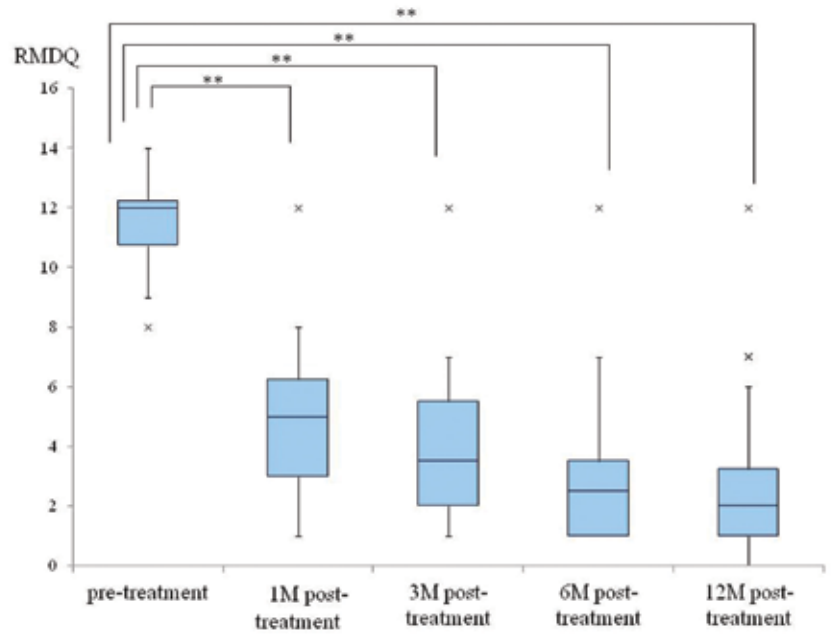

Fig. 3. *Mean Roland-Morris Disability Questionnaire (RMDQ) scores at pre-procedure, one, 3, 6, and 12 months post-treatment. Data are presented as median and lower limit, 25th, 75th and upper limit percentiles. Wilcoxon signed-rank test **P<0.01*

post-treatment, 4.05 ± 2.79 (range 1 – 12) at 3 months post-treatment, 3.30 ± 2.83 (range 1 – 12) at 6 months post-treatment, and 2.90 ± 2.97 (range 1 – 12) at 12 months post-treatment (Fig. 3).

These decreases in RMDQ scores were statistically significant ($P < 0.01$, Wilcoxon signed-rank test) when compare to pre-operative values (Fig. 3).

Fifteen of 23 (65.2%) patients had good ratings and 4 of 23 (17.4%) patients had moderate ratings at the 12-months follow-up (Table 2).

Table 2. *Clinical successful outcome at each follow-up period after intradiscal pulsed radiofrequency.*

Outcome	3 months	6 months	12 months
Good	4 (17.4%)	5 (21.8 %)	4 (17.4%)
Moderate	15 (65.2%)	14 (60.9%)	15 (65.2%)
No improvement	4 (17.4 %)	4 (17.4 %)	4 (17.4 %)

No improvement: there was no outcome over the 2 point NRS score improvement compared to the pre-teratment state.

After the intradiscal PRF treatment, none of the patients increased the amount of medication and none increased the types of medication taken. No patients complained of flare-up pain after the intradiscal PRF procedures. All procedures were considered technically successful. There were no complications of nerve root injuries, epidural space bleeding, discitis, or infection related to procedures. There were no cases of worsening motor or sensory status.

Discussion

The exact mechanism by which intradiscal PRF reduces discogenic pain is uncertain; however, intradiscal PRF is thought to decrease discogenic pain by 2 different mechanisms. First, high voltage PRF current applied intradiscally by means of Diskit needles may cause very strong electric fields and these could potentially have a biological effect on the nerve endings (21,24,25) that have been sprouting into the nucleus in the disc (4,5). The electric field generated is assumed to induce changes in the tissue that may explain changes in pain conduction (21,24). Exposure of PRF to the dorsal root ganglion can affect cellular function in the dorsal horn of the spinal cord, independently of thermal effects (26). Apparently, the electromagnetic field of PRF may enhance descending inhibitory pathways, specifically involving the noradrenergic and serotonergic systems (27). In addition, the nerve damage appears to be more

pronounced for C-fibers, known as principle sensory nociceptors, than for A-δ and A-β fibers (28). The second effect could possibly reflect an action of the electric field on immune cells, thus influencing the production of anti-inflammatory cytokines, resulting in decreased levels of pro-inflammatory cytokines such as interleukin (IL)-1b, tumor necrosis factor (TNF)-α, and IL-6 (29-33). The electric field of PRF have demonstrated effects on immune modulation, as there are studies that show proinflammatory cytokines, such as IL- 1 b, TNF-α, and IL-6 are attenuated by the electric field (32-34).

Chronic discogenic pain may result from mechanical stimulation of annulus fissures, or from delamination, in which the annular lamellae repeatedly stimulate nociceptors that may have been presensitized (5). Peng et al (35) reported that the natural history of discogenic LBP was chronic but persistent, and that the pain and disability in most patients did not improve over time.

IDET has been used as a procedure for managing chronic discogenic LBP in patients failing conservative treatments (10-13). However, meta-analyses and systematic reviews of the data on IDET produce contradictory results (14). Furthermore, most patients who underwent IDET suffer long-lasting (up to 2 months) post-procedure flare-up pain (36).

Teixeira and Sluijter (19) first reported on PRF treatment for discogenic pain. However, there has been only one investigation of intradiscal PRF with Diskit needles in patients with discogenic pain (20).

In the present study, the pain intensity scores (NRS) and RMDQ scores showed significant ($P < 0.01$) improvement at one, 3, 6, and 12 months after intradiscal PRF treatment. Intradiscal PRF resulted in 82.6% of patients reporting a successful clinical outcome after 12 months. Based upon our results, intradiscal PRF appears to be an effective and promising non-operative treatment for discogenic LBP.

A major advantage of intradiscal PRF with Diskit II® needles are that when used in discectomized discs it is relatively easy to place the Diskit needle, eliminating the need to thread a long heating portion of an IDET catheter. The Diskit needles are thin (20G) allowing treatment of discs with a residual height as low as 10-25% of the original height, while IDET electrodes are up to 17G and treatment can only be performed in discs that still have at least 50% of their original height. Intradical PRF is also an outpatient procedure, only local anesthesia is needed, and the procedure takes a very short amount of time. Furthermore, intradical PRF could eliminate the long-lasting (up to 2 months) flare-up pain linked to other techniques using radiofrequency thermocoagulation, such as IDET (36).

Intradiscal PRF appears to be a good alternative minimally invasive treatment to IDET (10-13) for discogenic pain which was resistant to other conservative therapies.

Teixeira and Sluijter (19) reported the effect of intradiscal PRF treatment in 8 patients via a numeric rating scale, and all patients had a drop of at least 4 points at the 3-month follow-up. The parameters applied for PRF were 60 V for 20 minutes, frequency 2 and 20 milliseconds pulse width, with a 15-mm active tip. Another study by Rohof (20) reported that 70.9% patients had a drop of at least 2 points at the 12-month follow-up and 56.5% of the patients had > 50% pain reduction at 12 months. The parameters applied for PRF were 60 V for 15 minutes, frequency 2 and 10 milliseconds pulse width, with a 20-mm active tip.

The clinical outcome of our study was apparently better than that of previous studies. It might have been attributed to the differences in the diagnostic method of discoblock (9).

Contrary to previous studies (20,37) using automated pressure-controlled discography (38) or manually controlled discography (39), we utilized discoblock as the inclusion criteria (9). This apparently may have led to the reliability of our dignostic method and the improvement in the quality of the data. Carefully selected patients with discogenic LBP, nonresponsive to conservative care, with definitive imaging and provocative discography and discoblock (9) seem to benefit clinically from intradiscal PRF in terms of pain reduction, functional, and quality-of-life improvement.

To achieve the optimal outcome through intradiscal PRF, further research is needed about the proper setting conditions of pulse width, pulse frequency, voltage, and stimulation time for applying PRF current, which is yet to be established.

Limitations

The limitations of this study were that it was not controlled and the number of patients was small. However, to lessen the possibility of natural improvement without PRF treatment in this study, patients who had shown no interval change of their pain intensity despite conservative treatment for at least 6 months were chosen.

Conclusion

Patients who underwent intradiscal PRF for chronic discogenic LBP showed significant improvements in terms of pain relief and reduction of disability. Intradiscal PRF appears to be a safe, minimally invasive treatment option for carefully selected patients with chronic discogenic LBP who have not responded to aggressive non-operative care. Further randomized placebo-controlled studies with longer follow-up periods or randomized studies of different pulse width or frequency are needed to elucidate the effects, as well as to explore the action mechanisms to reduce discogenic pain.

References

1. Andersson GBJ. Epidemiology of low back pain. *Acta Orthop Scand* 1998; 69:28-33.
2. Schwarzer AC, Aprill CN, Derby R, Fortin J, Kine G, Bogduk N. The prevalence and clinical features of internal disc disruption in patients with chronic low back pain. *Spine 1995; 20:1878-1883.*
3. Zhou YL, Abdi S. Diagnosis and minimally invasive treatment of lumbar discogenic pain – a review of the literature. *Clin J Pain* 2006; 22:468-481.
4. Gronblad M, Weinstein JN, Santavirta S. Immunohistochemical observations on spinal tissue innervation. A review of hypothetical mechanisms of back pain. *Acta Orthop Scand* 1991; 62:614-622.
5. Freemont AJ, Peacock TE, Goupille P, Hoyland JA, O'Brien J, Jayson MI. Nerve ingrowth into diseased intervertebral disc in chronic back pain. *Lancet* 1997; 350:178-181.
6. Burke JG, Watson RW, McCormack D, Dowling FE, Walsh MG, Fitzpatrick JM. Intervertebral discs which cause low back pain secrete high levels of proinflammatory mediators. *J Bone Joint Surg Br* 2002; 84:196-201.
7. Ulrich JA, Liebenberg EC, Thuillier DU, Lotz JC. ISSLS prize winner: Repeated disc injury causes persistent inflammation. *Spine* 2007; 32:2812-2819.
8. García-Cosamalón J, del Valle ME, Calavia MG, García-Suárez O, López-Muñiz A, Otero J, Vega JA. Intervertebral disc, sensory nerves and neurotrophins: Who is who in discogenic pain? *J Anat* 2010; 217:1-15.
9. Ohtori S, Kinoshita T, Yamashita M. Yamauchi K, Koshi T, Suzuki M, Orita S, Eguchi Y, Nakamura S, Yamagata M, Takaso M, Ochiai N, Kishida S, Aoki Y, Takahashi K. Results of surgery for discogenic low back pain: A randomized study using discography versus discoblock for diagnosis. *Spine* 2009; 34:1345-1348.
10. Saal JA, Saal JS. Intradiscal electrothermal treatment for chronic discogenic low back pain. Prospective outcome study with a minimum 2-year follow-up. *Spine* 2002; 27:966-974.
11. Saal JA, Saal JS. Intradiscal electrothermal treatment for chronic discogenic low back pain: A prospective outcome study with minimum 1-year follow-up. *Spine* 2000; 25:2622–2627.
12. Pauza KJ, Howell S, Dreyfuss P, Peloza JH, Dawson K, Bogduk N. A randomized, placebo-controlled trial of intradiscal electrothermal therapy for the treatment of discogenic low back pain. *Spine J* 2004; 4:27-35.
13. L utz C, Lutz GE, Cooke PM. Treatment of chronic lumbar discogenic pain with intradiscal electrothermal therapy: A prospective outcome study. *Arch Phys Med Rehabil* 2003; 84:23-28.
14. Appleby D, Andersson G, Totta T. Meta-analysis of the efficacy and safety of intradiscal electrothermal therapy (IDET). *Pain Medicine* 2006; 7:308-316.
15. Freeman BJ. IDET: A critical appraisal of the evidence. *Eur Spine J* 2006; 15:S448-457.
16. Urrutia G, Kovacs F, Nishishinya MB, Olabe J. Percutaneous thermocoagulation intradiscal techniques for discogenic low back pain. *Spine* 2007; 32:1146-1154.
17. Cosman EJ, Cosman ES. Electric and thermal field effects in tissue around radiofrequency electrodes. *Pain Med* 2005; 6:405-424.
18. Cohen SP, Van Zundert J. Pulsed radiofrequency: Rebel without cause. *Reg Anesth Pain Med* 2010; 35:8-10.
19. Teixeira A, Sluijter ME. Intradiscal high-voltage, long-duration pulsed radiofrequency for discogenic pain: A preliminary report. *Pain Med* 2006; 7:424-428.
20. Rohof, O. Intradiscal pulsed radiofrequency application following provocative discography for the management of degenerative disc disease and concordant pain: A pilot study. *Pain Practice* 2012; 125:342-349.
21. Cosman ER, Cosman ER. Electric and thermal field effects in tissue around radiofrequency electrodes. *Pain Med* 2005; 6:405-424.
22. Webster BS, Verma S, Pransky GS. Outcomes of workers' compensation claimants with low back pain undergoing intradiscal electrothermal therapy. *Spine* 2004; 29:435-441.
23. Fujiwara A, Kobayashi N, Saiki K, Kitagawa T, Tamai K, Saotome K. Association of the Japanese Orthopaedic Association score with the Oswestry Disability Index, Roland-Morris Disability Questionnaire, and Short-Form 36. *Spine* 2003; 28:1601-1607.
24. Bogduk N. Pulsed radiofrequency. *Pain Med* 2006; 7:396-407.
25. Cahana A, Vutskits L, Muller D. Acute differential modulation of synaptic transmission and cell survival during exposure to pulsed and continuous radiofrequency energy. *J Pain* 2003; 4:197-202.
26. Higuchi Y, Nashold BS Jr, Sluijter M, Cosman E, Pearlstein RD. Exposure of the dorsal root ganglion in rats to pulsed radiofrequency currents activates dorsal horn lamina I and II neurons. *Neurosurgery* 2002; 50:850-856.
27. Hagiwara S, Iwasaka H, Takeshima N, Noguchi T. Mechanisms of analgesic action of pulsed radiofrequency on adjuvant-induced pain in the rat: Roles of descending adrenergic and serotonergic systems. *Eur J Pain* 2009; 13:249-252.
28. Erdine S, Bilir A, Cosman ER, Cosman ER Jr. Ultrastructural changes in axons following exposure to pulsed radiofrequency fields. *Pain Practice* 2009; 9:407- 417.
29. Chua NH, Vissers KC, Sluijter ME. Pulsed radiofrequency treatment in interventional pain management: mechanisms and potential indications—a re-

view. *Acta Neurochir* 2011; 153:763-771.

30. Sluijter ME, Teixeira A, Serra V, Balogh S, Schianchi P. Intra-articular application of pulsed radiofrequency for arthrogenic pain—report of six cases. *Pain Practice* 2008; 8:57-61.
31. Schianchi PM, Sluijter ME, Balogh SE. Transforaminal pulsed radiofrequency for the treatment of cervical radicular pain: An alternative to steroid infiltration. *J Neurol Surg* 2012; 73:A017.
32. Rohde C, Chiang A, Adipouju D, Casper D, Pilla AA. Effects of pulsed electromagnetic fields on interleukin-1β and postoperative pain: A double-blind, placebo-controlled, pilot study in breast reduction patients. *Plastic & Reconstructive Surgery* 2010; 125:1620-1629.
33. Podhajsky RJ, Sekiguchi Y, Kikuchi S, Myers RR. The histologic effects of pulsed and continuous radiofrequency lesions at 42 degrees C to rat dorsal root ganglion and sciatic nerve. *Spine* 2005; 30:1008-1013.
34. Vallejo R, Tiley D, Vogel L, Benyamin R. Pulse radiofrequency attenuates cytokine expression in the spared nerve injury model. American Society of Regional Anesthesia Annual Meeting, San Antonio, TX, 2009.
35. Peng B, Fu X, Pang X, Li D, Liu W, Gao C, Yang H.Prospective clinical study on natural history of discogenic low back pain at 4 years of follow-up. *Pain Physician* 2012; 15:525-532.
36. Derby R, Seo KS, Kazala K, Anderson PA. A factor analysis of lumbar intradiscal electrothermal annuloplasty outcomes. *The Spine J* 2005; 5:256-262.
37. Jung YG, Lee DG, Cho YW, Ahn SH., Effect of intradiscal monopolar pulsed radiofrequency on chronic discogenic back pain diagnosed by pressure-controlled provocative discography: A one year prospective study. *Ann Rehabil Med* 2012; 36:648-656.
38. Carragee EJ, Lincoln T, Parmar VS, Alamin T. A gold standard evaluation of the "discogenic pain" diagnosis as determined by provocative discography. *Spine* 2006; 31:2115-2123.
39. Buenaventura RM, Shah RV, Patel V, Benyamin R, Singh V. Systematic review of discography as a diagnostic test for spinal pain: an update. *Pain Physician* 2007; 10:147-164.