Acute Histologic Effects and Thermal Distribution Profile of Disc Biacuplasty Using a Novel Water-Cooled Bipolar Electrode System in an In Vivo Porcine Model

Jeffrey D. Petersohn, MD,* Laura R. Conquergood, BSCE,† and Mark Leung, BScEng†

*PainCare, P.C. Linwood, New Jersey, USA; †Baylis Medical Company Inc., Montreal, QC, Canada

A B S T R A C T

Background. Thermal treatment of the lumbar intervertebral disc has been suggested for the treatment of chronic discogenic pain. Disc biacuplasty (D-BAC) is a novel procedure that uses two water-cooled radiofrequency electrodes in a bipolar configuration to heat a large volume of the posterior annulus fibrosus.

Methods. Seven porcine lumbar discs were treated with D-BAC to assess acute effects on the treated tissue in a “worst-case” in vivo model. Intradiscal and peridiscal temperatures were measured during treatment and histologic analysis was used to assess for evidence of acute thermal injury.

Results. Temperature monitoring at designated safety zones outside the disc demonstrated maintenance of near-physiologic conditions while temperature in the inner posterior annulus reached 65°C. Histologic sections of treated discs demonstrated no evidence of thermal damage to the dorsal root ganglia or spinal nerve roots when compared with controls. Increased coarseness of the fibrillar matrix and loss of cellular detail were noted in the nucleus pulposus of treated discs.

Discussion. Disc biacuplasty, in a porcine model, achieves suitable temperatures to induce thermal transition of collagen and thermoneurolysis while showing no evidence of damage to neural tissue in safety zones surrounding the disc.

Key Words. Low Back Pain; Intervertebral Disc; Biacuplasty; Histology; TransDiscal; Temperature Mapping

Introduction

The initial morphologic description of tears of the intervertebral disc by Lindblom [1] and reports of pain production with mechanical stimulation led to histologic evidence of innervation of the disc and a subsequent half-century of inquiry into the role of the posterior annulus in the generation of lumbar pain. Bogduk confirmed that the posterior annulus was reliably innervated by the sinuvertebral nerves while the lateral annulus was innervated by branches of the ventral rami and gray rami communicantes [2]. Coppes and Freeman showed that painful discs were more likely to demonstrate innervation of the inner third of the posterior annulus than nonpainful discs [3,4].

While MRI imaging of lumbar discs often demonstrates bulges, protrusions, desiccative changes, and/or annular tears, these findings lack both sensitivity and specificity and consequently, do not accurately predict the symptomaticity of an individual disc [5,6]. Provocative lumbar discography uses controlled reproduction of a patient’s usual lumbar pain by injection of pressurized liquid, typically radiocontrast, into the disc nucleus in order to identify a specific disc for treatment [7]. When provocative discography demonstrates a painful disc level, traditional therapeutic options have included physical therapy modalities and exercises, long-term opiate analgesics, disc decompression or surgical discectomy with interbody fusion. While clinical studies generally support the ther-
apeutic effectiveness of surgical discectomy and interbody fusion in the treatment of discogenic pain [8], the wide adoption of this procedure in the United States has drawn criticisms [8,9].

Several minimally invasive treatments for discogenic pain involve application of thermal energy to the posterior annulus and are hypothesized to be effective by two principal means: thermally induced closure of annular tears prevents the innervated posterior annulus from exposure to pro-nociceptive chemicals or milieu, such as metalloproteinases, interleukins or TNF-α, or; heating achieves neurolysis of the nerves within the posterior annulus, presumably including any areas of neo-innervation. Other potential means of effectiveness may include heat or radiofrequency (RF)-induced synthesis of heat shock proteins which have been shown to have a cytoprotective effect [10].

Disc heating has been attempted by several means: monopolar RF energy, thermoresistive element heating, and bipolar RF. In each application, the maximum temperature is achieved at the tip or surface of a device(s) and temperatures decline rapidly as the distance from the heat source increases [11–13]. Varied clinical outcomes were shown in studies of intradiscal heating using a thermoresistive catheter (SPINECATH, Smith & Nephew, Menlo Park, CA) [14–18]. Although several of these studies showed limited clinical improvement, others suggest efficacy with heating of the disc. It is the authors’ opinion that the range of results may be due to the limited volume of tissue heating and to variations in treatment techniques.

In an attempt to achieve more optimal heating of the human lumbar intervertebral disc, a new cooled percutaneous RF electrode system (Trans-Discal System, Baylis Medical, Montreal Inc., QC, Canada) was developed for disc biacuplasty (D-BAC). Two water-cooled needle probes (15 cm length, 18 gauge probe with 6 mm electrode tip) are placed into each posterolateral region of the disc (see Figure 1). While bipolar RF energy heats the tissue adjacent to and between the two needle probes, the tissue in immediate contact with each probe is actively cooled.

An internally cooled, bipolar RF system can heat a larger volume of tissue than a non-cooled equivalent as active cooling removes the constraint of maximum tissue temperature development at the electrode surface. By active probe cooling, continued delivery of RF energy produces ionic tissue heating and avoids the tissue charring which results in rising impedance, unpredictable RF energy delivery, and ineffective tissue heating. (see Figure 2).

Figure 1 (A) Magnified view of the electrode on the Trans-Discal Probe. (B) Schematic view of the electrode with arrows representing flow of water.

Figure 2 A temperature-distance graph showing the heating profile of two radiofrequency electrodes placed 3 cm apart. The dashed line represents non-cooled electrodes. The solid line represents cooled electrodes.
Isotherms developed around the TransDiscal System’s probes are shown in Figure 3. In operation, the cooled area is limited to a few millimeters around each electrode with surrounding spherical isotherms merging medially into a dumbbell-shaped heat distribution across the posterior annulus. In vivo, in addition to the cooled probes, several sinks remove heat actively: cerebrospinal fluid flow within the thecal sac; blood flow within the epidural venous plexus posteriorly; blood flow within the great vessels anteriorly radicular veins, and arteries laterally. Passive heat sinks include the adjacent cephalad, caudal, and lateral osseous and muscular spinal structures.

The purpose of this study was to examine the histologic changes and thermal distribution characteristics of the TransDiscal System in treatment of porcine discs searching for evidence of injury to nontarget nerve, osseous or muscular structures in order to assess safety.

Methods

Using a protocol approved by the Institutional Animal Care and Use Committee (L’Hôpital du Sacre Coeur, Montreal, QC, Canada), Landrace pigs were anesthetized with intramuscular ketamine (20 mg/kg) and xylazine (2 mg/kg). Endotracheal intubation was performed and anesthesia was maintained with isoflurane (2.0–2.5%) in O₂/N₂O.

Multiplanar C-arm fluoroscopic imaging was used to place 17 gauge introducers bilaterally in a conventional extrapedicular approach (lateral to the Superior Articular Processes) in a total of nine lumbar intervertebral discs in two animals. TransDiscal Probes (Baylis Medical Company Inc., Montreal, QC, Canada) with integrated electrode, dual temperature sensors and liquid cooling channels were placed through the introducers into the intervertebral disc. Radio- opaque markings on the probe allowed fluoroscopic verification of correct placement of the electrode in both anterior-posterior (AP) and lateral projections. Following probe placement, 22 gauge thermocouples were inserted through 20 gauge introducers into multiple predetermined locations, including the lateral posterior annulus, midline posterior annulus, midline anterior epidural space, and immediately posterior to the intervertebral disc in the lateral recess adjacent to the descending nerve root and dorsal root ganglion. The tip positions of the probes and monitoring thermocouples were reviewed in multiple AP, lateral, and oblique fluoroscopic views prior to initiation of the RF application (Figure 4). RF energy was applied using the RF generator (Baylis Medical Company Inc., PMG-115 TD), except in one disc from each pig which were used as instrumented controls.

A multichannel data acquisition system (Hotmux Data Loggers, DCC Corporation, Pennsauken, NJ) was used to record temperatures at all
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thermocouple sites. Data from the RF generator, including probe tip temperatures, were recorded with data acquisition software (Teraterm Pro 2.3, T. Teranishi, Wako, Saitama, Japan). Discs were heated with varied temperatures and treatment times (see Table 1) in order to achieve intradiscal temperatures suitable for collagen contraction and thermoneurolysis. Following each heating session, all probes and thermocouples were removed prior to study of additional levels in the same animal. Immediately following RF treatment of all discs, each animal was euthanized with intravenous bolus potassium chloride. The lumbar spine was removed en bloc and after identification of treated and control disc levels, fascial and muscular attachments were removed prior to formalin fixation for histologic analysis.

In total, nine disc samples from the lumbar spine of two pigs were submitted for histological evaluation. Discs were sectioned sagittally in 2–4 mm thick sections which included the cephalad and caudal vertebrae and intervertebral discs. The spinal cord was removed to facilitate processing. Left, right, and central disc sections were chosen for further analysis as well as any areas with macroscopic evidence of alteration. Sections were trimmed and decalcified using commercial solutions. Nerve roots and dorsal root ganglia were recovered from the areas located within the vertebrae at the treated and control disc levels. Disc sections, spinal cord sections, and nerve root tissues were infiltrated and embedded in paraffin and stained with hematoxylin and eosin.

Results

Disc biacuplasty treatment was completed on seven porcine lumbar intervertebral discs (2: L1-L2, 1: L2-L3, 2: L3-L4, 2: L4-L5); instruments were placed within two additional control discs (1: T12-L1 and 1: L2-L3). Temperatures in the treated discs reached averages between 45°C and 65°C as revealed by the thermocouple data (Figure 5 and Table 2). Low-power microscopy revealed slit-like voids in both the nucleus and annulus of samples sectioned along the sagittal plane. The voids originated from the dorsal edge of the sections and terminated at various locations within the central area of the disc, suggesting that the voids were created by the placement of the probes and temperature-monitoring equipment.

Histologic analysis showed no damage to neural structures surrounding the disc. No histomorphologic alterations were present in the ganglion and nerve roots sections examined when compared with the controls. Additionally, the cauda equina sections available after sectioning showed no morphologic changes.

Cellular changes were observed in the nucleus pulposus of treated discs when compared with controls. The central area of the control discs contained viable nucleus pulposus cells within a fibrillar basophilic matrix with no presence of cellular debris (Figure 6). In contrast, the treated discs exhibited increased coarseness of the fibrillar matrix and loss of cellular detail of the nucleus pulposus (Figure 7). Under gross microscopic

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<tr>
<th>Table 1</th>
<th>Treatment parameters for seven porcine intervertebral discs</th>
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<td>Set Temperature (°C)</td>
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<td>Disc 1</td>
<td>45</td>
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<td>Disc 2</td>
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<td>Disc 3</td>
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<td>Disc 5</td>
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<td>Disc 7</td>
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<th>Table 2</th>
<th>Temperature results for seven porcine intervertebral discs</th>
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<tr>
<td></td>
<td>Temperature</td>
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<tr>
<td>Inner third posterior annulus</td>
<td>61.1°C ± 6.5°C</td>
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<tr>
<td>Outer third posterior annulus</td>
<td>47.8°C ± 2.4°C</td>
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<tr>
<td>Outer third lateral annulus</td>
<td>44.5°C ± 5.2°C</td>
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<td>Adjacent to nerve root</td>
<td>45.5°C ± 5.0°C</td>
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Figure 5 Axial disc schematic showing TransDiscal probe placement and temperature measurement zones. Reported temperatures (average ± SD): (A) inner third posterior annulus: 61.1°C ± 6.5°C; (B) outer third posterior annulus: 47.8°C ± 2.4°C; (C) outer third lateral annulus: 44.5°C ± 5.2°C; (D) adjacent to nerve root: 45.5°C ± 5.0°C.
imaging, the sagittal sections showed no tissue charring adjacent to the slit-like voids associated with the instrumentation.

**Discussion**

In this *in vivo* porcine study of D-BAC, an immediate histologic examination of spinal and perispinal structures was performed in order to assess potential acute thermal injury to peridiscal tissues and to draw conclusions regarding safety. The investigation demonstrated no evidence of neural injury of the *cauda equina*, the dorsal root ganglia, nor nerve roots at any treatment levels as compared with unheated controls. There was no evidence of vertebral endplate necrosis nor of myonecrosis on gross examination. While only subtle changes occurred in the morphology of the disc, the significance of the changes in nuclear cellularity and increased granularity are unknown. The minor tissue disruption noted in the disc and epidural space was considered to be due to the extensive manipulation of instrumentation used, including trans-thecal thermocouple placement.

Recorded average inner posterior annulus temperature was 61.6°C ± 6.5°C with probe tip temperatures between 40°C and 45°C. Lateral and midline posterior outer annulus temperatures were 44.5°C ± 5.2°C and 47.8°C ± 2.4°C, respectively. The variations in these temperatures reflect variations in disc geometry and placement of instrumentation.

The average temperature of the thermocouple placed adjacent to the nerve root was 45.5°C ± 5.0°C. A retrospective analysis was completed on the placement of this thermocouple to provide an understanding for the high temperature and large deviation. For the five temperatures recorded, there were large variations in thermocouple placements. Radiographs were reviewed in an attempt to ascertain more precise positions for each thermocouple, but they did not give further insight due to limited fluoroscopic resolution and visual cluttering because of instrumentation superimposition. The histologic images of the nerve root structures at the treated levels provided no evidence of tissue damage which suggests that the temperature variations may have been instrumentation artifact and were of no clinical relevance.

*In vitro* studies demonstrate that collagen contraction takes place at 63–65°C, but other studies show that this transition may also occur at slower rates at lower temperatures [19,20]. Smith et al. showed that heating to a temperature of 42°C for longer than 2 minutes produced microscopic evidence of nerve destruction [21]. In this study, thermal monitoring demonstrated that temperatures achieved in the posterior annulus and nucleus were sufficient to initiate the proposed mechanisms of thermal action, such as collagen contraction and thermoneurolysis, while histologic evidence demonstrated a lack of effects on peridiscal neural structures.

While several animal models are used for study of degenerative disc disease, there is little consen-
sus regarding a satisfactory animal model for dis-
cogenic pain [22–24]. As there is no assurance that
evidence of destruction or modification of any
normal innervation of the posterior annulus would
be indicative of events which might occur in a
pathologically painful disc, histologic evidence for
neurolysis within the posterior annulus was not
sought in this study.

In the absence of a robust animal model for pain
treatment, a porcine model was selected for a
worst-case investigation of the specific effects of
heating, reasoning that the lesser disc height,
smaller disc volume, and thinner posterior annulus
of the porcine disc as compared with the human
disc would increase the likelihood of incurring
possible thermal damage. Thermal energy deliv-
ered and the maximal temperatures achieved dur-
ing use of bipolar RF in the disc can be affected
by probe separation distance, the volume of tissue
available to heat, and heat sink boundary condi-
tions. Porcine discs differ from human discs by
their smaller disc volume, lesser disc height, and
more widely spaced pedicles which result in the
probe tips being placed closer together and rela-
tively more anteriorly within the disc. These dif-
ferences imply that a greater relative volume of the
porcine disc will be heated, including greater
nuclear heating. As the porcine disc will have ther-
amal redistribution characteristics similar to the
human disc, this model provides a worst-case sce-
nario where unwanted peridiscal heating would be
expected to equal or exceed that observed in
humans. As well, anterior probe placement in the
porcine model produces greater nuclear heating
and this suggests that observed effects upon
nuclear cellularity might be lessened in human
application.

The TransDiscal System provides a percutane-
ous, minimally invasive treatment for discogenic
lumbar pain with its novel use of a liquid-cooled
probes and integrated temperature sensors. This
systematic study of the heat distribution in this
porcine worst-case scenario allows us to conclude
that this heating method produces a significant
gradient in temperature between the nuclear and
posterior annular structures and the extradiscal
structures. Therefore, if similar temperatures are
seen in the human intervertebral disc, this heating
is unlikely to produce damage to surrounding neu-
ral, muscular, or osseous structures.

While long-term histologic effects of D-BAC
may be investigated in a porcine model, given the
differences in natural history and clinical presenta-
tion of degenerative disc disease as compared
with symptomatic internal disc disruption, it is the
authors’ opinion that presently available non-
primate experimental models do not provide an
adequate basis for further study of mechanisms of
action or efficacy. Consequently, clinical trials of
the TransDiscal System will be required in order
to demonstrate the long-term safety and efficacy
of this technology in humans.

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