11-1-2022

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Retrospective Study

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Disclaimer: There was no external funding in the preparation of this manuscript.

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 03-07-2022
Revised manuscript received: 06-26-2022
Accepted for publication: 08-16-2022

Free full manuscript: www.painphysicianjournal.com

Background: The diagnosis and treatment of neuropathic pain is often clinically challenging, with many patients requiring treatments beyond oral medications. To improve our percutaneous treatments, we established a clinical pathway that utilized ultrasound (US) guidance for steroid injection and alcohol ablation for patients with painful neuropathy.

Objectives: To describe a collaborative neuropathy treatment pathway developed by a neurosurgeon, pain physicians, and a sonologist, describing early clinical experiences and patient-reported outcomes.

Study Design: A retrospective case series was performed.

Methods: Patients that received percutaneous alcohol ablation with US guidance for neuropathy were identified through a retrospective review of a single provider's case log. Demographics and treatment information were collected from the electronic medical record. Patients were surveyed about their symptoms and treatment efficacy. Descriptive statistics were expressed as medians and the interquartile range ([IQR]; 25th and 75th data percentiles). Differences in the median follow-up pain scores were assessed using a Wilcoxon signed-rank test.

Results: Thirty-five patients underwent US-guided alcohol ablation, with the average patient receiving one treatment (range: 1 to 2), having a median duration of 4.8 months until reinjection (IQR: 2.9 to 13.1). The median number of steroid injections that individuals received before US-guided alcohol ablation was 2 (IQR: 1 to 3), and the median interval between steroid injections was 3.7 months (IQR: 2.0 to 9.6). Most (20/35 [57%]) patients responded to the survey, and the median pain scores decreased by 3 units (median: -3, IQR: -6 to 0; $P < 0.001$) one week following the alcohol ablation. This pain reduction remained significant at one month ($P < 0.001$) and one year ($P = 0.002$) following ablation. Most (12/20 [60%]) patients reported that alcohol ablation was more effective in improving their pain than oral pain medications.

Limitations: Given the small sample size, treatment efficacy for alcohol neurolysis cannot be generalized to the broader population.

Conclusions: US-guided percutaneous treatments for neuropathic pain present a growing opportunity for interprofessional collaboration between neurosurgery, clinicians who treat chronic pain, and sonologists. US can provide valuable diagnostic information and guide accurate percutaneous treatments in skilled hands. Further studies are warranted to determine whether a US-guided treatment pathway can prevent unnecessary open surgical management.

Key words: Interventional ultrasonography, ablation techniques, neurolysis, interprofessional relations, pain clinics, peripheral neuropathy, neuroma, neuroma injection

Pain Physician 2022: 25:E1299-E1305

Mononeuropathies are common maladies, and many do not have optimally defined treatments. Initial management is often conservative through physical therapy and/or avoidance of aggravating activities. Medical therapies include the use of over-the-counter nonsteroidal anti-inflammatory

drugs or neuropathic agents, such as gabapentin or pregabalin; however, a high percentage of patients are nonresponsive to these conservative measures (1).

Anatomic landmark approaches have been used to deliver injectable therapies for painful mononeuropathy (2,3), but ultrasound (US)-guided steroid injections have gained traction in recent years, reducing the risks associated with blind injections and improving treatment efficacy (4). Previously, we described a high-resolution US technique to guide steroid injection for patients with mononeuropathy, including lesions that were difficult or impossible to target without sonographic guidance (5). However, steroid injections may have diminishing analgesic effects over time, leaving both patients and clinicians seeking alternative treatments. Open surgical management may be necessary, and we have previously reported on an approach using a sonologist in collaboration with a neurosurgeon (6). Seeking a middle ground between conservative management and surgery; however, our group has explored US-guided nerve ablation to control patients' symptoms. The purpose of this manuscript is to review our clinical experience of a sonologist collaborating with a pain physician to perform US-guided alcohol neurolysis under conscious sedation. Patient experiences with this strategy and treatment outcomes will be described.

Methods

This study was approved by the Thomas Jefferson University Institutional Review Board (protocol number 19331). A retrospective review of the procedure database of a single radiologist (LNN) collaborating with a fellowship-trained pain physician (DW or AN) was conducted to identify all patients that underwent US-guided alcohol neurolysis over a 7-year time period, which was the maximum timeframe available for our institutional electronic medical record (EMR). Demographic parameters, such as age and gender, were collected from the EMR. Information on the treatments was obtained, including the number of steroid injections, alcohol ablations, radiofrequency ablations, and surgical interventions (Table 1). Patients were

Table 1. *Patient characteristics*.

	Complete Cohort	No Follow-up Questionnaire	Questionnaire Completed	*P* value
Sample size	35	15/35 (43%)	20/35 (57%)	-
Age (mean ± standard deviation)	51.5 ± 15.0	47.5 ± 18.0	54.6 ± 11.8	0.169[a]
Gender (men)	18/35 (51%)	9/15 (60%)	9/20 (45%)	0.380[b]
Diagnosis				0.952[b]
Neuropathy	13/35 (37%)	6/15 (40%)	7/20 (35%)	
Neuroma	12/35 (34%)	5/15 (33%)	7/20 (35%)	
Mesh-Associated Neuropathy	10/35 (29%)	4/15 (27%)	6/20 (30%)	
Site of Pain				0.947[c]
Ilioinguinal Nerve	13/35 (37%)	6/15 (40%)	7/20 (35%)	
Abdominal Wall Neuroma	12/35 (34%)	5/15 (33%)	7/20 (35%)	
Lateral Femoral Caneous Nerve	4/35 (11%)	2/15 (13%)	2/20 (10%)	
Superior Cluneal Nerve	2/35 (6%)	0/15 (0%)	2/20 (10%)	
Sural Nerve	2/35 (6%)	1/15 (7%)	1/20 (5%)	
Amputation Stump Neuroma	2/35 (6%)	1/15 (7%)	1/20 (5%)	
Number of US-Guided Injections				
Steroid Injections [median (IQR)]	2 (1-3)	2 (1-3)	2 (1-3)	0.521[d]
Alcohol Ablations [median (IQR)]	1 (1-2)	1 (1-2)	1 (1-2)	0.805[d]
Subsequent Treatments				
Radiofrequency Ablation	1/35 (3%)	0/15 (0%)	1/20 (5%)	1.000[e]
Surgical Intervention	10/35 (29%)	4/15 (27%)	6/20 (30%)	1.000[e]
Months Follow-up [median (IQR)]	8.6 (3.3-49.5)	12.3 (4.7-53.1)	7.9 (3.1-11.3)	0.199[d]

Abbreviations: US, ultrasound; IQR, interquartile.
[a]t test. [b]Pearson chi-square. [c]Fisher-Freeman-Halton exact test. [d]Mann-Whitney U exact test. [e]Fisher's exact test.

subsequently surveyed to obtain information regarding the nature of their initial symptoms, the efficacy of alcohol-ablation treatment, and, where applicable, its relative effectiveness compared to oral medications and steroid injections.

Figure 1 outlines the flow diagram for patient care. Patients with neuropathy were identified clinically by a pain physician or neurosurgeon and referred for a diagnostic US. All US evaluations were performed by a single radiologist (LNN) with almost 30 years of clinical experience in musculoskeletal US, utilizing a multifrequency linear array probe with a peak frequency of 12 MHz (Philips iU22, Philips Medical Systems, Bothell, WA). Patients that were nonresponsive to conservative measures subsequently underwent US-guided corticosteroid injections. Injections were performed under US guidance, and 1% local anesthetic was given subcutaneously. Depending on the depth of the abnormality, a 25-G 1-1/2 inch hypodermic needle or 22-G 3-1/2 inch spinal needle was advanced into the perineural space. A mixture of betamethasone (0.5-1 mL), 1% lidocaine (1-2 mL), and 0.2 % ropivacaine (1-2 mL) was injected.

Patients who initially benefited from a corticosteroid injection, but had recurrent pain, were offered repeat US-guided steroid injections at a minimum of 3 months after the initial injection. Those with recurrent or refractory pain were referred for US-guided alcohol neurolysis. Alcohol neurolysis was performed in the operating room through collaboration between a radiologist (LNN), and a pain physician (DW or AN). A portable US unit (Sonosite M-Turbo, Bothell, WA) equipped with a 12 MHz multifrequency linear probe was used to guide the needle into the target under moderate sedation and local anesthetic with 1% lidocaine. Depending on the size of the abnormality being treated, 1-2 mL of 99% ethanol was injected into the nerve/neuroma. After 2 minutes, an injection of steroid and local anesthetic was performed into the area to ease postprocedure inflammation. Representative US images from alcohol neurolysis are shown in Fig. 2.

Following retrospective patient identification, patients were mailed a survey and supplied a reply envelope. Patients that did not respond to the initially mailed questionnaire were followed up by telephone (CJM) with the same survey questions (Table 1). The survey questions were adapted from the Visual Analog Scale and Likert scales, given their ease of use (1). The survey consisted of 3 questions:

1. How long did you have nerve pain before receiving any alcohol-ablation treatments?
2. What was your nerve pain when you were: first seen in the clinic by your pain physician, the day before your alcohol ablation, one week following ablation, one month following ablation, and one year following ablation?
3. Compared to medications taken by mouth, how would you rate the effectiveness of alcohol ablation for improving your nerve pain? The responses are: much better, somewhat better, no difference, somewhat worse, and much worse (Fig. 3).

To determine whether US-guided alcohol ablation was effective in reducing pain, the pain scores were adjusted by subtracting the subsequent pain scores from the initial pain score; this was done to compare the change in pain relative to the individual patient's baseline. The normality assumption was assessed using the Shapiro-Wilk statistical test, and the descriptive statistics of parameters that violated this assumption were expressed as medians and the interquartile range (IQR; 25th and 75th data percentiles). Differences in the median follow-up pain scores were assessed using a Wilcoxon signed-rank test. All statistical analyses were performed using GraphPad Prism version 9.3.1 (GraphPad Software Inc, San Diego, CA).

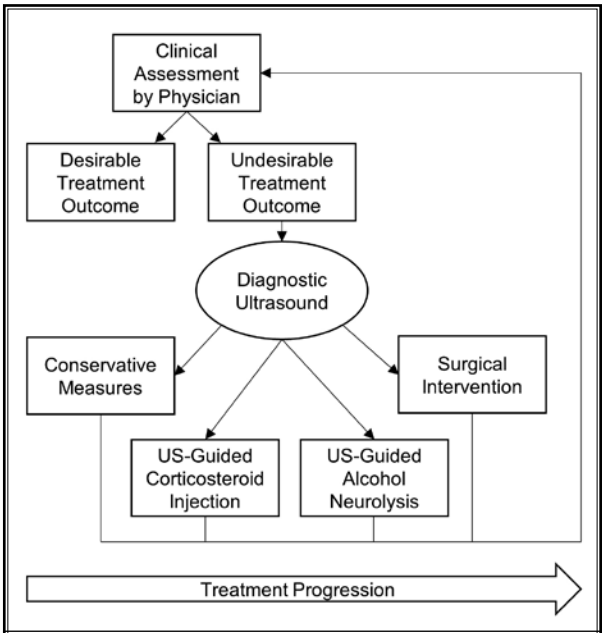

Fig. 1. *Patient treatment paradigm with treatment progression.*

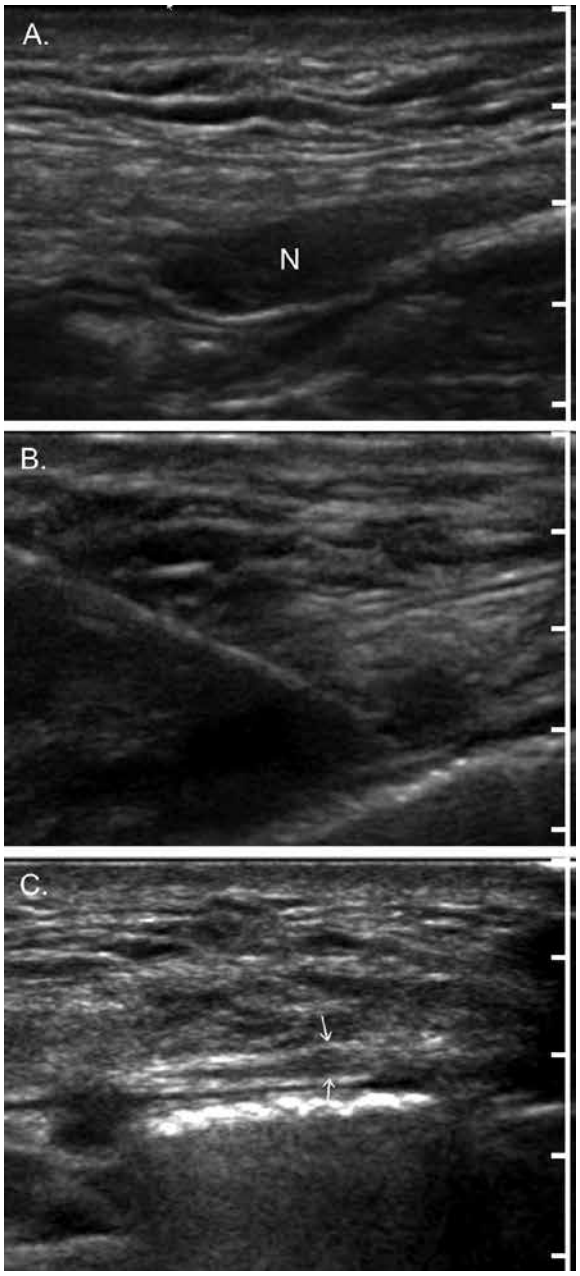

Fig. 2. *US-guided alcohol neurolysis for an inguinal neuroma. A 68-year-old man with chronic right inguinal pain refractory to medical and injected steroid therapy. A. Oblong right inguinal neuroma (N) measuring up to 1.2 cm in size. B. Satisfactory needle and injectate placement into the inguinal neuroma. C. A follow-up US obtained 8 months following alcohol neurolysis showed a small residual neuroma measuring up to 0.7cm.*
US, ultrasound.

Results

A total of 35 patients that underwent US-guided alcohol ablation were identified (Table 1). The average patient age was 51.5 ± 15.0, and 18/35 (51%) were men. The diagnosis for treatment included peripheral neuropathy in 23/35 (66%) and neuromas in 12/35 (34%). The ilioinguinal nerve (13/35 [37%]) and abdominal wall neuromas (12/35 [34%]) comprised the majority of the treated nerves, with the remaining treated areas listed in Table 1. The median number of steroid injections that individuals received before US-guided alcohol ablation was 2 (IQR: 1 to 3), and the median interval between steroid injections was 3.7 months (IQR: 2.0 to 9.6). The median number of US-guided alcohol-ablation patients received was 1 (IQR: 1 to 2), and the median interval between repeat alcohol ablations was 4.8 months (IQR: 2.9 to 13.1). Only 1/35 (3%) patient underwent subsequent radiofrequency ablation, and 10/35 (29%) required subsequent surgery for further management. Of the 10 patients that required surgery, half had pain associated with prior mesh hernia repair and the remaining half had abdominal wall neuromas secondary to prior abdominal surgery. The EMR captured a median follow-up of 8.6 months (IQR 3.3 to 49.5) for the cohort.

The majority (20/35 [57%]) of patients responded to our survey, and this group was no different in de-

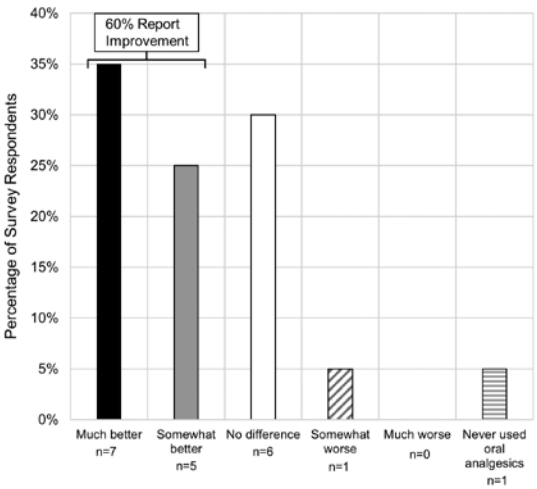

Fig. 3. *Relative benefit of US-guided alcohol neurolysis compared to oral pain medications.*
US, ultrasound.

mographic, illness, or treatment variables than those that were unreachable via the survey ($P \geq 0.169$; Table 1). Compared to their initial pain level, the survey respondents' pain was unchanged the day before their US-guided alcohol ablation (median: 0, IQR: 0 to 0; Fig. 4). However, one week following the alcohol ablation, the median relative pain scores decreased by 3 units (median: -3, IQR: -6 to 0; $P < 0.001$). Compared to baseline, this pain reduction remained significant at one month (median: -3.3, IQR: -7 to 0; $P < 0.001$) and one year (median: -2.3, IQR: -6.8 to 0; $P = 0.002$) (Fig. 4). Most (12/20 [60%]) patients reported that alcohol ablation was more effective in improving their pain than oral pain medications, with 7/20 (35%) stating that the ablation was much better and 5/20 (25%) stating that ablation was somewhat better than oral pain medications (Fig. 3). There were 6/20 (30%) that felt ablation was no different from oral pain medications and only 1/20 (5%) that felt that ablation was somewhat worse than oral pain medications.

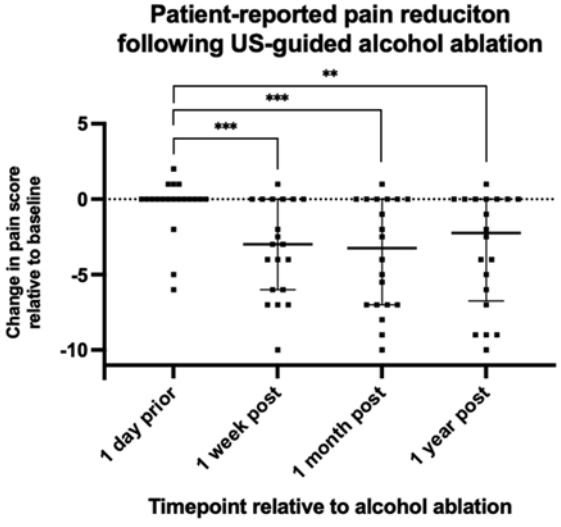

Fig. 4. *Patient-reported pain reduction following US-guided alcohol neurolysis relative to baseline neuropathic pain.* (**) signifies $P < 0.01$ and (***) signifies $P < 0.001$. US, ultrasound.

Discussion

The treatment of pain from neuropathy and neuromas can be challenging for both patients and physicians, requiring multimodal treatments and multidisciplinary teams. Previous studies (7-10) have demonstrated the technique and efficacy of ablative therapy using US-guided alcohol neurolysis, which we have also confirmed in this study. However, to our knowledge, no prior studies have described the benefits of the collaboration among neurosurgery, pain management, and radiologist in the comprehensive treatment of patients with painful neuropathy. This workflow (Fig. 1) allows patients to benefit from the clinical experience of a pain physician with the added diagnostic and image-guided capabilities of a sonologist; it should be noted that sonologists can be any physician with expertise in US and are not limited to radiologists. US offers several opportunities to guide patient management. First, sonographic identification of a pain generator provides valuable diagnostic information to the pain physician and provides a possible target for subsequent intervention. US can also be performed to follow lesions and assess treatment response and need for additional therapy; for example, the case described in Fig. 4 shows a stark decrease in size of a painful neuroma following alcohol neurolysis. We and others have shown that patients that experience recurrent neuropathic pain despite steroid injection can be effectively treated with US-guided alcohol ablation; however, in the absence of US guidance, it is difficult, if not impossible, to deliver the injectate to the targeted area, especially in circumstances where anatomic landmarks are not well-defined or not useful (3). We found that patients, on average, saw a 2 to 3 unit decrease in pain scores at one year following alcohol neurolysis, highlighting the durability of this treatment method (Fig. 4). However, if necessary, US-guided alcohol ablation can be repeated in the setting of inadequate neurolysis or recurrent pain. Finally, it should be noted that nearly a third of these patients progressed to surgery, but that aberrant postsurgical anatomy underpinned the pathophysiology in these patients. As such, alcohol neurolysis may have decreased efficacy in this patient subset.

Steroid injections have long been used to treat isolated neuropathy and have only recently been performed using imaging guidance. Nontargeted steroid administration runs the risk of inadvertent damage to the nerve or adjacent structures or reduced efficacy if the steroid is injected too distant from the target nerve. Other nonsurgical management options exist for isolated neuropathy. Pu et al (11) showed that radiofrequency ablation could treat postamputation pain from stump neuromas with an 82% success rate. Similarly, Oswald et al (12), prospectively evaluated the use of an electrical nerve stimulator for treating painful mononeuropathies, and 71% of patients experienced pain reduction. However, the beneficial effects of the stimu-

lator were not uniform among the treated areas; the patients with the most significant pain reduction were limited to treatments involving the brachial plexus and suprascapular nerve. Recently, cryoablation has also been used under either computed tomography (CT) or magnetic resonance (MR) guidance to treat neuropathy (13). Alcohol neurolysis has been used for decades to treat upper motor neuron-related spasticity, but comes with the drawback of losing cutaneous sensation following treatment. However, there are multiple areas where neuropathy commonly develops, and the loss of sensation is of no major consequence to the patient. For example, entrapment neuropathies of the lateral femoral cutaneous nerve, abdominal nerves, cluneal nerve branches, or nerves associated with surgical incision sites may all be amenable to alcohol neurolysis (1).

Previously, our group demonstrated the utility of US for both the diagnosis and intraoperative neurosurgical guidance for peripheral nerve lesions (6). We showed that US could be a valuable adjunct for diagnosing entrapment neuropathies along with clinical evaluation and electromyography. Furthermore, occasionally it is not possible to identify the cause of neuropathy surgically; however, intraoperative sonography could be used to guide the surgeon directly to the target lesion for targeted therapy. Given these experiences, we sought to apply some of these techniques to less invasive treatments, such as alcohol neurolysis. Several studies have demonstrated the utility of image guidance for percutaneous neurolysis (5,10-14), and few have shown the utility of real-time US guidance for neurolysis (5,7-12,15-17). It is somewhat surprising that more studies are not present in the literature, especially given the widespread availability of US compared to advanced imaging modalities, like CT and MR imaging. Similarly, US is a lower-cost alternative that can often provide higher resolution images than competing modalities. Furthermore, real-time US guidance facilitates minimally invasive treatments that otherwise would require open surgical therapy and its associated morbidity.

There are multiple challenges for the widespread adoption of US-guided therapies. For example, ultrasonography is extremely user-dependent and requires a high degree of technical skill and detailed knowledge of neuroanatomy. However, given the widespread prevalence of neuropathic pain, the unique challenge and expertise required may present an attractive opportunity for experienced sonologists to collaborate in clinical care. It must be kept in mind that although US can deliver exquisite anatomic and functional details in skilled hands, neuropathic pain may occur due to electrophysiological changes in a sonographically normal nerve. To combat this issue, it is our standard practice to always perform a US-guided steroid injection first for both diagnostic and therapeutic purposes; in this way, we can confirm the presence and location of a pain generator before any alcohol ablation. Following alcohol neurolysis, it is our practice to administer a combination of steroid and local anesthetic to ease postprocedural pain; as such, it is impossible to completely separate the beneficial effects of alcohol neurolysis from that of a repeat steroid administration. However, since all patients who receive alcohol ablation had either persistent or recurrent symptoms despite prior steroid injection, the improvement in pain scores following ablation is more likely due to the effects of the alcohol rather than repeat steroids alone. Similarly, the anti-inflammatory effects of steroids are short-lived relative to the effects of alcohol neurolysis; therefore, the overall treatment response likely reflects the effects of neurolysis to a greater degree than steroid administration. Although we were able to collect responses from most but not all of our study patients, and as such, there may be an inherent nonresponse bias that could influence these results. Similarly, given the retrospective nature of this study and the varying degrees of time between treatment and survey, differences in patient recall could also introduce bias. Finally, this study was limited by modest sample size. Although many of our patients benefited from prolonged pain relief following alcohol neurolysis, this study was designed to demonstrate the benefits of collaborative treatment, rather than to show efficacy for alcohol neurolysis, as has been shown in prior work (7-11,17).

Conclusions

US is a valuable and low-cost tool that can deliver physiologic and diagnostic information to the pain physician and neurosurgeon. Sonographic guidance is helpful for percutaneous therapies, including injectable steroids or alcohol ablation. By creating a patient care framework, we have shown that neurosurgeons, pain physicians, and sonologists can create a synergistic collaboration in the workup and treatment of neuropathic pain. Given this study's relatively small sample size and retrospective nature, generalization to broader patient populations is neither possible nor appropriate, but these results are encouraging for a growing relationship between these specialties.

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