Retrospective Review

Survival Analysis of Occipital Nerve Stimulator Leads Placed under Fluoroscopic Guidance with and without Ultrasonography

James H. Jones, MD[1], Alison Brown, MD[1], Daniel Moyse, MD[2], Wenjing Qi, PhD[3], and Lance Roy, MD[1]

From: [1]Department of Anesthesiology – Pain Division, Duke University Medical Center, Durham, NC; [2]Pain Specialists of Iowa, Des Moines, IA; [3]Department of Biostatistics and Bioinformatics, Duke University, Durham, NC

Address Correspondence: James Harvey Jones, MD Department of Anesthesiology – Pain Division, Duke University Medical Center 4309 Medical Park Dr. Durham, NC 27710 E-mail: jamesjns137@gmail.com

Disclaimer: There was no external funding in the preparation of this manuscript. Conflict of interest: Drs. Jones, Brown, Moyse, and Qi have no conflicts of interest to report. These authors have not received any reimbursement or honorarium in any other manner. Dr. Roy reports personal fees from Medtronic outside of the submitted work.

Manuscript received: 04-19-2017
Revised manuscript received: 06-04-2017
Accepted for publication: 06-13-2017

Free full manuscript: www.painphysicianjournal.com

Background: Electrical stimulation of the greater occipital nerves is performed to treat pain secondary to chronic daily headaches and occipital neuralgia. The use of fluoroscopy alone to guide the surgical placement of electrodes near the greater occipital nerves disregards the impact of tissue planes on lead stability and stimulation efficacy.

Objective: We hypothesized that occipital neurostimulator (ONS) leads placed with ultrasonography combined with fluoroscopy would demonstrate increased survival rates and times when compared to ONS leads placed with fluoroscopy alone.

Study Design: A 2-arm retrospective chart review.

Setting: A single academic medical center.

Methods: This retrospective chart review analyzed the procedure notes and demographic data of patients who underwent the permanent implant of an ONS lead between July 2012 and August 2015. Patient data included the diagnosis (reason for implant), smoking tobacco use, disability, and age. ONS lead data included the date of permanent implant, the imaging modality used during permanent implant (fluoroscopy with or without ultrasonography), and, if applicable, the date and reason for lead removal. A total of 21 patients (53 leads) were included for the review. Chi-squared tests, Fishers exact tests, 2-sample t-tests, and Wilcoxon rank-sum tests were used to compare fluoroscopy against combined fluoroscopy and ultrasonography as implant methods with respect to patient demographics. These tests were also used to evaluate the primary aim of this study, which was to compare the survival rates and times of ONS leads placed with combined ultrasonography and fluoroscopy versus those placed with fluoroscopy alone. Survival analysis was used to assess the effect of implant method, adjusted for patient demographics (age, smoking tobacco use, and disability), on the risk of lead explant.

Results: Data from 21 patients were collected, including a total of 53 ONS leads. There was no statistically significant difference in the lead survival rate or time, disability, or patient age with respect to the implant method with or without ultrasonography. There was a statistically significant negative effect on the risk of explant with regards to lead removal in smoking patients compared to non-smoking patients (hazard ratio 0.36). There was also a statistically significant difference in smoking tobacco use with respect to the implant method, such that a greater number of patients whose leads were placed with combined fluoroscopy and ultrasonography had a history of smoking ($P = 0.048$).

Limitations: This study is a retrospective chart review that had statistically significant differences in the patient groups and a small sample size.

Conclusion: This study assessed the survival rates and times of ONS leads placed with ultrasonography and fluoroscopy versus fluoroscopy alone. We did not observe an effect to suggest that the incremental addition of ultrasound guidance to fluoroscopy as the intraoperative imaging modality used during the permanent implant of ONS leads yields statistically significant differences in lead survival rate or time. Medical comorbidities, including age and smoking status, may play a role in determining the risk of surgical revision and should be considered in future studies.

Key words: Neuromodulation, peripheral nerve stimulation, occipital nerve stimulation, occipital neuralgia, chronic daily headaches, ultrasonography

Pain Physician 2017; 20:E1115-E1121

Peripheral stimulation of the greater occipital nerves is a proposed treatment modality for patients with occipital neuralgia and intractable, chronic, daily headaches (1-3). Effective neuromodulation demands accurate placement of the electrodes near the nerves and not within the surrounding occipital musculature (4). Surgical placement of occipital neurostimulator (ONS) leads is commonly guided using bony landmarks at the skull base that are visualized with fluoroscopy (3). Although fluoroscopy allows for proper alignment with bony landmarks, it does not provide information about the depth of insertion; electrode depth relative to the occipital nerve, tissue planes, and musculature has been proposed as an important factor in ONS outcome success (5). Improper placement of an ONS lead may adversely affect a patient's experience with neuromodulation who may have otherwise benefited from this therapy. Furthermore, imprecise placement of ONS leads may yield inconsistent results when transitioning from trial to permanent implant.

Surgical revision of ONS leads translates to increased healthcare costs and the potential for increased morbidity. Lead migration remains one of the most frequently encountered complications of ONS lead placement, often requiring surgical revision (6,7). Although anchors have been utilized in attempt to enhance lead stability, lead migration remains a significant problem (7). Furthermore, excessive direct stimulation of suboccipital muscles can cause an overall decreased effectiveness of neuromodulation, which may also require surgical revision. This muscle stimulation may be the consequence of stimulator leads that violate tissue planes. The accurate placement of ONS leads along tissue planes holds the potential to enhance lead survival, decrease lead migration, reduce healthcare costs, and improve patient experience.

Ultrasonography allows for the real-time identification of tissue planes and neurovascular structures without radiation exposure, bulky equipment, or need for additional personnel (such as radiology technicians) that accompany fluoroscopy. The use of ultrasound to facilitate the placement of ONS leads has been previously described (6,8,9). However, the statistical comparison of the survival rate and time for ONS leads placed with ultrasonography combined with fluoroscopy and those placed with fluoroscopy alone in a 2-arm retrospective study has not been reported in the medical literature. The main aim of this study was to determine if ONS leads placed with ultrasonography combined with fluoroscopy would demonstrate an increased survival rate and time when compared to leads placed with fluoroscopy alone. As secondary aims, we studied the impact of smoking tobacco use, age, and disability on lead survival rate and time.

Methods

Data Collection

This retrospective chart review was approved by the Institutional Review Board (IRB) at Duke University. The IRB waived the requirement for written informed consent.

We reviewed the medical records of patients with permanent ONS leads implanted by Duke University physicians from July 2012 to August 2015. Leads placed prior to July 2012 were not included in this review because ultrasound was not a frequently used modality for ONS lead placement at our medical center prior to that date, and therefore inclusion of leads placed prior to July 2012 risked skewing the statistical analyses.

The following current procedural terminology (CPT) codes were used to search the electronic medical record (EMR): 64555, 64585, 64590, and 64595. The charts with these CPT codes were then reviewed to verify that each identified patient had a permanent ONS lead implanted. If true, then the chart was interrogated for the following information: patient diagnosis (reason for implant), date of permanent lead placement, imaging modality used during the permanent lead placement (fluoroscopy with or without ultrasonography), patient age, medical disability (yes or no), and smoking history (yes or no). If applicable, the date and reason for lead removal were also collected. Patients were excluded if interrogation of the chart revealed a peripheral nerve stimulator lead not placed in the occipital region. Patients with both greater occipital and supraorbital leads were included for review, but only data regarding ONS leads were included in statistical analyses. All of the patients demonstrated effectiveness of greater occipital nerve stimulation by completing a trial prior to the permanent implant of the ONS lead. The numbers of patients identified and excluded from review are shown in Fig. 1.

The lead survival time was defined as the number of days elapsed between the date of lead implant and the date of lead removal. If a lead had not been removed by physicians at Duke University, then that lead was assumed to have remained in place, and the lead survival time was then calculated as the number of days from

the date of permanent lead implant to the date of data collection. The date of data collection was the same for all of the leads. The loss to follow-up was defined as a patient who did not present for the initial postoperative clinic visit. Lead migration was defined as either a sudden loss in neurostimulation efficacy or unpleasant stimulation of surrounding tissues coupled with objective measures, such as head x-ray or bedside ultrasound, when indicated.

Surgical Technique

Although multiple physicians utilized both imaging modalities (fluoroscopy with or without ultrasonography) when implanting the ONS leads reviewed in this study, similar techniques were utilized. For example, leads placed with fluoroscopy were inserted at the level of the dens and directed towards the inferior-lateral margin of the ipsilateral orbit. Figure 2 exemplifies ONS lead placement with fluoroscopy. Leads placed with ultrasonography combined with fluoroscopy were implanted posterior to the trapezius muscle on the occiput or the approximate location where the greater occipital nerve exits the trapezius muscle to innervate the scalp. The placement of leads using ultrasonography combined with fluoroscopy was in the same relative position to the dens and orbit as those placed with fluoroscopy alone. Therefore, the major potential difference in configuration between the 2 groups was the depth of insertion. Ultrasound-guided leads have a consistent depth of insertion. Fluoroscopy, when used alone, provides no specific measurement of depth. Figures 2 and 3 exemplify ONS lead placement with ultrasonography combined with fluoroscopy.

Statistical Analysis

Statistical analyses were performed to compare fluoroscopy versus ultrasonography combined with fluoroscopy as implant methods with respect to patient demographics. For categorical variables such as disability and smoking tobacco use, Chi-squared tests and Fisher's exact tests were used if the expected counts for all of the cells of the contingency table were more than 5 or the expected count for any cell was less than 5, respectively. For continuous variables, such as age at the time of implant, 2-sample t-tests and Wilcoxon rank-sum tests were used if both groups passed the normality tests or either group failed the normality tests, respectively.

Fluoroscopy and ultrasonography combined with fluoroscopy were additionally compared with respect to the lead survival rate and time using appropriate 2-sample t-tests. To assess the effect of the implant method on the risk of lead explant, survival analysis was applied and Cox proportional hazards model was used, adjusted for age at the time of implant, disability, and smoking tobacco use.

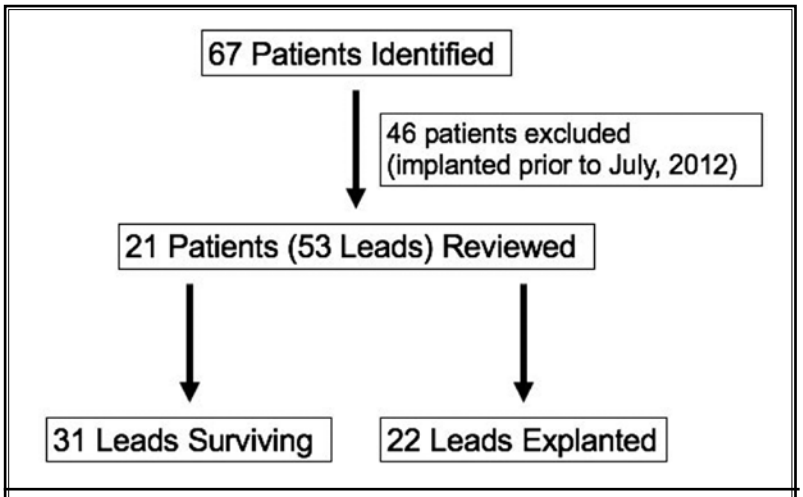
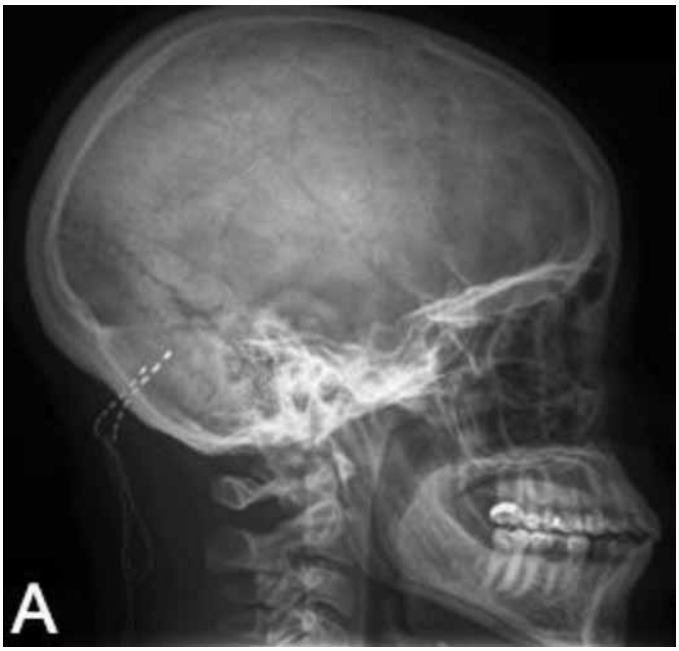


Fig. 1. *The number of patients identified and excluded from the review. A total of 67 patients were identified who had permanent ONS stimulator lead(s) implanted at Duke University Medical Center. After review, 21 patients met the inclusion criteria, including a total of 53 leads.*

Results

Patient Demographics

A total of 21 patients met the inclusion criteria for review in this study. There were no statistically significant differences ($P < 0.05$) in patient age at the time of implant or disability status between patients with ONS leads implanted with fluoroscopy versus those with leads implanted with ultrasonography combined with fluoroscopy. However, there was a statistically significant difference in the number of patients with a history of smoking tobacco between the 2 implant groups ($P = 0.048$). The most common diagnoses for neuromodulation were occipital neuralgia and chronic daily headaches. Other diagnoses included chronic migraine, cluster headache, post-craniotomy pain, and atypical face pain. The patient demographics with respect to the implant method are shown in Table 1.



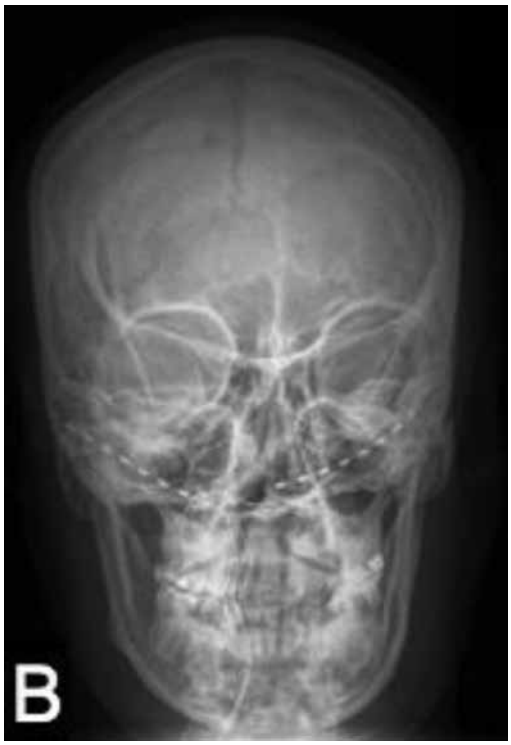


Fig. 2. *Fluoroscopy images of bilateral occipital neurostimulator leads. (A) Lateral fluoroscopic view. (B) Anterior-posterior fluoroscopic view.*

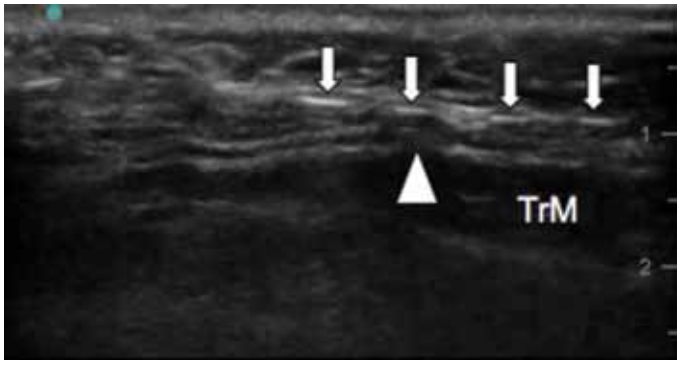


Fig. 3. *Ultrasound image of greater occipital nerve stimulator lead and surrounding tissues. Fluoroscopic images after final lead placement are shown in Fig. 2.*
TrM = trapezius muscle; Arrows = stimulator lead; Arrow head = approximate location of grater occipital nerve and occipital artery.

Lead Survival

A total of 53 leads were analyzed in this study. The ONS leads placed with fluoroscopy versus those placed with ultrasonography combined with fluoroscopy revealed no statistically significant difference in lead survival rate or lead survival time. For explanted leads that were originally implanted with fluoroscopy alone, the mean lead survival time was 380.25 days (standard deviation 278.40 days). For explanted leads that were originally implanted with ultrasonography combined with fluoroscopy, the mean lead survival time was 236.45 days (standard deviation 200.90 days). One lead was excluded from the calculation of lead survival time because the exact implant date was unable to be determined. Data regarding the survival of ONS leads with respect to implant method are displayed in Table 2.

The survival analysis showed no statistically significant effect with regards to implant method, disability, or patient age on the risk of explant. However, smoking tobacco use did reveal a statistically significant negative effect on the risk of explant. Compared to non-smoking patients, leads implanted in smoking patients demonstrated a 72% (hazard ratio 0.36) decrease in the risk of explant. All survival analysis results are shown in Table 3. Product-limit survival estimates with 95% Hall-Wellner Bands are displayed in Fig. 4.

Table 1. *Patient demographics by implant method.*

Patient Characteristics	Implant Method		*P*-value (D)
	F (N = 13)	U + F (N = 8)	
Age at time of implant (years) (A)	52.08 ± 14.17	46.25 ± 9.27	0.32
Disability (B)	1 (7.69%)	3 (37.5%)	0.25
Smoking tobacco use (B)	1 (7.69%)	4 (50%)	0.048
Diagnosis			
Occipital Neuralgia	7	7	
Chronic Daily Headaches	3	0	
Chronic Migraine	0	1	
Other (C)	3	0	

N = sample size; ONS = occipital neurostimulator; F = fluoroscopy; U = ultrasonography; U + F = ultrasonography combined with fluoroscopy. A: Statistics are mean ± standard deviation; B: Statistics are frequency (%); C: Other = cluster headache (N = 1), post-craniotomy pain (N = 1), and atypical face pain (N = 1); D: *P*-value for age at the time of implant is derived from 2-sample t-test; *P*-values for disability and smoking tobacco use are derived from Fisher's exact tests.

Table 2. *ONS lead survival by implant method.*

	Implant Method		*P*-value (C)
	F (N = 33)	U + F (N = 20)	
Explanted Leads (A)	14 (42.42%)	8 (40%)	0.86
Surviving Leads	19 (57.58%)	12 (60%)	
	F (N = 32)	**U + F (N = 20)**	
Lead survival time (days) (B)	380.25 ± 278.40	236.45 ± 200.90	0.07

N = sample size; ONS = occipital neurostimulator; F = fluoroscopy; U = ultrasonography. U + F = ultrasonography combined with fluoroscopy. A: Statistics are frequency (%); B: Statistics are mean ± standard deviation; C: *P*-value for explanted and surviving leads is derived from Chi-Square exact test; *P*-value for time to explant is derived from Wilcoxon rank-sum test.

Table 3. *Survival analysis results with regards to implant method and patient demographics.*

Parameter	Parameter Estimate	Standard Error	Hazard Ratio	*P*-value
Implant Method	0.37	0.45	1.45	0.41
Disability	-0.21	0.56	0.81	0.71
Smoking	-1.02	0.51	0.36	0.046
Age	-0.03	0.03	0.97	0.37

Lead Removal

There were multiple reasons for which ONS leads were removed, as shown in Table 4. Of the 12 leads that were removed due to migration, 10 leads (83.33%)

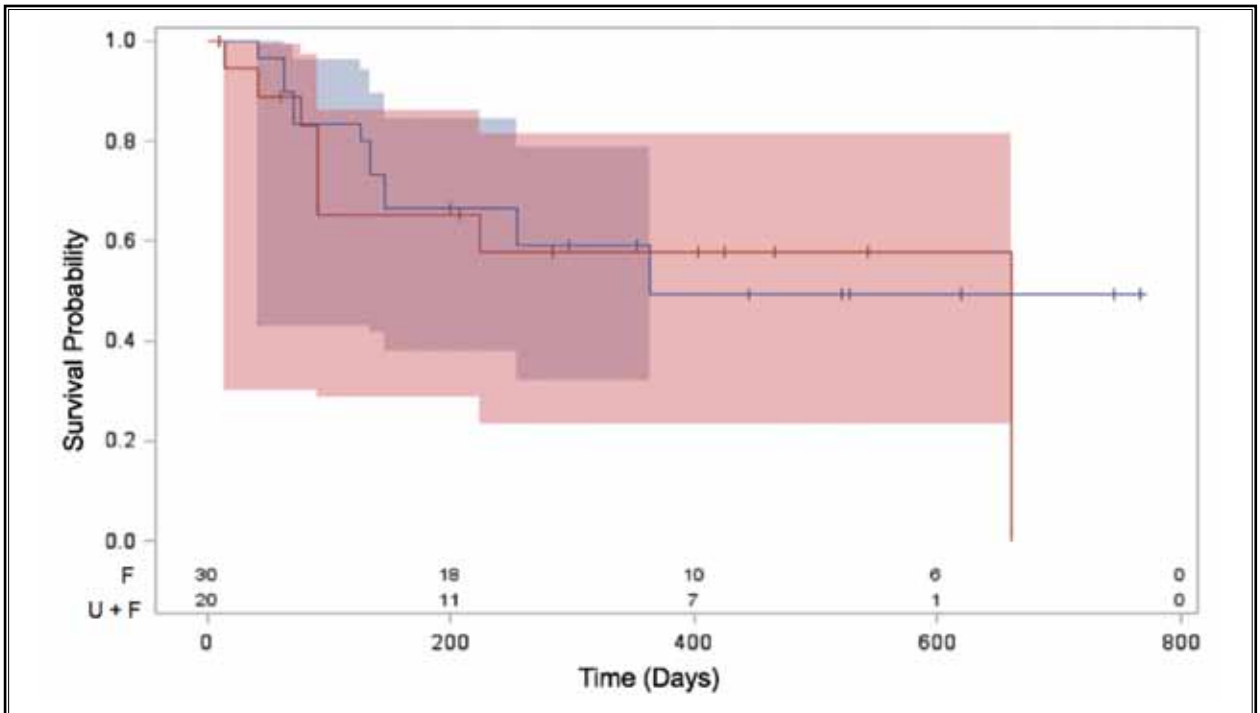


Fig. 4. *Product-limit survival estimates with number of leads at risk and 95% Hall-Wellner Bands for leads placed with fluoroscopy (F, blue line) and ultrasonography combined with fluoroscopy (U + F, red line).*

Table 4. *ONS lead removal by implant method.*

Reason for Removal	Implant Method	
	F (N = 14)	U + F (N = 8)
Lead migration	10 (83.33%)	2 (16.66%)
Ineffectiveness	4 (57.14%)	3 (42.86%)
Muscle stimulation	0	2 (100%)
Lead malfunction	0	1 (100%)

Values are presented as number (%). ONS = occipital neurostimulator; F = fluoroscopy; U = ultrasonography; U + F = ultrasonography combined with fluoroscopy.

were implanted with fluoroscopy alone, while 2 leads (16.66%) were implanted with ultrasonography combined with fluoroscopy. Additionally, of the 7 leads that were removed due to neurostimulation ineffectiveness, 4 leads (57.14%) were implanted with fluoroscopy alone, while 3 leads (42.86%) were implanted with ultrasonography combined with fluoroscopy.

Discussion

This retrospective chart review studied the impact of real-time intraoperative ultrasound guidance on ONS lead survival rate and time. Although the real-time visualization of tissue planes and assessment of lead depth in the suboccipital muscles may provide useful information to the physician at the time of ONS lead permanent implant, the addition of ultrasonography to fluoroscopy was not associated with a greater lead survival time. Furthermore, the addition of ultrasonography to fluoroscopy did not result in statistically significant differences in lead survival rate when compared to fluoroscopy alone.

Given that ONS leads are frequently implanted with the patient receiving conscious sedation and local anesthetic such that continuous interview with the physician is possible, the use of ultrasound to visualize the greater occipital nerve may prove unnecessary. In other words, appropriate stimulation as reported by the patient may provide adequate information regarding the lead placement, and visualization of the nerve may not be necessary. Additionally, it is unclear if ONS leads placed parallel to tissue planes exhibit decreased mobility relative to leads that traverse multiple fascial layers and muscle fibers, possibly stabilizing the lead. For explanted leads that were originally placed with fluoroscopy alone, lead migration was a common reason for removal. However, lead migration requiring surgical intervention was also noted for leads placed with the addition of ultrasound guidance to fluoroscopy. The incidence of lead migration was not a primary aim in this study and was not the focus of statistical analyses.

Several limitations in this retrospective study design are recognized in translating the results to clinical practice. The small sample size examined in this study may not sufficiently represent all of the patients who present for ONS lead insertion and may lack the power necessary to reveal differences in lead survival rate or time. Moreover, the leads reviewed in this study were implanted by several different physicians, including those with no prior exposure to formal ultrasound training. It is possible that ultrasonography by physicians with formal training in regional anesthesia or ultrasound techniques may increase the value of ultrasound as an implant method.

The patient groups analyzed in this study showed a statistically significant difference with respect to smoking tobacco. Of the 13 patients with leads placed with fluoroscopy alone, only one patient had a history of smoking tobacco. In comparison, of the 8 patients with leads placed with ultrasonography combined with fluoroscopy, 4 patients had a history of smoking tobacco. This unbalanced grouping of smoking tobacco in treatment groups could potentially make the statistical estimates biased. Smoking tobacco, a risk factor shown in this study to negatively affect the risk of explant, could act as a confounding variable and may jeopardize the internal validity of statistical analyses. Increasing the sample size may be necessary in future studies to overcome this limitation.

Lead survival may not be associated with the imaging modality utilized during permanent lead implant. Instead, lead survival (or, conversely, the risk of lead explant) may depend more on medical comorbidities. Smoking tobacco use did reveal a statistically significant negative effect on the risk of lead explant when adjusted for covariates in this study, thus implying a survival benefit for leads placed in patients smoking tobacco. This contradicts prior research, which has shown a negative correlation between tobacco use and spinal cord stimulation, particularly with respect to lead migration revisions (10). There was a statistically significant difference in patient groups regarding smoking tobacco use in this study, as mentioned previously. Therefore, these findings should be challenged prior to drawing clinical conclusions. Additional medical comorbidities, such as diabetes and peripheral vascular disease, may impact the integrity of tissues and inhibit healing following surgery and should be considered in future studies.

The lead survival time was defined in this study as the number of days that had elapsed from the date

of lead insertion to the date of lead removal or data collection, and not to the date at which the lead was noted to have migrated, began to stimulate surrounding musculature, or became ineffective. The definition of survival time utilized in this study necessarily over-estimates the amount of time that an ONS lead remained in the original, intended position. This inability to determine the exact effective lead lifespan due to lack of data could impact the results. Furthermore, imprecise measurement of lead survival time may lead to increased variability in survival times, as reported in this study. Although leads implanted with fluoroscopy alone demonstrated a trend towards increased survival time, the large standard deviations led to poor statistical power to detect the difference between the 2 treatment groups; thus diminishing the statistical and clinical significance of this result. Additionally, the diagnoses of lead migration, neuromodulation ineffectiveness, and muscle stimulation relied upon interview and physical examination of the patient and, when indicated, were supported with objective modalities to assess lead position including bed-side ultrasound or head x-ray. However, these diagnoses represent subjective, clinical determinations made by different physicians and serve as a source of bias.

Conclusion

There is insufficient evidence to propose that the addition of ultrasonography to fluoroscopy during the permanent implant of ONS leads yields statistically significant differences in lead survival rate or time when compared to fluoroscopy alone. Further investigation is necessary to assess the benefits of ultrasonography as they relate to the permanent implant of ONS leads including potential impact on lead migration, rate of revision, patient morbidity, neurostimulation effectiveness, healthcare costs, and operative time. The effects of medical comorbidities on lead survival rate and time should also be considered. A prospective, randomized trial comparing imaging modalities for ONS lead placement will provide important additional information on the utility of including ultrasound during both trial and permanent implants.

Author Contributions

Drs. Jones, Brown, Moyse, Qi, and Roy had full access to all of the data in the study, and each of them takes responsibility for the integrity of the data and the accuracy of the data analysis. Dr. Roy designed the study protocol. Drs. Jones, Brown, Moyse, Qi, and Roy managed the literature searches and summaries of previous related work and wrote the first draft of the manuscript. Drs. Jones, Brown, Moyse, Qi, and Roy provided revision for intellectual content and final approval of the manuscript.

Acknowledgments

The authors also wish to thank Dr. Buchheit for manuscript review and for his assistance in preparation of this manuscript. We also would like to thank the editorial board of *Pain Physician* for review of this manuscript.

References

1. Weiner RL, Reed KL. Peripheral neurostimulation for control of intractable occipital neuralgia. *Neuromodulation* 1999; 2:217-221.
2. Weiner RL. Occipital neurostimulation (ONS) for treatment of intractable headache disorders. *Pain Med* 2006; 7:S137-S139.
3. Kapural L, Mekhail N, Hayek SM, Stanton-Hicks M, Malak O. Occipital nerve electrical stimulation via the midline approach and subcutaneous surgical leads for treatment of severe occipital neuralgia: A pilot study. *Anesth Analg* 2005; 101:171-174.
4. Falowski S, Wang D, Sabesan A, Sharan A. Occipital nerve stimulator systems: Review of complications and surgical techniques. *Neuromodulation* 2010; 13:121-125.
5. Trentman TL, Dodick DW, Zimmerman RS, Birch BD. Percutaneous occipital stimulator lead tip erosion: Report of 2 cases. *Pain Physician* 2008; 11:253-256.
6. Skaribas I, Aló K. Ultrasound imaging and occipital nerve stimulation. *Neuromodulation* 2010; 13:126-130.
7. Zhou L, Ashkenazi A, Smith JW, Jen N, Deer TR, Zhou C. Long-term clinical outcome of peripheral nerve stimulation for chronic headache and complication prevention. *Anesth Pain Med* 2016; 6:e35983.
8. Eldrige JS, Obray JB, Pingree MJ, Hoelzer BC. Occipital neuromodulation: Ultrasound guidance for peripheral nerve stimulator implantation. *Pain Pract* 2010; 10:580-585.
9. Pittelkow TP, Pagani-Estevez GL, Landry B, Pingree MJ, Eldrige JS. Occipital neuromodulation: A surgical technique with reduced complications. *Pain Physician* 2016; 19:E1005-E1012.
10. De La Cruz P, Fama C, Roth S, Haller J, Wilock M, Lange S, Pilitsis J. Predictors of spinal cord stimulation success. *Neuromodulation* 2015; 18:599-602.