North American Spine Society Journal (NASSJ) 3 (2020) 100030

Contents lists available at ScienceDirect

North American Spine Society Journal (NASSJ)

journal homepage: www.elsevier.com/locate/xnsj

Clinical Studies

A prospective, single arm study of intraosseous basivertebral nerve ablation for the treatment of chronic low back pain: 12-month results

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A B S T R A C T

Background: The basivertebral nerve (BVN) has been a recently discovered target as a potential source for vertebrogenic chronic low back pain (CLBP). Prior randomized controlled trials have demonstrated safety and efficacy of BVN ablation for vertebrogenic CLBP, but minimal data exists regarding BVN ablation's clinical effectiveness with broader application outside of strict trial inclusion criteria.

Methods: Prospective, single arm, open label effectiveness trial of 48 patients from community spine and pain practices treated with BVN ablation. Inclusion criteria required more than 6 months of CLBP and type 1 or 2 Modic changes on MRI to be enrolled. Patients were followed post procedure for 12 months using ODI, VAS, EQ-5D-5L and SF-36 patient reported outcome metrics.Results: 47 patients successfully received BVN ablation and 45 patients completed 12 months of follow up. Mean reduction in ODI at 12 months was 32.31 +/- 14.07 ($p<0.001$) with 88.89% (40/45) patients reporting a ≥15 point ODI decrease at 12 months. Mean VAS pain score decrease was 4.31 +/-2.51 at 12 months ($p<0.001$) and more than 69% reported a 50% reduction in VAS pain scale. Similarly, SF-36 and EQ-5D-5L scores improved 26.27 +/-17.19 and 0.22 +/-0.15 (each $p<0.001$).

Conclusions: This data supports the clinical effectiveness of BVN ablation in the community practice setting, with similar 12 month improvements in patient reported outcomes as seen in previously published randomized control trials.

Background

Chronic low back pain (CLBP) is a common and debilitating condition, affecting 5–10% of the adult US population and impacting the lives of more than 30 million Americans [1-3]. The source of CLBP is challenging to identify and treat, resulting in long term disability and a disproportional consumption of healthcare resources at a significant rate [3]. Recent studies have highlighted the potential contribution of vertebrogenic sources of CLBP [4-6]. Altered force transfer and endplate loading occur through disc derangements secondary to degenerative disc disease, resulting in changes to endplate morphology and composition with additional impairment in permeability and transport; further accelerating disc degeneration [7]. Proinflammatory material in the disc triggers an inflammatory response in the bone marrow that sensitizes local nociceptors, and results in Modic changes visible on MRI [4, 8-11]. Although low back pain is a complex and multifactorial pathology, multiple studies have suggested the presence of Modic changes to positively correlate with chronic low back pain [12, 13].

The basivertebral nerve (BVN), enters the vertebrae through the posterior basivertebral foramen and then arborizes to innervate the superior and inferior endplates. Pain signals from the BVN are transmitted via the sinuvertebral nerve to the central nervous system [14]. Immunohistochemical studies of the BVN demonstrate the presence of PGP 9.5 and substance-P, supporting its role in nociceptive innervation [14-17]. Two level 1 trials have reported successful outcomes of radiofrequency (RF) ablation of the BVN compared to sham-control and standard care-control arms in patients with chronic vertebrogenic low back pain [18, 19].

Randomized control trials designed to test efficacy of a therapy are often more restrictive in inclusion and exclusion criteria to isolate treatment effects, and may not fully reflect the broader low back pain population encountered in typical spine clinics. A prospective single arm effectiveness study of BVN ablation, employing more permissive criteria, including use of extended release narcotics and prior lumbar discectomies, was initiated. An interim analysis was conducted and reported when the first 28 patients treated reached their 3-month post procedure visit [20]. Superiority of the primary endpoint was demonstrated with a change in ODI of -30.07 ± 14.52 points ($p < 0.0001$) and with 75% of patients reporting $a \geq 20$-point improvement in ODI. Pain scores were decreased by 3.5 points on a 0–10 scale at 3-months. Enrollments were stopped in the study with 50 study participants enrolled and 47 of these successfully treated. This manuscript reports the 12-month follow-up results for all patients enrolled and treated with BVN ablation at these two typical spine practices.

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https://doi.org/10.1016/j.xnsj.2020.100030
Received 27 May 2020; Received in revised form 29 July 2020; Accepted 15 September 2020
Available online 18 September 2020

Table 1
Lists the inclusion and exclusion criteria for the study.

Inclusion criteria	Exclusion criteria

• Skeletally mature patients with chronic (≥6 months) isolated lumbar back pain, who had not responded to at least 6 months of non-operative management
• Type 1 or Type 2 Modic changes at one or more vertebral body for levels L3-S1
• Minimum Oswestry Disability Index (ODI) of 30 points (100-point scale)
• Minimum Visual Analogue Scale (VAS) of 4 cm (10 cm scale)
• Ability to provide informed consent, read and complete questionnaires
	• MRI evidence of Modic at levels other than L3-S1
	• Radicular pain (defined as nerve pain following a dermatomal distribution and that correlates with nerve compression in imaging)
	• Previous lumbar spine surgery (discectomy/laminectomy allowed if > 6 months prior to baseline and radicular pain resolved)
	• Symptomatic spinal stenosis (defined as the presence of neurogenic claudication confirmed by imaging)
	• Metabolic bone disease, spine fragility fracture history, or trauma/compression fracture, or spinal cancer
	• Spine infection, active systemic infection, bleeding diathesis
	• Radiographic evidence of other pain etiology
	  • Disc extrusion or protrusion > 5 mm
	  • Spondylolisthesis > 2 mm at any level
	  • Spondylolysis at any level
	  • Facet arthrosis/effusion correlated with facet-mediated LBP
	• Beck Depression Inventory (BDI) > 24
	• 3 or > Waddell's signs
	• Compensated injury or litigation
	• Addiction behavior
	• BMI > 40
	• Contraindicated to MRI, allergies to components of the device, or active implantable devices, pregnant or lactating

Methods

Trial design

This study is a prospective, single arm, open label effectiveness trial of 48 patients treated with BVN ablation at two investigative sites in the U.S. from March 2018 to February 2019. The trial is registered on ClinicalTrials.gov as NCT03266107 and was sponsored by Relievant Medsystems, Inc. (Minneapolis, MN). The study was conducted under Institutional Board Review approval and participant informed consent. Upon receiving Food and Drug Administration 510(k) clearance, the protocol was revised to allow treatment of up to four vertebrae and treatment of nonconsecutive levels from L3 to S1. An evaluation of the impact of protocol revisions to the primary endpoint detected no significant differences, and no adjustment for difference was required.

Participants

Patients for the study were drawn from current low back pain clinic populations, referrals, or through patient self-referral. Consecutively identified patients were screened by investigative sites for medical history eligibility prior to MRI review for endplate changes and excluded pain sources. Eligibility was adjudicated prior to randomization by an independent orthopedic surgeon based on each patient's medical, clinical, and radiographic presentation. Primary inclusion requirements were CLBP with a duration of greater than 6 months with non-surgical management and Modic Type 1 or 2 changes at the levels targeted for treatment. Full inclusion and exclusion criteria are listed in Table 1.

Study interventions

Patients in the study were treated with BVN ablation for each level with Modic changes (L3 to S1) using the Intracept ® System (Relievant Medsystems, Minneapolis, MN USA). The procedure was performed under image guidance, under moderate conscious sedation or general anesthesia, and in an outpatient setting. Targeted location for electrode placement was approximately 30–50% across vertebral body width from the posterior wall, and in the same horizontal plane as the BVN on sagittal imaging as shown in Fig. 1. After confirmation of placement, thermal ablation was delivered for 15 min at 85 °C to create an approximately 1-cm spherical lesion within each vertebral body as shown in Fig. 2. Detailed information about the surgical technique was described previously in the literature [18]. All patients continued nonsurgical therapies as per the investigator's medical judgment and patient symptoms.

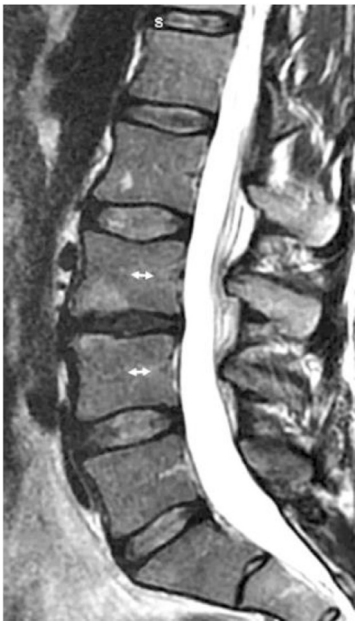

Fig. 1. Depicts the targeted location for the electrode placement at approximately 30–50% across vertebral body width from the posterior wall, and in the same horizontal plane as the BVN on sagittal imaging.

Outcome measures

Patients were followed at 6 weeks, and 3, 6, 9, and 12 months. Patient-reported clinical outcomes using validated questionnaires were

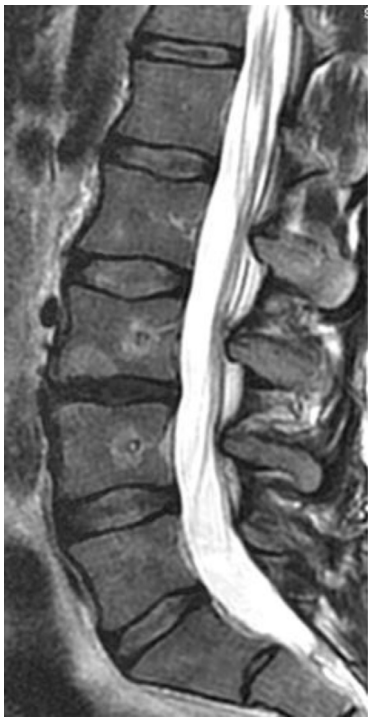

Fig. 2. Depicts the BVN ablation lesion at 6 weeks post procedure.

collected at each study visit. The primary endpoint was a measurement of functional impact at 3 months post BVN ablation using the Oswestry Disability Index (ODI) questionnaire, [21] scored on a scale of 0 (no disability) to 100 (complete disability), with a minimal clinically important difference (MCID) of a 15-point reduction [22]. Low Back Pain was assessed using a Visual Analog Scale (VAS) [23] ranging from 0 (no pain) to 10 (worst pain imaginable) with published MCID thresholds for pain improvement of 1.5–2.0 cm [22, 23]. Health Status and Quality of Life (QOL) were measured at each follow-up using the SF-36 [24, 25] and EQ-5D-5L [26-28] questionnaires. Published MCID for the physical component of SF-36 is 4.9[22] and 0.03 points [22] for the EQ-5D-5 L.

Targeting success was confirmed via a 6 weeks post-BVN ablation MR image (T1, T2, and STIR time constants) reviewed by an independent neuroradiologist to assess the degree of overlap of the ablation lesion with the terminus of the BVN for each treated vertebral body. Spinal and neurological adverse events (AEs) were collected at each study visit and adjudicated by an independent clinical event committee for relatedness to device therapy and procedure.

Statistical analysis

The study was 90% powered to detect a 15-point difference in ODI with a 2-sided overall alpha level of 0.05 for a required sample size of 45 study participants. A total of 50 patients were enrolled to allow for a 10% attrition rate. The study had a group-sequential design with an interim analysis conducted after 60% of the randomized participants completed their 3-month follow-up visit. Statistical significance was defined as $P < 0.025$ for the interim analysis for an overall alpha level of 0.05, resulting in early termination of the study enrollment for treatment superiority at 50 patients enrolled and 47 successfully treated.

The primary endpoint, change in ODI from baseline to 12 months, was estimated as a function of the baseline ODI using a regression analysis. Results were summarized using descriptive statistics. Tests of the changes between the baseline and post treatment values were performed with Stata v15 (Stata Corp., College Station, TX) using a Student's two-tailed *t*-test without imputation for missing values.

Results

Patient disposition

Screening was conducted for 120 consented participants, 48 BVN ablations were attempted, and 47 were successfully treated (one inability to access due to hard bone). Retention was high at 96% with 45 treated patients with 12 months of follow-up. See Fig. 3 Consort Flow Diagram.

Patient demographics & baseline characteristics

Baseline ODI was 47.13; VAS was 6.82; and median age was 44.5 years. The percentage of patients with LBP symptoms ≥ 5 years was 72.3% and 35/47 (75%) were working full-time, with 10/47 (21%) having missed work an average of 2.5 days due to LBP in the two weeks prior to baseline. Nearly half (48.9%) of the study participants had received lumbar epidural injections prior to baseline and 21.3% (10/47) had taken opioids in the 14 days prior to baseline. See Table 2.

Treatment results

Two vertebral bodies were treated in 77% of patients, 19% had three levels treated, and 4% had four levels treated. L5 was the most treated level at 95.7%, followed by S1 at 72.3%, and L4 in 44.7% of cases. Targeting was adjudicated as successful in 96% of patients treated (45/47) and in 98% of treated vertebral bodies (102/104). Targeting at S1 was deemed unsuccessful for two patients where a combination of S1 morphology and bone density prevented the curved cannula from reaching the BVN target. In these two cases, despite several attempts from both sides, acceptable positioning was not achieved, and the procedure was abandoned at the S1 level. These patients are included as intent-to-treat in the analysis.

ODI – primary endpoint

Statistically significant and clinically meaningful improvements in pain and function observed at the 3-month interim analysis time point[20] were maintained for all patient-reported outcomes through 12-months post treatment. Improvement in function was significant with a change in mean ODI of −30.33 ± 12.71 points from a baseline of 47.13 ± 9.87 ($p < 0.001$; CI 26.55–34.10); a difference of more than twice the MCID for ODI. Reduction in mean ODI remained significant at 12 months at −32.31 ± 14.07 ($p < 0.001$; CI 28.08–36.54). See Fig. 4.

Responder rates for ODI remained high at 12 months post BVN ablation treatment with 88.89%, (40/45) of patients reporting $a \geq$ 15-point improvement in ODI and 84.44%, (38/ 45) reporting $a \geq$ 20-point difference compared to baseline ($p < 0.001$). See Table 3 – ODI Results. A combined function and pain responder rate of 77.8% was demonstrated using thresholds of ≥ 15-point ODI and ≥ 2-point VAS improvements at 12-months following BVN ablation. Using a combined threshold of ≥ 20-point ODI and ≥ 2-point VAS a 75.56% responder rate was observed.

VAS pain scores

Similarly, significant improvements in VAS were seen at all follow-up timepoints through 12 months. Reduction in pain VAS score was nearly twice the established MCID of a 2 cm reduction with a change in mean VAS of −4.31 ± 2.51 at 12-months ($p < 0.001$). See Table 4. More than 68% of patients reported $a \geq$ 50% reduction in pain; 51% reported ≥ 75% reduction; and pain was completely resolved in 38% of patients at 12 months post BVN ablation. See Fig. 5.

Quality of life

Quality of life measurements were also significantly reduced at all timepoints from baseline. SF-36 total score was improved by

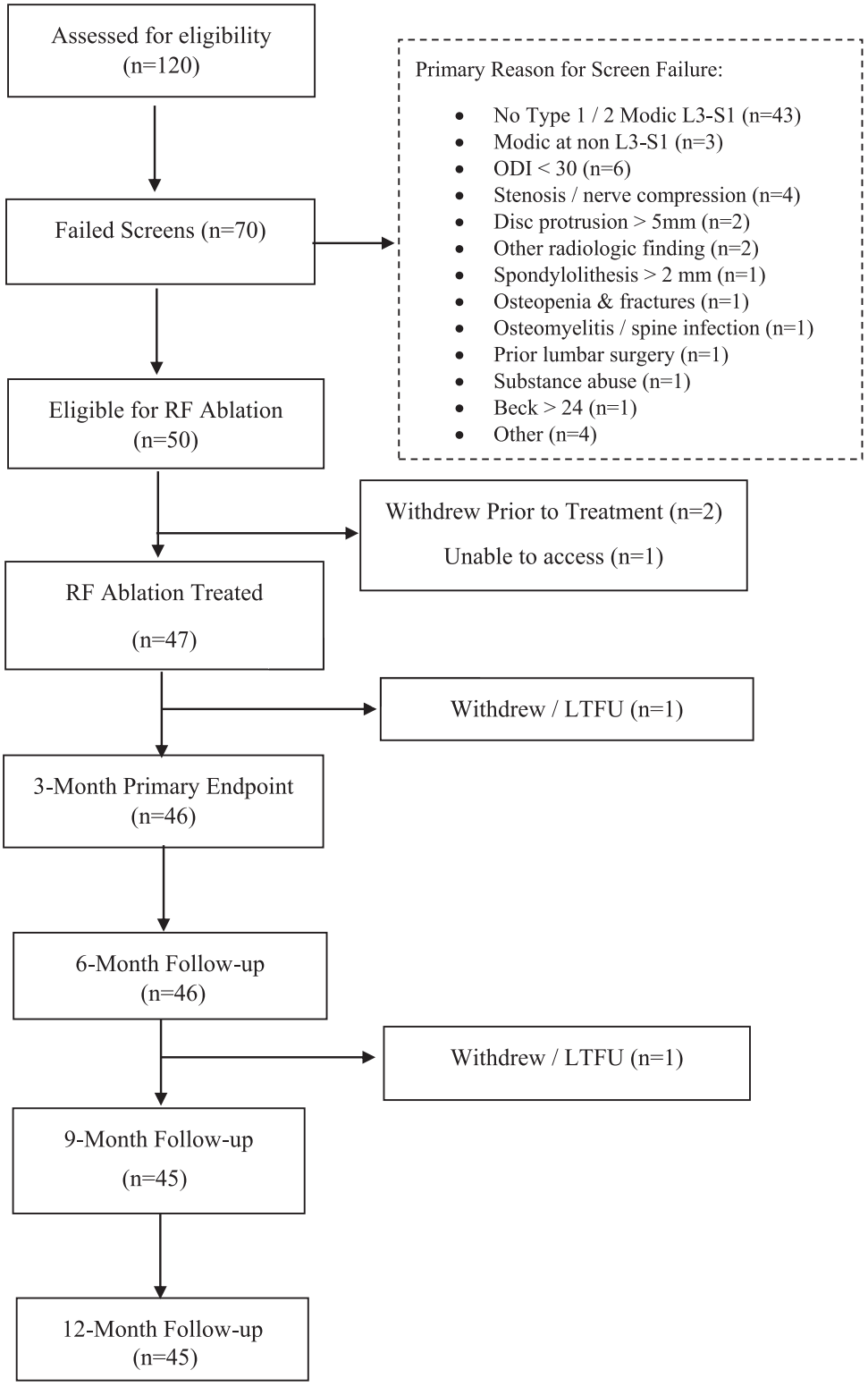

Fig. 3. Consort flow diagram of patients.

26.27 ± 17.19 and physical component scores (PCS) were increased by 17.53 ± 9.73 at 12 months; an improvement that is more than 3 times the MCID of 4.9. At 12-months post treatment, patients reported an EQ 5D 5L score of 0.63 an increase of 0.22 ± 0.15; an improvement that is more than 7 times the MCID of a 0.03 score increase. See Table 5.

Healthcare utilization

Only one patient (2%) received additional epidural injections in the 12 months post BVN ablation compared to 49% (23/47) prior to baseline. The injections were at 4 and 8 months and deemed for treatment of foraminal stenosis per independent review. One patient underwent

Table 2
Reports baseline characteristics of the study population.

Characteristic	(*N* = 47)
Age (years)	44.47 + 8.68 (47), 45, [25, 66]
Gender:	
Male	46.81%, (22/ 47)
Female	53.19%, (25/ 47)
Length of time Experience LBP	
< 6 months	0.00%, (0/ 47)
6 months to < 1 Year	0.00%, (0/ 47)
1 year to < 2 years	14.89%, (7/ 47)
2 years to < 3 years	10.64%, (5/ 47)
3 years to < 5 Years	2.13%, (1/ 47)
≥ 5 years	72.34%, (34/ 47)
Baseline Working Status *n*(%)	
Working	85.11%, (40/ 47)
Full-Time	74.47%, (35/ 47)
Part-Time	10.64%, (5/ 47)
Short-Term Disability	0.00%, (0/ 47)
Not Working Due to Back Pain	2.13%, (1/ 47)
Unemployed/Retired/At Home Provider	12.8%, (6/ 47)
Missed work due to LBP in past 2 weeks	21.28%, (10/ 47)
Number of days missed work (more than half a day) from low back pain in last two weeks *mean, SD, median, range*	2.50 + 2.32, 2, [0, 8]
Medications	
Opioid Medications use Prior to Procedure	21.28%, (10/ 47)
Total Opioid Average Daily Dose (14 Days Prior)	11.28 + 7.68 (10), 10, [1, 23]
Injections	
Epidural Injections	48.94%, (23/ 47)
Joint Injection	8.51%, (4/ 47)
Other Injection	4.26%, (2/ 47)
Modic Type by Level	
L3 (Inferior Endplate)	
Modic I	0.00%, (0/ 47)
Modic II	6.38%, (3/ 47)
L4	46.81%, (22/ 47)
Modic I	29.78%, (14/ 47)
Modic II	17.02%, (8/ 47)
L5	95.74%, (45/ 47)
Modic I	74.47%, (35/ 47)
Modic II	36.17%, (17/ 47)
S1	72.34%, (34/ 47)
Modic I	44.68%, (21/ 47)
Modic II	27.66%, (13/ 47)

Table 3
Reports ODI results at 3, 6, 9 and 12 months. Statistically significant functional improvements were reported at each timepoint.

	Mean ± SD (N), Median, Range or % (n/N)	*t*-test (*p*-value)	95% CI
ODI (3 Months Post Treatment) Primary Endpoint	**(*N* = 46)**		
Baseline ODI Score (Mean + SD, Median, Range)	47.13 + 9.87 (46), 44, [30, 72]		[44.20, 50.06]
3-Month ODI Score (Mean + SD, Median, Range)	16.80 + 12.69 (46), 16, [0, 52]		[13.04, 20.57]
Mean change in ODI score baseline to 3 months	30.33 + 12.71 (46), 30, [6, 58]	($p < 0.001$)	[26.55, 34.10]
Subjects with ≥ 15-point ODI decrease	91.30%, (42/ 46)	($p < 0.001$)	[79.21%, 97.58%]
Subjects with ≥ 20-point ODI decrease	82.61%, (38/ 46)	($p < 0.001$)	[68.58%, 92.18%]
ODI (6 Months Post Treatment)	**(*N* = 46)**		
Baseline ODI Score (Mean + SD, Median, Range)	47.13 + 9.87 (46), 44, [30, 72]		[44.20, 50.06]
6-Month ODI Score (Mean + SD, Median, Range)	14.83 + 11.46 (46), 13, [0, 50]		[11.42, 18.23]
Mean change in ODI score baseline to 6 months	32.30 + 13.69 (46), 30, [0, 70]	($p < 0.001$)	[28.24, 36.37]
Subjects with ≥ 15-point ODI decrease	95.65%, (44/ 46)	($p < 0.001$)	[85.16%, 99.47%]
Subjects with ≥ 20-point ODI decrease	80.43%, (37/ 46)	($p < 0.001$)	[66.09%, 90.64%]
ODI (9 Months Post Treatment)	**(*N* = 45)**		
Baseline ODI Score (Mean + SD, Median, Range)	46.98 + 9.92 (45), 44, [30, 72]		[44.00, 49.96]
9-Month ODI Score (Mean + SD, Median, Range)	14.53 + 12.09 (45), 12, [0, 50]		[10.90, 18.17]
Mean change in ODI score baseline to 9 months	32.44 + 13.70 (45), 34, [0, 60]	($p < 0.001$)	[28.33, 36.56]
Subjects with ≥ 15-point ODI decrease	91.11%, (41/ 45)	($p < 0.001$)	[78.78%, 97.52%]
Subjects with ≥ 20-point ODI decrease	86.67%, (39/ 45)	($p < 0.001$)	[73.21%, 94.95%]
ODI (12 Months Treatment)	**(*N* = 45)**		
Baseline ODI Score (Mean + SD, Median, Range)	46.98 + 9.92 (45), 44, [30, 72]		[44.00, 49.96]
12-Month ODI Score (Mean + SD, Median, Range)	14.67 + 13.00 (45), 12, [0, 50]		[10.76, 18.57]
Mean change in ODI score baseline to 12 months	32.31 + 14.07 (45), 34, [0, 58]	($p < 0.001$)	[28.08, 36.54]
Subjects with ≥ 15-point ODI decrease	88.89%, (40/ 45)	($p < 0.001$)	[75.95%, 96.29%]
Subjects with ≥ 20-point ODI decrease	84.44%, (38/ 45)	($p < 0.001$)	[70.54%, 93.51%]

Table 4
Reports VAS results at 3, 6, 9 and 12 months. Statistically significant pain reduction was reported at each timepoint.

	Mean ± SD (N), Median, Range or % (n/N)	*t*-test (*p*-value)	95% CI
VAS (3 Months Post Treatment)	**(*N* = 46)**		
Baseline VAS Score (Mean + SD, Median, Range)	6.82+1.03 (46), 7, [4, 9]		[6.52, 7.13]
3-Month VAS Score (Mean + SD, Median, Range)	3.04+2.39 (46), 2, [0, 9]		[2.33, 3.75]
Mean VAS score change baseline to 3 months	3.79+2.21 (46), 4, [−1, 7]	(*p*<0.001)	[3.13, 4.44]
% of subjects with ≥ 2.0 Pt VAS decrease	78.26%, (36/ 46)	(*p*<0.001)	[61.23%, 87.41%]
VAS (6 Months Post Treatment)	**(*N* = 46)**		
Baseline VAS Score (Mean + SD, Median, Range)	6.82+1.03 (46), 7, [4, 9]		[6.52, 7.13]
6-Month VAS Score (Mean + SD, Median, Range)	2.27+2.01 (46), 2, [0, 6]		[1.67, 2.86]
Mean VAS score change baseline to 6 months	4.56+2.04 (46), 5, [1, 8]	(*p*<0.001)	[3.95, 5.16]
% of subjects with ≥ 2.0 Pt VAS decrease	84.78%, (39/ 46)	(*p*<0.001)	[66.09%, 90.64%]
VAS (9 Months Post Treatment)	**(*N* = 45)**		
Baseline VAS Score (Mean + SD, Median, Range)	6.82+1.04 (45), 7, [4, 9]		[6.51, 7.13]
9-Month VAS Score (Mean + SD, Median, Range)	2.33+2.27 (45), 2, [0, 8]		[1.65, 3.02]
Mean VAS score change baseline to 9 months	4.49+2.17 (45), 5, [0, 8]	(*p*<0.001)	[3.83, 5.14]
% of subjects with ≥ 2.0 Pt VAS decrease	84.44%, (38/ 45)	(*p*<0.001)	[65.40%, 90.42%]
VAS (12 Months Post Treatment)	**(*N* = 45)**		
Baseline VAS Score (Mean + SD, Median, Range)	6.82+1.04 (45), 7, [4, 9]		[6.51, 7.13]
12-Month VAS Score (Mean + SD, Median, Range)	2.51+2.82 (45), 2, [0, 9]		[1.66, 3.36]
Mean VAS score change baseline to 12 months	4.31+2.51 (45), 5, [−1, 8]	(*p*<0.001)	[3.56, 5.07]
% of subjects with ≥ 2.0 Pt VAS decrease	80.00%, (36/ 45)	(*p*<0.001)	[62.91%, 88.80%]

Table 5
Reports QOL measurements from SF-36 Total Scores and EQ-5D-5 L Index at 3, 6, 9, and 12 months post BVN Ablation. Significant improvements were reported at all timepoints.

SF-36 Total Score	Mean ± SD, Median, Range	*t*-test (*p*-value)
SF-36 Total Score (3 Months)	**(*N* = 46)**	
Baseline SF-36 Total Score	54.17+13.38, 55, [18, 82]	
3-Month SF-36 Total Score	79.00+14.36, 82, [37, 97]	
Change baseline to 3 months post-treatment	24.83+15.51, 25, [−13, 51]	(*p*<0.001)
SF-36 Total Score (6 Months)	**(*N* = 46)**	
6-Month SF-36 Total Score	79.44+12.05, 80, [47, 100]	
Change baseline to 6 months post-treatment	25.27+14.69, 25, [−14, 49]	(*p*<0.001)
SF-36 Total Score (9 Months)	**(*N* = 45)**	
9-Month SF-36 Total Score	80.25+14.62, 84, [38, 100]	
Change baseline to 9 months post-treatment	25.75+17.46, 26, [−17, 72]	(*p*<0.001)
SF-36 Total Score (12 Months)	**(*N* = 45)**	
12-Month SF-36 Total Score	80.77+13.67, 84, [48, 100]	
Change baseline to 12 months post-treatment	26.27+17.19, 25, [1, 77]	(*p*<0.001)
EQ-5D-5 L Index	**Mean ± SD, Median, Range**	***t*-test (*p*-value)**
EQ-5D-5 L Index (3 Months)	**(*N* = 46)**	
Baseline EQ-5D-5 L Index	0.63+0.11, 1, [0, 1]	
3-Month EQ-5D-5 L Index	0.82+0.11, 1, [1, 1]	
Change baseline to 3 months post-treatment	0.19+0.13, 0, [0, 1]	(*p*<0.001)
EQ-5D-5 L Index (6 Months)	**(*N* = 46)**	
6-Month EQ-5D-5 L Index	0.84+0.12, 1, [1, 1]	
Change baseline to 6 months post-treatment	0.21+0.14, 0, [0, 0]	(*p*<0.001)
EQ-5D-5 L Index (9 Months)	**(*N* = 45)**	
9-Month EQ-5D-5 L Index	0.84+0.12, 1, [0, 1]	
Change baseline to 9 months post-treatment	0.21+0.14, 0, [0, 1]	(*p*<0.001)
EQ-5D-5 L Index (12 Months)	**(*N* = 45)**	
12-Month EQ-5D-5 L Index	0.85+0.13, 1, [1, 1]	
Change baseline to 12 months post-treatment	0.22+0.15, 0, [0, 1]	(*p*<0.001)

facet rhizotomy at the same level as treatment 7 months post BVN ablation. Of the 10 (21%) of patients taking opioids at baseline, 3(6.7%) reported actively taking opioids at 12 months post BVN ablation; a reduction of 70%. A comparison of ODI and VAS 12-month outcomes between patients that were actively using opioids or had received additional pain treatments (As Treated) and the patients treated with BVN ablation alone, demonstrated no statistically significant differences. See Table 6.

Patient satisfaction

Patients reported a high degree of patient satisfaction: 84.4% rated their condition as improved (60% vastly improved); 11% reported no change; and 4% indicated their condition had worsened. Eighty-nine percent (89%) of patients indicated they would have the BVN ablation again.

Work status

Many patients in this study (85%) were working full-time at baseline, with 10/47 (21%) having missed work for an average of 2.5 days due to LBP in the two weeks prior to baseline. At 12 months 3/45 (6.7%) of patients missed an average of 2 days due to LBP in the prior two weeks; a reduction of 70% of patients missing work for LBP and 20% reduction in days missed. At baseline, 15 patients averaged 1.04 days in the past

Table 6
A comparisons of ODI and VAS 12-month endpoints was performed between patients that were actively using opioids or had received injections / pain interventions post BVN ablation (As Treated), and the patients treated with BVN ablation alone (BVN Ablation Only). There were no statistically significant differences in outcomes.

Characteristics	As Treated	BVN Ablation Only	
	(*N* = 5)	(*N* = 40)	*p*-Value
Change in ODI (Baseline to 12 Months)	33.6 + 8.17 (5), 36, [22, 44]	32.15+14.71 (40), 33, [0, 58]	0.83
Change in VAS (Baseline to 12 Months)	3.78+1.40 (5), 4, [2, 5.2]	4.38+2.62 (40), 5.25, [−1, 8]	0.62

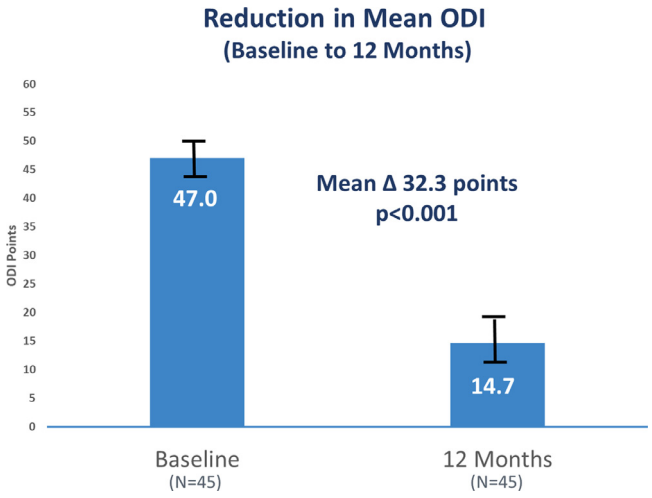

Fig. 4. Depicts the primary endpoint of change in mean ODI from baseline to 12 months post BVN ablation. Patient-reported significant improvements in function were observed.

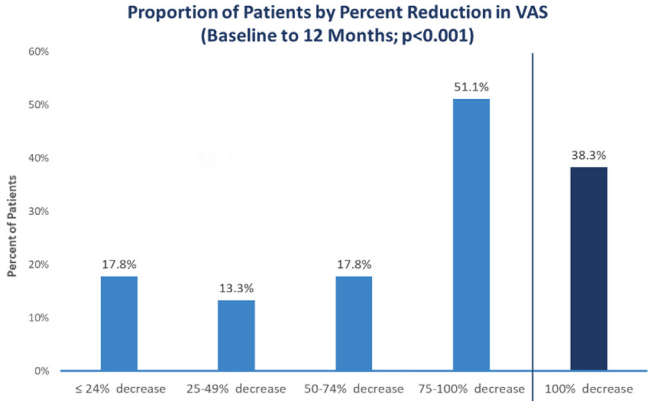

Fig. 5. Depicts the proportion of patients by percent reduction in VAS at 12 months. More than 69% of patients reported $a \geq 50\%$ reduction in pain; 51% reported ≥ 75% reduction; and pain was completely resolved in 38% of patients at 12 months post BVN ablation.

two weeks where they spent more than half of the day in bed. This was reduced by 87% to 2 patients at 12 months.

Adverse events

No serious device-related adverse events were reported through 12 months of follow-up. There were three (6.3%) non-serious device procedure-related events in 48 BVN ablation procedures/attempted procedures. One event was an aborted surgery for an inability to access the pedicle due to extremely hard bone. Two events were for potential pedicle breach with associated radiculitis. These two patients were treated with oral medications, with resolution of symptoms in a median of 91.5 days.

Discussion and conclusions

This study aimed to improve our understanding of the longer-term clinical effectiveness of basivertebral nerve ablation. While the efficacy has been established in two level 1 RCTs, [18, 19] effectiveness data from use of this therapy in daily practice had not yet been published. Although primary inclusion and exclusion criteria for this study population were consistent with the prior RCTs for comparison reasons, efforts were made to enroll patients reflective of a less homogeneous low back pain population. In alignment with this goal, patients with prior discectomies and extended release opioids were allowed and no limits on baseline patient reported outcomes (ODI, VAS) were enforced. There were no requirements of specific medications, conservative treatments, or injections that must have been attempted prior to enrolling, nor were there requirements for extensive diagnostic testing pre-procedure. Patients were enrolled based upon clinical judgment of symptoms consistent with vertebrogenic pain and MRI findings of Modic changes.

In this study, statistically significant and clinically meaningful improvements in pain and function observed at the 3-month interim analysis time point reported previously [20] were maintained with the full study cohort that demonstrated a mean ODI reduction of −30.3 points at 3 months compared to the interim analysis group who reported a reduction of −30.1 points. Similarly, decreases in VAS were consistent with the full cohort reporting a reduction of −3.97 at 3 months compared to −3.50 for the interim analysis group.

Our observations are similar to previously reported improvements in pain and function for the treatment arm patients from the two level 1 RCTs [18, 19]. In the SMART trial, BVN ablated patients reported a −20.9 reduction in mean ODI and −2.90 decrease in mean VAS at 3 months and a −23.4 reduction in mean ODI and a −2.76 decrease in mean VAS at 12 months [18]. Treatment arm patients in the INTRACEPT trial reported a reduction of −25.3 points in mean ODI and −3.46 decrease in mean VAS at 3 months post BVN ablation. In comparison, our study results are favorable with a reduction in mean ODI of −30.33 points and reduction in mean VAS of −3.79 at 3 months, and a decrease in mean ODI of −32.3 points and mean VAS of −4.31 at 12 months from baseline.

The observed treatment outcomes in the current study are superior to conservative treatments for CBLP where small effect sizes have been reported [29]. Likewise, reductions in ODI in this study are twice those reported in the literature for spinal injections for CLBP (−32.3 points compared to 11.9 to 13.9 points) with an average of 3.3 to 3.8 injections performed in the 12-month period [30, 31]. Similarly, RF medial branch neurotomy has demonstrated ODI reductions of 7.43–10.78 in randomized trials, [32, 33] however the duration of pain relief has been published to be 10.2–10.9 months and requires re-treatment. [34] In comparison our study demonstrates sustained clinical benefit through 12 months with a single procedure and recently published five-year results from the original RCT reported a −25.95 point reduction in ODI from baseline ($p < 0.001$) for BVN ablated arm patients at a median of 6.4 years. [35]

The safety profile for BVN ablation was excellent for this study, consistent with the literature. Basivertebral nerve ablation was successfully completed in 93.8% of the cases in this study, and in 98.2% of all published clinical cases to date [18-20, 36]. As with any surgical intervention, it is reasonable to counsel the patient that a procedure may be

aborted for safety, if anatomic or technical issues arise. In this study 2/47 (4.3%), of BVN ablated patients experienced radiculitis that resolved in a median of 91.5 days with oral medications. This is a low incidence rate that is consistent with reported rates of 2% to 9% for radiculitis [18, 19] but with longer resolution times compared to those reported of 42 days [19]. However, the time to resolution in our study is impacted by the small sample size (with only two events) and the follow-up visit schedule (6 weeks, and 3, 6, 9, and 12 months).

Strengths and weaknesses

These results expand upon the previously published interim data with longer follow-up and more patients, on the clinical effectiveness of basivertebral nerve ablation in typical spine practice. This is important for patients outside of the rigor of a randomized controlled trial. Limitations of this study include the open label design and a small study population. Although we did adequately power our study for the intended effect sizes of published MCIDs for ODI, our sample sizes are smaller compared with the prior RCTs on basivertebral nerve ablation and may explain the more favorable results seen in our study. However, these study results are consistent in observed treatment effects for multiple published studies on BVN ablation. Another limitation of our study was the involvement of only two study sites, thereby reducing the generalizability to other spine practices. In addition, industry support is a potential source of study bias. Despite the limitations, we believe these data inform clinicians seeking to integrate basivertebral nerve ablation into their practices, adding to the existing publications demonstrating safety and efficacy. Long-term follow-up of such patients is critical to understand the durability of basivertebral nerve ablation on meaningfully changing the trajectory of chronic pain for this specific subgroup of vertebrogenic low back patients.

Conclusions

Our study on basivertebral nerve ablation suggests maintenance of previously described improvements in ODI and VAS scores out to 12 months. We believe this data suggests that basivertebral nerve ablation in community spine and pain practices can result in similar outcomes as seen in prior highly controlled study protocols in this specific subgroup of vertebrogenic low back pain patients with radiographic criteria including type 1 or 2 Modic changes. While we continue to recommend thoughtful clinical application and clinical discretion of how this procedure is applied to patient care, we believe this data supports the clinical effectiveness and safety of basivertebral nerve ablation in community practice.

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