Differentiating Between Symptomatic Irreversible Pulpitis and Trigeminal Neuropathic Pain: Assessment of a Novel Method for Collecting Data on the Temporal Patterns of Pain

Nicholas Robert Sotak

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Committee:

Mark Drangsholt

Linda LeResche

Natasha Flake

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University of Washington

Abstract

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Nicholas Robert Sotak

Chair of the Supervisory Committee:

Mark Drangsholt

Department of Oral Medicine

Orofacial pain is a common experience and can prove diagnostically challenging. Symptomatic irreversible pulpitis (SIP) and trigeminal neuropathic pain (TNP) are two such conditions that prove difficult to distinguish for many clinicians. Commonly used diagnostic methods relying on clinical signs, symptoms, and the results of therapeutic trials may fail to identify TNP when it is present. A relatively unstudied aspect of orofacial pain conditions is the timing of painful symptoms. We piloted a novel method for the chairside collection of data on the temporal qualities of each condition and analyzed how easily people were able to provide the data, and what differences exist for SIP and TNP. All 35 subjects were able to provide the requested data with no or minimal assistance, and through their plots we were able to identify trends that may aid in differentiating between SIP and TNP. We also showed that clinical experts, using data collected from individual subjects, are able to differentiate between SIP and TNP. We conclude that further development of an easy to administer tool would serve as a useful aid in diagnosis of many pain conditions.

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Introduction and Background

A recent study found that 1 in 6 patients presenting to a dental office experienced orofacial pain in the previous 6 months, with a dentoalveolar location being the most prevalent site (Horst et al., 2015). Often the source of such pain is clearly identifiable. However, when clear clinical signs are lacking, painful conditions of the oral cavity can present significant diagnostic challenges. At times the result is unnecessary treatment (Linn, Trantor, Teo, Thanigaivel, & Goss, 2007). Differentiating between symptomatic irreversible pulpitis (SIP) and trigeminal neuropathic pain (TNP) is one example where correct diagnosis can prove difficult (Matwychuk, 2004), and respective therapies differ wildly (Yatani, Komiyama, Matsuka, Wajima, Muraoka, Ikawa, & Heir, 2014).

Symptomatic Irreversible Pulpitis

A diagnosis of SIP is reached when a clinician has determined an inflamed vital pulp is incapable of healing (American Association of Endodontists, 2009).

Causes of irreversible pulpitis involve chemical, mechanical, or, most commonly, bacterial challenge leading to severe inflammation within the pulpal tissues. One study examining the association between clinical diagnosis and histologic presentation of irreversible pulpitis found a match in 27 of 32 cases. Their histologic definition of irreversible pulpitis included presence of chronic inflammatory cells, areas of liquefaction necrosis, and invasion of bacterial biofilms. (Ricucci, Loghin, & Siqueira, 2014)

Typical treatment consists of either extraction of the affected tooth or complete removal of the infected/inflamed pulp tissue followed by restoration.

Trigeminal Neuropathic Pain

The International Association for the Study of Pain (IASP) specifies that labelling pain as neuropathic in origin is appropriate when the "pain is caused by a lesion or disease of the somatosensory nervous system" (International Association for the Study of Pain, December 14, 2017).

A notable distinction between SIP and TNP is that in SIP a cause for the pain complaint is established, whereas TNP is a clinical term that often presumes the existence of a lesion or disease. Processes by which TNP manifests vary, and may include changes in ion channel function and expression, second order nociceptive function, and inhibitory interneuronal function (Colloca et. al., 2017).

Treatments are non-surgical in nature and typically involve medications that target pain signaling pathways. For the purposes of our study, we focused on presentations of TNP where symptoms involved a tooth or tooth-bearing area that could have reasonably been confused for SIP.

Avoiding misdiagnosis in cases without an obvious cause can be challenging when only traditional signs and symptoms are considered. Most practitioners commonly ask about symptom onset, intensity, duration, aggravating and alleviating factors, and location. Typically, these questions are asked to differentiate between SIP and other problems, and to localize the area of concern. Common chairside tests used to evaluate the pulpal status of teeth, while widely used, can yield varying results. A recent systematic review to assess the accuracy of common practices used in

determining pulpal condition (i.e. whether a tooth's pulp is healthy, has reversible pulpitis, or irreversible pulpitis), including the presence of certain symptoms, like having a toothache, was unable to find sufficient evidence to determine the value such methods (Mejare et. al., 2012). While this conclusion speaks to the need for additional high quality research, the result may not be surprising given the number of variables that can influence a patient's response to testing that is ultimately subjective (Levin, 2013; Newton, Hoen, Goodis, Johnson, & McClanahan, 2009).

The issues with chairside diagnosis are often compounded by patients, who have been shown to be able to correctly identify the source of SIP 73.3% of the time, but only 30% of the time if they do not have periradicular symptoms (McCarthy, McClanahan, Hodges, & Bowles, 2010). Given that a recent study found the frequency of non-odontogenic toothache to be about 3.4% among those receiving endodontic therapy (Nixdorf, 2010), it is not surprising that in individual cases where pain is poorly localized, and treatment of the first tooth is unsuccessful in relieving symptoms, treatment of the second most suspect tooth resolves the complaint. Unfortunately, these types of serial treatments may result in confirmation bias, leading to dismay in cases where treatments of the second, third, fourth, etc. site fails to reduce pain. This dismay may be compounded by the fact that teeth may develop neuropathic pain following endodontic therapy (Okeson, 2014).

In addition to the issues concerning definitive treatment, therapeutic trials may also result in confusion when etiology is unclear, even when suspicion of TNP is present. Antibiotic trials to rule out infection would understandably have no effect on TNP, but they have also been shown to have no significant effect on SIP (Keenan, Farman, Fedorowicz, & Newton, 2006). Local anesthetic injections produce equivocal results in TNP depending on the specific pathology

(Abiko, Matsuoka, Chiba, & Toyofuku, 2012), but can also provide unclear results in SIP (Kung, McDonagh, & Sedgley, 2015). Analgesic trials are potentially informative given the ineffectiveness of anti-inflammatory drugs in treating TNP, and although a recent systematic review found evidence for their effectiveness in treating post-operative pain with an endodontic origin (Aminoshariae, Kulild, Donaldson, & Hersh, 2016), there is little evidence for their effectiveness in resolving pain symptoms associated with SIP, unless endodontic therapy is also provided.

The difficulties in diagnosing TNP prior to attempting therapy directed at SIP are clear, and an additional aid in chairside diagnosis would be understandably welcome. Chronobiology is one area which may prove useful in differentiating TNP from SIP. Little research has been completed specific to this area; however, studies that have focused on diabetic neuropathy, post-herpetic neuropathic pain, "toothache", osteoarthritis, and other conditions have found each condition to have consistent temporal qualities (Gilron & Ghasemlou, 2014; Labrecque, & Vanier, 1995). If TNP and SIP are similarly characteristic within their respective presentations, understanding the temporal patterns may help clinicians dealing with diagnostically difficult cases reach an accurate diagnosis earlier, before irreversible therapy has been initiated.

In exploring the possibility of using temporal patterns to aid in diagnosis, it is not only necessary to determine what the patterns are, and whether it is possible for patients to describe those patterns accurately, but also to ensure our data collection methodology is repeatable. Therefore, we proposed the following questions:

Can patients depict the temporal patterns of symptomatic irreversible pulpitis, or trigeminal neuropathic pain, while in the clinic, using a pictorial tool that results in a drawing of the "pain wave form"?

Are the depicted temporal patterns repeatable?

Can the temporal patterns of symptomatic irreversible pulpitis and trigeminal neuropathic pain be used to differentiate them?

Hypotheses:

The ability of patients to accurately describe their symptom temporality will vary according to age, education level, number of previous visits, and days since treatment was initiated.

The repeatability of a patient's temporal pattern will depend on number of previous visits, treatment initiation between recording of patterns, and proficiency in describing their symptom pattern during the initial visit.

Symptomatic irreversible pulpitis and trigeminal neuropathic pain conditions have distinctive temporal trends and patterns which enable differentiation.

Aims:

1. *Develop a feasible clinical method of measuring pain temporal patterns.*
    a. *Measure feasibility*
    b. *Measure repeatability*
2. *Describe the temporal patterns of symptomatic irreversible pulpitis.*
3. *Describe the temporal patterns of trigeminal neuropathic pain.*
4. *Explore the chairside accuracy of patient recall of symptom intensity and timing.*
5. *Explore what factors influence the ability of patients to:*
    a. *Accurately recall symptom temporality*
    b. *Successfully create "a pain waveform"*

Methods

Sample:

Subjects were recruited from the Dental Urgent Care Clinic (DUCC), Oral Medicine Clinical Services (OMCS), and Graduate Department of Endodontics Clinic (Grad. Endo.) at the University of Washington's School of Dentistry and met the following criteria:

***I**nclusion*

1. *Diagnosis, or presumed diagnosis, of either TNP involving a tooth or tooth-bearing area, or SIP made by an experienced dentist.*
2. *Ability to communicate in English.*
3. *Must have experienced symptoms within past 10 days.*

Exclusion

1. *Experienced painful orofacial symptoms not related to TNP or SIP within past 30 days, and are unable to differentiate those symptoms from TNP or SIP.*
2. *Unable to complete a visual analog scale.*
3. *Under 18 years of age.*

No subjects were required, or asked, to delay treatment initiation or continuation, for the purposes of completing the study tasks.

Procedures

The study was determined to have a minimal potential for harm, and was exempted from full review by the University of Washington's institutional review board. Informed consent was obtained for all study participants.

All subjects were be asked to complete a questionnaire to collect the following demographic and treatment information: Gender, age, race, education level, socioeconomic status, current or past occupation, months since onset of pain, days since last experienced symptoms, days since treatment was initiated, and perceived level of pain control.

Through a structured interactive and instructive interview process, subjects were guided in creating time-dependent pain waveforms. Waveforms described typical diurnal patterns, patterns from disease onset to present, and allowed for open-ended expression as well. All subjects were prompted to produce a waveform that described their "most typical" diurnal pattern for days when they experienced pain. The interview process began with an explanation of what a time-dependent plot is, how we would like them to create it, and then allowed subjects

an opportunity to produce a waveform. Increasing levels of assistance were provided to subjects who were unable to successfully create a waveform they felt represented their symptoms well. The level of assistance was recorded on a scale of 0 to 3, with level 3 being the most assistance. Certain clarifying questions were answered informally, or relevant parts of the interview script were re-read, when a subject required help that fell below the threshold set for requiring formal assistance. After a plot was completed, subjects were given the opportunity to clarify and describe certain aspects of their plot by labeling the axes and pain intensity line. Although deciding what to label was at the subject's discretion, they received a prompt to include any labels they felt would help someone understand their plot better. All subjects were required to label the x-axis on both the second and third plots, described below. The Protocol details procedural specifics, including when and how formal assistance was provided, and provides complete interview scripts.

Three plots were created on standardized forms to allow for qualitative and quantitative comparison. Each had a VAS-like 100mm long y-axis with labels for "No Pain" at (0,0), and "Most Pain Imaginable" at the vertical terminus, and was not labeled numerically. The first plot (Plot #1) had an x-axis specified as being diurnal, with labeled tick marks at (0,0) "Wake Day 1", and the x-axis terminus for "Wake Day 2". The x-axis for this plot and all others was approximately 240mm long. The first plot's x-axis also specified "Sleep" based on a subject's estimated nightly bedtime. This was indicated on the plot by having subjects place a dash mark on the x-axis and then write the word "sleep" underneath it. The first plot will be referred to as the "diurnal plot". The second plot (Plot #2) had an x-axis with labeled tick marks at (0,0) for "First Onset" and the x-axis terminus for "Today". This plot will be referred to as the "history plot". The x-axis was

unlabeled on the third plot (Plot #3) to allow the subject to express patterns on a timescale of their choosing, and will be referred to as the "freeform plot". Plots were completed in order using the interview method described previously, with changes to the script based on the plots' timescales.

Second, subjects were asked to complete a 3-day take home pain diary. Verbal and written instruction on how to complete the diary was provided. At a minimum, subjects were asked to provide entries for "Pain upon waking", every time a significant change in their symptoms took place or every 4 hours, pain just before falling asleep, and pain levels during the night upon waking (if waking occurs). Pain levels were recorded on a VAS along with the time and any associated activity.

Within the constraints of the study timeline, and subjects' schedule, subjects with a diagnosis of trigeminal neuropathic pain were asked to repeat the interview process at their next regularly scheduled clinic visit. The interview process was conducted as previously described to complete three additional plots (Plot #4, Plot #5, Plot #6 – similar to plots #1, #2 and #3, respectively).

At no point was a subject's diagnosis recorded on any plot.

Analysis

Comparison of demographic data and level of assistance required by participants in the two diagnostic groups was performed using an unpaired student t-test for continuous variables and either the Chi Square test or the Fisher Exact test for categorical variables, where appropriate. Significance was set at $p<0.05$.

Subjects' pain diaries were used to create diurnal plots of the individual's pain symptoms by converting VAS results into vertical measures and placing them on a standardized form similar to that used by subjects during the interview process when completing the diurnal plot. VAS results were placed on the x-axis according to the subject's time entry along with any associated activity. A subject's wake time was established as the start of the hour of their first entry for the day, or as a time specified by a subject (usually written as an associated activity).

When possible, pain diary plots, first, and second interview plots were compared qualitatively.

For each unlabeled diurnal plot we recorded high pain, low pain, periods of no pain while awake, presence of pain at night, number of pain flares during the day, number of pain flares after sleep, pain at waking, pain at sleep, and "pain load". Additionally, subjects' history plots were analyzed for whether their pain had worsened or improved over time. A description of this process is provided below. All needed measurements were completed by hand using a digital caliper. Comparisons of the two diagnostic groups were completed using either an unpaired t-test or the Chi-square test. The following definitions and rules were followed for each measure:

High pain: highest point drawn on the plot, not to exceed 100mm, measured from the x-axis.

Low pain: lowest point drawn on the plot during waking hours. If no line was above the x-axis during waking hours, low pain was assigned a value of 0.

Period of no pain while awake: Presence of at least one point between waking and sleep where the pain intensity line indicated no pain, or the pain intensity line was absent (excluding points within 5mm of either waking or sleeping).

Presence of pain at night: Pain intensity above 10mm after the onset of sleep, with a distinct positive slope after the point of sleep, but before the terminus of the x-axis.

Number of pain flares during the day: Increased pain intensity with a slope of no less then 1 and amplitude over of at least 20mm above the point from which run is to be calculated. Pain must decrease with a slope of no greater than -1 and the decrease must begin no more than 40mm (approximately 4 hours) beyond the start of flare. Slope was calculated measuring total rise from level of pain intensity immediately prior to the flare, with run measured to only to the highest point of the flare. Decreasing slope was similarly measured, with rise measured from the level of pain intensity immediately following the flare. Only counted for flares before the point of sleep.

Number of pain flares during after sleep: Counted using the rules applied for flares during the day, but only counting flares after the point of sleep.

Pain at waking: Level of pain intensity corresponding with the point "Wake Day 1". Lines starting within 5mm of the y-axis were considered as having intersected the y-axis. The absence of a line within 5mm of the y-axis was assumed to mean there was no pain present.

Pain at sleep: Level of pain intensity at the point of sleep. Lines terminating within 5mm of the point of sleep were counted as pain at the point of sleep. No line present within 5mm of the point of sleep was considered to mean there was no pain present.

Pain load: Pain intensity lines were split into segments with each segment being as long as possible, and generally no shorter than 5mm. The area under each segment was calculated by multiplying the x-axis dimension by the y-axis dimension. For non-horizontal segments, the area of a corresponding triangle was calculated and either added to (positive sloping segments) or subtracted (negative sloping segments) from the area of the previously calculated rectangles. The final units were "pain-intensity hours".

Pain intensity trend: A line of best fit was visually determined using a straightedge. Plots were placed in two groups, with one group consisting of plots with positively sloping lines and the other group having plots with lines that were either negatively sloping or flat.

Additionally, both the study team and ten individuals with no relevant clinical background, who were also naïve to the study, qualitatively grouped the diurnal plots to look for general patterns and trends. Forty separate diurnal plots were included in the sample, which contained 36 initial plots (one subject with SIP created two initial diurnal plots), and 4 plots collected at follow-up. First plots were compared only using subjects' unlabeled diurnal plots with the following instructions given:

1. Sort the plots into groups based on their shape and any other characteristics you feel are important.

2. Create no more than 2 groups.
3. Every plot must be placed in a group, and may not be placed in more than one group.
4. Provide a brief description of each group in the space provided.
5. Record the graph numbers (upper right) in the cells under the group description.

Each of the volunteers' two groups were compared using the chi-square test to determine whether a tendency to group plots based on the associated clinical diagnosis existed. Additionally, a scoring method assigning a "percent TNP" was used to help describe group homogeneity, with scores of 0.00 or 1.00 being 100% SIP or TNP, respectively. Because there were unequal numbers of TNP (25) and SIP (15) plots, each SIP plot was weighted with a score of 1 and 2/3, versus 1 for TNP, so that final scores would better reflect the potential for random sorting to produce groupings with scores of 0.50 (50% TNP and 50% SIP).

Finally, two of the study team members, one board certified by the American Board of Endodontics and the other board certified by the American Academy of Oral Medicine, were asked to assign a diagnosis of either TNP or SIP to each subject's full suite of labeled plots. The combined results were compared to the clinical diagnosis with sensitivity, positive predictive value, and accuracy reported.

Results

Table 1: Patient Characteristics

		SIP	TNP	Total	
N		14	21	35	
Age (mean years, range)		43.00 (18-62)	51.81 (24-80)	48.29 (18-80)	0.118
Gender					0.133
	Male	*8*	*6*	*13*	
	Female	*7*	*15*	*22*	
Educational Level					0.329
	<HS	*1*	*0*	*1*	
	HS	*7*	*6*	*13*	
	AA	*4*	*5*	*9*	
	BA/S	*2*	*4*	*6*	
	Graduate	*1*	*6*	*7*	
Race					0.366
	Black	*2*	*0*	*2*	
	Native American/Alaska Native	*0*	*0*	*0*	
	Asian/Pacific Islander	*1*	*2*	*3*	
	White	*12*	*18*	*30*	
	Hispanic	*0*	*1*	*1*	
Onset (months)					**<0.0001**
	Less than 1	*12*	*0*	*12*	
	1-5	*1*	*1*	*2*	
	6-12	*0*	*0*	*0*	
	Over 12	*1*	*20*	*21*	
Days Since Treatment Initiated (mean days, range)		*3.64 (0-30)*	*1696.48 (60-4380)*		**<0.0001**
Perceived Level of Pain Management (mean %, range)		*54.29 (10-100)*	*57.14 (0-90)*	*56 (0-100)*	0.762
Clinic					
	OMCS	0	21	21	
	DUCC	9	0	9	
	Grad. Endo.	5	0	5	

<HS, less than high school education; HS, high school diploma; AA, associates degree; BA/S, bachelors level degree; Graduate, graduate school level degree or professional degree. OMCS,

Oral Medicine Clinical Services; DUCC, Dental Urgent Care Clinic; Grad. Endo., Graduate Endondontics Clinic.

During the period of active recruitment from May 2018 through October 2018, 52 potential subjects were identified as likely meeting eligibility criteria and approached for recruitment. Of those approached, 35 met inclusion and exclusion criteria and agreed to participate. Three did not ultimately meet eligibility criteria, and the remaining 14 declined participation.) Of those who participated, 14 had a clinical diagnosis of symptomatic irreversible pulpitis and 21 had a clinical diagnosis of trigeminal neuropathic pain. Participant characteristics are shown in Table 1. Ages ranged from 18-80 years with those diagnosed as having SIP averaging 43 years, and those with TNP averaging almost 52 years old. Although not statistically significant, SIP tended to have an equal number of men and women with the diagnosis, whereas TNP tended to have more women diagnosed. Race, education, and level of perceived pain management were also not significantly different between groups.

TNP and SIP were notably different in time since onset, with pain associated with SIP having started almost exclusively less than 1 month prior to recruitment and TNP almost exclusively over 12 months. The difference in time since initial therapy was similarly stark with SIP typically having had some kind of treatment started less than 4 days prior to study enrollment and TNP well over several years.

Not displayed in Table 1 are the occupations subjects listed as being their most recent. Figure 1 shows an aggregate of the occupations named by the included subjects.

Equipment Operator, Physical Calibration Technician, Stay at home dad, Hotel room service, Apt Manager, Supervisor, Research Assistant, Pizza dresser/Student, Stay at home mom, Unload trucks, Pilot, Immigration Customs Enforcement, Airline Pilot, Program worker in Middle School, Hairdresser, Xray technologist, ER Tech, Executive director, Stay at home mom, Medical Science Liason, Stay at home mom - previously kindergarten teacher, Budget analyst, RN, Pier Agent, Knitting instructor, Electronic Engineer, Housewife, Flight Attendant, Driver, HR Manager, Financial Analyst, Metal Artist, RN, Truck Driver

Figure 1: *List of subjects' self-identified "most recent occupation".*

All 35 subjects successfully completed the initial interview with only 5 requiring "Level 1" assistance as outlined in the protocol. Besides all but one of those requiring assistance having a diagnosis of TNP, there was no discernable association with clinical or demographic factors. Only 9 subjects returned completed pain diaries, and just 4 diagnosed with TNP were able to complete a second interview. Second interview plots, for the subjects who were able to complete a second interview, were included in the analysis as if they represented an additional subject. Reliability and validity testing was not performed due to low numbers of second interviews and returned diaries. One subject completed two diurnal plots, one with medication and one without. Both were included in the analysis.

Table 2: Plot characteristics		**TNP**		**SIP**		
		Mean	***SD***	***Mean***	***SD***	***p***
Diurnal Plot						
High Pain (mm)		*58.32*	*21.35*	*66.83*	*21.66*	0.250
Low Pain (mm)		*13.42*	*12.65*	*17.56*	*24.39*	0.562
Period of no pain while awake (%)		*16.00*		*36.00*		0.160
Pain at night (%)		*24.00*		*50.00*		0.098
Flares (#)	*Awake*	*0.84*	*1.46*	*1.73*	*1.39*	0.070
	Asleep	*0.32*	*0.97*	*0.73*	*1.77*	0.430
Pain upon waking (mm)		*22.77*	*22.91*	*24.86*	*27.96*	0.814
Pain at Sleep (mm)		*40.46*	*22.55*	*30.54*	*30.18*	0.297
Pain Load (Pain intensity hours)		*606.28*	*321.55*	*624.66*	*420.54*	0.889
History Plot						
Pain History (% w/ positive slope)		*28*		*71*		**0.008**

As seen in Table 2, there were no statistically significant differences between the two groups' diurnal plots, but there were some trends. Notably, subjects with a diagnosis of TNP tended to be less likely to have pain at night (24%) compared to those with SIP (50%) , had fewer pain flares during the day (mean of 0.84 vs. 1.73) and night (mean of 0.32 vs. 0.73), and were less likely to experience periods of no pain while awake (16% vs. 36%). Irrespective of diagnosis, subjects tended to have similar overall amounts of pain, shown as the pain load.

The history plot analysis revealed a significant difference between diagnoses, with just 28% of subjects with TNP indicating increasing pain over their disease course, while 71% of those with SIP had increasing pain.

Table 3: Volunteer Plot Grouping

Volunteer	Group A	Group B	p
1	62.3%	43.3%	0.273
2	47.4%	51.6%	0.800
3	59.0%	43.8%	0.364
4	56.0%	40.7%	0.354
5	35.1%	65.8%	0.060
6	49.2%	54.5%	0.819
7	50.7%	49.4%	0.935
8	44.4%	56.5%	0.462
9	45.7%	56.9%	0.505
10	31.0%	54.5%	0.237

Results from the grouping exercise performed by volunteers (Table 3) showed that, generally, people without any relevant clinical training did not naturally separate plots based on the associated diagnosis. One volunteer created groups that were roughly 35% TNP and 66% TNP, this resulted in groups that were bordering on being statistically different.

Table 4: Clinical Expert Plot Grouping

		Clinical Diagnosis		
		TNP	SIP	PPV
Grouping Result	TNP	*42*	*4*	0.91
	SIP	*0*	*24*	1.00
	Sensitivity/Specificity	1.00	0.86	
			Accuracy	0.94

PPV, Positive Predictive Value. The value for the sensitivity measure of TNP is the value for the specificity measure for SIP. Likewise, the value for the sensitivity measure for SIP is the value for the specificity measure for TNP.

Expert grouping (Table 4) using the full suite of plots resulted in marked separation of the conditions, with high an overall accuracy of 0.94.

Discussion

Trigeminal neuropathic pain and symptomatic irreversible pulpitis can be difficult to distinguish in the clinic. The goal of this pilot study was to investigate the feasibility of chairside data collection using a novel interactive interview to produce time-dependent waveforms of patients' pain experiences. Through this process we compared the plots of patients with these two orofacial pain conditions, looking for differences that may help clinicians in reaching a correct diagnosis.

We found that people, regardless of age, gender, education level, race, professional background, time since diagnosis, time since treatment was initiated, or their level of perceived pain management were able to successfully complete the interview process with no, or minimal

assistance. This is encouraging, because the interview method was time-consuming and would be difficult to employ in a feasible way for most clinics with fiscal concerns. Using the results from the interview method, we believe a form that provides instruction to patients can be developed. This would allow for a streamlined collection of data that could then be easily reviewed by a clinician.

Though subjects were easily able to complete the interview process, due to the low numbers that completed pain diaries, we cannot say whether plots from the first interview represent "real-time" collection of pain intensity measures (like the pain diary). Furthermore, having inadequate numbers of subjects that completed second interviews also prevented us from testing the repeatability of the plotting exercises. We hypothesized that this would have depended not only on a subject's ability to recall their pain experience, but also on certain treatment factors (e.g. having root canal therapy or a drastic change in a medication regimen) that would have significantly altered a subject's pain between interviews. The diaries that were returned, and plots from the second interviews that were conducted, showed some similarities, but were not exact replicas of the initial interview plots. In some cases this should be expected. Every subject was interviewed during a clinical visit at which they were being treated from their condition. In the case of subjects with a diagnosis of SIP, definitive treatment (root canal therapy or extraction of the involved tooth) was often provided that would typically resolve their pain complaint. For those with a diagnosis of TNP, modifications to therapy would be expected to have an effect on pain level. Exploring these factors was beyond the scope of this study, but would be worth investigating in the case of TNP as a way of measuring the effectiveness of therapy.

Almost all of those with SIP received initial treatment on the day of data collection. Given the nature of SIP, initial treatment in the form of an edondontic procedure, or an extraction, typically results in a marked reduction of pain. This was reflected in the diaries that were returned, with two of the subjects failing to complete three days of entries and instead providing hand written notes indicating they had no pain and didn't see the point in finishing the three days. In one case the School of Dentistry was thanked for providing expert care. Subjects with TNP received ongoing treatment for their pain, and likely because of the chronic nature of the condition, their diary plots and second interview plots were more similar to their initial plots than were those of subjects with SIP.

Differences between subjects' recalled patterns and real-time patterns, while important to note, may not be as important for chairside diagnosis. Especially in the case of SIP, where immediate treatment can completely resolve pain, clinicians must base their decision on information patients perceive to be accurate, such as the recalled patterns collected in this study.

Analysis of the diurnal plots showed trends, but no statistically significant differences between conditions. With a higher number of subjects some of these differences may become statistically significant, however. Further, many of the trends identified in the analysis fall in line with current perceptions regarding SIP and TNP, especially during sleep. One aspect of the plots that was very similar was pain load. This measure, with units of pain-intensity hours, attempted to convey a sense of the pain burden experienced by each subject. On average, the numbers appear remarkably close. How the subjects experienced the pain was different, however. Based on both qualitative and quantitative analysis, subjects with SIP typically had shorter periods of more

intense pain, whereas those with TNP typically had longer periods of more moderate pain. During analysis of both the diurnal plots and pain diaries, it was one study investigator's contention that TNP plots were "boring".

Two of the most statistically significant findings (time since treatment initiation, months since onset) are likely a reflection of the nature of the clinic where data was collected. TNP is often a chronic condition, and patients are often referred to OMCS after many months or years of inadequate management. This made it unlikely to find patients with new onset TNP during the recruitment period, and also lays bare the need for more timely referrals.

Perhaps the most telling finding of our analysis is that the typical course for TNP is to get better over time, and, while acknowledging the potential for pulpal necrosis resulting in reduced pain, the typical course for SIP is to get worse. Though we cannot know with certainty how TNP behaves near onset, it is clear from our analysis that in the near term SIP will not get better without treatment. In the context of this study, faced with a patient who has *worsening* pain over the course of days, most treating clinicians would be likely to provide surgical care. This is not inappropriate and is supported by our analysis. With this in mind, a red flag for clinicians should be the patient who has had a consistent, or very slightly improving, pain over the course of weeks or months, especially if they lack clear clinical findings indicating SIP. The potential confounder, alluded to above, is the case where a tooth with SIP becomes necrotic. Assuming pain from an abscess does not develop, the potential reduction in pain could theoretically mimic the course of TNP. It is likely clear clinical signs (e.g. having no response to vitality testing) would be present in these cases, however.

In order to help determine whether each condition produced temporal patterns that were inherently different, we used volunteer sorters without any relevant clinical background who were also naïve to the study question. Using these volunteers allowed the study team to analyze groups that were created with less bias, and ultimately helped to indicate whether each condition tended to produce consistent patterns within the diagnosis, but show differences between the diagnoses. We did not attempt to control how volunteers grouped the plots, and this may have resulted in non-relevant criteria being used for sorting. Initially, we instructed volunteers to sort plots into "no more than 5 groups". This additional freedom allowed for volunteers to use criteria that had no relevance to the distinguishing between SIP and TNP. For example, one volunteer created a group that included only plots with "Level of Assistance: 1" labeled in the lower right corner of the page the plot was created on. This label simply indicated to the study team that a particular plot had been created with "Level 1" assistance. In an attempt to reduce the degree to which non-relevant criteria were used, we decided to repeat the exercise with volunteers instructed to sort plots into only two groups. Still, it may have been helpful to provide volunteers with more instruction, or propose a vignette they could base their sorting on. The best performing volunteer described his groups as "Volatile spikes in pain throughout the day" and "Constant pain levels, varies little prior to sleep". These descriptions are in line with the stereotyped patterns of SIP and TNP, and tend to reflect the findings from our quantitative analysis.

Expert grouping was conducted with the full suite of plots. We chose to give our experts all the data to better simulate an actual clinical encounter, and the results reflect this. The utility of

subjects' temporal patterns seems to become more obvious when they are combined with the information subjects volunteered on their various plots. What became clear during our analysis was that only considering diurnal patterns (i.e. only looking at the unlabeled diurnal plots) was not very useful for differentiating between diagnoses of SIP and TNP.

It should be mentioned that although we did not analyze the freeform plots, they provided a way for subjects to convey what they felt was important about the timing of their pain experiences. While some subjects simply repeated the diurnal or history plot, others chose to detail pain flares, or a pattern that occurred over the course of days. Future data collection that focuses on these aspects may discover trends that we were unable to detect in our analysis.

This was a pilot study and there are lessons we learned during the collection of data. First, many subjects indicated the presence of pain while sleeping. In fact, while we expected some subjects to be awakened from sleep and experience pain, 61.5% of the diurnal plots indicated some level of pain during sleep with 87.5% of those (53.4% of the sample population) having continuous pain (i.e. no periods of 0 pain) during sleep. Pain is a conscious experience. Therefore, by definition, people cannot have pain during sleep, and our results are likely a reflection of an apparent misunderstanding in how pain is defined. Despite this, we analyzed unlabeled plots to reduce bias, so plot lines were taken at face value. This was despite the fact that a handful of subjects indicated verbally to the interviewer, or wrote on their labeled plots, they in fact had no pain during sleep, or were awoken during sleep by their pain, and produced plots that misrepresented their statements. One subject stated she felt no pain during sleep, but that she knew it was still there, and her plot reflected this belief. This was a major hindrance during

analysis, and future studies should be sure subjects understand that during sleep hours, they should have no pain unless they are awoken. We attempted to filter out plots that were likely a misrepresentation by setting criteria that only counted plots having a set minimum pain intensity after sleep, and also indicated at least a period of increasing pain after sleep. This method likely failed to capture what subjects truly experienced, and educating subjects on how pain is defined, clarifying that they should be experiencing no pain while asleep, and splitting data collection between sleep and wakefulness would likely help make the differences in how the two conditions behave more clear.

A second lesson involved the presence of other neuropathic and non-neuropathic pain in subjects. Though our exclusion criteria attempted to separate out people who could not distinguish between their pain from either SIP or TNP and other pain, like myalgia, it is impossible to say whether or not these subjects' plots reflected more than a single condition. Our study design was not able to adequately separate out these participants during analysis, and excluding them from the study would have made recruitment much more difficult. Despite the drawbacks, we ultimately included them because applying our findings as an aid in undiagnosed cases is more realistic if the data reflect the experiences of a typical patient.

Finally, it is likely subjects with a diagnosis of TNP represent a group that is more diverse than our study was designed to account for. The heterogeneity of our subjects' TNP plots may reflect this, and future investigations with greater numbers of subjects, looking only at TNP, may find subtypes of TNP that have distinct temporal patterns of their own.

Conclusion

Taken as a whole, we have shown that typical patients are capable of producing time-dependent waveforms that describe their temporal pain patterns. We have also shown that the temporal patterns of TNP and SIP have trends that could aid in diagnosis, and the collection of more data in the form of an easy to administer chairside handout will make these trends clearer. Our experience also makes clear that on the individual level, clinical evaluation is still paramount. Several subjects created plots – especially diurnal plots – that appeared stereotypically as SIP or TNP, but had a diagnosis of the other condition. Reaching a correct diagnosis requires integration of all aspects of a person's clinical presentation and pain experience. Temporal patterns of pain can be a useful tool in the diagnostic armamentarium of the expert clinician.

Moving forward we hope that with the creation of an easy to administer tool, plots can be routinely collected for both SIP, TNP, as well as other painful conditions. Further analysis of high numbers of plots from many different conditions may yield several stereotyped patterns which would serve as valuable aids in diagnostically challenging cases, and potentially provide for a more rapid application of effective therapy.

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Protocol

1 Instructions

1.1 How this document should be used.

This protocol is intended to guide an interviewer in the collection of data that will be used to analyze a subject's "pain experience waveform". Where indicated, interviewers will be asked to read specific instructions to study participants. Explanations, and clarifications, in some instances will not be allowed, unless indicated in this document. The intent is for the interview of each participant to be as standardized as possible.

1.2 Consent

A consent form is attached in the Appendix (8.1). It is important for all participants to understand what is being studied, how the data will be used, and any potential risks to themselves or their personal information. Informed consent is required for all study subjects, and they are required to indicate this by signing the consent form before their participation in the study begins.

1.3 Chart Review/Confirmation of diagnosis

It is important that each subject's preliminary, or definitive, diagnosis is determined prior to participation. A diagnosis of symptomatic irreversible pulpitis (SIP) or trigeminal neuropathic pain (TNP) fitting the inclusion criteria will be confirmed by a chart review, This will be conducted by accessing the subject's University of Washington School of Dentistry EHR, also known as axiUm. Relevant clinical notes and/or attachments will be reviewed. For both TNP and SIP a diagnosis will be determined based on clinical signs, patient report, and treatment response (if treatment has been initiated). Because either diagnosis may be "presumed" at the time of study initiation, subjects will be contacted after treatment initiation and/or completion to confirm that treatment targeted towards their diagnosed condition was successful.

1.4 Demographic/History Questionnaire

Each participant will complete a questionnaire (9.2) to record basic demographic information, and certain aspects of subjects' individual treatment and symptom histories. This questionnaire must be completed immediately after introducing the participant to the study (2.1).

1.5 Timeline: Interview #1, Pain Diary, Interview #2

Each participant will go through the same basic process. Interview #1 and #2 will be conducted in one of three dental clinics, depending on existing appointments, availability, and other logistics. Ideally, interviews will be conducted on days when a subject already has an appointment at the dental school. If this is not possible, the subject will be scheduled to return to the dental school for the interview at a later date.

The take home pain diary will be completed between interviews #1 and #2, and should include 3 days.

1.6 Criteria for when assistance is required

Assistance completing the tasks during Interviews #1 and #2 will be given under the following circumstances:

1. Participant asks for help, or indicates by words or action they do not understand what to do.
2. Participant draws a line that has more than one pain intensity for a given time point.
3. Participant asks a clarifying question.
4. Participant indicates they cannot recall their symptom pattern.

In all cases, the participant must respond affirmatively to the prompt, "Do you need [more] help?"

1.7 Levels of assistance

When assistance is required (1.6) it will be standardized and the level of assistance needed will be recorded for each task according to 1.7.2-1.7.5.

1.7.1 Level 0: No assistance required.

For this level, the participant was able to complete the task after 3.1 without further explanation.

1.7.2 Level 1: Show examples of time dependent plots

This level of assistance includes showing participants example plots (9.4) and pointing out relevant features. Interviewers will say the following:

> "Here is an example of the type of plot we are asking you to create. Notice how, as time goes on, the level of pain changes. We know your pain most likely will not look like the pain shown here. This is just an example to show you what the various ups and downs of the plots mean. At some points, the level of pain decreases, and at some points it increases or remains relatively constant. When the line suddenly stops, or drops to zero, that means the pain also stops. When the line is steeper in an upward direction, that means the level of pain increased rapidly. Sometimes this happens when a person does something to irritate an area, but it can also happen without any apparent cause. Likewise, a line that is steeper in a downward direction usually means pain decreased more rapidly. This can often happen with an activity that relieves pain, like taking medication or a hot shower, and falling asleep. It can also happen without any apparent cause."

1.7.3 Level 2: Guide subject in creating scatter plot, connect line

Have the participant create a scatterplot by asking them about his or her pain level as various points during a typical day. Have the subject begin at the lefthand side of the x-axis and continue placing points until they have reached the right-hand terminus. Use the following description to start:

"At this point, we would like you to change how you are creating the plot. Instead of drawing a continuous line, think about specific times and what your level of pain was. Then, on the plot, from left to right, place a dot over a specific time, at a distance above the horizontal line that corresponded to your level of pain at that time."

Use the following prompt, or a similar propmpt, for successive points as needed:

"Are there any other points you would like to place?"
[Yes] No action.
[No] Take the plot and continue with the protocol.

Once the subject has finished placing points, the interviewer will connect successive points using a ruler to make straight lines.

1.7.4 Level 3: Draw plot for subject with their input

When this level of assistance is reached, the subject will no longer be responsible for drawing. Instead, the interviewer will draw a line with the subject's input. The interviewer may make motions on the plots, without leaving a mark, as a way of communicating what he or she feels the subject means, but the interviewer will not suggest a pattern. The interviewer will use the following description to start:

"At this point I would like to draw the plot for you, with your input. I will ask you about your level of pain over the course of time, and have you indicate by showing me where a point should be placed, or where the line should change direction. You may also describe a general pattern to me, and tell me where during the time period there are significant changes to your level of pain."

As the process continues, the interview may ask the following types of questions to help determine the proper pattern to draw:

"At the beginning of the day, immediately upon waking, do you have any pain?"
"How long after waking does your pain start? What level is it?"
"When you eat breakfast/lunch/dinner does your pain change? How does it change?"
"Does your pain ever wake you from sleep? If so, when you wake up, how long does it take for the pain to start?"
"Do you have/have you had periods of no pain? When?"

If the subject meets the criteria for further assistance, the threshold for 1.7.5 has been reached.

1.7.5 Failure to draw plot

Subject states drawn plot does not represent their pain well, or subject is unable to complete the task after Level 3 assistance. If a subject reaches this point, end the task and continue to the next task at Level 0 (1.7.1)

1.8 Confirmation of plot representing pain experience

Investigators must ensure each plot accurately represents the participant's recalled symptom pattern. Therefore, when a participant appears to be finished with one of the tasks, the investigator conducting the interview must ask the participant if he or she is done and if the plot represents his or her symptom pattern. An affirmative response concludes the task. A negative response results in the participant being given more time to make modifications. The interviewer will use the phrases similar to the following prompts:

> For checking to see if a participant is finished:
> "Do you feel like you need to work on this more, or do you think this is a good representation of your pain pattern?"
>
> If the participant responds in a way that indicates he or she is either not finished, or does not feel the plot represents his or her symptom pattern:
>
> If Level 0-2 "Okay, go ahead and make whatever changes are needed."
> If Level 3 "Okay, where do you think changes need to be made?"

The participant, or investigator, depending on the current level of assistance will then modify the plot and repeat the necessary above steps until the participant is satisfied, or terminates the task. If the participant terminates this process and confirms the plot does not represent their pain pattern, this will be counted as a "Failure to draw plot".

1.9 Plot labeling

Once an investigator confirms the participant has finished, and is satisfied, with his or her plot, the plot must be **first copied**, and then the original plot labeled. Labels are placed at the discretion of the participant, meaning, no labels will be suggested to the participant. The "free form plot" x-axis should have a labeled timescale. If the participant fails to label this appropriately, the investigator will ask them to label it. Investigators may also prompt the participants to label certain other aspects of the plot, however. For example, when pain sharply increases, decreased, or otherwise changes the investigator may ask the participant, "Did something at this point to cause this change?" Before these types of prompts are asked, the participant should be given the opportunity to label the plot how they see fit.

Plot lines should not be changed at this point, other than modifying labels. When the participant is finished labeling, end the task.

2 Introduction to Participant

2.1 Describe what we are measuring, describe concept of time dependent plot, give subject general instructions for completing each plot.

Each participant will be given the same standard introduction to the study, an overview of what they will be expected to do, and a brief explanation of the general concepts. This introduction should be sufficient for some participants to complete each task. After consent has been given, interviewers will read the following statement while holding up a blank copy of the diurnal plot, and pointing out the features as they are described:

> "During this interview I will be asking you to create a drawing that helps describe your pain pattern. The type of drawing you will create is called a time-dependent plot. On the left side of the plot, there is a vertical line labeled at the top and bottom. The bottom of this line is says "No Pain" and at the top it says "Most Pain Imaginable". The bottom of the plot has a horizontal line. Think of this line like a timeline. Each spot on the line represents a moment in time. So, as you move across the line from left to right, time is progressing.
>
> You will be drawing a line that shows your level of pain intensity changing with time. When your pain goes up, the line goes up. When your pain goes down, the line goes down. If you have no pain during a specific time, the line would be down at the bottom, right over the "time line".
>
> There may be points when you aren't sure what level of pain you experienced, or it has changed. I would like you to draw what is most typical, or what you can remember. If you aren't sure, or are confused, just let me know. If you need help with a specific task, tell me. The goal of this interview is to get the most accurate information we can, and if that means you feel you cannot recall something accurately, it is important I know so that I do not record incorrect information."

3 Interview #1

For each task, read the "Explanation to Participant", allow the participant to attempt completing the task, and provide assistance following the guidelines set forth in sections 1.6 and 1.7. When the participant appears finished, follow the instructions in section 1.8, and then 1.9.

3.1 Explain task #1: Diurnal plot

Explanation to Participant:

> "The first plot I would like you to create is for your pain symptoms over the course of a 24 hour period. The left end of the horizontal line represents the moment you wake up to start your day. The right end of the line represents the

moment just before you wake up to start your next day. Depending on how many hours of sleep you have each night, some portion of this plot will represent the time you are asleep. I would now like you to indicate on the horizontal line when you typically fall asleep."

Help the participant to accurately place a mark on the x-axis that roughly indicates when he or she falls asleep. It may help to ask what time the participant goes to bed, what time they wake up, and then suggest placing a mark that allows for the proper proportion of the line to be occupied by sleep.

"Now, I would like you to begin drawing the line. You may make changes along the way, and can indicate corrections by putting an "x" over incorrect lines and/or drawing an arrow pointing to the correct area. You will have a chance to label the plot at the end, for now please only draw lines. Finally, if your pain isn't always the same, try to think of your most typical symptomatic day, or a day that best represents your pain pattern. Okay, go ahead."

3.2 Complete task #1

3.3 Explain task #2: History plot

Explanation to Participant:

"For this plot, I would like to have you draw a line that represents how your pain has changed since it first started. The left end of the horizontal line is when you first noticed the pain. The right end of the horizontal line is today. This line will not be as detailed as the line in the first plot you drew. Think about average level of pain during any one day, week, or month. Think about if there were points since this started that it got a lot worse, or better. You may make changes along the way, and can indicate corrections by putting an "x" over incorrect lines and/or drawing an arrow pointing to the correct area. You will have a chance to label the plot at the end, for now please only draw lines. Okay go ahead."

3.4 Complete task #2

3.5 Explain task #3: Freeform plot

Explanation to Participant:

"For this plot, I would like you to draw a line that you feel best represents your pain experience. The vertical line is still pain intensity, and the horizontal line still represents time. The difference is, the horizontal line no longer has a specific period of time defined. You get to decide how much time is represented by the line. It could be seconds, minutes, hours, days, or longer. For some people, this is an opportunity to describe very detailed changes in their pain. For others, this may be an opportunity to show a pattern that recurs over the course of days. Anything you feel best represents your experience can be drawn. You may make changes along the way, and can indicate corrections by putting an "x"

over incorrect lines and/or drawing an arrow pointing to the correct area. You will have a chance to label the plot at the end, for now please only draw lines. Okay, go ahead."

3.6 Complete task #3

4 Pain Diary

The pain diary will be used as an alternative method for collecting time dependent date. The diary should be completed for 3 days, and will be collected during Interview #2.

4.1 Describe what a pain diary is, how subject should use it, and when an entry should be made.

The participant will be introduced to the concept of a pain diary. Next, instructions for use will be given. Each pain diary packet will have the introduction and instructions for use printed inside the first page.

Introduction to the Pain Diary:

"Now that we have completed the interview, I would like to introduce the next task to you. For the next few days, I would like you to complete what is called a pain diary. This is a record of your pain intensity over the course of time, as you experience it. Unlike the plots, we are using a horizontal line to measure pain intensity. Other than its orientation, it will appear very similar to the vertical line in the plots. Please place a single mark on each line."

Instructions for use:

"There are many ways to complete a pain diary. We would like you to use this standardized form, so that we can be sure everyone is giving us the same kind of information, and we can compare your diary to other participants.

1. Each entry should have:
    a. Pain intensity
    b. Time of entry
    c. Associated activity, if any
2. At a minimum, record entries:
    a. Immediately upon waking for the day, or if awoken during the night
    b. Every 4 hours
    c. Just before sleep onset
    d. Any time a significant change in pain is noticed

3. Do not change an entry after recording it
4. If you forgot to put in a time, or associated activity, only correct this if you are sure that your recall is accurate. If you weren't sure what time is was (an example may be when you make an entry during the night), indicate a time range.
5. Bring the diary with you for your second interview

4.2 Provide example entry.
See 8.6

4.3 How results will be transformed into time dependent VAS.
Once the Pain Diary is returned during Interview #2, the data will be transformed such that the horizontal VAS entries will become vertical VAS data points. Using the time the entry was made, the data points will be placed on a standardized diurnal plot, with a scale identical to those used during the interviews. Lines will be connected between points, and the plots will be copied, and then original plot labelled according to any associated activities, or events, endorsed in the diary by the participant.

5 Interview #2

Interview #2 will be conducted the same way as Interview #1, with the exception that interviewers may welcome participant back, and let them know they will be going through the same basic process.

5.1 Explain task #4: Diurnal plot
See 3.1

5.2 Complete task #4

5.3 Explain task #5: Disease history plot
See 3.3

5.4 Complete task #5

5.5 Explain task #6: Freeform plot
See 3.4

5.6 Complete task #6

6 Appendix

6.1 Consent Form
6.2 Demographic/Treatment/History Questionnaire
6.3 Example plot to show subjects
6.4 Blank standardized plots #1/#4, #2/#5, #3/#6
6.5 Pain Diary Example Entry page

UNIVERSITY OF WASHINGTON CONSENT FORM

Plotting Temporal Patterns of Tooth Pain

Researchers:

Nicholas Sotak, DMD, Graduate Student, Department of Oral Medicine, University of Washington, 253-970-7321 (PI)
Mark Drangsholt, DDS, PhD, Professor and Chair, Department of Oral Medicine, University of Washington
Linda LeResche, ScD, Professor, Department of Oral Medicine, University of Washington
Natasha Flake DDS, PhD, MSD, Associate Professor, Department of Endodontics, University of Washington

24-hour emergency telephone number: If you are experiencing tooth pain and want to talk to someone immediately, call 206-598-6l90 and ask for the Oral Medicine Attending Dentist on call, 24 hours a day. If you have a question about study procedures, please contact Study PI Nicholas Sotak.

Researchers' statement

We are asking you to be in a research study. The purpose of this consent form is to give you the information you will need to help you decide whether to be in the study or not. Whether or not you choose to be in the study will not affect your treatment at the School of Dentistry. Please read the form carefully. You may ask questions about the purpose of the research, what we would ask you to do, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions, you can decide if you want to be in the study or not. This process is called "informed consent." We will give you a copy of this form for your records.

PURPOSE OF THE STUDY

The purpose of this research study is to test a new interview and data collection method, and to compare the timing and intensity of pain experienced for two painful conditions. We would like to compare results from volunteers who have a diagnosis of symptomatic irreversible pulpitis to those with a diagnosis of trigeminal neuropathic pain. The process we will use is described in the procedures section of the consent form.

STUDY PROCEDURES

The procedures described below are part of a research study and are purely voluntary. If you agree to be in this study, you will be asked to sign this consent form before any study procedures are done. You will be asked to come to the University of Washington Oral Medicine Clinic, Dental Urgent Care Clinic, or the Graduate Endodontics Clinic for study procedures.

Overview of study participation

Total time of study participation includes a take home form to be completed over the course of three days, and two clinic visits with each estimated to take between 15 minutes and 1 hour.

Details of study participation

You will complete a questionnaire that gathers basic information about you, and your condition. Your dental records will be reviewed to confirm study eligibility and a diagnosis of one of the conditions we are studying.

You will have two interviews done by one of the study examiner/dentists in one of the study clinics. The interviews will include drawing tasks, along with questions related to the timing, intensity, and factors influencing your pain symptoms. We will also give you a form to complete at home over the course of three days.

Interview questions will be limited to factors directly related to your condition. At times, the answers to the interview questions, or items written in the take home form, may be sensitive in nature.

Completing the questionnaire and interview will take about 30-60 minutes, the interview is repeated at the second study visit, and will take about 15-30 minutes.

You are free not to complete any aspect of the interview or answer any question.

RISKS, STRESS, OR DISCOMFORT

Although we will make every effort to keep your information confidential, no system for protecting your confidentiality can be completely secure. It is still possible that someone could find out you were in this study and could find out information about you. Your personal information will not be used in any published reports about this study.

BENEFITS OF THE STUDY

You will not directly benefit if you take part in this study. The results of the study will help us gather information from volunteers that will guide future research. We will also learn if there are any pain differences between the two conditions we are studying. Our results might help clinicians better diagnosis these conditions.

CONFIDENTIALITY OF RESEARCH INFORMATION

The information you provide in this study will be kept confidential and will be analyzed along with information from other participants. The data you provide will be identified only by a study number. The link between your name and your study number will be kept in a separate file from the data and both will be accessible only to the investigators. Identifiable data will be kept in accordance with University of Washington policy.

Government or university staff sometimes review studies such as this one to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal risk of harm.

OTHER INFORMATION

You may refuse to participate and you are free to withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled.

You will be compensated for the time spent completing the interview and questionnaire.

Printed name of study staff obtaining consent | Signature | Date

Subject's statement

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later about the research, or if I believe I have been harmed by participating in this study, I can contact one of the researchers listed on the first page of this consent form. If I have questions about my rights as a research subject, I can call the Human Subjects Division at (206) 543-0098. I give permission to the researchers to use my medical records as described in this consent form. I will receive a copy of this consent form.

Printed name of subject | Signature | Date

CC: Subject
Investigator

Plotting Pain Questionnaire

Subject ID_____

1. Gender (Female, Male, Transgender, etc): _____ 2. **Age:** _____

3. **What is the highest grade (or year) of regular school you have completed?** ***(check one.)***
Elementary/Middle School: __01 __02 __03 __04 __05 __06 __07__08
High School: __09 __10 __11 __12
College/Junior College: __13 __14 __15 __16
Graduate School: __17 __18 __19 __20+

4. What is the highest degree you earned? (check one.)
__No degree/diploma
__High school diploma or equivalency (GED)
__Associate degree (junior college) or vocational degree/license
__Bachelor's degree
__ Master's degree
__ Doctorate or Professional degree (e.g. MD, JD, DDS, PhD)

5. How many people are currently living in your household, including yourself? ___

5a. Of these people, how many are children 18 years old or younger? ___

6. Which of these categories best describes your total combined family income for your household for the past 12 months? This should include income (before taxes) from all sources, wages, rent from properties, social security, disability and/or veteran's benefits, unemployment benefits, workman's compensation, help from relatives (including child payments and alimony), and so on.
__ less than $25,000
__$25,000-<$50,000
__$50,000-<$75,000
__$75,000-<$100,000
__$100,000-<$150,000
__$150,000 or more
__Don't Know/Not sure
__ Decline to respond

7. Most recent occupation: _____

Plotting Pain Questionnaire

Subject ID_____

8. Race:

- ☐ Black
- ☐ Native American/Alaska Native
- ☐ Asian/Pacific Islander
- ☐ White
- ☐ Mixed Race
- ☐ Other:_____

Questions 9-12 refer to the pain you are currently seeking treatment for.

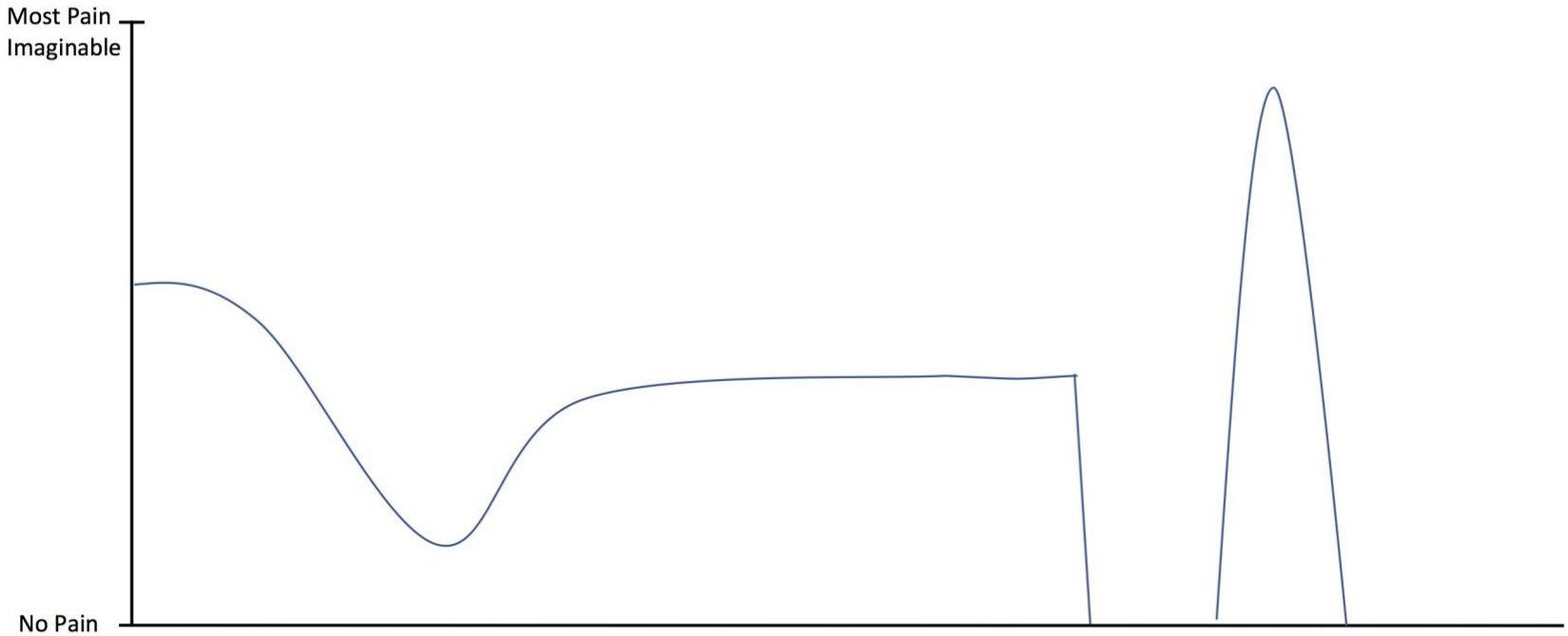
9. Months since onset of oral pain *(check one.)*:

__Less than 1
__1-5
__6-12
__12+

10. Days since last experienced oral pain: _____ *(If you experienced pain today, write '0')*

11. Days, or months, since treatment was started: _____ *(circle)* Days Months

12. Perceived level of pain management *(0% means nothing is helping, 100% means pain is completely controlled)*: _____%



Example Plot

ID:

Plot #1/4

Level of Assistance:

ID:

Plot #2/5

Level of Assistance:

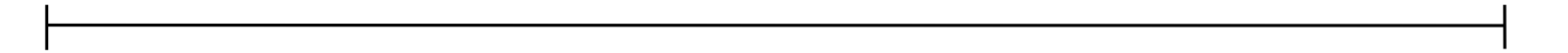
ID:

Plot #3/6

Level of Assistance:

ID:

Date: Time:

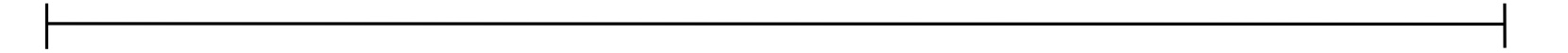


No Pain

Most Pain Imaginable

Associated Activities/Events (if any):

Date: Time:

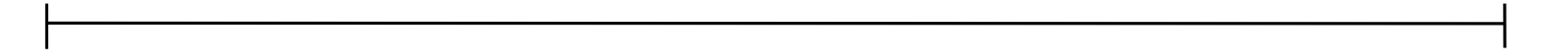


No Pain

Most Pain Imaginable

Associated Activities/Events (if any):

Date: Time:

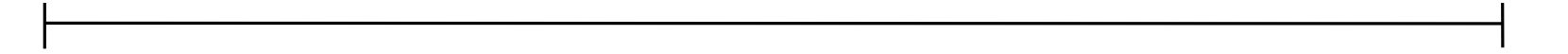


No Pain

Most Pain Imaginable

Associated Activities/Events (if any):

Date: Time:



No Pain

Most Pain Imaginable

Associated Activities/Events (if any):