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A randomized double-blind controlled trial of intra-annular radiofrequency thermal disc therapy – A 12-month follow-up

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ABSTRACT

The discTRODE™ probe applies radiofrequency (RF) current, heating the annulus to treat chronic discogenic low back pain. Randomized controlled studies have not been published. We assessed the long-term effect and safety aspects of percutaneous intradiscal radiofrequency thermocoagulation (PIRFT) with the discTRODE™ probe in a prospective parallel, randomized and gender stratified, double-blind placebo-controlled study. Twenty selected patients with chronic low back pain and a positive one-level pressure-controlled provocation discography were randomized to either intra-annular PIRFT or intra-annular sham treatment. A blinded interim analysis was performed when 20 patients had been followed for six months. The 6-month analysis did not reveal any trend towards overall effect or difference between active and sham treatment for the primary endpoint: change in pain intensity (0–10). The inclusion of patients was therefore discontinued. After 12 months the overall reduction from baseline pain had reached statistical significance, but there was no significant difference between the groups. The functional outcome measures (Oswestry Disability Index, and SF 36 subscales and the relative change in pain) appeared more promising, but did not reach statistical significance when compared with sham treatment. Two actively treated and two sham-treated patients reported increased pain levels, and in both groups a higher number was unemployed after 12 months. The study did not find evidence for a benefit of PIRFT, although it cannot rule out a moderate effect. Considering the high number, reporting increased pain in our study, we would not recommend intra-annular thermal therapy with the discTRODE™ probe.

1. Introduction

Different percutaneous techniques, coagulating the annulus fibrosus, have been introduced for the treatment of chronic discogenic low back pain (CDLBP). The first non-controlled and non-randomized case-controlled studies of Intradiscal Electrothermal Therapy (IDET) reported long-lasting pain relief [8,20,29], but the efficacy data from later randomized controlled trials have been less impressive [15,27]. DiscTRODE ™ is another system, where radiofrequency (RF) current is applied in order to heat the posterior annulus [17]. The treatment is termed percutaneous intradiscal radiofrequency thermocoagulation (PIRFT) [35]. The efficacy data are limited, but significant pain reduction has been reported in one non-controlled [11] and one case-controlled study [14]. Encouraged by promising results in a small pilot study, we decided to perform a randomized placebo-controlled study on PIRFT using the discTRODE™. The objective of the study was to assess the long-term effect and safety. We hypothesized that heating the posterior annulus by radiofrequency current could lead to a long-lasting and significant reduction in pain related to internal disc disruption.

2. Materials and methods

2.1. Design

To test the hypothesis we conducted a prospective parallel, randomized and gender stratified, double-blind placebo-controlled study. We assumed that penetrating the annulus might in itself have biological effects. To examine whether the pain-relieving effect was caused by the heat lesion or not, the discTRODE™ probe was therefore inserted into the annulus in both groups. The patients included had tried all kinds of conventional treatment, and

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the study did not delay other established treatment modalities. We observed the outcome variables for 12 months, with a planned interim analysis when 20 patients had been followed for 6 months. Before the study started we decided that if the blinded interim analysis showed (1) no trend towards benefit on the primary outcome (change in pain intensity), (2) any increased pain or (3) decreased score on functional outcomes, the inclusion of patients into the study would be discontinued. If RF thermal therapy was found more effective than sham therapy, we would, after the trial, offer active treatment to those who were given sham therapy.

The study was performed in accordance with the Helsinki declaration [37] and approved by the Ethical Committee for Medical Research of Health Region II in Norway. The assessment and procedures were carried out at the Pain Clinic, in the Department of Radiology and at The Interventional Centre at Oslo University Hospital, Rikshospitalet. Participants were not offered economic inducements, but the treatment was free of charge. The participants were given extensive written and verbal information about the trial, the potential benefits and risks before giving their written consent. The presentation of the study follows the CONSORT recommendations for randomized, controlled clinical trials [26].

2.2. Patient selection

The inclusion and exclusion criteria are listed in Table 1a and b, while the flow diagram in Fig. 1 shows the selection and treatment allocation of patients. Chronic low back pain (CLBP) patients, who responded to medial branch blocks at the three lower lumbar segments or to transforaminal epidural steroid injection at the suspected level of pathology, were excluded. In order to select patients with a high probability of discogenic pain, we performed a three-level (L3/L4, L4/L5 and L5/S1) pressure-controlled provocation discography. To be qualified for provocation discography two neuroradiologists in consensus had to demonstrate findings of moderate structural degeneration of at least one of the three lower lumbar discs on an MRI scan taken within the last 6 months. Moderate structural degeneration included; reduced disc height but not more than 30%, disc protrusion less than 4 mm, and decreased water content or high intensity zones (HIZ). The discography was performed according to the standards prescribed by the International Spine Intervention Society [9]. The change in pain intensity was assessed with an 11-graded numeric rating scale (0–10), with "no pain" and worst pain imaginable" as anchors. Patients were found eligible if the discography reproduced typical ("concordant") and intensive low back pain (>7/10) at only one of the three levels. The procedure was discontinued if the patients felt unacceptable pain. To identify the location of relevant annular tears an axial computed tomography (CT) scan was taken immediately after and within 1 h of the discography.

2.3. Randomization

The patients were allocated to either active intra-annular thermal treatment or sham treatment in ratio 1:1 in gender-stratified [25,34] blocks of eight by use of random numbers. The block size and randomization codes were not revealed until all measurements had been entered into the database after a 12-month observation.

Table 1a
Inclusion criteria.

(1)	Age of 20 to 65 years
(2)	Unremitting low back pain for more than 6 months
(3)	Pain intensity $\geqslant$5 of maximum 10 (NRS) and low back pain greater than leg pain
(4)	Exacerbated by sitting and relieved by laying
(5)	No neurological deficits and negative straight raised leg test (Laseque)
(6)	No previous surgical interventions
(7)	Failure to improve with conservative treatment (physical and manual therapy and non-opioid medications)
(8)	Signs of disc degeneration (MR scan) or posterior annular tear (CT scan)
(9)	Disc height reduction less than 30% and disc protrusion less than 4 mm
(10)	Positive one-level pain provocation discography

Table 1b
Exclusion criteria.

(1)	Acute infection
(2)	History of drug abuse
(3)	Psychological, cognitive disturbances or somatic disorder which could affect the outcome
(4)	Previous lumbar spine surgery
(5)	Abnormal neurological examination
(6)	Radicular pain by history or examination
(7)	Structural spinal deformities or vertebral canal stenosis
(8)	Intervertebral disc herniations equivalent to or greater than 4 mm or sequestered intervertebral disc herniations
(9)	Pregnancy
(10)	Allergy to contrast media or drugs to be used in the procedure

2.4. Treatment protocol

The treatment procedure was performed four to six weeks after the discography as we did not know whether the injected contrast agent could influence the outcome. The patients were placed in prone position and monitored with ECG and pulse oximetry. They were allowed intravenous incremental doses of analgesics (alfentanil 0.25–0.5 mg) but no sedation. Being awake throughout the procedure, the patients were able to respond if a nerve root was exposed to thermal or mechanical stimulation.

The insertion of the discTRODE™ probe was carried out with one single operator (LM) under aseptic conditions and intermittent multiplane fluoroscopic guidance. The skin and the paravertebral muscles were anesthetized with 5 ml of lidocaine 10 mg/ml. From a posterolateral approach a 17 Gauge introducer was inserted into the outer annular part of the disc at the most painful side. With the introducer in optimal position, just inside the annulus confirmed by fluoroscopy and by impedance measurements lower than 400 Ohm [14] a flexible discTRODE™ probe (Radionics RFG-3C, Valleylab, Tyco Healthcare Group LP 5920 Longbow Drive, Boulder, Colorado 80301–3299 USA) was navigated in-between the posterior annular layers of the target disc and medially to cover the dorsal annulus and if possible the annular tears. Exact electrode position was ascertained by a computerized three-dimensional tomography. We graded the final, accepted probe position on a three-point scale; (1) the electrode optimally placed along the posterior wall of the annulus fibrosus, with the tip covering the annular fissure, (2) the electrode partly placed along the posterior wall of the annulus fibrosus, and (3) the electrode directed into deeper annular layers towards the nucleus pulposus. If needed, the electrode was repositioned.

When we had accepted the position of the discTRODE™ probe, the treatment allocation (enclosed within a sealed envelope marked with patient number only) was revealed to the investigator responsible for RF-generator control. To keep the patient blinded the sound from the RF generator was shut off. The operator and the independent assessor were not present during the RF-treatment procedure, and they and the patients were kept blinded throughout the 12-month observation period of the trial.

In the active treatment group the annulus fibrosus was subjected to RF heating. We followed a 10-min protocol recommended by the Radionics and published by Finch [13] with an incremental heating, starting at 50 °C, increasing by 5 °C every second minute, and ending with a 4-min interval at 65 °C. The sham group was exposed to a similar intervention, but the annulus was not exposed to RF heating. After completing the procedure, but before the

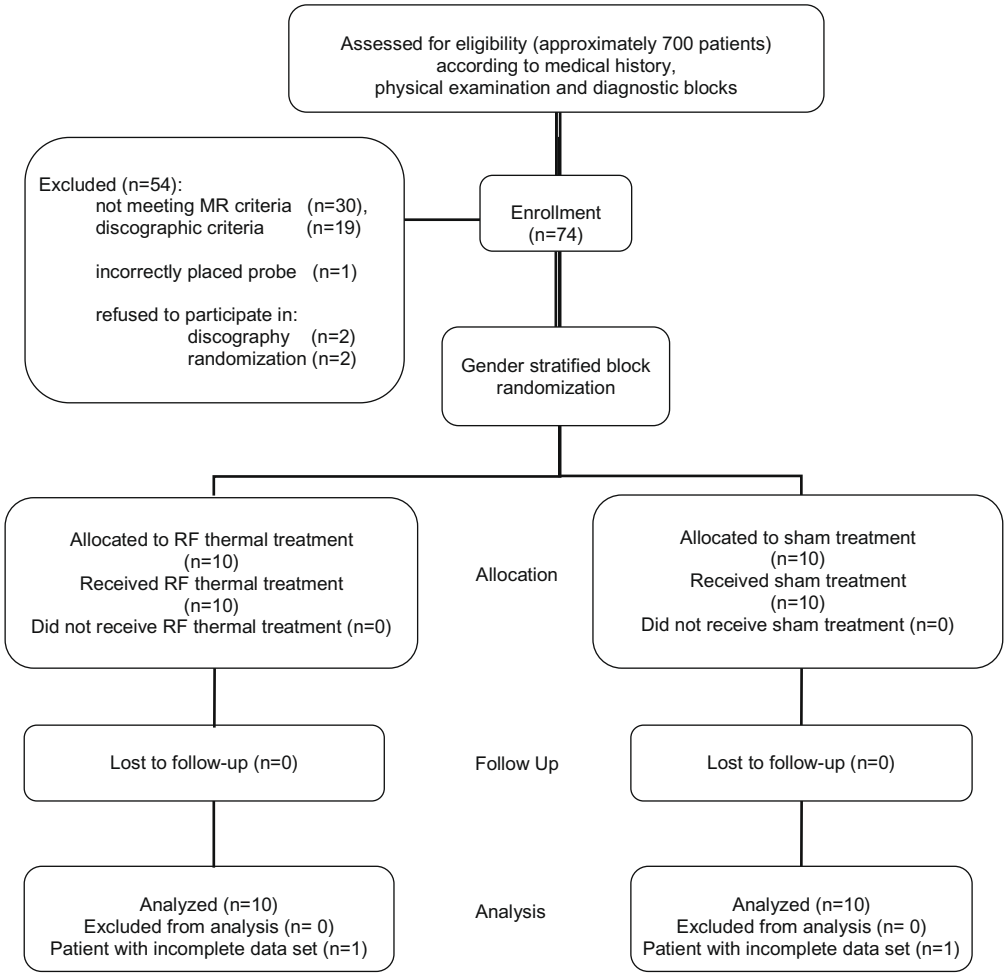

Fig. 1. The diagram shows the flow of patients treated with intra-annular radiofrequency thermal or sham treatment with the discTRODE™ probe. The patients were selected according to medical history, physical examination and the response to diagnostic blocks of the lumbar medial branches and lumbar nerve roots and to diagnostic provocative discography. To be qualified for provocative discography an MRI scan of the three lower lumbar discs should demonstrate only moderate signs of structural degeneration.

introducer and electrode were withdrawn, 2 ml of bupivacaine 5 mg/ml and 10 mg of cefuroxim were injected into the disc. The patient was discharged from the hospital after 1 h with no physical restrictions. Paracetamol was recommended orally for postprocedural pain.

2.5. Follow-up and data collection

The follow-up and data collection were carried out by a specially trained nurse (blinded for treatment allocation) for baseline and at follow-ups 1, 3, 6 and 12 months post-procedure. Sociodemographic variables such as age, gender, and type of work (physically or not physically demanding work) were included. The patients were asked about disability (due to back pain or other reasons), daily consumption of analgesics (non-opioids, weak opioid, carisoprodol or strong opioids) and other treatment modalities (e.g. physiotherapy, manual and chiropractic therapy, injections, acupuncture or psychotherapy) in use just prior to treatment.

2.5.1. Primary outcome measure – numeric change in pain intensity

Change in self-reported pain intensity was the primary outcome. To measure pain intensity we applied four 11-pointed numeric rating scales (0–10) (NRS) for "worst pain", "average pain", "least pain" for the last 24 h and "pain right now" as in the Brief Pain Inventory (BPI) [5–7]. A decrease of two or more on the 11-point NRS was considered clinically significant. Patients were distributed into two categories; those with a reduction in numeric pain intensity equivalent to or more than two points and those without.

2.5.2. Secondary outcome measure – patient's categorical impression of change in experienced pain

To evaluate patients impression of changes in experienced pain we included a 5-graded patient-reported, categorical, verbal rating scale (VRS): "How is your pain now as compared to that before treatment: (1) worse, (2) unchanged, (3) <50% improvement, (4) $\geqslant$50% improvement or (5) pain free"?

2.5.3. Secondary outcome measure – functioning and health-related quality of life

In accordance with the principles of the IMMPACT recommendations pain intensity was supplemented by emotional and functional outcome measures [33]. We applied four standardized questionnaires: (1) the second part of Brief Pain Inventory (BPI) which includes seven numeric scales to assess the degree to which pain interferes with function or daily life activities [6,7,21], (2) the Short-Form General Health questionnaire 36 (SF-36) (version 2), assessing health status on a one week recall [24,36], (3) the Oswestry Low Back Pain Disability Questionnaire Version 2.0; developed to examine the physical condition and effect of treatment among low back pain patients [12] and (4) the Patient-Specific Functional Scale, counting the number of four individually chosen activities of daily life (ADL) which the person was disabled to practice before, but that recovered after the treatment [28,32].

2.5.4. Blinding test

As a test on how effective the blinding was, the patients and the assessor were asked after the last 12-month follow-up what kind of treatment they believed they had been given.

2.6. Statistics

For the statistical analyses we used the SPSS statistical package, version 14.0 (SPSS, Chicago, Illinois). Sample size was calculated by the nomogram depicted by Altman [1] and Sample Power 2, SPSS and based on the results in the Pauza IDET study [27] and our pilot data with a mean difference in pain relief between active and sham treatment of 2.0 and a standard deviation of 2.6. Accepting a power of 80% and a level of statistical significance (alpha value) of 0.05, we calculated the sample size needed to be 50 (25 in each group).

The continuous variables were compared to baseline using the General Linear Model; Repeated Measurements and the GLM, Univariate ANCOVA in order to adjust for different baseline levels in pain intensity as the residuals were found normally distributed by the Q–Q plot and the Kolmogorov–Smirnov test. Comparisons between the groups were carried out by the two independent samples Student *t*-test and by the Mann–Whitney test for the SF 36 health domains Role Physical and Role Emotional which were not normally distributed. The continuous variables are presented as means with standard deviations.

Although all patients had pain intensity >5/10 when referred to the study, four of the patients reported baseline pain intensity <5/10 on the day of treatment". The primary endpoint, pain intensity, was subjected to both intention-to-treat and per-protocol analyses (excluding these four patients). Fisher's exact test was applied to compare groups on categorical variables. The null-hypothesis (suggesting no change) was rejected, and the difference was considered statistically significant if the *p*-value was less than 0.05. The data analysis of the secondary outcome variables presented is considered exploratory. Consequently, multiple tests were done without multiplicity correction [3].

3. Results

Between August 2003 and January 2006 we recruited 74 patients with chronic low back pain from a total of approximately 700 referrals (see Fig. 1). Of the 44 patients who were found eligible for discography, only 23 were invited to participate in the study. In one patient we were not able to place the discTRODE™ probe adequately close to the annulus, as the probe advanced into the nucleus. This patient was excluded from the study and instead given active, unblinded treatment with no benefit after 12 months. Two patients refused to participate. Thus, twenty patients were randomized to active thermal or sham intra-annular treatment; 10 patients in each group.

A blinded interim analysis of pain intensity was performed, as planned, when 20 patients had completed a follow-up of 6 months. The analysis did not reveal any trend towards overall effect or difference between active treatment and sham treatment for the primary endpoint "change in pain intensity". Two actively and three sham-treated patients experienced even increased pain. Due to ethical reasons the inclusion of new patients was therefore discontinued. The 20 patients, who had been included, were followed up for another 6 months.

3.1. Demographic data

The demographic and clinical features of the participants at baseline are demonstrated in Table 2. The use of other treatment modalities and pain medication did not differ significantly between the groups during the follow-up period.

3.2. Primary outcome measure - change in pain intensity

Individual levels of "worst pain" and changes in "worst pain" are visualized in Fig. 2a–d. Table 3 presents the mean values of "worst", "average", "minimal" pain and "pain right now" at baseline and throughout the follow-up. When including the patients, intended to treat, mean baseline pain intensity did not differ statistically between the groups, with the exception of "pain right now" which was significantly lower in the active group (*p*: 0.046). After active treatment we found only a slight reduction in mean pain intensity, for worst pain −1.0 (SD 2.2) at 6 months and −1.4 (SD 3.3) at 12 months. In the sham-treated group the corresponding change was 0.0 (SD 2.4) and −1.6 (SD 2.5), respectively (Table 3). Intention-to-treat analyses of the four pain intensity scores showed no significant differences between the groups (active vs. sham group), neither at 6 nor at 12 months, and still not when adjusting for different baseline levels (ANCOVA). Mean group difference in "worst pain", 95% confidence intervals and the probability that the null hypothesis is true (*p*-value), were respectively: −1.5 (CI: −3.6, 0.6) (*p*: 0.14) at 6 months and −0.3 (CI: −3.1, 2.5) (p: 0.81) at 12 months.

After excluding the four patients with a too low baseline pain level (per-protocol analyses) the effect of active RF on the four pain intensity scores was still not superior to sham treatment. Group comparison of "worst pain" (ANCOVA) gave the following mean difference with 95% confidence intervals and *p*-value: −1.0 (CI: −3.5, 1.5) (*p*: 0.41) at 6 months and −0.5 (CI: −4.2, 3.1) (*p*: 0.76) at 12 months.

We also carried out test analyses where we replaced the low baseline levels with 5/10, consistent with the criterion for inclusion. Even with this change we found no statistical difference between the groups, neither at 6 nor at 12 months.

At 6 months two of the actively treated patients reported more than 2 of 11 points pain reduction, compared with three patients in the sham group. At 12 months three of the actively treated patients reported more than 2 of 11 points pain reduction, while the number had increased to five patients in the sham group (Table 5).

Table 2
Demographic and clinical features before radiofrequency (RF) thermal and sham therapy.

Feature	RF group (*n* = 10) *N*	Sham group (*n* = 10) *N*	Comparison *P*[*]
Male	3	3	1.0
Female	7	7	1.0
Age in years (mean ± SD)	44.7 ± 10.1	39.6 ± 8.9	0.25
Employment			1.00
Unemployed	3	2	
Working	7	8	
Work class			0.65
Manual	0	0	
Sedentary	4	5	
Mixed	6	5	
Duration of pain			1.00
6–12 months	0	0	
12–24 months	1	2	
>24 months	9	8	
Pain distribution			0.54
Only back pain	2	2	
Also in buttock	4	4	
Also in thigh	2	3	
Also in leg	2	1	
Treated disc			1.0
L5–S1	6	7	
L4–L5	4	3	
L3–L4	0	0	

[*] The *p*-values are based on the Student *t*-test for continuous data or on the Fisher exact test for categorical data.

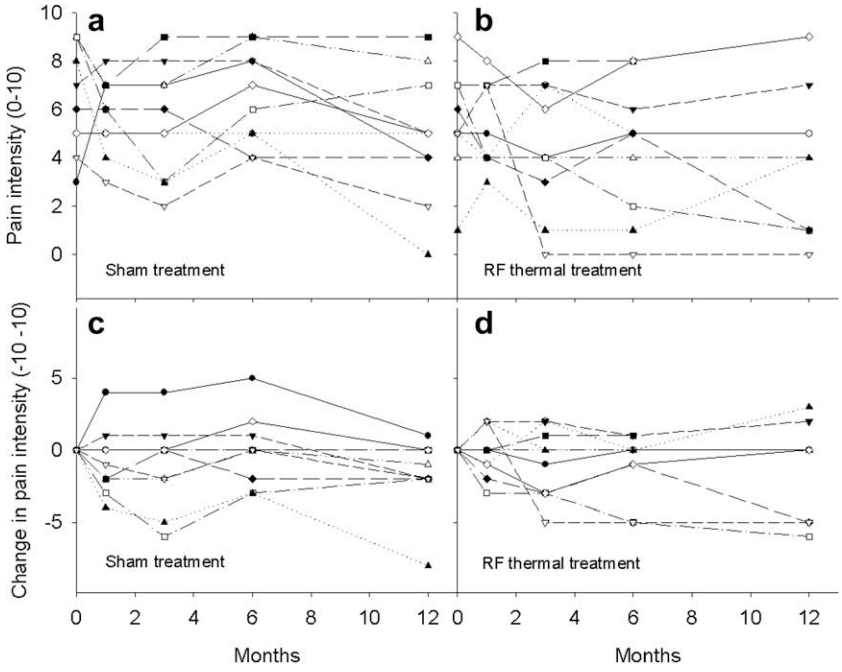

Fig. 2. Individual pain intensity scores following intra-annular radiofrequency thermal or sham treatment with the discTRODE™ probe. Graphs of patients who were subjected to intra-annular radiofrequency thermal ($n = 10$) and sham therapy ($n = 10$) with the discTRODE™ probe, showing numeric levels in "worst pain" (a and b) and "change in worst pain" (c and d) before and 1, 3, 6 and 12 months after treatment. One patient in the active group did not respond to the 12-month follow-up.

3.3. Secondary outcome measures

3.3.1. Patient's categorical impression of change in experienced pain

Categorical changes in experienced pain are presented in Table 5. Three actively treated patients reported ⩾50% improvement of pain at 6 months, and the number increased to five at 12 months, one of them was pain free. Only one of the sham-treated patients reported more than 50% improvement.

3.3.2. Health-related quality of life

The Brief Pain Inventory (BPI) (second part) reported comparable baseline levels between the groups on how pain influenced daily life (Table 3). After active therapy the mean levels improved, but reached statistical significance only for pain influence on work (at 3 and 6 months) and enjoyment of life (at 3 and 12 months). The improvements, however, did not differ significantly from sham therapy.

The mean reduction of Oswestry disability Index scores (improvement) did not reach statistical significance when compared with baseline and sham therapy (Table 4).

The scores of the eight subscales of SF 36 are shown in Table 4. The mean baseline levels did not differ between the groups. After 6 and 12 months we measured scores in favor of active treatment, although the group difference did not reach statistical significance.

3.3.3. Functional ability

The Patient-Specific Functional Scale on activities of daily life showed a tendency of improved functioning after both active and

Table 3
Outcome measurements on pain intensity and pain interferences on function (BPI) among patients subjected to intra-annular radiofrequency thermal or sham treatment.

Item	Baseline					6 months						12 months					
	Active ($n = 10$)		Sham ($n = 10$)			Active ($n = 10$)		Sham ($n = 9$)				Active ($n = 10$)		Sham ($n = 10$)			
	Mean	(SD)	Mean	(SD)	p	Mean	(SD)	Mean	(SD)	p		Mean	(SD)	Mean	(SD)	p	
BPI pain intensity last 24 h*																	
Worst pain	5.4	(2.1)	6.5	(2.2)	0.27	4.4	(2.7)	6.5	(2.0)	0.06		4.0	(3.0)	4.9	(2.7)	0.50	$
Least pain	2.3	(1.4)	2.7	(2.6)	0.68	2.5	(2.0)	3.5	(2.8)	0.36		1.8	(1.3)	3.2	(2.5)	0.14	
Average pain	4.6	(1.8)	5.5	(2.0)	0.30	3.7	(2.2)	5.3	(1.8)	0.09		3.2	(2.3)	4.9	(2.1)	0.12	
Pain now	3.8	(1.5)	5.4	(1.8)	0.046	3.2	(2.2)	5.1	(2.4)	0.08		3.6	(2.6)	4.5	(2.9)	0.47	
BPI pain interference on*																	
General activity	5.5	(2.9)	5.8	(2.1)	0.80	3.7	(2.7)	5.8	(2.4)	0.08		4.2	(3.1)	5.0	(3.0)	0.60	
Mood	5.5	(3.1)	4.4	(2.1)	0.37	3.6	(2.7)	4.3	(2.5)	9.55		3.7	(3.2)	3.8	(2.9)	0.93	
Walking ability	3.4	(3.3)	3.4	(2.9)	1.0	2.0	(1.8)	3.1	(2.6)	0.28		2.0	(1.8)	3.3	(2.6)	0.23	
Work	5.3	(2.5)	6.6	(2.2)	0.27	3.3	(2.4)	5.7	(2.3)	0.06	$	3.3	(3.0)	5.6	(3.0)	0.09	
Relations to others	3.9	(2.4)	3.8	(2.3)	0.91	2.5	(2.6)	3.5	(2.2)	0.52		2.8	(2.9)	3.1	(3.2)	0.83	
Sleep	4.5	(3.4)	4.4	(2.8)	0.97	3.2	(2.7)	4.0	(2.8)	0.71		3.1	(3.0)	4.3	(3.3)	0.39	
Enjoyment of life	5.2	(3.2)	4.3	(3.2)	0.56	3.5	(2.8)	3.2	(2.3)	0.75		2.9	(3.1)	3.1	(3.0)	0.76	$

The groups are compared by Student t-test, and p-values are presented without Bonferroni correction for multiple comparisons. Comparisons to baseline are carried out with the GLM, Repeated measurements; $ means a statistically significant difference from baseline for both groups combined ($p < 0.05$).

* BPI, Brief Pain Inventory; pain intensity and pain interference on function are assessed by numeric 11-graded numeric rating scales. The higher the score, the worse the outcome.

Table 4
Functional and life of quality outcome measurements among patients subjected to intra-annular radiofrequency thermal or sham treatment.

Item	Baseline					6 Months						12 Months					
	Active (n = 10)		Sham (n = 10)			Active (n = 10)		Sham (n = 9)				Active (n = 10)		Sham (n = 10)			
	Mean	(SD)	Mean	(SD)	p	Mean	(SD)	Mean	(SD)	p		Mean	(SD)	Mean	(SD)	p	
SF-36**																	
Bodily pain	39.5	(17.9)	32.5	(14.8)	0.35	43.7	(30.1)	35.3	(18.6)	0.46		51.6	(23.8)	39.5	(24.2)	0.29	
Physical functioning	49.0	(20.2)	52.5	(24.2)	0.73	59.0	(23.1)	64.0	(20.4)	0.61	$	65.0	(21.7)	57.5	(21.4)	0.46	
Role physical	27.5	(41.6)	5.0	(10.5)	0.13	27.5	(44.8)	15.0	(24.2)	0.45		41.7	(45.1)	15.0	(31.6)	0.16	
Role emotional	73.3	(43.9)	40.0	(43.9)	0.11	80.0	(35.8)	30.0	(36.7)	0.01#		77.8	(37.3)	46.7	(42.2)	0.11	
Social functioning	60.0	(25.5)	55.0	(25.1)	0.66	68.8	(30.2)	63.8	(23.2)	0.68		73.6	(26.8)	66.3	(28.3)	0.57	
Mental health	66.8	(12.7)	68.0	(13.9)	0.84	71.6	(15.9)	74.8	(12.7)	0.63		76.9	(14.1)	70.0	(14.5)	0.31	
General health	66.4	(19.7)	49.7	(17.7)	0.06	65.9	(20.0)	50.7	(15.2)	0.07		75.2	(10.3)	59.4	(21.2)	0.06	$
Vitality	40.0	(22.2)	30.5	(15.7)	0.28	46.0	(17.9)	39.0	(16.5)	0.38	$	52.8	(22.7)	37.0	(16.7)	0.10	
ODI***	31.6	(10.2)	30.4	(15.3)	0.84	25.2	(14.8)	28.2	(13.1)	0.64		20.0	(16.2)	30.0	(17.1)	0.20	

The p-values are presented without Bonferroni correction for multiple comparisons. Comparisons to baseline are carried out with the GLM, Repeated measurements; $ means statistically significant difference from baseline for both groups combined ($p < 0.05$).
The groups are compared by Student t-test or Mann–Whitney test# when not normally distributed.
** SF36, the short form 36 questionnaire subscales range from 0 to 100, and a high level indicates good health.
*** ODI, The Oswestry Disability Index score varies from 0 to 100, a high score is associated with a high degree of disability.

sham therapies (see Table 5). The number of patients, who regained at least three individually chosen activities, was slightly higher in the active group than in the sham group (3 vs. 2) after 6 months. The ratio increased to 4 vs. 1 patient after 12 months, but the difference did not reach statistical significance. The number of patients who were unemployed due to disability, contrastingly increased during the 12-month follow-up from 5 subjects (25%) at baseline to 9 (45%) at 6 months and 10 (50%) at 12 months, but the differences between the groups did not reach statistical significance.

3.3.4. Other outcome measures

The proportions of patients, who received other treatment modalities during the observation period, remained low in both groups, and the consumption of analgesics did not change significantly during the follow-up or differ between the groups.

We found no difference in the positioning of the discTRODE probe between the groups (see Table 6). Any serious adverse effects attributable to the treatment were not reported. On MRI scans taken 3 months after treatment we found no reduction in the bulging or herniation of the discs. (baseline pictures were lacking in two patients). New disc bulging was observed in one and herniation in two patients (none of these reported worse symptoms), but we found no signs of injury related to the treatment.

3.3.5. Blinding

After 12 months eight of ten in the active group, believed they had received RF treatment, one believed he got sham treatment, whereas another did not respond. It should be noted that six of the actively treated patients required alfentanil 0.5–1.0 mg for procedural heating pain. In the sham group six of the patients suggested sham treatment, while four believed they received active treatment. Four sham-treated patients had been given alfentanil 0.5 mg, and in two of the cases this was related to incisional pain. The assessor suggested correct treatment for six in the active group, and seven in the sham group.

3.3.6. Protocol violation

Four patients reported baseline pain values, obtained on the day of treatment, below the accepted level for inclusion. Intention-to-

Table 5
The categorical distribution of patients with regard to change in experienced pain and functional status after intra-annular radiofrequency thermal and sham treatment.

	RF thermal treatment (n = 10)*				Sham treatment (n = 10)			
	1 mo	3 mo	6 mo	12 mo	1 mo	3 mo	6 mo	12 mo
Absolute change in worst pain intensity								
Not improved ⩾ 2points**	8	6	8	6	6	6	7	5
Improved ⩾ 2points**	2	4	2	3	4	4	3	5
Relative change in pain intensity***								
Worse	2	2	2	2	3	4	3	2
Unchanged	3	3	4	2	4	3	4	5
Improvement < 50%	3	0	1	0	2	3	2	2
Improvement ⩾ 50%	2	4	2	4	1	0	1	1
Pain free	0	1	1	1	0	0	0	0
Patient-Specific Functional Scale****								
0 activity	6	4	4	3	4	6	5	7
1 activity	2	1	1	1	3	2	2	0
2 activities	2	3	2	1	3	1	1	2
3 activities	0	2	3	1	0	1	2	1
4 activities	0	0	0	3	0	0	0	0
Improved (“sum”)	4	6	6	6	6	4	5	3

No group differences were found statistically significant at 6 and 12 months (Fisher exact test).
* One patient did not response at the 12-month follow-up.
** The absolute changes <2 points and ⩾2 points are based on numeric pain scores.
*** The relative changes in pain intensity are based on categorical statements from the patient.
**** The Patient-Specific Functional Scale (PSFS) counts the number of persons who regained 0–4 individually chosen activities.

Table 6
Distribution of final probe position before treatment ($n = 20$).

Grading	1	2	3
Number in the active group	6	2	2
Number in sham group	3	5	2
Sum of patients	9	7	4

Probe position was graded according to a three-point scale; (1) the electrode optimally placed along the posterior wall of the annulus fibrosus, with the tip covering the annular fissure, (2) the electrode partly placed along the posterior wall of the annulus fibrosus, and (3) the electrode directed into deeper annular layers towards the nucleus pulposus. The group difference was not statistically significant (Fisher exact test).

treat and per-protocol analyses were therefore carried out for the primary outcome measures (the four numeric pain intensity scales from BPI). Two patients violated the prescribed protocol slightly; as they did not respond to all the questions in the questionnaires. One actively treated patient did not meet at the 12-month follow-up, nor respond to later telephone calls. One patient in the sham group did not answer four questions in the second part of BPI, but the rate of the missing values did not exceed 2% of all the measurements.

The grading of final accepted probe positions is presented in Table 6. In two of the actively treated patients the probe did not reach the two most optimal positions (grade 3). The individual responses on pain intensity, however, did not differ much from those with a more optimal probe position.

4. Discussion

This is the first properly designed double-blind comparison of percutaneous intradiscal radiofrequency thermal (PIRFT) and sham therapy for CDLBP using the discTRODE™ probe. Previous RCTs have applied straight needles inserted into the nucleus pulposus [2,10]. Although the sampled size is limited, our results do not support the use of PIRFT. The study was designed to include 2×25 patients with a 12-month follow-up, but before the start of the study we decided to carry out an interim analysis when 20 patients had completed a 6-month follow-up. The blinded interim analysis of the primary end point revealed no trend towards overall effect or difference between active and sham treatments for the primary endpoint. Most of the patients reported a small and clinically not meaningful change on the primary outcome although the confidence intervals included treatment effects larger than expected ($\geqslant 2$). At 6 months 2 actively and 3 sham-treated patients (25%) reported even increased pain intensity compared with baseline, and the number of unemployed due to disability had increased from 5 (25%) to 9 (45%). According to predefined stopping rules (see Section 1) the inclusion of patients was therefore discontinued.

We were indeed concerned that this reduction in the number of patients reduced the statistical power of the analyses and increased the risk of type 2 error. However, with such a small reduction in mean pain intensity, we found it ethically unacceptable to continue the trial. We would need to include an additional large number of patients for invasive and painful discography and potentially risky intradiscal sham treatment.

At 12 months mean change in pain intensity was still small and clinically not meaningful. The phenomenon that some patients improved between 6 and 12 months might be attributed to reasons other than PIRFT [15,16].

We observed, on the other hand, somewhat more promising results in the secondary outcomes. After 6 months 3 (30%) of the actively treated subjects reported at least 50% pain relief vs. 1 (10%) in the sham group, and the number had increased to 5 (50%) vs. 1 (10%) after 12 months. The numeric scale for pain intensity has been shown to be a sensitive measure for detecting treatment effect [4], and was therefore used as the primary outcome. The contrasting results in categorical impression of change in experienced pain, could reflect the difficulties patients have in remembering pain intensities, with an overestimation of baseline pain [22,23].

We were also surprised by the improvements in function scores (SF 36, ODI and BPI), particularly since more patients had become unemployed. We might speculate whether the follow-up visits or even the small reduction in pain could have a positive context-sensitive influence on the functional status – or possibly, the reduced work load for those who had become unemployed gave a feeling of more energy and improved quality of life.

4.1. Comparison with previous studies on intra-annular thermal therapy

Our results agree with the negative results from the IDET study by Freeman et al. [15], but contrasts to promising efficacy data from non-controlled [11,29,30], case-controlled [6,8,22] and the randomized placebo-controlled IDET study by Pauza et al. [27]. Pauza et al. demonstrated a statistically significant pain reduction (VAS) of 2.4 (SD 2.3) after 6 months, statistically different from sham therapy by 1.2 (SD 2.7) [27]. In our study we observed a reduction of "worst pain" 6 months after active treatment by only 1.0 (SD 2.2) and at 12 months by 1.4 (SD 3.3). The number of actively treated patients who improved their pain scores by 2 points or more, was only 2 (20%) at 6 months and 3 (30%) at 12 months. In the sham group the corresponding numbers were actually higher 3 (30%) at 6 months and 5 (50%) at 12 months. The proportion of responders among sham-treated patients was similarly high in the Pauza study; 38% [27].

Previous data on PIRFT are more limited. A small comparative study by Kapural [19] reported a pain reduction of 2 points at 12 months, which was inferior to the change after IDET treatment (6,5 points). In a non-randomized study by Erdine et al. 60% of the participants reported decreased pain intensity, and 66% improved physical function on the SF 36 subscale [11]. Finch et al. reported a change in pain intensity after treatment with the discTRODE™ probe of 37% compared with 3% in the non-treated, unblinded controls [14]. It is well established that unblinded studies frequently overestimate the treatment effect [18,31]. We do not believe that population differences explain the contrasting results.

An invasive procedure will carry the risk of worse pain. At 12 months 2 of 10 patients (20%) reported increased pain in both groups. In the study by Pauza et al. the corresponding numbers were 6% in the active group but 33% in the sham group [27]. The increased number of unemployed patients in our population from 25% to 50% through the 12-month follow-up could reflect the spontaneous variation of chronic low back pain, or be related to the trauma following a painful provocation discography, the insertion of a discTRODE probe or heating of the annulus fibrosus. However, we could not find any correlation between unemployment, change in pain intensity and the deterioration on the Patient-Specific Functional Scale on the activities of daily life.

4.2. Procedural considerations

To explain the poor results compared to those of other studies procedural differences should be considered. The patients in our study were treated at only one level where discogenic pain could be provoked by pressure discography, while 38% of the patients in the Pauza study were treated at the two lower levels [27]. Different techniques between IDET™ and discTRODE™ for heating tissue could also explain the contrasting results. The IDET employs a different principle of heating. The tip of the electrically resistive heating probe is placed circumferentially along the inner and posterior side of the annulus and is gradually heated to 90 °C during a period

of 13 min and then maintained for 4 min to create a temperature in the annulus between 60 and 65 °C [29]. The total lesion time is thus longer (17 min) compared with our protocol for discTRODE™ (10 min).

The clinical effect of any intervention is certainly dependent on the quality of the procedure. In the present study the procedure was therefore performed by one single and well-trained operator. The final probe position was well documented with three-dimensional tomographic X-ray images. Although the probe was less optimally placed in 2 of the 10 actively treated patients, this did not seem to explain the lack of treatment effect.

Some of the actively treated patients might have been unblinded due to pain during the heating procedure. This should rather increase a treatment effect, and cannot be the reason for the negative result.

5. Conclusion

Within a highly selected group of CDLBP with positive pressure discography the study did not find evidence for a benefit of PIRFT, although it cannot rule out a moderate effect. Considering the high number of patients with increased pain 12 months later, we do not recommend intra-annular thermal therapy with the discTRODE™ probe.

Conflict of interest

The authors do not have other financial or other relationships that might lead to a conflict of interest.

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