



**TITLE:** **IDET – Intradiscal Electrothermal Therapy  
for Treatment of Back Pain**

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## **INTRADISCAL ELECTROTHERMAL THERAPY FOR TREATMENT OF BACK PAIN (IDET)**

### **INTRODUCTION**

The technology of Intradiscal Electrothermal Therapy (IDET) for the treatment of chronic back pain was reviewed by the Blue Shield of California Medical Policy Committee on Quality and Technology on June 9, 1999. The decision at that time was that IDET did not meet technology assessment criteria. The California Technology Assessment Forum has been asked to conduct another review as the scientific literature has evolved over the past four years.

### **BACKGROUND**

#### Back pain

Low back pain is the most common cause of morbidity and chronic pain in the US with an incidence approaching 20% (Deyo *et al.* 1987). In most cases, the causes of both acute and chronic back pain are benign. The physiologic basis for low back pain is complex, in part because of its complex anatomy. The spine is comprised of bones, joints, ligaments, fatty tissue, multiple layers of muscles, and nerves. These structures are supplied by an intricate arterial and venous system and lie in close proximity to the skin with its sensory receptors. Spinal structures and tissues that possess either unmyelinated nerves or substance P or related peptides are assumed to have the capacity to cause pain.

Such structures include the posterior facet joints, bones and periosteum, muscles, tendons, fascia, ligaments, nerve roots, dorsal root ganglia, dura mater, and the intervertebral disc (Haldeman 1999).

The specific tissue responsible for back pain is identified in less than 20% of cases (Frymoyer 1988). In most cases a trial of conservative treatment is appropriate. A more aggressive diagnostic evaluation is usually done in cases of progressive neurologic deficit, bowel or bladder incontinence, a history of cancer, or significant trauma (Swenson 1999).

## **BACKGROUND**, continued

Up to 40% of chronic low back pain has been reported to originate from the intervertebral disc (Schwarzer *et al.* 1995). Internal disc disruption has been postulated as a cause of discogenic pain, but there is controversy surrounding its diagnosis and management. It is differentiated from other potentially painful degenerative processes such as degenerative disc disease and segmental instability. There has been controversy in the literature about the extent of innervation of the disc. It is now clear that fine nerve endings penetrate the outer one-third of the annulus and may cause pain (Weinstein *et al.* 1988; Houpt *et al.* 1996). The disc resembles a jelly-filled donut composed of a series of firm fibrous rings (annulus fibrosis) surrounding a soft core (nucleus pulposus). A number of disc injuries can potentially lead to pain. These include annular tears, disc protrusions with extrusion of the nucleus pulposus, and disc herniation, in which some of the nucleus pulposus escapes through the annulus. These events cause pain by stretching or tearing peripheral disc fibers or by generating an inflammatory reaction in adjacent spinal tissues (Swenson 1999).

Low back pain caused by intervertebral disc damage may be insidious or sudden in onset. Pain is usually at the center of the back and may radiate to the buttocks or thighs. It is usually increased by sitting and improved by lying down. Pain usually improves within two weeks, but may require up to twelve weeks for complete resolution. The pain caused by disc tears does not differ significantly from that associated with disc bulge and herniation. Up to 90% of acute episodes of intervertebral disc damage resolve spontaneously with chronic pain developing in about 10% of cases (Swenson 1999).

Magnetic resonance imaging (MRI) is an important tool for the diagnosis of internal disc disruption. If the MRI is normal, disc disruption can be ruled out. MRI findings suggestive of internal disc disruption include concentric, radial and transverse tears of the annulus fibrosis. Radial tears are most frequently associated with pain on discography (Moneta *et al.* 1994). Discography, while controversial, is considered to be the most important tool in the diagnosis of internal disc disruption (Holt 1968; Weinstein *et al.* 1988). Information from discography should include the morphology of the disc being injected, the disc pressure and volume of fluid accepted by the disc, the subjective pain response, and the pain response at adjacent disc levels.

## **BACKGROUND**, continued

Reproduction of the severity and character of the patient's pain during disc injection are necessary for discography to be considered positive.

Patients with clear discogenic pain often benefit from complete surgical removal of the intervertebral disc and vertebral fusion. Measurable decreases in preoperative pain have been noted in over 80% of patients in various series (Lee *et al.* 1995). Minimally invasive intradiscal techniques and percutaneous procedures have recently been employed as an alternative to conventional surgical methods. These have included chemonucleolysis, manual percutaneous discectomy, automated percutaneous discectomy, laser-assisted discectomy, endoscopic posterolateral discectomy, and laparoscopic discectomy and fusion (Fehlings 1996; Maroon *et al.* 1996).

### Thermal therapy

Recently, controlled heat has been used in the treatment of joint disease. For example, both laser and radiofrequency energy have been applied to the joint capsule of the shoulder in order to shrink collagen. Collagen tissue shrinkage is caused by the rupture of hydrogen bonds linking collagen fibrils (Shah *et al.* 2001) transforming the native triple helix conformation to a contracted, "random coil conformation." Temperatures achieved with laser are difficult to target and control. Because of impedance limitations, radiofrequency energy is relatively ineffective for heating disc tissue and has difficulty covering the full expanse of the intervertebral disc. A third form of heat delivery, electrothermal energy using a thermal resistive coil allows for thermocoagulation of a larger tissue segment, more precise temperature control, and temperature feedback.

Intradiscal electrothermal therapy permits controlled delivery of heat to the intervertebral disc via a thermal resistive coil embedded within a catheter. The technique is usually performed under local anesthesia with intravenous sedation. General anesthesia is contraindicated, as the patient must be awake for monitoring of signs of nerve root irritation. After placement of a 17-gauge needle into the center of the disc, the intradiscal catheter is introduced through the needle and positioned adjacent to the posterior annulus with fluoroscopic guidance. The strong outer layers of the annulus deflect the electrode, guiding it in a circumferential course toward the affected side.



## **BACKGROUND**, continued

The catheter temperature is then gradually raised following a standard protocol to 90° C over 13 minutes and is maintained at 90° C for 4 minutes. This creates an annular temperature of 60-65° C. After heating, prophylactic antibiotics and local anesthetic are injected intradiscally and the catheter is withdrawn. The therapy is an outpatient procedure that takes approximately one hour.

After surgery, the patients are encouraged to walk and do light stretching. Bending, lifting, and prolonged sitting are restricted for 8-12 weeks. Low intensity stabilization exercises are begun during the second month. Athletic activities are delayed until two to three months after surgery.

Several mechanisms have been proposed to explain the effects of intradiscal electrothermal treatment. Heating may cause shrinkage of collagen fibrils leading to stabilization through remodeling (Lee *et al.* 2001; Shah *et al.* 2001) or sealing annular tears, but this is controversial (Kleinstueck *et al.* 2001; Narvani *et al.* 2003). No loss of disc height or other changes were seen on MRI three to fourteen months after the procedure (van Kleef *et al.* 1996). The leading hypothesis is that heating the disc globally may decrease enervation from pain fibers. It has been shown that irreversible damage to nerve tissue occurs at temperatures above 42° C. However, two cadaver studies suggested that the temperature changes from this procedure were not sufficient to raise temperatures above the 42° C required for neuronal cell death (Troussier *et al.* 1995; Houpt *et al.* 1996). However, these studies have been criticized because the heating element was placed in the middle of the disc and not within the annulus. A subsequent study using the Oratec SpineCATH method reported that sufficient temperatures were generated to achieve denervation (Ashley *et al.* 1999).



## **Technology Assessment (TA)**

**TA Criterion 1: The technology must have final approval from the appropriate regulatory bodies.**

The SpineCATH Intradiscal Catheter (Oratec, Menlo Park, CA) received 510(k) clearance from the FDA on February 4, 1998 for use “for the coagulation and decompression of disc material to treat symptomatic patients with annular disruption of contained herniated discs.” The radiofrequency generator SMK Cannula and Radionics TIC Cannula (Radionics, Burlington, MA) received 510(k) clearance in 1996. The Radionics RF Disc Catheter Electrode System received 510(k) clearance on October 23, 2000.

TA criterion 1 is met.

**TA Criterion 2: The scientific evidence must permit conclusions concerning the effectiveness of the technology regarding health outcomes.**

The literature search identified published reports from thirteen centers presenting outcome data for intradiscal electrothermal therapy as treatment for chronic discogenic low back pain. Two studies were randomized clinical trials (Barendse *et al.* 2001; Pauza *et al.* 2003). One cohort study used concurrent controls who participated in a rehabilitation program (Karasek *et al.* 2000; Bogduk *et al.* 2002). The nine other studies were case series,; several with multiple publications (van Kleef *et al.* 1996; Derby *et al.* 2000; Saal *et al.* 2000a; Saal *et al.* 2000b; Singh 2000; Endres *et al.* 2002; Gerszten *et al.* 2002; Saal *et al.* 2002; Spruit *et al.* 2002; Lutz *et al.* 2003). The studies are summarized in Table 1. Two different catheter systems were used in these studies. The majority of the studies used the IDET device manufactured by Oratec, which uses a resistance coil to generate heat (Derby *et al.* 2000; Saal *et al.* 2000a; Saal *et al.* 2000b; Singh 2000; Endres *et al.* 2002; Gerszten *et al.* 2002; Saal *et al.* 2002; Saal *et al.* 2002; Spruit *et al.* 2002; Lutz *et al.* 2003; Pauza *et al.* 2003). There are two studies of the device by Radionics, which uses radiofrequency energy (van Kleef *et al.* 1996; Barendse *et al.* 2001). Studies in progress include at least one European randomized clinical trial and a multicenter cohort of at least 400 patients.

**Table 1: Studies of Intradiscal Therapy for Chronic Back Pain**

Study	N	Follow-up	Patients	Procedure	Pain VAS	Oswestry Disability Scale	Additional information
<b>Randomized trials</b>							
Pauza 2003	IDET 37 Sham 27	6 months	Texas LBP > 6 months Age 18-65 years Unsuccessful conservative treatment Normal neurological exam, negative straight leg raise, pain provoked on discography, abnormal nucleogram. No nerve compression on MRI. No radiculopathy. <20% disc height loss. Posterior tear of annulus fibrosis on CT.	Oratech device: IDET: electrode heated to 90° C over 13 minutes and maintained for 4 minutes: total 17 minutes.  Intradiscal injection cefazolin or gatafloxin.  Outcome assessment blinded.	<i>6 mo</i> Pre Post IDET 6.6 4.2 Sham 6.5 5.4 P=0.045	<i>6 mo</i> Pre Post IDET 31 20 Sham 33 28 P=0.05	Per protocol rather than intention to treat analysis. 13% lost to follow-up at 6 months. 22% IDET report pain same or worse vs. 54% sham. Pain improved >75% in 22% of IDET patients vs. 4% of sham patients. No differences in SF-36 changes between groups.
Barendse 2001	RF 13 Sham 15	8 weeks	Netherlands LBP > 1 year Age 30-65 years Unsuccessful conservative treatment. Pain relief with anesthetic discography. Neurologist evaluation to rule out radiculopathy.	Radionics RF device: Radiofrequency energy for 90 seconds at 70° C.  Outcome assessment blinded.	<i>2 mo</i> Pre Post RF 6.5 5.9 Sham 5.5 4.4 P=NS (>0.1)	Pre Post RF 44 41 Sham 41 35 P=NS (>0.1)	Different device from other studies.
<b>Concurrent controls</b>							
Karasek (2000, 2002)	IDET 36 Control 17	3 months	Oregon LBP > 3 months 150 patients without disc prolapse, tumor, infection. Discography on 110: 53 had internal disc disruption. Insurance approval in 36, denied in 17.	IDET: electrode heated to 90° C for 17 minutes.  Intradiscal injection cefazolin.	<i>3 mo</i> Pre Post IDET 8.0 3.5 Sham 8.0 8.0 P<0.001  <i>12 mo</i> Pre Post IDET 8.0 3.0 Control 8.0 7.5 P=0.005	Incompletely measured. 41% improvement in 14 patients. No comparison with controls.	24 mo similar to 12 month data. 54% had >50% pain relief, 20% were completely pain free. No multivariable adjustment for differences between groups.

Study	N	Follow-up	Patients	Procedure	Pain VAS	Oswestry Disability Scale	Additional information
Case series							
Cohen 2003	IDET 79	6 months	<p>Boston and Washington DC LBP&gt;6 months. Discogenic. Unsuccessful conservative treatment Normal neurological exam, pain provoked on discography, abnormal nucleogram. No nerve compression on MRI. No segmental instability.</p> <p>Note: Prior surgery at level, leg pain, and the presence of annular leak on discography were not exclusion criteria at beginning of study period (they are in current guidelines for use of IDET).</p>	<p>IDET: electrode heated to 90° C for 16.5 minutes.</p> <p>Intradiscal injection cefazolin and bupivacaine post-procedure.</p>	<p>6 mo Pre Post IDET 6.1 3.7 No p given.</p> <p>38/79 (48%) reported more than 50%pain relief (Positive).</p> <p>Positive (n=38) 6 mo Pre Post IDET 5.9 2.1 P not given. Est: P&lt;0.0001</p> <p>Negative (n=41) 6 mo Pre Post IDET 6.2 5.1 P not given. Est: P&lt;0.01</p>	Not assessed.	<p>Obese patients (&gt;20% above ideal body weight) had worse outcomes (p=0.01). 90% of obese patients had poor outcomes.</p> <p>Trend towards worse outcomes in patients treated at 2 levels versus 1 level.</p> <p>8/79 patients (10%) reported complications: Headache that resolved in 1 week. Paresthesias in 3 resolved &lt; 1 month. Foot drop resolved 6 weeks. Worse pain in 3, 2 with disc herniation treated with surgery with good relief.</p>
Lutz 2003	IDET 33	15 months mean	<p>New York LBP&gt;6 months. Unsuccessful conservative treatment Normal neurological exam, negative straight leg raise, pain provoked on discography, abnormal nucleogram. No nerve compression on MRI. No prior surgery, no segmental instability. No radiculopathy.</p>	<p>IDET: electrode heated to 80-90° C for 16.5 minutes.</p> <p>Intradiscal injection cefazolin.</p>	<p>? mo Pre Post IDET 7.5 3.9 P&lt;0.001</p>	Not assessed.	<p>Roland-Morris Disability Questionnaire 13.9 to 7.3 (p&lt;0.001). 77% of patients would repeat procedure for the same outcome.</p>
Saal 2000, 2002	IDET 62	24 months	<p>1116 patients referred for specialty care. LBP&gt;6 months. Unsuccessful conservative treatment Normal neurological exam, negative straight leg raise, pain provoked on discography, abnormal nucleogram. No nerve compression on MRI. No radiculopathy.</p>	<p>IDET: electrode heated to 90° C over 13 minutes and maintained for 4 minutes: total 17 minutes.</p> <p>Intradiscal injection cefazolin.</p>	<p>6 mo Pre Post IDET 6.6 3.7 P&lt;0.001</p> <p>Stable over time: 12 mo 3.5 24 mo 3.4</p>	Not assessed.	<p>Statistically significant improvements in SF-36 physical function and bodily pain subscales at 6 months. Both continue to improve slightly at 12 and 24 months. 18/25 had increased</p>

Study	N	Follow-up	Patients	Procedure	Pain VAS	Oswestry Disability Scale	Additional information
Case series							
Gerszten 2002	IDET 27	12 months	Pennsylvania Consecutive patients. LBP>6 months Unsuccessful conservative treatment Normal neurological exam, negative straight leg raise, pain provoked on discography, abnormal nucleogram. No nerve compression on MRI. No instability on imaging. No radiculopathy.	IDET: electrode heated to 90° C over 13 minutes and maintained for 4 minutes: total 17 minutes.  Intradiscal injection cefazolin.	Not done.	12 mo Pre Post IDET 34 30 P not reported	Improvement in SF-36 role functioning-physical. No p values reported.
Spruit 2002	IDET 20	6 months	Netherlands Consecutive patients. LBP>6 months Unsuccessful conservative treatment Normal neurological exam, negative straight leg raise, pain provoked on discography, abnormal nucleogram. No instability on imaging.	IDET: electrode heated to 90° C over 13 minutes and maintained for 4 minutes: total 17 minutes.  Intradiscal injection cefazolin.	6 mo Pre Post IDET 6.5 5.1  P=0.046	6 mo Pre Post IDET 43 37  P=NS	Similar results at 3 and 6 months. Significant improvements on SF-36 subscales: vitality and bodily pain, but not the other 6 subscales.
Endres 2002	IDET 54	3-24 months	Wisconsin LBP>9 months Unsuccessful conservative treatment Normal neurological exam, negative straight leg raise, pain provoked on discography, abnormal nucleogram. No instability on imaging. Disruption to outer third of annulus on CT. No nerve compression on MRI. No prior surgery.	IDET: electrode heated to 90° C over 13 minutes and maintained for 4 minutes: total 17 minutes.  Intradiscal injection cefazolin.	Average reduction 2.6 P<0.001 Median reduction 3.	Not assessed.	23% no change or worse pain. 13% minimal decrease in pain. 65% report clinically significant reduction in pain. Significant improvements in sitting time and walking tolerance.

Study	N	Follow-up	Patients	Procedure	Pain VAS	Oswestry Disability Scale	Additional information
Singh 2000*	IDET 21	1-6 months	Consecutive patients. LBP>6 months Unsuccessful conservative treatment Normal neurological exam, negative straight leg raise, pain provoked on discography, abnormal nucleogram. No nerve compression on MRI. No radiculopathy.	IDET: electrode heated to 80-90° C for 16.5 minutes.  Intradiscal injection cefazolin.	3 mo Pre Post IDET 6.2 3.9 P<0.001	Not assessed.	
Derby 2000*	IDET 32	6 months 12 months	Consecutive patients. LBP>6 months Normal neurological exam, negative straight leg raise, pain provoked on discography, abnormal nucleogram. No radiculopathy.	IDET protocols varied: heated to 75-150° C, total duration 13.5-16.5 minutes.	12 month decline in VAS 1.84 (SD2.38)	Not assessed.	62% better 25% unchanged 13% worse
Van Kleef 1996	RF 39	2 months > 9 months	Netherlands LBP > 1 year Age 30-65 years Unsuccessful conservative treatment Pain relief with anesthetic discography. Neurologist evaluation to rule out radiculopathy.	Radionics RF device: Radiofrequency energy for 90 seconds at 70° C.	Not assessed.	Not assessed.	21/39 (54%) reported >50% pain relief using a 4 point Likert scale at 2 months and 16 (41%) at > 9 months.  This was pilot study for RCT: Barendse 2001 above.

**TA Criterion 2: The scientific evidence must permit conclusions concerning the effectiveness of the technology regarding health outcomes (continued)**

The patient selection criteria were similar for all studies. Participants had chronic back pain of at least 3-12 months duration that had failed conservative therapy with anti-inflammatory medications, narcotics, physical therapy, and corticosteroid injections. Most required discography that demonstrated pain with low pressure at the affected disc and demonstrated posterior annular disruption. The affected discs could not have lost >50% of their height and no more than 2 discs could be affected. There could be no evidence of nerve root compression on neurologic exam or imaging with CT or MRI. Patients with spinal stenosis, spondylolisthesis, disc herniation, or prior surgery were excluded.

The benefits of treatment for low back pain include pain relief, decreased disability/restoration of function, cessation of narcotic therapy and return to work. The primary outcome measure used in all studies was change in the pain score as measured by a 10-point visual analog scale (VAS). Changes of two points or greater are generally considered clinically significant. Disability was measured by the 100 point Oswestry Disability Scale (ODS). Many studies also used the Short Form 36 (SF-36) and its eight subscales to measure changes in health related quality of life. A change of seven or greater on each 100 point scale is considered clinically significant.

Potential harms that could occur as a result of intradiscal therapy include spinal injury and worsened symptoms.

TA criterion 2 is met.

Level of evidence: 1, 3, 5

**TA Criterion 3: The technology must improve the net health outcomes.**

Comparative trials

Pauza *et al* conducted a randomized clinical trial of the Oratec IDET device at a single private practice clinic in Texas (Pauza *et al.* 2003). A major strength of the study was the careful implementation of sham therapy as a control. The study is in press and is of moderate overall quality. Of 4253 patients screened by telephone, 1360 were considered potentially eligible and underwent consultation and physical exam. Of these, 260 were confirmed as eligible and underwent discography. Sixty-four patients met discography criteria and were randomized in a 3:2 proportion to intradiscal therapy or sham therapy. Thirty-seven were randomized to intradiscal therapy and 27 to sham therapy. The primary reasons for ineligibility were unwillingness to follow the protocol, excess disc height loss, radicular pain, and failed discography.

The sham therapy consisted of the same protocol as the active therapy including conscious sedation, IV antibiotics, placement of a guide needle into the affected disc, and the same sounds and length of time in the procedure room. The randomization schedule for an individual participant was revealed after the guide needle was in place. A similar proportion in each group thought that they had received active therapy when asked immediately after the procedure (74-78%).

The primary outcome measures were changes at 6 months in pain by VAS, disability by the ODS, and quality of life by the SF-36. Staff blinded to the patients' allocation assessed outcome measures. Per protocol, rather than intention-to-treat analysis, was performed due to protocol deviations by five patients in the active therapy group and three in the sham group. In the active therapy group, one patient died, one had inadequate catheter placement, one was censored because a broken leg after the procedure interfered with outcome assessment, and two were censored because new injuries affected outcome assessment. In the sham therapy group, one patient was lost to follow-up, and two were found to have undisclosed exclusion criteria present at randomization (neurologic illness, compensation claims, and illicit opiate use). Thus, outcome data at 6 months were available for 56/64 (87%) patients randomized. Pain improved 2.4 points in the electrothermal therapy group compared with 1.1 points in the sham group (p=0.045).

**TA Criterion 3: The technology must improve the net health outcomes (continued)**

Comparative trials, continued

Disability scores improved 11 points in the electrothermal therapy group compared with 5 points in the sham group ( $p=0.05$ ). There were no significant differences between groups in the changes in the 8 subscales of the SF-36. Pain was the same or worse for 22% of the participants randomized to electrothermal therapy and for 54% of the participants randomized to sham therapy. No patient suffered adverse events.

The major strength of the Pauza study is its careful implementation of sham IDET in the control group. The effectiveness of the blinding was confirmed by the fact that equal proportions of patients in each group believed that they had received active therapy. Unfortunately, by reporting only per protocol data and not an intention to treat analysis, the authors weaken the conclusions that can be drawn from their study. The current standards of clinical trial execution and analysis call for complete outcome ascertainment, even if subjects are found to have violated the study protocol after randomization. Studies should be large enough so that randomization results in roughly equal numbers of subjects with protocol violations in each arm of the study. They should have adequate power to overcome the bias towards a null result that may occur because of protocol violations. The study should have attempted to measure the primary outcomes in the protocol violators and the patients with intercurrent injuries. Then, both intention-to-treat and per protocol analyses could be performed and presented in the publication.

Barendse *et al* (2001) conducted a similar small, randomized clinical trial of a device which heats the disc using radiofrequency energy rather than electrothermal energy (Radionics RF probe). Patients were recruited at a University-based pain clinic in the Netherlands. Two hundred eighty-seven patients with a history of at least one year of chronic low back pain were screened. Eighteen patients were randomized, thirteen to active therapy and fifteen to sham therapy. The patients randomized to sham therapy were older (45.2 vs. 40.8 years), had shorter length of pain (38 vs. 60 months) and had lower pretreatment pain levels (5.5 vs. 6.5 on VAS). An investigator blinded to treatment allocation did outcome assessments. The primary outcome measures were “success” defined as a reduction of 2 points on the VAS or  $\geq 50\%$  reduction in pain, and changes at 8 weeks in pain by VAS and disability by the ODS.

**TA Criterion 3: The technology must improve the net health outcomes (continued)**

Comparative trials, continued

Results from both unadjusted analyses and analyses adjusting for gender, age, pretreatment duration of pain, and average pretreatment pain intensity were presented. Eight weeks after treatment there were 2 successes in the sham group and 1 success in the treatment group. VAS scores decline 1.1 points in the sham group and 0.6 points in the treatment group. Similarly, the ODS decline was 4.9 in the sham group and 2.6 in the treatment group. None of the differences were statistically significant and the trends were all for better outcomes in the sham group than the radiofrequency group.

There were several differences between the studies that might explain the different outcomes. The primary differences in the intervention were the energy delivery system (radiofrequency energy rather than electrothermal energy), the heating protocol (90 seconds at 70° C vs. 13 minutes gradual heating to 90° C followed by 4 minutes at 90° C), and the placement of the heat source (center of disc vs. peripherally along the posterior annulus). Higher temperatures for a longer period of time may be necessary for effective therapy. The identification of discs amenable to therapy was also different: the study using radiofrequency energy required >50% relief of pain with injection of local anesthetic into the disc while the electrothermal therapy study required reproduction of the patients pain with modest increase in pressure of the affected disc.

Karasek and Bogduk published the only prospective cohort study of intradiscal electrothermal therapy using concurrent controls (Karasek *et al.* 2000; Bogduk *et al.* 2002). Thirty-six patients with chronic low back pain at a private practice clinic in Oregon were treated with intradiscal therapy and then compared to 17 patients in the same clinic who met the eligibility criteria for intradiscal therapy, but did not undergo the procedure as their insurance did not authorize coverage for the procedure. The control group received non-operative therapy including physical rehabilitation. The control group was older (45 years vs. 39 years, *p* not given), but otherwise appeared similar. No adjustments were made for differences at baseline. Median pain scores on the VAS improved from 8.0 to 3.5 at 3 months in the treated group, while scores were unchanged at 8.0 in the control group (*p*<0.001). The scores for both groups improved by an additional 0.5 at 1 year follow-up and the between group differences were still statistically significant (*p*<0.005).

**TA Criterion 3: The technology must improve the net health outcomes (continued)**

Comparative trials, continued

Follow-up data at 2 years were similar. The Oswestry Disability scale was measured in 14 treated patients with no controls so no comparisons can be made. In the treatment group, 8/15 (53%) patients who were not working at the time of the procedure had returned to work by the 6- month follow-up. In the control group, 1/5 (20%) returned to work. Complications were not mentioned.

It is difficult to conclude from this study alone, that intradiscal electrothermal therapy is superior to physical rehabilitation because the study did not adjust for the potential influence of selection bias leading to differences between groups in baseline characteristics. The method for determining group assignment was not blinded and could have been biased. However, the difference in the reduction in VAS pain scores between those treated with IDET and those treated conservatively was larger than would be expected from selection bias alone.

Case series

Saal *et al* have published one- and two-year follow-up data from the largest prospective case series: sixty-two patients with chronic low back pain unresponsive to non-operative care who received intradiscal therapy (Saal *et al.* 2000a; Saal *et al.* 2000b; Saal *et al.* 2002). Outcome measures included self-reported pain on a visual analog scale (VAS) and a validated measure of health related quality of life (SF-36). At 6 months, the VAS score decline from 6.6 to 3.9 ( $p<0.001$ ) and these improvements were preserved at 1 and 2 years of follow-up. There were also significant improvements on 2 of the 8 SF-36 subscales, physical function and bodily pain at 1 year (Saal *et al.* 2000a) and all 8 subscales by year 2 ( Saal *et al.* 2002). At year one, 83% of patients receiving worker's compensation returned to work and 97% of those receiving private pay returned to work. No adverse events or complications were reported.

**TA Criterion 3: The technology must improve the net health outcomes (continued)**

Case series, continued

Taken together, the 9 case series report on 367 patients treated with intradiscal electrotherapy (van Kleef *et al.* 1996; Derby *et al.* 2000; Singh 2000; Endres *et al.* 2002; Gerszten *et al.* 2002; Saal *et al.* 2002; Spruit *et al.* 2002; Lutz *et al.* 2003). Seven of the series measured pain using a VAS and all reported a statistically and clinically significant improvement (Derby *et al.* 2000; Singh 2000; Endres *et al.* 2002; Saal *et al.* 2002; Spruit *et al.* 2002; Lutz *et al.* 2003). Of note, the average improvements reported in the case series are larger (3-4 points) than the 2.4 point reduction found in the clinical trial (Pauza *et al.* 2003). Only 2 case series measured the ODS and neither reported statistically significant improvements (Gerszten *et al.* 2002; Spruit *et al.* 2002). Improvements in SF-36 subscales were inconsistent across studies (Saal *et al.* 2000a; Gerszten *et al.* 2002; Saal *et al.* 2002; Spruit *et al.* 2002). The two year follow-up data in the larger studies suggest that the benefits are durable and that there are no unexpected long-term adverse effects (Bogduk *et al.* 2002; Saal *et al.* 2002).

Complications

Several case reports have described complications of intradiscal electrothermal therapy. There have been 2 reports of procedure-associated cauda equina syndrome (Hsia *et al.* 2000; Ackerman 2002), one report of vertebral osteonecrosis (Djurasovic *et al.* 2002), and one of a large disc herniation (Cohen *et al.* 2002). Given the lack of information about the total number of procedures being performed, it is not possible to quantify the risk of these complications. In a large retrospective registry of 1,675 patients treated with intradiscal electrothermal therapy, there were 19 catheter breakages, 5 transient nerve root injuries, 1 partially resolved nerve root injury, and 6 cases of disc herniation (Saal and Saal, 2000). This suggests that the incidence of complications is less than 1%. Finally, a recent case series (Cohen *et al.* 2003) reported a much higher complication rate (8/79, 10%). Most of these were transient neurologic symptoms that resolved spontaneously. However, two of the patients had new disc herniation on MRI and two of the patients required surgery for pain relief. Certainly, larger cohort studies are needed to better define the risk for these complications.

**TA Criterion 3: The technology must improve the net health outcomes (continued)**

Summary

These case-series consistently show improvements in health outcomes by comparing follow-up with baseline measurements. However, case series are generally inadequate study designs for assessing treatment effectiveness. A major limitation is that many explanations for the change cannot be evaluated. Before-after studies do not account for placebo effects or the natural history of the disorder being studied. Pain is an outcome that has commonly been shown to be subject to large placebo effects. The study of Pauza *et al* (Pauza *et al.* 2003) clearly demonstrates that the placebo effect plays a role in intradiscal electrothermal therapy: 33% reported greater than 50% improvement in pain with one patient reporting complete relief of pain. Blinding is important because the subjective experience of pain can be affected by expectations of a positive treatment effect or by the perceived expectation of benefit from a clinical evaluator. Furthermore, the expectation of a positive treatment effect has been shown to lead to motivational and effort changes, which introduce a serious source of bias into study results.

The cohort study with concurrent controls (Karasek *et al.* 2000) suggests a benefit to intradiscal thermal therapy, but did not account for baseline differences between groups and is subject to selection bias due to unblinded assignment to the treatment groups. The randomized trial of the IDET system compared to sham therapy (Pauza *et al.* 2003) supports the case-series and non-randomized comparative trial. Randomization and allocation concealment were well done, loss to follow-up was similar in the two groups, and outcome assessments were blinded to treatment allocation. Unfortunately, confidence in this study's results is undermined by the lack of complete follow-up (87%) and no intention-to-treat analysis.

**TA Criterion 3: The technology must improve the net health outcomes (continued)**

Summary, continued

A further concern is the relatively high (10%) complication rate reported in a recent case series (Cohen *et al.* 2003). This is much higher than the 0.7% (12/1675) reported in a prior case series (Saal *et al.* 2002) from an IDET database. The discrepancy may be explained by differences in data collection. The more recent study asked patients prospectively about complications, while the prior study based its findings on physician response to a questionnaire. Physicians may be less likely to recall transient complications and may be reluctant to report complications at their center.

TA criterion 3 is not met for the Oratec IDET system.

TA criterion 3 is not met for the Radionics RF system.

**TA Criterion 4: The technology must be as beneficial as any established alternatives.**

Patients with chronic discogenic low back pain are faced with the choice of long-term pain management or surgery. Alternatives to intradiscal electrothermal therapy include conventional surgical discectomy with spinal fusion, percutaneous discectomy, laser-assisted discectomy, endoscopic posterolateral discectomy, and laparoscopic discectomy with spinal fusion. A recent Cochrane review concluded that there was no scientific evidence regarding the effectiveness of any form of surgical decompression or fusion for degenerative lumbar spondylosis compared with natural history, placebo or conservative treatment (Gibson *et al.* 2000). It is important to note that in this review the authors included all conditions involving the discs, vertebrae, and associated joints grouped as “degenerative lumbar spondylosis” of which discogenic low back pain was a sub-population.

**TA Criterion 4: The technology must be as beneficial as any established alternatives (continued)**

Intradiscal electrothermal therapy is offered as a way to avoid spinal fusion when conservative therapy has failed. Given that there are no established alternatives (Gibson *et al.* 2000), evidence that the therapy improves net health outcomes compared to continued conservative management would be sufficient to meet TA Criterion 4. The 3 comparative studies (Karasek *et al.* 2000; Barendse *et al.* 2001; Pauza *et al.* 2003) evaluate the efficacy of intradiscal electrothermal therapy versus continued conservative management. Intradiscal therapy using the Radionics RF system was no better than sham therapy (Barendse *et al.* 2001). Therapy with the Oratec IDET system significantly improved pain and reduced disability in comparative trials (Karasek *et al.* 2000; Pauza *et al.* 2003). Long term follow-up studies (Bogduk *et al.* 2002; Saal *et al.* 2002) suggest that the benefits are durable. However, case reports of significant treatment related complications (Hsia *et al.* 2000; Ackerman 2002; Cohen *et al.* 2002; Djurasovic *et al.* 2002) remind us that procedures that are marketed as “minimally invasive” still may be associated with devastating complications and should not be recommended lightly. Furthermore, the therapy is far from universally successful. In the one randomized clinical trial, only 40% of treated patients had  $\geq 50\%$  pain relief and 22% reported unchanged or worsening of pain (Pauza *et al.* 2003).

TA criterion 4 is not met for the Oratec IDET system.

TA criterion 4 is not met for the Radionics RF system.

**TA Criterion 5: The improvement must be attainable outside the investigational setting**

The published data on the Oratec device represent intradiscal electrothermal therapy used in both university and private practice settings. At least 16 centers currently provide the therapy. Oratec recommends a one-day training course for physicians interested in providing intradiscal electrothermal therapy with their catheter. The technique is not technically demanding for clinicians experienced in spinal catheter placement (anesthesiologists, orthopedic surgeons, neurosurgeons), though care must be taken to avoid injury to exiting nerve roots.

**TA Criterion 5: The improvement must be attainable outside the investigational setting (continued)**

It is likely that patient selection will be the more important determinant of clinical improvements with wider dissemination of the techniques. In the Pauza trial (Pauza *et al.* 2003), over 4000 people were screened to randomize 64 patients and of 260 patients who underwent discography, 196 did not meet the criteria for therapy. Strict adherence to the indications for therapy should allow for similar clinical benefits outside the investigational setting. The International Spinal Injection Society has published practice guidelines and protocols for intradiscal electrothermal annuloplasty that should be used by researchers in the field. However, given that clear benefits of the procedure have not been established in the investigational setting, it is impossible to make any statements about the use of the device outside the investigational setting.

Given the minimal published data on the Radionics RF device, it is impossible to make any statements about the use of the device outside the investigational setting.

TA criterion 5 is not met for the Oratec IDET system.

TA criterion 5 is not met for the Radionics RF system.

## **RECOMMENDATION OF OTHERS**

### **Blue Cross Blue Shield Association (BCBSA)**

In August 2002 the Medical Advisory Panel of the BCBSA reviewed this topic and determined that percutaneous intradiscal radiofrequency thermocoagulation for chronic discogenic low back pain did not meet the Technology Evaluation Center TEC criteria.

### **Centers for Medicare and Medicaid Services (CMS)**

CMS has not evaluated this technology for determination of coverage. Three local CMS carriers consider the procedure to be investigational at this time.

### **California Orthopedic Association (COA)**

A California Orthopedic Association representative attended the meeting and indicated that the COA was in agreement with the recommendation and that the studies did not meet criteria three, four, and five.

### **California Association of Neurologic Surgeons (CANS)**

The CANS Board of Directors agreed on May 10, 2003 that that their position is the same as 1999 when they determined that CANS cannot endorse Intradiscal Radiofrequency Thermocoagulation as an accepted treatment for back pain due to lack of conclusive scientific evidence of its efficacy.

### **Society of Interventional Radiology (SIR)**

SIR has indicated that they do not have a formal position regarding IDET. Representation at the meeting has been requested.

### **International Spinal Injection Society (ISIS)**

A position statement and representation at the meeting have been requested. ISIS Practice Guidelines and Protocols for Intradiscal Electrothermal Annuloplasty are available through the Internet.

### **American Academy of Physical Medicine and Rehabilitation (AAPMR)**

The AAPMR has indicated that they do not have a formal position regarding IDET. Representation at the meeting has been requested.

## CONCLUSION

Treatment options for chronic low back pain caused by intervertebral disc damage are limited. When patients fail conservative therapy with anti-inflammatory medications, corticosteroid injections, and rehabilitative therapy, their remaining options are long-term pain management or surgical discectomy with spinal fusion. Catheter-based intradiscal thermal therapy has been studied as a less invasive alternative to discectomy with spinal fusion.

The published evidence consists of 3 comparative trials (n=145 total) and 9 case series (n=367) examining the effectiveness of two different thermal delivery systems. There were two studies of the Radionics RF system: a pilot study in which 21/39 patients studied reported greater than 50% relief of pain. This prompted a high quality, double blind clinical trial in which 28 patients were randomized to either active treatment or a sham procedure. The study was underpowered to detect a difference between groups, but the trend was towards worse outcomes for pain and disability in the treatment group. Thus, there are little data to support the use of the Radionics device for the relief of chronic discogenic pain.

The majority of the studies of intradiscal thermal therapy utilized the Oratec IDET system. The patient selection criteria are very specific: candidates must have back pain for more than 6 months without improvement, no evidence of nerve root impingement on neurologic exam or MRI, and pain must be reproduced on provocative discography. Eight case series including 328 patients consistently found a significant improvement in pain measured with a visual analog scale. A non-randomized comparative trial of intradiscal electrothermal therapy compared to physical rehabilitation found significantly better improvements in pain in the treatment group compared with controls at three months.

## **CONCLUSION**, continued

These benefits were preserved at one and two year follow-up. However, the authors did not control for potential differences between the groups at baseline and there was significant potential for selection bias. There was one randomized clinical trial of 64 patients randomized to either IDET therapy or sham therapy that was adequately powered to detect a clinically meaningful improvement in pain. At six month follow-up there was a significant improvement in both pain and disability when compared to placebo. There were no important adverse events and no procedure related complications. The study had adequate allocation concealment and the outcome assessments were blinded to treatment allocations. However, the authors report only a per protocol analysis as 13% of the patients were not included in the final sample due to protocol violations. The lack of an intention-to-treat analysis weakens the conclusions of the study. Taken together, the consistent findings of the seven case series, the cohort study with concurrent controls, and the randomized clinical trial support the efficacy of intradiscal electrothermal therapy using the IDET system. However, the benefits are modest: 22% of patients in the randomized clinical trial reported the same or worse pain at the six--month follow-up evaluations. Furthermore, case reports have documented that the procedure carries a small risk for serious adverse events including osteonecrosis, disc herniation, and cauda equina syndrome. Further clinical trials large enough to demonstrate unequivocal efficacy with acceptable complication rates are needed to establish IDET as a clinically useful procedure.

## **RECOMMENDATION**

It is recommended that intradiscal electrothermal therapy with the Radionics RF system does not meet California Technology Assessment Forum (CTAF) TA criteria.

It is recommended that intradiscal electrothermal therapy with the Oratec IDET system does not meet CTAF TA criteria.

**October 8, 2003**

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