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Systematic Review

# Effectiveness of Thermal Annular Procedures in Treating Discogenic Low Back Pain

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**Background:** Persistent low back pain refractory to conservative treatment is a common problem that leads to widespread impairment, resulting in significant costs to society. The intervertebral disc is a major source of persistent low back pain. Technologies developed to treat this problem, including various surgical instrumentation and fusion techniques, have not reliably provided satisfactory results in terms of either pain relief or increased function.

Thermal annular procedures (TAPs) were first developed in the late 1990s in an attempt to treat discogenic pain. The hope was that they would provide greater value than fusion in terms of efficacy, morbidity, and cost. Three technologies have been developed to apply heat to the annulus: intradiscal electrothermal therapy (IDET), discTRODE, and biacuplasty. Since nerve ingrowth and tissue regeneration in the annulus is felt to be the source of pain in discogenic low back pain, when describing the 3 above techniques we use the term "thermal annular procedures" rather than "thermal intradiscal procedures." We have specifically excluded studies treating the nucleus. TAPs have been the subject of significant controversy. Multiple reviews have been conducted resulting in varying conclusions.

**Study Design:** A systematic review of TAPs for the treatment of discogenic low back pain.

**Objective:** To evaluate the effectiveness of TAPs in treating discogenic low back pain and to assess complications associated with those procedures.

**Methods:** The available literature on TAPs in treating discogenic low back pain was reviewed. The quality assessment and clinical relevance criteria utilized were the Cochrane Musculoskeletal Review Group criteria for interventional techniques for randomized trials, and the criteria developed by the Newcastle-Ottawa Scale criteria for observational studies. The level of evidence was classified as good, fair, or limited (or poor) based on the quality of evidence developed by the U.S. Preventive Services Task Force. Data sources included relevant literature identified through searches of PubMed and EMBASE from 1966 through December 2011, and manual searches of the bibliographies of known primary and review articles.

**Outcome Measures:** The primary outcome measure was pain relief of at least 6 months. Secondary outcome measures were improvements in functional status.

**Results:** For this systematic review, 43 studies were identified. Of these, 3 randomized controlled trials and one observational study met the inclusion criteria.

Using current criteria for successful outcomes, the evidence is fair for IDET and limited (or poor) for discTRODE and biacuplasty procedures regarding whether they are effective in relieving discogenic low back pain. Since 2 randomized controlled trials are in progress on that procedure, assessment of biacuplasty may change upon publication of those studies.

**Limitations:** The limitations of this systematic review include the paucity of literature and non-availability of 2 randomized trials which are in progress for biacuplasty.

**Conclusion:** In summary, the evidence is fair for IDET and limited (or poor) for discTRODE and biacuplasty is being evaluated in 2 ongoing randomized controlled trials.

**Key words:** Spinal pain, chronic low back pain, discogenic pain, thermal procedures, annular procedures, IDET, biaculoplasty, disctrode

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Chronic pain is a major source of disability. It has significant social and economic impact (1,2). Almost two-thirds of the adult United States population has back pain at some point in their lives (3). The prevalence of low back pain is increasing in many populations, as exemplified by an increase from 3.9% in North Carolina in 1992 to 10.2% in 2006 (4). The prevalence of low back pain in German adults is more than 70%, with direct costs per patient of €1,332 ($1,900) (5). In a Finnish study, the incidence of low back pain lasting more than one month in a cohort of those younger than 40 years old was 11.2% (6).

Low back pain has significant societal costs, with hospitalization for nonspecific low back pain in active duty military personnel of 19.1/1,000 persons per year (7). Low back pain was reported in almost 40% of adolescents (8). The cumulative incidence of low back pain in a Canadian population was almost 20%, while in the American active military population, it was 40.5/1,000 persons per year (3,9). Most episodes were mild, but less than one-third recovered in one year; of those who did recover, almost one-third had a recurrence in 6 months. The persistence of low back pain has been documented in several studies (10-13).

The major sources of persistent low back pain have been identified as multifactorial. They include the lumbar intervertebral discs, the facet joints, and the sacroiliac joint (14-20). The intervertebral disc is the source of pain in between 7% and 39% of all persistent pain cases (21). While many patients respond well to conservative management, about 5% of patients with a component of discogenic pain will have persistent pain (22). The diagnosis and treatment of discogenic pain has been frustrating and variable (23). Various therapies, including fusion, disc replacement, injection therapies, and thermal annular procedures (TAPs) have been utilized, with considerable controversy over the efficacy of any of these procedures (24-33). Operative procedures are associated with a high morbidity level, so that interest in alternative treatments with less morbidity remains high (34).

TAPs are an option for offering a therapeutic alternative between conservative therapy and fusion. The intervertebral discs are composed of a central nucleus pulposus containing water and glycogens surrounded by a restraining laminated ligamentous annulus. The discs allow for the distribution of load as the spine moves. With aging, the disc desiccates and the annulus tears (35,36). This degeneration is a universal phenomenon which starts early in life (37). While many mechanisms have been provided to explain why lumbar disc degeneration leads to pain, an attractive explanation is the growth of nerves capable of expressing pain deep into the annular structures. Granulation tissue is present in the same area as part of the healing process; this tissue contains a number of mediators, such as cytokines, prostaglandin E2, interleukin(IL)-6, and IL-8 which can sensitize the nociceptors, so that loading within a physiological range can lead to pain (38,39). The goal of the application of heat across the damaged annulus is to denervate the annulus, leading to pain relief (40). An alternative hypothesis is that the heat reconfigures collagen structure (41). Both hypotheses have been criticized (42). Derby et al (39) have reviewed the proposed mechanisms of action and have concluded that the mechanism is unclear.

Heat was first used to treat discogenic low back pain in 1996, using a convection technology with a 5 cm active tip placed at the nucleoannular junction (43). This technology is marketed under the name intradiscal electrothermal therapy (IDET). Finch et al (44) developed a technology which applied heat to the posterior annulus using ionic heating created by a monopolar radiofrequency device marketed under the name discTRODE. A third technology to create heat across the posterior annulus uses a cooled bipolar radiofrequency device marketed as biacuplasty (45).

The Centers for Medicare and Medicaid Services have described these procedures as thermal intradiscal procedures (46). Given that these therapies are united by their application of heat to the annulus, and given that some studies have dealt, irrelevantly, with treating the nucleus, we have adopted the phrase "thermal annular procedures" as being more accurately descriptive of the procedure.

TAPs have been the subject of several reviews, including one in this journal in 2009 (21,29,46-57). The United Kingdom's National Institute for Clinical Excellence (53) published a review of percutaneous intradiscal radiofrequency thermocoagulation (PIRFT) in 2004, finding that IDET should be restricted. Gibson and Waddell (47), in a review published in 2005 concerning the surgical treatment of degenerative disc disease, found that limited evidence on the IDET procedure suggested that the procedure was ineffective. This review was criticized by Andersson et al (58) at the time of its publication for methodological shortcomings. They said there was a lack of critical assessment of the reviewed studies as well as a mischaracterization of the procedure. Andersson et al published

a systematic review in 2006 (52), finding that IDET had the same symptom amelioration as fusion without the complications of fusion. Appleby et al (48), in a manufacturer-sponsored meta-analysis of the data supporting IDET, found that although there were variations in the results of the various studies, "the pooled results provide compelling evidence of the relative efficacy." Freeman (49), in a review published in 2006, found that the evidence for IDET was weak. Freeman updated his conclusions in a book chapter in 2010 (59). The American Pain Society (APS) guidelines, authored by Chou and Huffman (50), found that there was conflicting evidence regarding IDET's efficacy and that the quality of the evidence was poor. Chou and Huffman (50) also looked at PIRFT, but used this term to refer to either Coblation®, a technology which used radiofrequency to decompress the nucleus, or to the application of radiofrequency energy within the nucleus (60). Neither procedure treated the annulus, so they are not germane to the current discussion.

Urrútia et al (54) also looked at both IDET and PIRFT, again defining PIRFT as having the catheter "placed in the center of the disc rather than the annulus." Urrutia et al (54), however, also included a study by Kapural et al (61) that compared IDET with discTRODE , so that they, like Chou and Huffman (50), appear to be comparing dissimilar procedures. Urrutia et al (54) found that the evidence did not support the effectiveness of IDET. The 2009 review by the Helm et al (29) of TAPs found that IDET provided functionally significant relief in approximately one-half of appropriately selected patients, but that there was minimal evidence to support the use of discTRODE or biacuplasty. Levin (55), publishing a review of prospective, double blind, placebo controlled trials in 2009, found that IDET is modestly effective in carefully selected patients. Chou and Huffman (50), responding in the same issue as Levin published in, clarifies the APS position as being that there is insufficient evidence to judge whether IDET (or the other TAP procedures) is effective.

Kabbara and Hayek (56) found that IDET may be useful in a selected group of patients, but evidence did not exist for a wider use of IDET. Kallewaard et al (21), as a part of the evidence-based medicine reviews published in *Pain Practice*, authored a review of the treatment of discogenic low back pain. They found insufficient evidence to support either IDET or biacuplasty. Interestingly, an older therapy, radiofrequency ablation of the gray ramus communicans, was recommended.

These reviews have significant treatment implications and have been used to support denied coverage of these procedures (2,62). The use of an insufficient evidence determination to support denied coverage is disquieting (63). Carragee et al (64), in an article coauthored by Urrútia et al (54), used Urrútia et al's study of IDET as an example of a technology which was initially popular and which was later shown to be ineffective. Freeman and Merdian (65) concluded that IDET was not effective.

Henschke et al (57), writing in the *European Spine Journal* in 2010, found that there was low quality evidence that IDET is more effective than placebo at relieving pain, but not functional status, at 6 months. Because IDET is the most widely studied of the 3 technologies evaluated here, it was the focus of these reviews.

The purpose of the current review is to perform a systematic survey of the literature regarding the effectiveness of TAPs for the treatment of chronic low back pain of discogenic origin. The evidence will be assessed in light of the previous reviews.

The second question to be addressed is the severity and risk of complications associated with these techniques.

## 1.0 Methods

### 1.1 Research Protocol

A systematic review of randomized trials, observational studies, and reports of complications dealing with TAPs for the treatment of discogenic pain of at least 6 months' duration will be performed. Attendant to this review will be an analysis of complications of these procedures.

### 1.2 Eligibility Criteria (Criteria for Including and Excluding Studies in the Systematic Review)

Inclusion criteria were patients suffering with chronic intractable low back pain for at least 6 months due to intradiscal disorder. Only percutaneous TAPs were evaluated. All the studies providing appropriate management with outcome evaluations of 6 months or longer and statistical evaluations were reviewed. Reports without appropriate diagnosis, nonsystematic reviews, book chapters, and case reports were excluded. The patients must have been at least 18 years old. Study participants must have failed conservative therapy, including medication management and physical therapy.

### 1.3 Outcome Measures

The primary outcome parameter was pain relief. The secondary outcome measures were functional improvement; change in psychological status; return to work; reduction or elimination of opioid use, other drugs, or other interventions; and complications.

At least 2 of the review authors independently, in an unblinded standardized manner, assessed the outcomes measures. Any disagreements between reviewers were resolved by a third author and consensus.

### 1.4 Key Questions and Analytic Framework

The purpose of the current review is to perform a systematic survey of the literature regarding the effectiveness of TAPs for the treatment of chronic low back pain of discogenic origin. The evidence will be assessed in light of the previous reviews.

The second question to be addressed is the severity and risk of complications associated with these techniques.

### 1.5 Databases and Other Information Sources Used to Identify Relevant Studies

A comprehensive literature search was conducted of English language studies from 1966 through December 2011. Databases included in the search were Medline, EMBASE, Cochrane Review Database, and Google Scholar. Other sources included Clinical Trial Registry, systematic reviews, narrative reviews, and cross-references to the reviews. Bibliographies of reviewed papers were also examined. In addition, authors known to be active in the field were contacted.

### 1.6 Search Strategy

The search strategy focused on chronic discogenic back pain treated with TAPs. The search terminologies include degenerative disc disease, intervertebral disc degeneration, intra-annular radiofrequency thermal disc therapy, intradiscal electrothermal therapy, low back pain, discography, and treatment.

At least 2 of the review authors independently, in an unblinded, standardized manner, performed each search. Accuracy was confirmed by a statistician. All searches were combined to obtain a unified search strategy. Any disagreements between reviewers were resolved by a third author and consensus.

### 1.7 Study Selection Process

Only studies of clinical relevance were assessed. Clinical relevance was assessed according to the Cochrane Back Review Group (66,67). Table 1 shows the questions used to assess clinical relevance. At least 3 clinical relevance questions had to be positive for a study to be considered clinically relevant.

In an unblinded, standardized manner, 2 review authors screened the abstracts of all identified studies against the inclusion criteria. All articles with possible relevance were then retrieved in full text for comprehensive assessment of internal validity, quality, and adherence to inclusion criteria.

### 1.8 Methodological Quality Assessment

The quality of each individual article used in this analysis was assessed by modified Cochrane review criteria (Table 2) (68) for randomized trials, and the Newcastle-Ottawa Scale for observational studies (Tables 3 and 4) (69,70). The case series format for the Newcastle-Ottawa Scale was used for all studies with more than one group; otherwise, the cohort format was used. Nonrandomized observational studies were included only if at least 50 patients were enrolled or at least 25 in each group if there were comparison groups.

Table 1. *Clinical relevance questions.*

| | P (+) | N (-) | U (unclear) |
|---|---|---|---|
| A) Are the patients described in detail so that you can decide whether they are comparable to those that you see in your practice? | | | |
| B) Are the interventions and treatment settings described well enough so that you can provide the same for your patients? | | | |
| C) Were all clinically relevant outcomes measured and reported? | | | |
| D) Is the size of the effect clinically important? | | | |
| E) Are the likely treatment benefits worth the potential harms? | | | |

Scoring adapted and modified from Staal JB, et al. Injection therapy for subacute and chronic low-back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824 (67).

Table 2. ***Randomized controlled trials quality rating system.***

| | | | |
|---|---|---|---|
| A | 1. Was the method of randomization adequate? | A random (unpredictable) assignment sequence. Examples of adequate methods are coin toss (for studies with 2 groups), rolling a dice (for studies with 2 or more groups), drawing of balls of different colors, drawing of ballots with the study group labels from a dark bag, computer-generated random sequence, pre-ordered sealed envelopes, sequentially-ordered vials, telephone call to a central office, and pre-ordered list of treatment assignments. Examples of inadequate methods are alternation, birth date, social insurance/ security number, date in which they are invited to participate in the study, and hospital registration number. | Yes/No/Unsure |
| B | 2. Was the treatment allocation concealed? | Assignment generated by an independent person not responsible for determining the eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about eligibility of the patient. | Yes/No/Unsure |
| C | Was knowledge of the allocated interventions adequately prevented during the study? | | |
| | 3. Was the patient blinded to the intervention? | This item should be scored "yes" if the index and control groups are indistinguishable for the patients or if the success of blinding was tested among the patients and it was successful. | Yes/No/Unsure |
| | 4. Was the care provider blinded to the intervention? | This item should be scored "yes" if the index and control groups are indistinguishable for the care providers or if the success of blinding was tested among the care providers and it was successful. | Yes/No/Unsure |
| | 5. Was the outcome assessor blinded to the intervention? | Adequacy of blinding should be assessed for the primary outcomes. This item should be scored "yes" if the success of blinding was tested among the outcome assessors and it was successful or:<br>–for patient-reported outcomes in which the patient is the outcome assessor (e.g., pain, disability): the blinding procedure is adequate for outcome assessors if participant blinding is scored "yes"<br>–for outcome criteria assessed during scheduled visit and that supposes a contact between participants and outcome assessors (e.g., clinical examination): the blinding procedure is adequate if patients are blinded, and the treatment or adverse effects of the treatment cannot be noticed during clinical examination<br>–for outcome criteria that do not suppose a contact with participants (e.g., radiography, magnetic resonance imaging): the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed when assessing the main outcome<br>–for outcome criteria that are clinical or therapeutic events that will be determined by the interaction between patients and care providers (e.g., co-interventions, hospitalization length, treatment failure), in which the care provider is the outcome assessor: the blinding procedure is adequate for outcome assessors if item "4" (caregivers) is scored "yes"<br>–for outcome criteria that are assessed from data of the medical forms: the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed on the extracted data. | Yes/No/Unsure |
| D | Were incomplete outcome data adequately addressed? | | |
| | 6. Was the drop-out rate described and acceptable? | The number of participants who were included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and drop-outs does not exceed 20% for short-term follow-up and 30% for long-term follow-up and does not lead to substantial bias a "yes" is scored. | Yes/No/Unsure |
| | 7. Were all randomized participants analyzed in the group to which they were allocated? | All randomized patients are reported/analyzed in the group they were allocated to by randomization for the most important moments of effect measurement (minus missing values) irrespective of non-compliance and co-interventions. | Yes/No/Unsure |
| E | 8. Are reports of the study free of suggestion of selective outcome reporting? | In order to receive a "yes," the review author determines if all the results from all pre-specified outcomes have been adequately reported in the published report of the trial. This information is either obtained by comparing the protocol and the report, or in the absence of the protocol, assessing that the published report includes enough information to make this judgment. | Yes/No/Unsure |
| F | Other sources of potential bias: | | |
| | 9. Were the groups similar at baseline regarding the most important prognostic indicators? | In order to receive a "yes," groups have to be similar at baseline regarding demographic factors, duration and severity of complaints, percentage of patients with neurological symptoms, and value of main outcome measure(s). | Yes/No/Unsure |

Table 2 (cont.). ***Randomized controlled trials quality rating system.***

| | | | |
|---|---|---|---|
| | 10. Were co-interventions avoided or similar? | This item should be scored "yes" if there were no co-interventions or they were similar between the index and control groups. | Yes/No/Unsure |
| | 11. Was the compliance acceptable in all groups? | The reviewer determines if the compliance with the interventions is acceptable, based on the reported intensity, duration, number, and frequency of sessions for both the index intervention and control intervention(s). For example, physiotherapy treatment is usually administered over several sessions; therefore, it is necessary to assess how many sessions each patient attended. For single-session interventions (e.g., surgery), this item is irrelevant. | Yes/No/Unsure |
| | 12. Was the timing of the outcome assessment similar in all groups? | Timing of outcome assessment should be identical for all intervention groups and for all important outcome assessments. | Yes/No/Unsure |

Adapted and Modified: Furlan AD, Pennick V, Bombardier C, van Tulder M; Editorial Board, Cochrane Back Review Group. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. *Spine (Phila Pa 1976)* 2009; 34:1929-1941 (68)

Table 3. ***Newcastle-Ottawa quality assessment scale: Case control studies.***

| |
|---|
| **Selection** |
| 1) Is the case definition adequate?<br>a) yes, with independent validation*<br>b) yes, e.g. record linkage or based on self reports<br>c) no description |
| 2) Representativeness of the cases<br>a) consecutive or obviously representative series of cases *<br>b) potential for selection biases or not stated |
| 3) Selection of Controls<br>a) community controls *<br>b) hospital controls<br>c) no description |
| 4) Definition of Controls<br>a) no history of disease (endpoint) *<br>b) no description of source |
| **Comparability** |
| 1) Comparability of cases and controls on the basis of the design or analysis<br>a) study controls for _____ (Select the most important factor.) *<br>b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.) |
| **Exposure** |
| 1) Ascertainment of exposure<br>a) secure record (e.g. surgical records) *<br>b) structured interview where blind to case/control status *<br>c) interview not blinded to case/control status<br>d) written self report or medical record only<br>e) no description |
| 2) Same method of ascertainment for cases and controls<br>a) yes *<br>b) no |
| 3) Non-Response rate<br>a) same rate for both groups *<br>b) non respondents described<br>c) rate different and no designation |

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.
Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp (69).

Table 4. *Newcastle-Ottawa quality assessment scale for cohort studies.*

| **Selection** |
|---|
| 1) Representativeness of the exposed cohort<br>a) truly representative of the average _____ (describe) in the community *<br>b) somewhat representative of the average _____ in the community<br>c) selected group of users (e.g. nurses, volunteers )<br>d) no description of the derivation of the cohort |
| 2) Selection of the non exposed cohort<br>a) drawn from the same community as the exposed cohort *<br>b) drawn from a different source<br>c) no description of the derivation of the non exposed cohort |
| 3) Ascertainment of exposure<br>a) secure record (eg.. surgical records)*<br>b) structured interview *<br>c) written self report<br>d) no description |
| 4) Demonstration that outcome of interest was not present at start of study<br>a) yes *<br>b) no |
| **Comparability** |
| 1) Comparability of cohorts on the basis of the design or analysis<br>a) study controls for _____ (select the most important factor) *<br>b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.) |
| **Outcome** |
| 1) Assessment of outcome<br>a) independent blind assessment *<br>b) record linkage *<br>c) self report<br>d) no description |
| 2) Was follow-up long enough for outcomes to occur<br>a) yes (select an adequate follow-up period for outcome of interest) *<br>b) no |
| 3) Adequacy of follow-up of cohorts<br>a) complete follow-up — all subjects accounted for *<br>b) subjects lost to follow-up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow-up, or description provided of those lost) *<br>c) follow-up rate < ____% (select an adequate %) and no description of those lost<br>d) no statement |

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.
Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp (69).

Only the randomized trials meeting at least 6 of 12 inclusion criteria were utilized for analysis. However, studies scoring lower were described and provided with an opinion and critical analysis.

Observational studies had to meet a minimum of the 50% criteria for cohort studies and case-control studies. Studies scoring less were also described and provided with an opinion and a critical analysis.

### 1.9 Data Extraction Process

Each study was evaluated by at least 2 authors for stated criteria and any disagreements were discussed with a third reviewer. If there was a conflict of interest with the reviewed manuscript concerning authorship or any other type of conflict, the involved authors did not review the manuscript for quality assessment, clinical relevance, evidence synthesis, or grading of evidence. No such conflicts occurred.

#### *1.9.1 Methods for Handling Missing Information*

Missing information was evaluated on a case-by-case basis. If the data available were insufficient to evaluate the study, or if the data did not meet the endpoint criteria, the study was excluded.

#### *1.9.2 Information to Be Extracted From Included Studies*

The primary outcome parameter was pain relief. The secondary outcome measures are functional improvement, change in psychological status, return to work, continued opioid use, other drugs or other interventions, and complications.

The studies were evaluated according to clinical relevance, the strength of evidence, and the recommendation.

#### *1.9.3 Summary Measures*

Summary measures included 50% or more reduction of pain in at least 40% of the patients, or at least a 3 point decrease in pain scores and a relative risk of adverse events, including side effects

### 1.10 Analysis of Evidence

The analysis of the evidence was performed based on United States Preventive Services Task Force (USPSTF) criteria as illustrated in Table 5, criteria which have been utilized by multiple authors (71).

The analysis was conducted using 3 levels of evidence ranging from good to fair to limited (or poor).

At least 2 of the review authors independently, in an unblinded, standardized manner, analyzed the evidence. Any disagreements between reviewers were resolved by a third author and consensus. If there were any conflicts of interest (e.g., authorship), those reviewers were recused from assessment and analysis.

### 1.11 Outcome of the Studies

In the randomized trials, a study was judged to be positive if the TAP therapy was clinically relevant and effective, either with a placebo control or active control. This indicates that the difference in effect for the primary outcome measure is statistically significant on the conventional 5% level. In a negative study, no difference between the study treatments or no improvement from baseline is identified. Further, the outcomes were judged at the reference point with positive or negative results reported at one month, 3 months, 6 months, and one year.

For observational studies, a study was judged to be positive if the TAP was effective, with outcomes reported at the reference point with positive or negative results at one month, 3 months, 6 months, and one year. However, observational studies were only included in the evidence synthesis if there were fewer than 5 randomized trials meeting inclusion criteria for evidence synthesis for each modality (i.e., IDET, discTRODE, and biacuplasty).

## 2.0 Results

Figure 1 shows a flow diagram of study selection.

Six prospective, double-blind, randomized controlled trials were identified (60,72-76). Of the 6 randomized controlled trials, 3 dealt with intranuclear procedures, either radiofrequency or steroid injection, and were excluded (60,74,76).

Thirty-eight observational studies were found (43,44,61,77-111). Twenty-six of the observational studies did not meet the current criteria for inclu-

Table 5. *Method for grading the overall strength of the evidence for an intervention.*

| Grade | Definition |
|---|---|
| Good | Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes (at least 2 consistent, higher-quality RCTs or studies of diagnostic test accuracy). |
| Fair | Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes (at least one higher-quality trial or study of diagnostic test accuracy of sufficient sample size; 2 or more higher-quality trials or studies of diagnostic test accuracy with some inconsistency; at least 2 consistent, lower-quality trials or studies of diagnostic test accuracy, or multiple consistent observational studies with no significant methodological flaws). |
| Limited or Poor | Evidence is insufficient to assess effects on health outcomes because of limited number or power of studies, large and unexplained inconsistency between higher-quality trials, important flaws in trial design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes. |

Adapted and modified from methods developed by US Preventive Services Task Force (71).

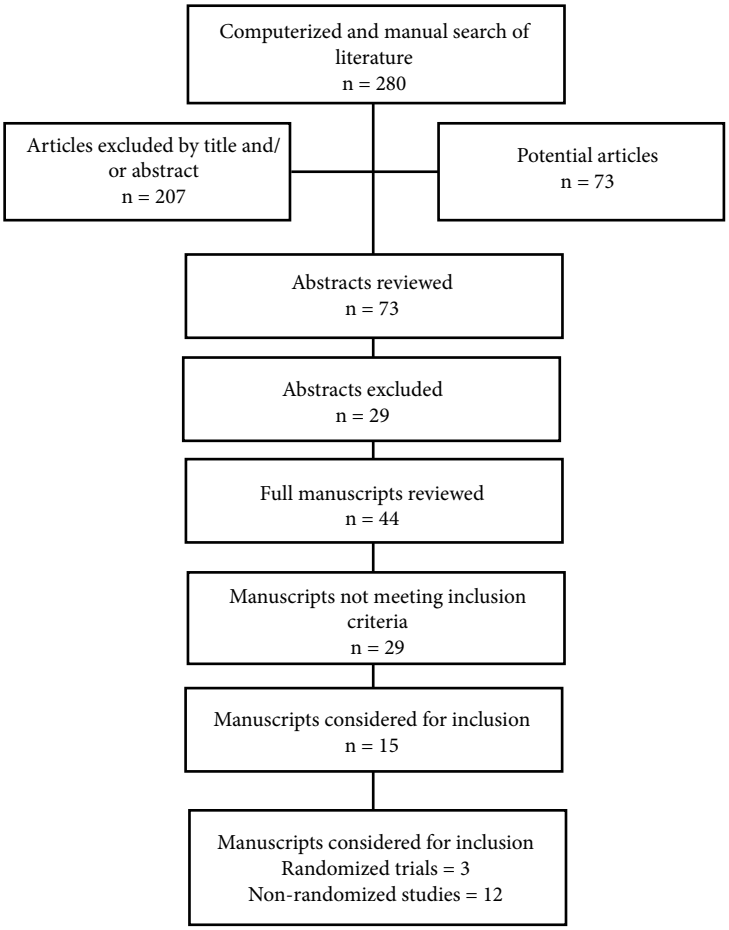


Fig. 1. *Flow diagram illustrating published literature evaluating thermal annular procedures.*

sion (43,44,61,77,79-82,84,88,89,92-100,103,105-107, 110,111). Table 6 shows the 3 randomized controlled trials (60,74,76) and 26 observational studies excluded and their reason for exclusion (43,44,61,77,79-82,84,88,90,92-100,103,105-107,110,111). Multiple studies, whether meeting the inclusion criteria or not, had the same patient group reported on in different papers (43,77,81,82,84,85,97,100,102-104,111).

There were 12 observational studies which did meet the inclusion criteria (78,83,85-87,89, 91,101,102,104,108,109). Of these 12, 4 (85,101,102,104) had previous reports on the same patient group (43,84,100,103,111). Only the most recent study was used, except in one instance where the second study (111), while more recent, was published in a journal sufficiently difficult to find as to warrant the review of the more accessible version (102). There was no difference in the duration of follow-up or conclusions between the 2 studies. The characteristics of these 12 observational studies looking at distinct patient groups and 3 randomized trials, which were accepted for further review, are shown on Table 7.

Table 7 shows the characteristics of studies considered for inclusion.

## 2.1 Clinical Relevance

Of the 15 randomized controlled trials and observational studies which met the inclusion criteria, 14 met the criteria for clinical relevance, with a score of at least 3 out of 5. The clinical relevance findings are shown in Table 8. All 3 randomized controlled trials were clinically relevant. Of the 11 observational studies, only one (108), a review of insurance files, was not clinically relevant.

Table 6. *List of excluded randomized trials and nonrandomized studies.*

| Manuscript Author(s) | Number of Patients | Treated vs. Control | Reason for Exclusion | |
|---|---|---|---|---|
| | | | Follow-up Period | Other Reason(s) |
| RANDOMIZED CONTROLLED TRIALS | | | | |
| Barendse et al (60) | 28 | 13 intranuclear radiofrequency 15 needle placement without radiofrequency | 8 weeks | Dealt with intranuclear radiofrequency rather than an annular procedure |
| Cao et al (74) | 120 | 6 arms of 20 each | 6 months | Dealt in intranuclear injection of steroids rather than an annular procedure |
| Erçelen et al (76) | 37 | 19 Intranuclear radiofrequency-120 sec 18 Intranuclear radiofrequency-360 sec | 6 months | Dealt with intranuclear radiofrequency rather than an annular procedure |
| OBSERVATIONAL STUDIES | | | | |
| Saal & Saal (43) | 25 | IDET | Mean 7 months | Same database as Saal 2002 |
| Finch et al (44) | 46 | 31 treated with discTRODE /15 controls | 12 months | Failure to meet criteria of > 50 patients |
| Kapural et al (61) | 42 | 21 IDET/21 discTRODE | 12 months | Failure to meet criteria of 25 patients in each group |
| Mekhail & Kapural (79) | 34 | IDET | 12 months | Failure to meet criteria of > 50 patients |
| Kapural et al (80) | 34 | 17 IDET 1-2 level disc disease/17 IDET multilevel disc disease | 12 months | Failure to meet criteria of 25 patients in each group |
| Kapural et al (81,82) | 15 | Biacuplasty | 6 month/12 month | Failure to meet criteria of > 50 patients |
| Assietti (84) | 50 | IDET | 24 | Duplicate of Assietti 2010, as an abstract presentation |
| Cohen et al (88) | 9 | IDET | 6 months | Failure to meet criteria of > 50 patients |
| Derby et al (90) | 36 | IDET | 12 months | Failure to meet criteria of > 50 patients |
| Derby et al (92) | 35 | IDET | 16 months | Failure to meet criteria of > 50 patients. Same patient population as Derby 2004. |
| Endres et al (93) | 54 | IDET | 3 months to 2 years | Data provided were inadequate for any type of conclusion in a relatively small number of patients in a retrospective evaluation. |
| Ergün et al (94) | 39 | IDET | 18 months | Failure to meet criteria of > 50 patients |
| Freedman et al (95) | 41 | IDET | 6-46 months | Failure to meet criteria of > 50 patients |
| Gerstein et al (96) | 27 | IDET | 12 months | Failure to meet criteria of > 50 patients |
| Karasek & Bogduk (77,97) | 53 | 36 treated with IDET/17 control | 12 months/24 months | Failure to meet criteria of 25 patients in each group. Both studies evaluated same data base. |
| Lee et al (98) | 51 | 32 IDET one level; 19 IDET multilevel | 24 months | Failure to meet criteria of 25 patients in each group |
| Lutz et al (99) | 33 | IDET | Mean 15 months | Failure to meet criteria of > 50 patients |
| Maurer & Squillante (100) | 78 | IDET | 24 months | Same patient population as Maurer 2008 |
| Saal & Saal (103) | 62 | IDET | 12 months | Same database as Saal 2002 |
| Singh (105) | 23 | IDET | 6 months | Failure to meet criteria of > 50 patients |
| Spruit & Jacobs (106) | 20 | IDET | 6 months | Failure to meet criteria of >50 patients |

Table 6 (cont.). *List of excluded randomized trials and nonrandomized studies.*

| Manuscript Author(s) | Number of Patients | Treated vs. Control | Reason for Exclusion | |
|---|---|---|---|---|
| | | | Follow-up Period | Other Reason(s) |
| Teixeira & Sluijter (107) | 8 | Intranuclear pulsed radiofrequency | 3 months | Deals with an intranuclear rather than annular procedure |
| Kapural et al (110) | 3 | Thoracic biacuplasty | 12 months | Failure to meet criteria of > 50 patients; thoracic pain |
| Jawahar et al (111) | 53 | IDET | Up 72 months | Duplicate patient population as Nunley et al (102) |

Table 7. *Assessment of randomized trials and nonrandomized studies for inclusion criteria.*

| Manuscript Authors | Type of Study | Number of Patients | Treatment vs. Comparator | Length of Follow-up | Outcome Parameters | Comments |
|---|---|---|---|---|---|---|
| RANDOMIZED | | | | | | |
| Pauza et al (72) | R, PC | 64 | IDET=37<br>Sham=27 | 6 months | VAS, ODI, SF-36 | 40% of patients had 50% relief |
| Freeman et al (73) | R, PC | 57 | IDET=38<br>Sham=19 | 6 months | VAS, ODI, SF-36, ZDI, MSPQ | No improvement in either group |
| Kvarstein et al (75) | R, PC | 20 | discTRODE=10<br>sham=10 | 12 months | VAS, ODI, SF-36 | No difference between treated and control |
| OBSERVATIONAL | | | | | | |
| Derby et al (78) | RE | 109<br>IDET=74<br>Injection=35 | IDET vs restorative injections | 6-18 months | VAS | Analysis of patients treated from 1/00 to 10/02. Pain relief of 1.27 for IDET and 2.2 for injection. 35% of IDET patients were worse; 0% of injection patients were worse. |
| Tsou et al (83) | P | 93 | IDET | 3 years | Percent improvement – 100%, > 50%, < 50%, no change or increase | The results were positive in short-term and long-term with 62% at 3 months, 74% at 6 months, 63% at one year, 60% at 2 years, and 48% at 3 years. |
| Assietti et al (85) | P | 50 | IDET | 24 months | VAS, ODI, Prolo Score | 68% improvement at 24 months. Predictors of success include discographic pain concordance, disc height (Pfirrmann Grade), HIZ, and percentage of annulus covered. |
| Bryce et al (86) | P | 86 | IDET | 18 months | VAS, RMDQ | Significant relief in women and age 18-45; relief in males lasted 3-6 months |
| Cohen et al (87) | RE | 79 | IDET | 6 month | VAS | 48% of patients had > 50% relief at 6 months. Obesity is a risk factor. |
| Davis et al (89) | RE | 60 | IDET | 12 months | Surgical treatment for back pain after IDET | 48 of 60 patients completed the interview process. 6 patients had surgery at one year and 4 more at 2 years. 37% of patients were satisfied with the procedure at one year. |
| Derby et al (91) | RE | 99 | IDET | 18 months | VAS | Analysis of 129 patients treated from 1/6/99 to 1/6/00. 30 had fusion and were excluded. 83% had leg pain without sciatica. 63.9% of patients had mean pain relief of 3.28/10. Relief of low back and leg pain was correlated. |

Table 7 (cont.). *Assessment of randomized trials and nonrandomized studies for inclusion criteria.*

| Manuscript Authors | Type of Study | Number of Patients | Treatment vs. Comparator | Length of Follow-up | Outcome Parameters | Comments |
|---|---|---|---|---|---|---|
| Maurer et al (101) | RE | 56 | IDET | 6 months | VAS, SF-36 | 75% had ≥ 2 point improvement in pain severity or ≥ 10 point improvement of SF-36 domains. |
| Nunley et al (102) | RE | 53 | IDET | 12 months | VAS, ODI | Mean reduction in VAS was 62%; mean reduction in ODI was 69%. |
| Saal & Saal (104) | RE | 58 | IDET | 24 months | VAS, SF-36, Sitting tolerance | 50% of patients had a ≥ 4 point improvement in VAS |
| Webster et al (108) | RE | 142 | IDET | Mean 22 months | Narcotic use, Lumbar injections, Surgery | 142 cases obtained from workers' compensation files |
| Wetzel et al (109) | P | 78 | IDET | 24 months | VAS, ODI | Mean reduction in VAS of 2.8. |

R = Randomized
PC = Placebo control
P = Prospective
RE = Retrospective
IDET = Intradiscal Electrothermal Therapy
VAS = Visual analog scale
ODI = Oswestry Disability Index
SF-36 = Short Form-36 Health Survey
ZDI = Zung Depression Index
MSPQ = Modified Somatic Perception Questionnaire
RMDQ = Roland Morris Disability Questionnaire

Table 8. *Clinical relevance of included studies.*

| Manuscript Author(s) | A) Patient Description | B) Description of Interventions and Treatment Settings | C) Clinically Relevant Outcomes | D) Clinical Importance | E) Benefits vs Potential Harms | Total Criteria Met |
|---|---|---|---|---|---|---|
| RANDOMIZED CONTROLLED TRIALS | | | | | | |
| Pauza et al (72) | + | + | + | + | + | 5/5 |
| Freeman et al (73) | + | + | + | + | + | 5/5 |
| Kvarstein et al (75) | + | + | + | + | + | 5/5 |
| OBSERVATIONAL STUDIES | | | | | | |
| Derby et al (78) | + | + | + | + | + | 5/5 |
| Tsou et al (83) | + | + | + | + | + | 5/5 |
| Assienti et al (85) | + | + | + | * | + | 5/5 |
| Bryce et al (86) | + | + | + | - | + | 4/5 |
| Cohen et al (87) | + | + | + | + | + | 5/5 |
| Davis et al (89) | + | + | + | + | + | 5/5 |
| Derby et al (91) | + | + | + | + | + | 5/5 |
| Maurer et al (101) | + | + | + | + | + | 5/5 |
| Nunley et al (102) | + | + | + | + | + | 5/5 |
| Saal & Saal (104) | + | + | + | + | + | 5/5 |
| Webster et al (108) | - | + | - | + | - | 2/5 |
| Wetzel et al (109) | + | + | + | + | + | 5/5 |

+ = positive; - = negative

Scoring adapted and modified from Staal JB, et al. Injection therapy for subacute and chronic low-back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824 (67).

There were 3 randomized trials that evaluated TAP (72,73,75), 2 that evaluated IDET (72,73) and one that evaluated discTRODE (75). Pauza et al (72) and Kvarstein et al (75) achieved a Cochrane score indicating high quality; Freeman et al (73) scored moderate quality. Freeman et al's (73) treatment and control groups differed in that there were more patients with Waddell signs in the treatment group versus. control (13.2% versus 5.3%) and more disability (10.5% versus 0%).

## 2.2 Methodological Quality Assessment

A methodological quality assessment of the randomized controlled trials meeting inclusion criteria was carried out utilizing Cochrane review criteria as shown in Table 9. Studies achieving Cochrane scores of 9 or higher were considered as high quality; 6 to 8 were considered as moderate quality; and studies scoring less than 6 were excluded. Two of the 3 studies were of high quality (72,75) whereas one trial was of moderate quality (73).

A methodological quality assessment of the 12 observational studies meeting inclusion criteria was carried out utilizing Newcastle-Ottawa Scale as illustrated in Table 10. All 12 studies were cohort studies. Cohort studies achieving scores of 10 or higher were considered high quality; 7 to 9 were considered moderate quality; studies scoring less than 7 were considered low quality and were excluded. As the Newcastle-Ottawa scale is structured in such a way that studies without a control cannot score 7 or above, those studies without a control which scored 6 were also included: as they could not be scored positively for either the selection of the non-exposed cohort or for the comparability of cohort criterion, their correct denominator should be 11 rather than 13. Studies without control groups scoring 6 met, therefore, at least 50% of the criteria and were included.

No observational study was high quality using the current criteria. One was moderate quality (78) and five were included as having no control group and scoring 6 (83,85,89,91,102). The remainder were considered low quality were not included. (86,87,101,104,108,109).

## 2.3 Study Characteristics

Table 11 illustrates the study characteristics of 3 randomized controlled trials (72,73,75), the one moderate quality observational study (78), and 5 studies (83,85,89,91,102) scoring 6 on the Newcastle-Ottowa scale.

## 2.4 Analysis of Evidence

The results of the analysis of evidence as to whether TAPs provide relief from discogenic low back pain are shown in Table 12.

Table 9. *Methodological quality assessment of randomized trials.*

| | Pauza et al (72) | Freeman et al (73) | Kvarstein et al (75) |
|---|---|---|---|
| Randomization adequate | Y | U | Y |
| Concealed treatment allocation | U | U | U |
| Patient blinded | Y | Y | Y |
| Care provider blinded | N | Y | Y |
| Outcome assessor blinded | Y | Y | Y |
| Drop-out rate described | Y | Y | Y |
| All randomized participants analyzed in the group | Y | Y | Y |
| Reports of the study free of suggestion of selective outcome reporting | Y | Y | Y |
| Groups similar at baseline regarding most important prognostic indicators | Y | N | Y |
| Co-interventions avoided or similar | Y | U | U |
| Compliance acceptable in all groups | Y | Y | Y |
| Time of outcome assessment in all groups similar | Y | Y | Y |
| **Score** | 10/12 | 8/12 | 10/12 |

Y = yes; N = no; U = unsure

Table 10. *Methodological quality assessment of cohort studies.*

| | Derby et al (78) | Tsou et al (83) | Assieti et al (85) | Bryce et al (86) | Cohen et al (87) | Davis et al (89) |
|---|---|---|---|---|---|---|
| **Selection** | | | | | | |
| 1) Representativeness of the exposed cohort | | | | | | |
| a) truly representative of the average pt with discogenic pain in the community * | X | X | X | X | | X |
| b) somewhat representative of the average pain patients in the community * | | | | | X | |
| c) selected group of users e.g. nurses, volunteers | | | | | | |
| d) no description of the derivation of the cohort | | | | | | |
| 2) Selection of the non exposed cohort | | | | | | |
| a) drawn from the same community as the exposed cohort * | X | | | | | |
| b) drawn from a different source | | | | | | |
| c) no description of the derivation of the non exposed cohort | | | | | | |
| 3) Ascertainment of exposure | | | | | | |
| a) secure record (eg surgical records) * | X | X | X | X | X | X |
| b) structured interview * | | | | | | |
| c) written self report | | | | | | |
| d) no description | | | | | | |
| 4) Demonstration that outcome of interest was not present at start of study | | | | | | |
| a) yes * | X | X | X | X | X | X |
| b) no | | | | | | |
| **Comparability** | | | | | | |
| 1) Comparability of cohorts on the basis of the design or analysis | | | | | | |
| a) study controls for discogenic low back pain * | X | | | | | |
| b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.) | | | | | | |
| **Outcome (Exposure)** | | | | | | |
| 1) Assessment of outcome | | | | | | |
| a) independent blind assessment * | | | X | | | X |
| b) record linkage * | X | X | | | | |
| c) self report | | | | | | |
| d) no description | | | | X | X | |
| 2) Was follow-up long enough for outcomes to occur | | | | | | |
| a) yes (select an adequate follow up period for outcome of interest)* | X | X | X | X | X | X |
| b) no | | | | | | |
| 3) Adequacy of follow up of cohorts | | | | | | |
| a) complete follow up - all subjects accounted for * | X | X | X | | X | X |
| b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) + | | | | | | |
| c) follow up rate < ____% (select an adequate %) and no description of those lost | | | | | | |
| d) no statement | | | | X | | |
| **SCORE** | 8/11 | 6/11 | 6/11 | 4/11 | 5/11 | 6/11 |

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

Table 10 (cont.). *Methodological quality assessment of cohort studies*.

| | Derby et al (91) | Maurer et al (101) | Nunley et al (102) | Saal & Saal (104) | Webster et al (108) | Wetzel et al (109) |
|---|---|---|---|---|---|---|
| **Selection** | | | | | | |
| 1) Representativeness of the exposed cohort | | | | | | |
| a) truly representative of the average patient with low back pain in the community * | X | X | | X | | X |
| b) somewhat representative of the average pain patients in the community * | | | X | | X | |
| c) selected group of users e.g. nurses, volunteers | | | | | | |
| d) no description of the derivation of the cohort | | | | | | |
| 2) Selection of the non exposed cohort | | | | | | |
| a) drawn from the same community as the exposed cohort * | | | | | | |
| b) drawn from a different source | | | | | | |
| c) no description of the derivation of the non exposed cohort | | | | | | |
| 3) Ascertainment of exposure | | | | | | |
| a) secure record (eg surgical records) * | X | X | X | X | X | X |
| b) structured interview * | | | | | | |
| c) written self report | | | | | | |
| d) no description | | | | | | |
| 4) Demonstration that outcome of interest was not present at start of study | | | | | | |
| a) yes * | X | X | X | X | X | X |
| b) no | | | | | | |
| **Comparability** | | | | | | |
| 1) Comparability of cohorts on the basis of the design or analysis | | | | | | |
| a) study controls for _____ (select the most important factor) * | | | | | | |
| b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.) | | | | | | |
| **Outcome (Exposure)** | | | | | | |
| 1) Assessment of outcome | | | | | | |
| a) independent blind assessment * | | | | | | |
| b) record linkage * | X | | X | | X | |
| c) self report | | | | X | | |
| d) no description | | X | | | | X |
| 2) Was follow-up long enough for outcomes to occur | | | | | | |
| a) yes (select an adequate follow up period for outcome of interest)* | X | X | X | X | X | X |
| b) no | | | | | | |
| 3) Adequacy of follow up of cohorts | | | | | | |
| a) complete follow up - all subjects accounted for * | X | X | X | X | | |
| b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)* | | | | | | X |
| c) follow up rate < ____% (select an adequate %) and no description of those lost | | | | | | |
| d) no statement | | | | | | |
| **SCORE** | **6/11** | **5/11** | **6/11** | **5/11** | **5/11** | **6/11** |

Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp (69).

Table 11. *Results of randomized controlled trials and observational studies of thermal annular procedures.*

| Manuscript Author(s) | Number of Patients & Selection Criteria | Control/ Comparator | Outcome Measures | Time of Measurement | Results | Strengths Weaknesses | Methodological Quality Assessment Scores |
|---|---|---|---|---|---|---|---|
| | | | | | | | |
| Pauza et al (72) | 64 patients recruited from referral and media. Back pain > leg pain of 6 months duration. Failure of 6 weeks of conservative care. Less than 20% loss of disc height. Score< 20 on Beck Depression Inventory. No radicular pain. No previous surgery or structural deformities. No workers' compensation. Positive discography with annular tear on post discography computed tomography scan, among other criteria. | 37 IDET 27 sham In treatment group, catheter passed 100% across annulus. In sham, introducer passed to annulus and patient shown image of catheter being passed on fluoro screen with appropriate sound during treatment. Powered for 40 IDET/27 sham. | VAS, SF-36, ODI<br><br>25%, 50% and 75% relief at 6 months | Before treatment 6 months evaluation by blinded evaluator | About 75% had pain > 20 months. No improvement on various SF-36 scores. 56% of IDET group improved by more than 2 on VAS; 38% of control did. These improvements are not significant by current standards. 38% of IDET had > 58% relief; 33% of sham did. The number needed to treat to get 75% relief was 5. Subgroup analysis was done with those with ≥ 7 and ≤ 6 on VAS. | Strengths: High quality efficacy randomized controlled trial. Annulus coverage was 100% of 1,360 potentially eligible candidates; 64 were enrolled. Weaknesses: Powered for operator not blinded for procedure. 40% of treated got 50% improvement in VAS; 33% of control did. | 10/12 |
| Freeman et al (73) | 57 patients in 3 spine surgery practices. Symptomatic low back pain of at least 3 months duration, no radicular findings, disc degeneration on MRI, positive discography at one or 2 levels with annular tear. < 50% loss of disc height at treated level. | 38 IDET/19 sham procedure with surgeon and patient blinded. Catheter passed with 75% annular coverage in all cases; treatment has generator attached; sham did not. Powered for 50 treated/25 sham. Enrolled stopped because of inability to enroll. | VAS, LBOS, ODI, SF-36, ZDI, MSPQ<br><br>Blinded assessment | 6 weeks, 6 months | VAS scores are not provided. Mean duration of pain 40 months, with maximum of 180 months in IDET group and mean of 66 in sham, with maximum of 180 months. No significant change in any of the functional scores. | Strengths: Randomized controlled trial. Weaknesses: No placebo response. Lack of conformity between control and treated, with more Waddell's signs and disability in treated. Over 50% of both groups were on workers' compensation. Annulus coverage was 75% VAS results were not reported. | 8/12 |
| Kvarstein et al (75) | 20 patients 10-65. LBP > leg pain of 6 months duration. No neurological findings. No previous surgery. Failure to respond to conservative treatment. Disc degeneration on MRI. < 30% loss of disc height and disc protrusion of < 4 mm. One positive level on discography. No previous spine surgery or structural deformity. | 10 discTRODE 10 Sham All patients had catheter placed across posterior annulus. Patient and operator blinded as to whether current was delivered. | VAS, with reduction of 2 significant. Verbal rating scale of pain. BPI, SF-36<br><br>ODI Patient specific functional scale | 1,3,6, 12 months | No differences between treated and sham groups at 6 months. Study halted. | Strengths: Highly controlled efficacy study, structured as randomized controlled trial. Weaknesses: Highly controlled, small study. | 10/12 |

Table 11 (cont.). *Results of randomized controlled trials and observational studies of thermal annular procedures.*

| Manuscript Author(s) | Number of Patients & Selection Criteria | Control/ Comparator | Outcome Measures | Time of Measurement | Results | Strengths Weaknesses | Methodological Quality Assessment Scores |
|---|---|---|---|---|---|---|---|
| OBSERVATIONAL STUDIES | | | | | | | |
| Derby et al (78) | Failure to respond to conservative therapy, including IDET. 24 of 35 had more than 3 discs involved. 7 of 35 had IDET at previous disc. Previous lumbar fusion at other levels or laminectomy at treated level accepted. No neurological symptoms. Disc protrusion ≤ 2 mm. Positive discogram with annular tear. Disc height≥50%. No spondylolisthesis or severe stenosis. | 109 74 IDET/ 35 injection therapy with chondroitin, glucosamine, DMSO, bupivacaine mixture with contrast medium and 50% dextrose. 6 injection discs had treatment at level previously treated by IDET. One had injection at level other than treated by IDET. | VAS Patients' subjective impression of improvement | 6-18 months Clinic visits or telephone interview | More flare-up of pain in injection than IDET group, but duration of flare-ups longer in IDET (~1 vs. 4 weeks) 2.2 pain relief in injections vs 1.2 in IDET. ~50% of IDET patients reported feeling better vs 65% of injection therapy. | Strengths: Only observational study of sufficient size with a comparator group. Weaknesses: Members of comparator group previously treated with IDET. | 8/11 |
| Tsou et al (83) | 93 consecutive patients undergoing IDET at 134 disc levels from October 2004 through January 2007 were prospectively evaluated. Discogenic disease with chronic low back pain evaluated by multiple means including discography. | NA | Percent improvement – 100%, > 50%, < 50%, no change increase | 3 years | The results were positive in short-term and long-term at 3 months 62%, at 6 months 74%, at 1 year 63%, at 2 years,60%, and at 3 years 48% showed satisfactory improvement. | Strengths: A positive prospective evaluation in a practical setting with a relatively large number of patients with strict selection criteria. Weaknesses: Prospective, but nonrandomized study. | 6/11 |
| Assietti et al (85) | 50 patients with lumbar discogenic pain identified by MRI and provocation discography were treated with IDET and were followed for 24 months. | NA | VAS, ODI | 24 months | 68% improvement at 24 months. Predictors of success include discographic pain concordance, disc height (Pfirrmann Grade), HIZ and percentage of annulus covered. | Strengths: A prospective evaluation with strict selection criteria. Weaknesses: Nonrandomized, observational study with a relatively small number of patients. | 6/11 |

Table 11 (cont.). *Results of randomized controlled trials and observational studies of thermal annular procedures.*

| Manuscript Author(s) | Number of Patients & Selection Criteria | Control/ Comparator | Outcome Measures | Time of Measurement | Results | Strengths Weaknesses | Methodological Quality Assessment Scores |
|---|---|---|---|---|---|---|---|
| Davis et al (89) | 60 patients with discogenic pain with a positive discogram were treated with IDET. | NA | Surgical treatment for back pain after IDET. | 12 months | 48 of 60 patients completed the interview process. 6 patients had surgery at one year and 4 more at 2 years. 37% of patients were satisfied with the procedure at one year. | Strengths: A prospective evaluation comparing an important variable (i.e., to avoid the necessity for surgical intervention with independent evaluations after one year). Weaknesses: Nonrandomized, observational study with a relatively small sample. The data were included for only 38 of the 60 patients. The estimated proportion of patients undergoing fusion was 15% at one year and 30% at 2 years. | 6/11 |
| Derby et al (91) | A retrospective evaluation was performed in 99 patients undergoing procedures from January 1999 through January 2000. Data were included for only 99 patients because of the 129 patients undergoing IDET procedures, 30 of them underwent subsequent surgery and were excluded from the study. | NA | VAS | 18 months | 63.9% of patients had mean pain relief of 3.28/10. Relief of low back and leg pain was correlated. | Strengths: A study performed in a practical setting in interventional pain management. Weaknesses: A retrospective evaluation with a relatively small number of patients with large exclusions even though ultimate results were shown to be positive. | 6/11 |
| Nunley et al (102) | 134 patients were treated using IDET for their discogenic low back pain. 53 patients undergoing IDET with low back pain of discogenic origin were assessed. | NA | VAS, ODI | 12 months | Mean reduction in VAS was 62%; mean reduction in ODI was 69%. | Strengths: A rare prospective study evaluating only workers' compensation patients. Weaknesses: Non-observational, relatively small study. | 6/11 |

VAS = visual analog scale; ODI = Oswestry Disability Index; LBOS = Low Back Outcome Score; CT= computed tomography; SF-36= Short Form-36 Health Survey; IDET = Intradiscal Electrothermal Therapy; MSPQ = Modified Somatic Perception Questionnaire; LBP = low back pain; ZDI=Zung Depression Index; BPI= Brief Pain Inventory

Table 12. *Results of randomized and observational studies on the effectiveness of thermal annular procedures.*

| Study | Study Characteristics | Methodological Quality Scoring | Participants | Pain relief and Function | Results at 6 months | Comments |
|---|---|---|---|---|---|---|
| **RANDOMIZED TRIALS** | | | | | | |
| Pauza et al (72) | R, PC | 10/12 | 37 IDET/27 sham | No significant change in mean VAS. 40% of treated had ≥ 50% relief; 33% of control had ≥ 50% relief. | P | High quality study showing weak evidence of effectiveness. |
| Freeman et al (73) | R, PC | 8/12 | 38 IDET/19 sham | No improvement in treated or placebo. | N | Absence of improvement in placebo denotes fatal flaw. This study is rejected for methodological shortcomings. |
| Kvarstein et al (75) | R, PC | 10/12 | 20, 10 discTRODE/10 sham | No improvement in treated or sham. | N | High quality study showing lack of efficacy for discTRODE. |
| **OBSERVATIONAL STUDIES** | | | | | | |
| Derby et al (78) | RE | 8/11 | 74 IDET/35 injection therapy | Neither group showed > 3 point improvement in VAS or 50% improvement in VAS or 40% improvement in functional scores. | U | Using contemporary criteria, this study does not show efficacy of the procedure. It does suggest that injection therapy might be of benefit. |
| Tsou et al (83) | P | 6/11 | 93 IDET | 3 months (62%), 6 months (74%), one year (63%), 2 years (60%), 3 years (48%). | P | Positive study utilizing contemporary diagnostic criteria with provocation discography and appropriate follow-up measures. |
| Assietti et al (85) | P | 6/11 | 50 IDET | 68% improved at 24 months | P | A relatively small prospective evaluation with positive results with contemporary diagnostic and functional measures. |
| Davis et al (89) | RE | 6/11 | 60 IDET | NA | N | A poorly conducted evaluation with a large number of dropouts and negative results. |
| Derby et al (91) | RE | 6/11 | 99 IDET | 64% | P | A retrospective evaluation with a large number of dropouts ultimately with positive results. |
| Nunley et al (102) | RE | 6/11 | 53 IDET | VAS reduction 62% ODI reduction 69% | P | A prospective evaluation in a very difficult population – namely, workers' compensation patients with discogenic pain. |

R = randomized; PC = placebo control; RE = retrospective; P = Prospective; IDET – Intradiscal Electrothermal Therapy; VAS=Visual Analog Scale

### 2.5 Efficacy and Effectiveness

Efficacy deals with tightly controlled studies that determine whether a procedure achieves the desired end-point in a very specific population. Effectiveness studies examine whether a procedure works in the more heterogeneous population actually seen in clinical practice. This distinction is not always clearly understood. For example, Pauza et al (72), who evaluated 1,360 patients to select 64, has been criticized for being overly selective and not applicable to the general population. Given that Pauza et al (72) performed a high quality efficacy study, criticisms that his study does not deal with effectiveness are irrelevant.

Of the 4 studies that met the current criteria relating to study size and quality for inclusion (72,73,75,78), only Pauza et al(72) showed efficacy for the IDET procedure. There was a statistically significant ($P$ = .037) improvement in VAS scores between the treated and the controlled, with 40% of the control group getting more than 50% relief. At the same time, 33% of the placebo group had more than 50% relief and the change in the VAS, while significant between the control and placebo group, was less than 3. Thus, while Pauza et al's study does show efficacy of the procedure, the extent of the relief is modest. There are an additional 4 observational studies (83,85,91,102) which showed positive results for IDET.

Freeman et al (73) has been soundly criticized. We have already noted that the control and treated groups were dissimilar. There is also the methodological flaw that a 2-point improvement in VAS is listed as an outcome under the Methodology section, but no VAS scores are provided (112). Further, Kapural and Mekhail (113) criticized it for its failure to control for factors known to be associated with adverse outcomes, such as multilevel disease, workers' compensation status, and obesity. However, these criticisms pale in light of the failure to have a placebo effect. The importance of this failure is best described by Carragee (114). Dr. Carragee is a strong and eloquent supporter of the position that various back interventions are ineffective. Thus, his opinions on the importance of the lack of response in the control group are of great significance. He feels that no effect on the sham group is a major flaw: "Decades of detailed research on patients with [low back pain] have consistently shown at least some improvement after any nonspecific intervention on the basis of natural history, regression to the mean, and the placebo effect. Yet we see no effect of the sham injection at all. A failure to see this nonspecific effect is troublesome" (114). Freeman et al's article should be excluded for unidentified structural flaws that led to a lack of response in the placebo group. In comparison, Pauza et al (72) found that one out of 3 in the placebo groups got 50% relief. In like manner, Kvarstein et al's (75) data show that about 30% of the sham treated groups had 50% relief. The data suggest that the Freeman study is an outlier and should be discarded.

Kvarstein et al (75) showed no benefit from the discTRODE procedure. These findings are supported by a lower quality study by Kapural et al (61), which showed that discTRODE had a less favorable outcome than IDET.

There is a third technology, cooled biacuplasty, for which there are currently no high-quality publications. A highly controlled prospective, randomized, placebo-controlled efficacy study finished enrolling patients about December 2011, and a second randomized controlled trial is in progress (115). The results of these studies are pending. Future reviews should evaluate those studies based on the appropriate standards. There are no currently available high quality studies which document the efficacy of biacuplasty.

### 2.6 Level of Evidence

Level of evidence was based on USPSTF criteria stratified as good, fair, or limited (or poor). Good evidence includes consistent results from well-defined, well-conducted studies in representative populations that directly assess effects on health outcomes with at least 2 consistently higher quality RCTs. In contrast, fair evidence is somewhat broad. Fair means that the evidence is sufficient to determine an effect on health outcomes, but the strength of the evidence is limited by the number, quality, size, or consistency of included studies, the evidence's generalizability to routine practice, or the indirect nature of the evidence on health outcomes. Finally, a limited (or poor) grading is when there is no sufficient evidence to assess effects on health outcomes because of the limited number or power of studies, large and unexplained inconsistencies between higher quality trials, important flaws in the trial design or conduct, gaps in the chain of evidence, or the lack of information on important health outcomes as shown in Table 1. TAPs are met with a paucity of literature and with opposing views concerning randomized trials, even though some of the trials were performed very poorly and have major flaws.

#### *2.6.1 IDET*

IDET was evaluated in 2 randomized trials (72,73); however, only one study was of high quality (72) and showed positive results with 40% of treated patients getting greater than 50% relief compared to 33% of the control group. This study also utilized an appropriate selection process and outcome measures. In contrast, the negative study (73) was of moderate methodological quality scoring, but had multiple flaws and negative results. Further, of the 6 observational studies (78,83,85,89,91,102), 4 studies showed positive results (83,85,91,102), one study showed negative results (89), and one study showed undetermined results (78).

Consequently, based on the above evidence of one positive randomized trial, 4 positive observational studies meeting the inclusion criteria, negative evidence from one poorly performed randomized trial (73) and an observational study (89), and undetermined results from another observational study (78), the evidence supporting the efficacy of IDET is weakly fair.

#### *2.6.2 discTRODE*

There was only one study evaluating discTRODE (75) which showed no benefit from the procedure; therefore, the evidence is limited (or poor).

#### *2.6.3 Biacuplasty*

There is insufficient evidence to rate the effectiveness of biacuplasty for treating low back pain. Since 2 randomized controlled trials are in progress on that procedure, the assessment of biacuplasty is deferred pending publication of those studies. Therefore, the evidence is limited (or poor).

## 3.0 Complications

While some serious complications of TAPs have been reported, they are rare at the level of case reports. Cohen et al (87) reported up to a 10% complication rate, but the majority of these complications were transient. Of 8 patients, 3 had transient paresthesias or numbness. One had transient foot drop. One patient had an increase in his disc protrusion at the treated level, but this increase was diagnosed 10 months after the procedure, so any causal relation to the procedure is unclear. Another patient had a disc protrusion at a treated level 17 months after surgery, leading to additional surgery, but again, the time lag makes a causal relation unclear. Another patient had an increase in headaches, again for no determinable cause and with no evidence of dural leak. Other authors have reported similar side effects, but felt that there were complications. For example, Freeman et al (73) reported transient, self-limited paresthesias, in both the treated and control groups, but reported that there were no complications.

Cohen et al (116), in a separate study, and Eckel and Ortiz (117) noted post-IDET disc herniation. Discitis, osteonecrosis, and the development of Grade 1 anterolisthesis have been reported (89,118). Orr and Thomas (119) reported a case in which the catheter broke off, was left in the annulus resulting in the catheter migrating to the intradural sac. This led to radiculopathy and surgical removal of the catheter fragment. Ackerman (120) and Hsia et al (121) have reported cauda equine syndrome. Derby et al (39) reported a review of 1,675 IDET procedures and 35,000 medical device reports from the Food and Drug Administration. There were 6 nerve root injuries, 5 of which were related to the placement of the introducer needle. They resolved spontaneously. Six cases of disc herniation were reported, 2 of which required discectomy. Nineteen cases of catheter breakage were reported.

Kapural and Cata (122) reported that obesity, smoking, and a history of diabetes were not associated with a higher incidence of complications. They provide a nice summary of complications from percutaneous procedures.

There are no published cases of complications from discTRODE, but adverse events may be underreported and may include possible permanent ablation of traversing motor roots (122). There are no reported complications from biacuplasty (82).

The incidence of complications from TAP, particularly IDET and biacuplasty, therefore, is low and the complications are generally minimal and self-limited. The procedures should be considered low risk for serious adverse events.

## 4.0 Discussion

This systematic review evaluating the effectiveness of TAPs for treating discogenic low back pain shows fair evidence for IDET at 6 months, limited or poor evidence for discTRODE, and limited or poor evidence for biacuplasty. The lack of evidence for discTRODE and biacuplasty is primarily based on a paucity of the literature. Thus, upcoming studies may resolve some of these issues. However, in reference to IDET, there have been 2 randomized trials. The advantages and disadvantages of each study have been extensively discussed. The pending publication of randomized trials studying biacuplasty may shed light on some of the issues.

Discogenic low back pain is a common and vexing health problem. The initial best treatment is conservative, with continued activity, physical therapy, analgesics, and muscle relaxants being the core treatment. Patients who have an incomplete response to this therapy should be considered for injection therapy as a part of the treatment plan. Refractory cases have limited treatment options. Fusion has been viewed by some as a definitive answer and, indeed, one of the articles evaluating IDET used the need to proceed to fusion as an endpoint, although why the need for surgery should be considered a failure of a TAP is not explained. The future course of those patients who had surgery after IDET was not detailed, so we have no insight into the efficacy of surgery in patients who had IDET based upon that study (89).

TAPs were developed as intermediate therapies between conservative treatment and the uncertain benefits of fusion. Three technologies have been developed: IDET, discTRODE, and biacuplasty.

These findings are similar to a 2009 systematic review of TAPs (29), which found that the evidence supporting IDET to be II-2. The criteria by which articles are judged for quality have changed. There are new requirements regarding the number of patients enrolled and new criteria by which to score quality, with a higher emphasis on comparator groups. Despite this, the evidence remains similar. Fifteen observational studies included in the 2009 paper were excluded, along with additional studies published since then.

## 5.0 Conclusion

A systematic review of the literature regarding the use of the 3 technologies currently available for the application of thermal energy to the annulus to treat chronic discogenic low back pain shows that one of these procedures, IDET, is effective for short-term (6 months) treatment of discogenic pain. However, the evidence is limited for discTRODE and biacuplasty at present.

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