DESIGN, DEVELOPMENT, AND VALIDATION OF VIBROTACTILE THRESHOLD EVALUATOR FOR WORKPLACE SCREENING OF CARPAL TUNNEL SYNDROME

by

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STATEMENT OF DISSERTATION APPROVAL

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ABSTRACT

Carpal tunnel syndrome (CTS) is the number one cause of disability at work in the United States. Loss of time at work and worker's compensation expenditure caused by CTS is more than that caused by any other condition. However, workplace surveillance is likely to help in detecting CTS at a stage that is treatable at a significantly lower cost. Vibrotactile threshold (VT) testing can be used for this purpose. The VT is the smallest displacement applied (as a sinusoid) to a finger innervated by the median nerve that can be detected by the patient. Vibrotactile threshold evaluation can be a versatile tool for applications involving haptics interfaces, for evaluating peripheral neuropathies, and for studying the effects of chemotherapy induced neuropathies.

This dissertation presents the prototype design of a vibrotactile threshold evaluator for the workplace (VTEW), which is portable, and configurable in terms of the probe diameter (1-6 mm), surround diameter (8-10 mm), applied frequency (1-250 Hz), angle of probe (0-120^0), and displacement of probe (1-1500 μm) and is operated with a customizable LabView interface. The VTEW also incorporates a special mount for the probe stimulus to test the subjects in at least two distinctive postures of the hand.

Subjects were tested using an existing validated device, Vibrotactile Threshold Tester (VTT) and VTEW. Subjects were tested at 50 Hz with VTT and VTEW for validation. The effect of flexion on VT was observed by testing the subjects on VTEW at 50 Hz with their dominant hand in neutral posture and again with their dominant hand in provocative flexion. Use of low frequency for testing in VT studies is uncommon due to hardware constraints. However, low frequency studies could be potentially useful for investigating the effects of chemotherapy on the perception of pain. Thus, subjects were also tested at 4 Hz using VTEW to obtain preliminary data. Finally, an age regression model was developed to correct for the changes occurring in VT with age.

To God in all forms, my husband, parents, sister, and all the teachers who have inspired me.

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CHAPTER 1

INTRODUCTION

This chapter introduces the dissertation with background of and motivation for vibrotactile threshold testing, physiology of carpal tunnel syndrome along with current methods of diagnosis. This is followed by a discussion of the hypotheses tested, the contributions of this work, and an overview of the layout of the dissertation.

1.1 Background

1.1.1 Background and motivation

Bernardino Ramazzini, who has been regarded as the founder of occupational medicine, mentioned in his work De Morbis Artificum Diatriba, translated as Diseases of Workers, in 1713 about the serious conditions that arose from bad postures. He further suggested that a short break from these postures could result in a significant improvement of these conditions. He regarded the continuous movement of the fingers and hands for the clerks as the prime reason for a decreased power of the hand [1]. His advice for keeping the body in a natural posture mirrors the concepts of modern ergonomic principles [2]. Occupational diseases have been recognized as the root cause of the majority of the healthcare claim expenses and a major hurdle to a person's job satisfaction and performance. Carpal tunnel syndrome (CTS), a well known occupational disease, is a nerve entrapment syndrome. The median nerve supplies the sensation to the

thumb, index finger, middle finger, and half of the ring finger. Any compression of this nerve can cause a collection of symptoms such as pain, tingling and numbness in the hand. Patients also report an urge to shake the symptomatic hand, as well as an increase in the severity of symptoms at night or early morning [3-4]. Workers involved in extensive computer use, manual material handling or assembly line jobs, involving repetitive motions of hand, are more likely to be diagnosed with CTS. Studies have shown that although CTS is an occupational disease, the likelihood of a person showing the symptoms may increase with factors such as Body Mass Index (BMI), gender, diabetes, level of stress and use of tobacco or alcohol [5]. However, it has also been suggested that the severity rate of CTS may not necessarily increase due to these symptoms [6]. CTS has been reported to cost over $20 billion in workers compensation and over 31 days of lost work per case. Surgeries related to CTS cost over $1 billion annually and have been reported as the most common cause of surgeries for hand and wrist [7-8].

Understanding the consequences of CTS and or any other occupational disease underlines the need for an effective workplace screening tool for detecting workers who may still be at an early stage of this condition. This will significantly help in preventing the exacerbation of the condition by using tools such as ergonomic evaluation of the workplace, recommending rest period or surgery for carpal tunnel release. Detection at an early stage also helps in cutting down the compensation cost, since at this stage the condition is not too severe and can be treated at a lower cost.

This dissertation presents a newly designed vibrotactile testing device, called the vibrotactile threshold evaluator for the workplace (VTEW) for quick and reliable CTS

screening. In addition to CTS screening, this device is capable of testing at lower frequencies (<6 Hz) for application in testing for chemotherapy-induced neuropathy.

1.1.2 CTS: causes, risk factors and symptoms

1.1.2.1 Human hand anatomy. The human hand facilitates flexion-extension, and radial and ulnar deviation. This is achieved by an intricate mechanism of movement of anatomical structures (bones, tendons and ligaments). The human hand has 27 bones, of which 8 bones are carpal bones, 5 bones are metacarpal bones and the remaining 14 bones are digital bones (proximal, intermediate and distal phalanges). The carpal tunnel is a channel formed by eight carpal bones of the wrist covered by a tough ligament called the flexor retinaculum. This channel contains nine tendons and the median nerve. The median nerve supplies sensation to the thumb, index finger, middle finger, and half of the ring finger. Insufficient space in the carpal canal can cause a direct pressure on the median nerve in the event of change in the volume due to inflammation or fluid retention. The little finger and the other half of the ring finger have sensation supplied by the ulnar nerve, which does not travel through the carpal tunnel.

1.1.2.2 Causes, symptoms and risk factors of CTS. The human wrist can suffer a lot of trauma due to the mobility it offers [9]. Since there is very limited space within the carpal canal, anything that causes an increase in the pressure in this canal can result in an entrapment of the median nerve (due to increased pressure). This impingement of the median nerve causes CTS. CTS is characterized by classic symptoms such as parathesia, pain, atrophy of thenar muscles and numbness [10-11]. Sensory weakness in the digits supplied by median nerve and lower grip strength is also observed. These symptoms are

exacerbated nocturnally and are reported to radiate all the way from the wrist to the shoulder [12].

Aberrant anatomy of the wrist (cysts, anomalous flexor tendons, etc.), infections, inflammatory conditions (connective tissue disease, rheumatoid arthritis, etc.), metabolic conditions (diabetes, hypothyroidism, etc.) and the conditions causing an increased carpal canal volume (obesity, edema, pregnancy, etc.) [13-14] have been recognized as the potential risk factors for CTS. In addition, other factors that may increase the risk of CTS are age, height, gender, weight, smoking, medical history, alcohol consumption, menopausal status, etc. [5, 11, 15]. These factors increase the fluid level in the carpal canal, which results in a decrease in the volume available for the contents of carpal canal. Hence, the median nerve is impinged. Consequentially, irritation of the nerve produces pain, numbness and tingling.

The trauma caused by occupational movements of the wrist is a well recognized risk factor for CTS. Prevalence of injuries to the wrist has been reported with repetitive motions of the wrist and its dependence on gender has been highlighted [5, 13]. However, studies have shown that predisposing patient factors are usually present to initiate and aggravate the symptoms of CTS [16]. It is important to note that CTS has a "multifactorial etiology" involving both occupational and nonoccupational risk factors, which makes it more complex to understand and treat [17].

1.1.3 Methods of diagnosis for CTS

1.1.3.1 Clinical tests. In order to provide a clear diagnosis, electrophysiological tests are performed. These nerve conduction velocity (NCV) tests are considered the "gold standard" for CTS detection. This involves attaching electrodes at various locations

on the hand. Electric impulses are then sent to stimulate the median nerve. The time it takes for the action potential to travel from one location to another is recorded. This value is then compared to that of normal (asymptomatic) and healthy individuals to evaluate the extent of nerve damage, if any. In case of nerve impingements, the time it takes for a nerve to receive a signal and to carry a certain distance is increased. This is termed as the distal sensory latency. Thus, an increased conduction time and decreased conduction velocity provides a way of understanding the state of the median nerve. However, it is important to note that distal motor latency can occur in other conditions like nerve lesions and polyneuropathies also, which makes it necessary to conduct further tests like electrostimulation of the median nerve itself to confirm CTS [18]. In addition, even with abnormally slow NCV results, it is possible for the subject to show no other CTS symptoms. This may be due to the presence of another condition or a person's adaptability to the condition.

The drawbacks of NCV testing are the requirements of extensive training and experience to conduct this test. The cost of training and hiring a certified technician for the testing and the equipment cost ($12,000-$16,000) for NCV testing makes this method prohibitively expensive to be used as a frequent scanning tool. Moreover, the subjects undergoing this test may feel a discomfort arising from involuntary movements of hand on experiencing the electric impulses even though the test is not invasive.

Even with sophisticated tests like the NCV test, it is possible that a person can be misdiagnosed for CTS. This can happen if the person has another condition that causes neuropathy. Thus, it has been suggested that every subject should be asked to fill out a survey with questions regarding medical history and other existing ailments. Several

questionnaires and clinical scales have been devised in an attempt to accurately evaluate a patient's condition before conducting the test [19]. Since a standardized method of diagnosis is important, an item pool to be used by physicians has also been listed in the literature for recording patient's characteristics such as gender, age and BMI with the history of their symptoms, coexisting conditions and the diagnosis results of nonclinical tests [20].

1.1.3.2 Nonclinical tests. Nonclinical tests such as Phalen's test and Tinel's test, although not confirmatory for CTS, are used for screening. Phalen's test involves flexing the wrist of the subject for 1 min. This forced flexion causes artificial pinching of the median nerve and an increased pressure in the carpal canal. The result is considered positive for CTS if the subject experiences an aggravation of symptoms (pain, numbness or tingling) within the area innervated by median nerve.

Tinel's test is performed by gently tapping the wrist above median nerve. This tapping action can be used to spot an irritation in the median nerve by eliciting a tingling sensation, confirming CTS [11, 21-22].

The Semmes-Weinstein monofilament test was used in the past for detecting cutaneous sensibility by using a thin metallic rod of very small diameter to prick a subject's hand. The force of application may be controlled and calibrated based on diameter and bending of the filament. The subject is asked to look away and report when he or she feels the pressure [18, 23].

The straight arm raise (SAR) test involves raising the arm above the head while keeping the elbow extended and wrist in neutral posture for 1 min. This test relies on the occurrence of reduced blood flow (neural ischemia), due to gravity, on aggravating the

symptoms of nerve entrapment [24]. Another similar test, which is referred to as the hand elevation test is performed by raising the hand of the subject above the head for 1 min. The subject is declared to have CTS if they report symptoms within 1 min. These two tests rely on the exacerbation of CTS symptoms by decreasing the blood supply to the median nerve.

With nonclinical tests such as Phalen's and Tinel's test, a major concern is the criteria for test results. These tests are too qualitative to define what constitutes a positive result. In other words, the level of pain or tingling at which the result will be positive for these tests cannot be standardized. In addition, the results of different nonclinical tests may not agree based on the individual symptoms of a person. For instance, a person may have no pain but paraesthesia associated with CTS or vice versa.

1.2 Hypotheses tested

Reviewing relevant literature on VT testing methodology emphasized the lack of standardized testing hardware, testing protocol, and data analysis methods. It was found that even though pertinent questions have been raised, tools to gain insight into the realm of vibrotactile perception have either not been produced or lack considerably in terms of diagnostic and screening capabilities. While VT testing as a screening tool may be versatile, it is not without limitations. Understanding the very nature of mechanoreceptive channels and the lack of controlled stimulation was the motivation for this project to develop a tool that is customizable to be used for testing a variety of conditions by changing testing parameters.

In order to validate the use of the new device designed as part of this dissertation, the vibrotactile evaluator for the workplace (VTEW), the initial goal was to compare the

results obtained at a fixed frequency from the VTEW, and a previously validated device, the VTT. The review of the literature showed that 50 Hz may stimulate a variety of mechanoreceptive channels and previous studies have shown the utility of 50 Hz for testing a variety of ergonomic risk factors [25-28]. VT depends on the testing frequency and the testing protocol used in addition to the hardware parameters such as *probe* and *surround* diameter. The VTT is capable of testing at 50, 150, and 250 Hz. Thus, **Hypothesis 1** states that there is a correlation between the VT at 50 Hz obtained from the VTT and the VT at 50 Hz obtained from the VTEW.

Dependence of the VT on testing frequency may be further explored by testing the same subjects using different frequencies with VTEW. **Hypothesis 2** states that that a subject will have a lower sensitivity when tested at a low frequency of 4 Hz as compared to a higher frequency of 50 Hz.

Use of quantitative tests (Phalen's and Tinel's) to evaluate nerve health is common practice in clinical setting. It could be useful to use these tests in conjunction with the VT testing to screen for CTS. **Hypothesis 3** states that if a test subject is positive for Phalen's and /or Tinel's test, his/her sensory threshold will be elevated.

Median nerve provocation has been shown to aggravate the symptoms of CTS. Individuals who have history of CTS or have been experiencing CTS-like symptoms have been shown to have severe aggravation of symptoms by postprovocative flexion as compared to normal or asymptomatic individuals [26, 28-30]. However, VT testing during flexion has only been minimally explored in the literature [30-31]. **Hypothesis 4** states that a comparison of pre- and during- provocation VT will show a larger difference

for symptomatic subjects as compared to asymptomatic subjects (where symptomatic is defined as a positive result on Phalen's and/or Tinel's test).

Medical history and self-reported symptoms of a subject being tested have been used along with the qualitative and clinical tests to gain insights on the causes and risk factors for the conditions like CTS. Questionnaires and structured survey forms with ratings for pain and discomfort have been shown to be useful in screening for CTS [32].

1.3 Contributions

The concept of using VT testing for evaluation of neuropathies has been around since the 1920s. Several devices exist to show the techniques and hardware utilized to use this method for clinical purposes. However, an easy to use, cost effective, portable, ergonomically designed tool that does not require extensive training to implement in a workplace setting has not been successfully developed [31]. The reliability and repeatability of VT measurement has been one of the biggest concerns for researchers in this field.

A major contribution of this dissertation is the extensive literature review that provides an engineering perspective to the advancement in VT testing techniques for hand therapists who can incorporate this technique for evaluation in the clinical setting. The extensive comparison of devices with respect to hardware, testing protocols, and testing parameters can be used as a guideline for future devices. The limitations and concerns related to VT measurements have been discussed in detail to present the challenges in using this technique. These challenges necessitate the use of standardized measuring practices for accurate comparison.

This leads to the second major contribution of the design and fabrication of a testing device with vastly increased flexibility in testing parameters compared to existing devices. This was motivated to allow customization such that a wide variety of study parameters can be implemented, allowing comparison to many different previous studies and devices, while also providing a means to carry out entirely new studies. Thus, this dissertation also presents a measurement unit that incorporates a voice coil to provide vibration stimulus with feedback control in place to control the displacement (design requirements are discussed in Chapter 4). An ergonomic design presents a unique opportunity for testing in several different hand postures. A wide range of frequencies and amplitude testing offers applications in haptics (providing feedback through user's sense of touch for control and creation of virtual objects and improvement in remote control of machines in teleoperations), chemotherapy-induced neuropathies, and dying-back neuropathies along with CTS screening.

The third major contribution of this dissertation is the design and implementation of a validation study, including the recruitment of nearly 60 subjects, to test the hypotheses outlined in Section 1.2.

1.4 Overview

The subsequent chapters in this dissertation are submitted or prepared for submission to be conferences and journals.

An early conference abstract is included in Chapter 2. This paper describes the initial planning for the VTEW design and validation.

In Chapter 3, an extensive review of the VT history and comparison of existing devices is included in a review article under revised review to the *Journal of Hand*

Therapy. This review also includes the overview of mechanism of vibrotactile perception for human hand and the parameters that affect the VT. Recommendations for testing VT based on the review of literature are intended to serve as a brief guide for future studies in VT testing.

Chapter 4 is a draft manuscript that will be submitted to the *ASME Journal of Medical Devices* that reports on Hypotheses 1, 2, and 3, and includes the description of VTEW design specifications, features, testing protocol used, and studies for validation of VTEW by comparing the results obtained from VTEW and VTT at 50 Hz testing frequency. Additionally, VTEW was also used for testing at 4 Hz to compare the VT at the two frequencies (4 and 50 Hz). The effect of age on VT for all the subjects was investigated and an age correction has been presented and compared to the age correction previously published for VTT.

The draft manuscript in Chapter 5 reports on Hypotheses 4 and 5, and explores the effect of hand postures on VT evaluation using VTEW. An additional study was conducted to investigate the changes in VT with change in hand posture. The subjects recruited for this study were tested in a neutral hand posture at 50 Hz with VTEW. The same subjects were then asked to change their hand posture into fully flexed hand posture and tested again at 50 Hz with VTEW. The use of this method for screening CTS symptomatic population at workplace has been discussed. Subjects were asked to fill out a survey form to gain information about their age, height, BMI, handedness, type of profession, and presence and extent of hand pain and discomfort. Comparison of methods for evaluation and screening of CTS have been discussed.

Finally, Chapter 6 concludes the dissertation and provides suggestions for future work.

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CHAPTER 2

DESIGN OF A PORTABLE VIBROTACTILE THRESHOLD TESTER FOR WORKPLACE SCREENING OF CARPAL TUNNEL SYNDROME

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The abstract in the following pages was published in the 5th annual regional National Occupational Research Agenda (NORA) Young/New Investigators Symposium, SLC, UT. April, 2007.

2.1 Abstract

Musculoskeletal disorders associated with repetitive and forceful motions of the hands and wrists have been reported as the largest contributor of workers' compensation costs excluding the costs associated with work related injuries of the back. Carpal tunnel syndrome (CTS) is a combination of symptoms resulting from the impingement of the median nerve that supplies sensation and motor control to thumb, index finger, and middle finger. Improvements in the posture of the hands and wrists along with regular and frequent rest breaks have been shown to help prevent CTS at work. Early detection of CTS has been shown to have a significant impact on reducing the number of cases that reach the level of nerve damage that requires surgery. The aim of this project is to design a portable device for an early detection of CTS via workplace screening. The tests conducted with this portable device can be used to track the nerve condition of employees at fixed intervals of time or to evaluate the impact of particular workstations. If a patient is diagnosed with an altered sensation response, he or she can be asked to undergo more sophisticated and accurate CTS testing techniques such as nerve conduction velocity (NCV) testing and corresponding physician assessment. The portable vibrotactile threshold tester (PVTT) for workplace screening of CTS uses the vibrotactile threshold (VT) testing method, which determines the smallest amplitude of vibration that can be detected by a subject's middle finger. Increases in VT have been associated with the progression of CTS. Prolonged and exaggerated flexion of the wrist can cause the VT to increase more dramatically for a symptomatic hand as compared to an asymptomatic hand. Thus, testing subjects at different hand and wrist angles may be useful for determining very small changes in the nerve health corresponding to the changes in VT

recorded. The PVTT designed for this project has an ergonomic design with capability of testing subjects at several different wrist flexion angles. The two-interval forced choice psychophysical testing protocol will be used. The amplitude, frequency, and displacement of the testing probe can be customized. The subject's response will also be recorded. A set of asymptomatic subjects will be recruited from the University of Utah student population and another set of symptomatic subjects will be recruited from the School of Music at the University of Utah.

CHAPTER 3

PROGRESS IN VIBROTACTILE THRESHOLD EVALUATION TECHNIQUES: A REVIEW

The manuscript in the following pages has been accepted for publication with the Journal of Hand Therapy.

ARTICLE IN PRESS

SCIENTIFIC/CLINICAL ARTICLE

Progress in Vibrotactile Threshold Evaluation Techniques: A Review

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ABSTRACT: Vibrotactile threshold (VT) testing has been used for nearly a century to investigate activation of human somatosensory pathways. This use of vibrotactile stimuli provides a versatile tool for detecting peripheral neuropathies, and has been broadly used for investigation of carpal tunnel syndrome. New applications include investigation of drug-induced neuropathies and diabetes-related neuropathies. As a feedback device, the vibrotactile stimuli could be used as an information delivery system for rehabilitative feedback devices for upper limb musculoskeletal disorders or as information channels for the visually impaired. This review provides a comprehensive review of the advancement in VT measurement techniques over time and a comparison of these techniques in terms of various hardware features used and the testing protocols implemented. The advantages and limitations of these methods have been discussed along with specific recommendations for their implementation and suggestions for incorporation into clinical practice.

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Human skin is able to respond to a myriad of sensations due to the presence of a very specific but diverse assortment of sensory receptors. These receptors provide a unique way of sensing explicit stimuli, converting signals as diverse as light wavelengths, chemicals, and pressure waves into colors, taste, and sounds. The aim of this article is to begin by understanding the concept of how a human brain perceives touch and vibration and build up to comprehending the use of this sensation (or an abnormality in sensation) to evaluate peripheral neuropathies. Devices that can evaluate the sense of touch and vibration will be discussed and compared in terms of specific features such as hardware construction, frequencies at which the tests are performed, and the methods of psychophysical testing. A brief background of neurology and psychophysical testing is provided to make this literature review useful for readers with diverse backgrounds.

New applications of nerve health evaluation using vibrotactile testing include investigating peripheral sensory neuropathy in individuals who have received drugs with neurotoxic potential for treatment of cancer (e.g., taxanes, cisplatin) and inflammatory conditions such as arthritis.[1,2] In cancer treatment, neuropathy is often a dose-limiting complication. It is possible that continual monitoring with vibrometry might allow oncologists to be more confident in providing aggressive, efficacious treatment. In addition, use of quantitative vibrometry may allow closer monitoring of insulin-resistant and type 2 diabetic patients to promote lifestyle changes that can slow, stabilize, or even reverse peripheral nerve damage. Vibrometry may also contribute to translational investigations of drug treatments for diabetic neuropathy.

A traditional vibrometry application is the evaluation of carpal tunnel syndrome (CTS), a well-known upper extremity musculoskeletal disorder that results from compression of the median nerve in the human hand,[3,4] and thus most of the literature on vibration and touch testing has focused on the detection of CTS. Compared with clinical standards for testing for CTS, such as nerve conduction velocity (NCV) tests, ultrasound, or magnetic resonance imaging (MRI), vibrotactile testing is a low-cost and fast method, which provides the ability to cost-effectively evaluate nerve health on a regular basis in the workplace.[5–7]

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The availability of low-cost components to build devices that can provide a specified vibrotactile feedback enables new opportunities for rehabilitation such as feedback devices for upper limb musculoskeletal disorders,[8] use of vibrotactile feedback for manipulating objects in a virtual environment for physical rehabilitation, and using vibrotactile feedback as a mobility aid for the visually impaired.[9]

TACTILE PERCEPTION IN THE HUMAN HAND

The human hand has sophisticated mechanisms for sensing stimuli such as pain, temperature changes, joint position, and mechanical deformation of the skin. Sensory receptors are responsible for the initial interaction with the stimulus before it is transformed into an electrical signal coded to be transmitted by afferent nerve fibers to the central nervous system.[10,11]

Each sensory receptor is sensitive to a distinct type and pattern of energy and responds to a selective amount of stimulus for activation. Irrespective of the type of stimulus energy experienced by a sensory receptor, the stimulus is converted to an electrical signal (i.e., action potential discharge) that is then conducted through the central nervous system, illustrated schematically in Figure 1. Thus, all sensory receptors share a common mode of sending and processing signals. The human brain processes information from not just one, but many such sensory receptors when presented with external stimuli.[10,11] Although human beings experience a wide range of sensations such as colors, tastes, and tones, these are all the result of perceptions formed by the brain based on the transduction of an external stimulus received by the sensory receptors. Each sensory receptor processes information from a given stimulus in four different ways—modality, location, intensity, and timing. Vision, touch, taste, smell, and hearing have been identified as basic sensory modalities.[11]

Vibration and touch are both forms of tactile stimulation, as both produce distortion of the cutaneous surface. These distortions of the skin generate waves that are transmitted through the skin that are analogous to tremors traveling through the earth's crust.[12] When these distortions reach the membrane of a mechanoreceptor (MR), the membrane is also distorted causing stretch-sensitive ion channels to open and allowing ions to flow across the receptor membrane and to produce membrane depolarization that generates action potentials, which travel to the sensory cortex and produce a tactile sensation that could be either a touch or vibration depending on the type of receptor being activated. There are a variety of MRs within and just below the skin that respond to such displacements. Each receptor has unique filtering characteristics that allow it to respond preferentially to different types of distortion and produce sensations ranging from touch (low frequency displacement), to "flutter vibration" (moderate frequency) to "vibration" (high frequency).[13]

Tactile perception can be understood by considering the aspects of basic categories of information conveyed. Modality refers to the type of stimulus that a receptor can sense and respond to. Cutaneous modalities corresponding to tactile perception include touch, warming, cooling, pain, and itch, where submodalities of touch include texture, edges, and rigidity. Four types of MRs—Meissner's corpuscles, Merkel cells, Pacinian corpuscles (PCs), and Ruffini endings—are responsible for sensing these submodalities. Because these receptors are present in dense population throughout the hand, the location of touch is sensed by the active receptors not only at a given time, but also over a period of time. The action potential frequency and discharge duration produced by the active receptors signals the intensity and duration (defined by when the receptors start firing to when they stop) of the stimulus.[10,11,14,15]

The location and morphology of an MR determines the particular type of response that will be generated when activated by a stimulus that is in the adequate range to excite the receptor. MRs can be classified in several ways depending on features such as location, function, resolution, and adaptation rates.[10,11,14,16–18] These are summarized in Table 1.

A direct consequence of the varying adaptation rates of MRs is the ability of these receptors to act as filters to a range of frequencies. This property results in the ability of these receptors to respond to external stimuli in a manner that is unique and distinguishable for each type of receptor, especially at lower stimulus intensity. For instance, although a stimulus

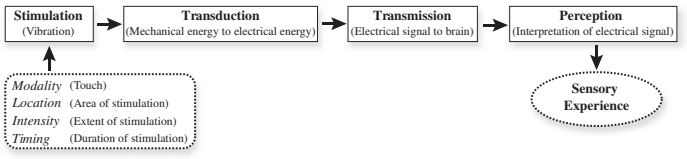

FIGURE 1. *Process of sensing an external stimulus by sensory system (adapted from[11]).*

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TABLE 1. **Classification of MRs**[10,11,14]

Classification Basis		*Type of MR*	*Comments*
Location	Superficial skin	MC	Located under the fingerprint ridges of hand, these receptors adapt rapidly and offer high sensitivity to mechanical stimuli.
		MD	Slowly adapting response formed by clusters of these structures.
	Deep subcutaneous tissue	PC	Similar to Meissner's corpuscles in morphology, larger but less densely distributed.
		RE	Senses skin stretch.
Adaptation rate	Slowly adapting	MD	Receptors can sense changes in stimulation over time and space. Rapidly adapting receptors stop firing when stimulus is constant, whereas slowly adapting receptors gradually adapt to a signal. When referring to adaptation rate, MDs are also called SA-I, REs are called SA-II, MCs are called RA-I, and PCs are called RA-II.
		RE	
	Rapidly adapting	MC	
		PC	
Excitation frequency	≤6.3 Hz	MD	Frequencies listed are ranges that can be used if a single frequency is used for the test. If multiple frequencies are used, then the discrete frequencies recommended to be used are 3.15, 4, or 5 Hz for MD; 20, 25, or 31.5 Hz for MC; 100, 125, or 160 Hz for PC. Note that REs are primarily active in sensing skin stretch and are not clinically useful for detecting a frequency response. This is likely due to their large size (five times larger in area than MD).
	16–32 Hz	MC	
	≥100 Hz	PC	
Function	Form and texture	MD	Sensitive to spatial features of an object such as edges, curvature, and orientation.
	Low frequency skin motion perception, grip, fluttering	MC	Provides feedback for gripping objects in hand and stroking or brushing of an object against the hand.
	High frequency vibration	PC	Accounts for human ability to sense high frequency vibrations by evoking action potential for every cycle.
	Perception of hand conformation and deep tissue strains	RE	Responsible for sensations perceived when the skin is stretched and the shape of the hand is changed.
Resolution	Fine	MC	Resolution is dependent on the size of receptive field and the density of receptors present in the area of stimulation.
		MD	
	Coarse	PC	
		RE	

MR = mechanoreceptor; MC = Meissner's corpuscles; PC = Pacinian corpuscles; RE = Ruffini's endings; MD = Merkel disk.

frequency range of 5–50 Hz appears to excite all MRs, it appears that PCs get excited more effectively in a stimulus frequency range of 100–300 Hz.[10,14,19] This type of quantitative sensory testing can be used as a means to identify earliest signs of nerve damage.[20–25] Thus, it is important to understand the parameters that affect this type of screening method for peripheral neuropathies to design an appropriate sensory test.

THE VIBROMETRY TECHNIQUE FOR EVALUATING NERVE HEALTH

Tests conducted for training the deaf to identify and interpret sounds by using the sense of touch have been used since the early 1920s.[26] The methodology of understanding auditory capacity of human beings was applied to the response elicited by a vibrating stimulus against the skin. It was hypothesized that just as a human ear can discern several frequencies within 10 octaves, the sense of touch should also have a range of frequency that can be felt.[26–28] The choice of frequencies for testing was purely experimental and was not based on the specific range of frequency that is now known and documented to excite a unique type of receptor. These early tests indicated that custom-designed hardware was necessary to understand the realm of touch sensitivity[26,29] in contrast to the simple tuning fork approach (derived from auditory tests) used in early experiments to investigate the range of frequency that could be felt by a human hand.[30]

Audiometry refers to tests of hearing ability, and the instrument used to conduct these tests is an audiometer, which provides different frequencies

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and pitches as a stimulus for the subject.[28] Because testing the sense of touch originated from hearing tests, it was aptly called vibrometry and the instruments that have been used were given a general name of vibrometers.[5,6,26,30–32] In the following sections, the fundamentals of vibration measurement, the features of a typical vibrometer, the various parameters that can affect the results, and the different testing protocols that have been used will all be discussed in detail.

Measurement of Vibration

Vibration can be thought of as an oscillatory motion of a body about an equilibrium point, and can be periodic or nonperiodic. For the purpose of this review, only sinusoidal (periodic) vibration will be discussed because it has been successfully used to excite all types of MRs. Because sound (pressure) waves are generated by an oscillating body, sound and vibration studies have been frequently analogous. This analogous nature of audiometry and vibrometry has been a key factor in the development of vibrometric devices and measurement practices.[33]

The amplitude of a sound wave is typically reported in pressure units (Newton per square meter, N/m^2), with the decibel (dB) used to provide a measurement of relative intensity of a pressure wave when compared with a reference level. Use of dB is practical when the ratio between two amplitudes is of more significance than absolute amplitude value and for audiometric measurements, the decibel reference level is the assumed minimum threshold of hearing ($0.00002\ N/m^2$).

Unfortunately, early vibrometeric measurements borrowed the use of the dB scale, which has led to a great deal of confusion. Vibrometry results that are reported in dB often refer to a change in intensity, with ''low intensity'' meaning a larger amplitude, and ''high intensity'' meaning a smaller amplitude. The use of dB units, originally intended to measure sound and pressure waves are somewhat unintuitive when applied to measuring and quantifying vibration. Measuring the amplitude of sound corresponds to a change in pressure with each oscillation, whereas measuring the amplitude of a vibration refers directly to the peak-to-peak distance of the oscillation about a fixed reference point. Also, the variation in amplitudes that can be detected on skin occurs over a relatively small range, which does not necessitate the use of a logarithmic scale to visualize changes.

Lately, the trend for reporting vibrometric measurements has been toward using the displacement of vibrating body from a fixed reference. This displacement, commonly reported in micrometers, is equal to one-half the amplitude of the oscillation, and thus provides a more insightful parameter for estimating threshold of vibration perception.[5] When compared with older studies that use dB, the amplitude in dB can be calculated from the ratio of the square of the measured amplitude (A_1) to the square of a selected reference amplitude (A_0), as in Eq. 1.

$$dB = 10 \log_{10}\left(\frac{A_1}{A_0}\right) = 20 \log_{10}\left(\frac{A_1}{A_0}\right) \quad (1)$$

Vibrometer Features

The international standards for mechanical vibration[34,35] provide recommendations for the various components and aspects of a vibrometer. The components of a vibrometer include a stimulator for producing vibration stimulus, a probe that transmits the vibration stimulus to the finger and is in direct contact with the subject's finger, and an optional firm surround encircling the probe to provide a finger rest, as shown in Figure 2. An optional finger or hand support (not shown in Figure 2) may also be included. In addition, a sensor for accurately determining the vibrating probe's position is desirable for correctly identifying the threshold of perception.

Parameters Affecting Vibrotactile Threshold Testing

The vibrotactile threshold (VT) is defined as the smallest displacement that can be detected by the individual undergoing a test. For a given individual, the VT varies depending on the type of hardware used, the psychophysical testing protocol used, the personal characteristics of the subject tested, and the testing procedure adopted. To account for the changes in the VT and to be able to use this tool for testing purposes, it is essential to understand the individual effect of these parameters.[36] The many factors affecting VT are detailed in Table 2.

The probe configuration, which includes the actual size and shape, and the location, affects the VT considerably. Because excitation of MRs is achieved directly by the stimulating probe, it is not surprising that the population of the MRs excited corresponds to the size of the probe. Increasing the size of contact decreases the VT because the sensitivity of the MRs

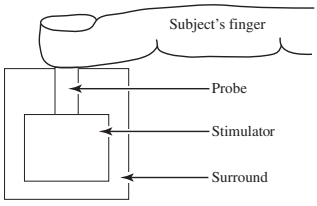

FIGURE 2. *Components of a typical vibrometer.*

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TABLE 2. **Factors Affecting the VT**

Parameter Affecting VT		*Effect on VT*	*Studies*
Hardware	Probe diameter	Decreased VT with increase in contact area.	[22,37]
	Surround	Absence of surround has been shown to cause an increase in VT at lower frequencies and a decrease in VT at higher frequencies.	[39,52]
Testing procedure	Vibration frequency	Choice of testing frequency affects temporal summation of PC channel.	[97]
	Amplitude	Correlation shown to exist between amplitude and perceived pitch of vibration.	[98]
	Contact location	No apparent effect on lower frequencies (with small contact area) but at higher frequencies, all locations except extreme tip of the finger shows decreased VT.	[22,37,40,99]
	Adaptation (training) frequency	Adaptation frequency (in the form of continued stimulation) has been shown to affect VT and the preactivation of MRs has been shown to stimulate the MRs to actively sense the variation in stimulus frequency.	[66,69–71,100]
	Wrist posture	Flexion of wrist may cause exaggerated CTS symptoms due to increased CT pressure.	[55,57,101–106]
Subject's characteristics	BMI	Obese subjects may have decreased sensory conduction.	[43,51]
	Age	Elevated VT with age possibly due to decrease in sensory input to brain.	[5,38,42,43,96,107]
	Alcohol and tobacco use	VT lower for drinkers than nondrinkers, with VT of drinkers highest among heavy drinkers (>180 drinks/d)	[5,43,48]
	Skin temperature	VT appears to increase with decreasing skin temperature. ISO 13091-1 recommends maintaining skin temperature in the range of 27–35°C and the testing room temperature in the range of 20–30°C.	[5,22,34,43,108,109]
	Skin hydration	No apparent effect of hydration level on VT was found but the perception of texture of a surface may be altered by hydration and skin condition.	[44]
	Gender	Females tend to have a higher perceived intensity of vibration stimulus than males. It was also found that discomfort associated with vibration may also be higher for females as compared with males.	[5,49]
	Upper limb disorders	Increased VT was reported for subjects with musculoskeletal disorders.	[73]
	Menstrual cycle	VT tends to be higher during menstruation and lower during nonmenstruation.	[45]
	Preexisting conditions	Preexisting neuropathies, exposure to vibration, musculoskeletal disorders, diabetes, peripheral neuropathies, and excessive burns have been shown to affect VT.	[23,24,58,63]
Psychophysical algorithm	Method of limits/ Von-Bekesy/staircase Forced choice	Choice of algorithm may cause a shift in VT.	[5,20,22,79,110]

PC = Pacinian corpuscles; VT = vibrotactile threshold; MR = mechanoreceptor; CTS = carpal tunnel syndrome; BMI = body mass index.

increases when a larger population is excited.[37,38] In addition, because some MRs are "edge detectors" (i.e., type I slowly adapting receptor), they are likely to exhibit enhanced activation by a probe with greater edge-to-surface area ratio.[10,14] Also, the probe size can alter the types of MRs that will be excited by a device at a particular frequency, so a careful selection of an appropriate probe size is necessary.

The surround for the probe affects the VT further by effectively limiting the area of stimulation. In other words, the vibration supplied by the probe is not transmitted to the entire finger, but the area within the surround. A decrease in the gap between the surround and the probe simulates an increased probe size and a corresponding increase in the VT is observed.[37–41]

The vibrotactile sensitivity shows a notable decline with age, resulting in a significant increase in VT, and thus, age must be accounted for during a VT evaluation.[5,42] Personal characteristics that have been frequently reported to affect the VT are skin temperature, skin hydration, and menstrual cycle.[41,43–45] The effect

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of skin temperature on VT has been studied by varying the skin temperatures in a controlled manner and recording the VT at each temperature; the temperature effect increases with an increase in the stimulus frequency of the stimulus.[5] However, studies often fail to mention whether or not a fixed limb temperature was maintained.[6,32,46,47] The effects of alcohol consumption on neurological perception is complex, with all drinkers having slightly lower VT compared with nondrinkers, and heavy drinkers (those consuming >180 drinks per month) having the highest VT among all drinkers; however, significant associations between VT and alcohol consumption have not been identified.[48] Gender affects the perceived stimulus intensity, with females showing a greater vibrotactile sensitivity at high frequencies than males, and sensitivity to change in a stimulus more apparent at certain frequencies (31.5, 63, 125 Hz) in females than males.[43,49,50]

Obesity has been suspected as a factor leading to altered metabolism causing slower motor latencies, and eventually leading to peripheral neuropathy.[51] Body mass index (BMI) and the VT have been shown to have a significant correlation.[5,43] However, in some studies focused on BMI, gender was not found to affect the slope of decline in vibrotactile sensitivity with age.[5,42] Such contradictory study results in the literature emphasize the need for standardization of testing devices and protocols so that any actual differences can be more clearly attributed to subject characteristics rather than differences in equipment or protocols.[5,41]

The frequency of stimulation used for testing determines the type of MR excited (Table 1). MRs are differentiated by the size of receptive fields and other distinctive features (e.g., shape, size, and locations). This results in the selective excitation of PCs at frequencies above 100 Hz. Merkel discs are active below 6.3 Hz, and Meissner's corpuscles are activated between16 and 32 Hz.[6,10,14,18] These unique properties of individual MRs have been used to develop vibrometry techniques to identify information about the innervating nerve.[52–54] For an impaired nerve, the VT is increased, meaning that a larger displacement is necessary for sensation to be observable by the individual. It is important to note, however, that although VT may be increased, the etiology may vary significantly for different conditions. For instance, low sensitivity of MRs originating from degeneration of distal axons may cause an increase in VT in the case of dying-back neuropathies such as diabetes and chemically induced neuropathies. In contrast, the VT may be increased in the case of CTS because action potentials are blocked at the area of entrapment of the median nerve, whereas the MRs may retain full sensitivity as long as they receive adequate blood flow.[55,56]

This feature can be exploited to examine and evaluate nerve health and MR response of a subject. For instance, clinical symptoms of neuropathies caused by hand–arm vibration syndrome (HAVS) can be similar to the symptoms of CTS. Careful VT testing can be used to distinguish between these, because an increase in the VT at a frequency of approximately 256 Hz is indicative of early CTS.[57–59] Identification for HAVS requires testing at multiple frequencies (e.g., 8, 16, 32.5, 65, 125, 250, and 500 Hz).[15,60] A ''tactilogram'' or ''vibrogram'' can be drawn by plotting the testing frequency on the X-axis and the VT expressed in dB on the Y-axis. For a normal subject, the trend is typically almost a straight line parallel to X-axis for frequencies between 8 and 125 Hz interrupted by a peak in the range 125–250 Hz due to a higher perception of PCs as compared with other types of MRs.[32] However, for a subject exposed to HAVS, the distinctive peak within the frequency range of 125 and 250 Hz starts becoming smaller to almost flat depending on the extent of exposure.[59,61]

The range of frequencies that has historically been used is broad (Table 3). Some studies used a stimulus picked randomly from a particular frequency range for testing the subjects.[46,62] It appears that often the choice of testing at a particular frequency is dependent on the hardware limitations. For instance, due to such equipment constraints, several studies have performed tests at 100 and 120 Hz.[12,63–65] These frequencies appear to have been implemented because they are related to the operating frequency of the supply voltage (50 Hz with a 220 V supply, 60 Hz with a 110 V supply). Thus, selection may have been more of an ''engineering convenience'' than a scientifically driven decision.

The effect of continued stimulation has been shown to elevate VT and this phenomenon has been referred to as ''vibration adaptation.''[30,66] Adaptation to a frequency offers an insight in the mechanism and scope of receptor ability of detecting a vibration stimulus. Because the magnitude of a stimulus and the perceived intensity during recovery from an adaptation frequency follows the same law (Stevens' power law[67]) that governs a test frequency response for a receptor, it appears that the role of adaptation is not a reflection of fatigue of receptor system.[66,68] Providing an adapting frequency (i.e., a different frequency than that used for testing) before the actual test improves the ability of the receptors to discriminate between frequencies. This has been credited to the ''preactivation'' of mechanosensory channels, which then respond more actively as the variation in stimulus is decreased.[53,66,69–72]

Psychophysical Testing Protocol Used

Psychophysics is a branch of psychology, first developed by Gustav Theodor Fechner, which explores the relationship between a particular physical

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TABLE 3. **Frequency Selection and Applications of VT Testing**

Reference	*Frequency (Hz)*	*Application*
[41]	31.5 and 125	VT and normative data from five European centers.
[80]	31.5 and 125	VT for Malaysian population.
[111]	4, 32, and 125	Nerve conduction and sensorineural function in dental hygienists.
[112]	120	VT of computer users and nonusers.
[56]	100	Sensory perception in female computer users and nonusers.
[81]	25, 40, 80, 100, 150, 250, and 300	VT for patients with trigeminal neuralgia.
[75]	30 and 200	Tactile perception in subjects with hypersensitivity to touch.
[82]	8, 16, 31.5, 63, 125, 250, and 500	Using VT for early detection of peripheral neuropathies.
[46]	8, 16, 31.5, 63, 125, 250, and 500	VT for various neuropathies.
[96]	120	VT for peripheral nervous system damage caused by neurotoxins.
[113]	4, 6.3, 20, and 32	Changes in VT to diagnose peripheral neuropathy by focusing separately on different mechanoreceptive channels over time.
[59]	16, 32, 63, 125, 250, and 500	Exposure to hand-arm vibration and elevated VT.
[114,115]	20–3,000	Peripheral neuropathy in subjects exposed to hand-arm vibration.
[83]	4, 25, 31.5, 63, 125, 250, 400, and 500	VT perception and hand-arm vibration syndrome in Poland.
[116]	125	Use of thermotactile testing for vibration-induced neuropathy.
[117]	120	Use of vibrometry methods for detection of CTS.
[118]	1, 10, and 300	Effectiveness of VT diagnostic method for CTS.
[119]	120	VT for detection of CTS (sensitivity and specificity measured).
[120]	120	Changes in vibrotactile threshold and the effect of keyboard usage in subjects experiencing repetitive strain injury.
[74]	100	Effect of upper limb disorders on VT.
[43]	120	Covariates of VT including skin temperature, height, and age.
[42]	100	Changes in vibrotactile sensitivity with age and other factors including BMI, height, and glucose level.
[121]	30 and 200	Effect of age on vibration detection threshold.
[122]	31.5 and 125	Change in normal values of vibrotactile and thermotactile thresholds between males and females with age.
[45]	120	Effect of menstruation on vibrotactile threshold.
[51]	Two ranges: 2–20 and 10,000–20,000	Effect of obesity on sensory nerve-response amplitudes.
[76]	20, 50, 100, and 200	Vibrotactile frequency discrimination in hairy and glabrous skin.
[77]	20, 80, and 160	Detection of vibration threshold on hairy and glabrous skin.
[44]	1, 10, 100, and 250	Effect of immersing skin in water on VT.
[123]	100	Effect of time on sensory perception on computer users.
[37]	8, 16, 31.5, 63, 125, and 250	Effect of location of measurement on the VT.
[38]	10, 25, 50, 80, 120, 160, 200, 250, 320, and 400	Effect of a rigid surround for spatial summation.
[18]	0.4–500	Receptors for tactile sensations at different frequencies.
[124]	5, 6.3, 8, 10, 12.5, 16, 20, 25, 31.5, 40, 50, 63, 80, 100, 125, 160, 200, 250, 315, and 400	Effect of local vibration on vibrotactile perception.
[125]	50	Effect of rapid displacements of skin on sensory perception.
[79]	16, 31.5, 63, and 125	Dependence of psychophysical method on VT.
[40]	31.5, 63,125, and 250	VT using two methods of controlling the contact of probe on skin.
[69]	25 and 200	Effect of preexposed skin to the two-point stimulus discrimination.
[126]	25 and 200	Ability to distinguish between two-point stimulus on skin.
[127]	10 and 25	Multipoint stimulus using portable tactile device.
[84]	25 and 200	Effect of two-site vibrotactile stimuli at variable distances.
[32]	8, 16, 33, 65, 125, 250, and 500	Use of vibrograms for assessing vibrotactile perception.
[6]	8, 16, 33, 65, 125, 250, and 500	Use of digital vibrograms as tools for sensory testing.
[128]	30, 60, 120, 240, and 480	Validation of high-resolution vibrometry for CTS detection.
[73]	Learning 100, testing 31.5, 63, 125, and 250	Validation of device to measure VT in asymptomatic population.
[129]	120	Validation of a portable device to measure VT with age and gender.

VT = vibrotactile threshold; CTS = carpal tunnel syndrome; BMI = body mass index.

stimuli and the way it is perceived by a subject. A stimulus that can be objectively identified and perceived must have a threshold, meaning that below a certain threshold, the stimulus cannot be perceived, while above the threshold the stimulus can be perceived. Several methods have been developed to test stimulus perception.[21,41,73] For VT testing, the protocols that have been used most frequently in the literature are method of limits (MOLs),[5,21,41,42,46,74–78] and the Von-Bekesy algorithm, which is a type of MOL,[37,40,46,77,79–83] and the forced-choice method (FCM).[21,37,41,69,74,84] MOL can be either ascending or descending, where the stimulus is gradually increased to the point of detection or decreased to the point of no perception, respectively. In the Von-Bekesy algorithm, continuous stimulation is applied with varying amplitude. The test is started at a selected frequency with large amplitude so the subject

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can easily detect the stimulus. The amplitude of the stimulus is then reduced in steps until it is no longer detectable. At this point, the staircase is reversed starting with a subthreshold amplitude and increased until detected, until the threshold is isolated.[34,79] In FCM, the subject is presented with the stimulus in predefined intervals of time and the subject is asked to identify the particular interval in which the stimulus occurred. Studies involving these different testing protocols are summarized in Table 4.

The choice of testing protocols has typically been dependent on the type of equipment used, with MOL used most frequently. It appears that protocols for commercially available VT equipment have often been selected based on the time efficiency and not the efficacy of the protocol. Using older equipment, a drop of 3–6 dB was found between the MOL and Von-Bekesy protocols, with FCM lower than the threshold obtained by Von-Bekesy by a drop of 2.2 dB. The lower thresholds identified with FCM may be due to the subject finding it easier to differentiate between signal and no signal than to identify the signal as it gets smaller or larger, or may be due to the response characteristics of MR system.[79]

The presence of bias related to MOL and FCM has been recognized but this bias has not been empirically estimated.[5,79] A consensus has not been reached on recommendation of one particular procedure, so equipment should provide sufficient flexibility in testing protocol because it is difficult to directly compare results when different testing methods are used.

COMPARISON OF TECHNIQUES CURRENTLY IN USE

Originally developed from audiometric testing devices used to screen the extent of hearing damage, the early vibrometry devices used in the 1970s show clear modifications of the audiometric devices that

TABLE 4. **Psychophysical Testing Protocols Used for VT Testing**

Reference	*Psychophysical Method*	*Description of Study*
42	MOLs	Amplitude changed in steps of 0.5 μm, at 100 Hz.
121	MOLs	Amplitude changed in steps of 0.17 μm at 200 Hz and 1.03 μm at 30 Hz.
74	MOLs	Amplitude increased in steps of 0.01 μm at 100 Hz.
75	MOLs	Amplitude decreased in steps of 1 μm at 200 Hz, 3 μm at 30 Hz.
59	MOLs	Amplitude increased and decreased at the rate of 3 dB/sec.
113	MOLs	Amplitude increased and decreased at the rate of 2 dB/sec.
51	MOLs	Six tests, with amplitude rates between 0.1 and 130 μ/sec, with 4-sec interval.
37	Von-Bekesy	Amplitude increased at the rate of 5 dB/sec before the first response, followed by 3 dB/sec after the first response.
83	Von-Bekesy	Amplitude increased and decreased at the rate of 4 dB/sec before the first response, followed by 2 dB/sec after the first response.
80	Von-Bekesy	Amplitude increased and decreased at 3 dB/sec, ISO 1309-I equipment.
73	Von-Bekesy	Amplitude increased and decreased at the rate of 5 dB/sec; frequencies included 31.5, 63, 125, and 250 Hz.
40	Von-Bekesy	Amplitude: initial rate was 5 dB/sec, and testing step rate was 3 dB/sec.
122	Von-Bekesy	Amplitude rate of 3 dB/sec; measurements taken for at least six reversals.
77	Von-Bekesy	Various durations (100, 400, 800 msec), and step sizes at different frequencies (for hairy or glabrous skin: 14.6 or 4.6 μm at 20 Hz, 5.0 or 1.2 μm at 80 Hz, 1.7 or 0.4 μm at 160 Hz).
46,82	Von-Bekesy	Standardized frequencies in one-octave bands used, with every frequency tracked for 35 sec (audiometry techniques used).
81	Von-Bekesy	Use of Von-Bekesy attenuator to drive Goodman's V-47 vibrator.
44	Two-alternative forced choice	Amplitude decreased by 1 dB after three correct responses and increased by 1 dB after one incorrect response.
18	Two-alternative forced choice	Amplitude decreased/increased by 1 dB/sec for correct/incorrect responses.
127	Two-alternative forced choice	Interprobe distance varied (5, 10, 20, and 30 mm).
43	Two-alternative forced choice	Amplitude decreased by 10% after two out of three correct responses.
76	Two-alternative forced choice	Three trials at each frequency (20, 50, 100, 200 Hz) repeated every 5 sec, with a 1-sec vibration train superimposed on a 1-mm step.
38	Three-alternative forced choice	Amplitude decreased by 3 dB until two reversals, then by 2 dB until the third reversal, then by 1 dB after three consecutive correct responses.
41	MOLs, Von-Bekesy	MOLs: 5 dB step; Von-Bekesy: amplitude rate: 3 dB/sec.
79	Forced choice, Von-Bekesy	Forced choice: amplitude decreased by 2 dB after three correct responses and increased by 2 dB after one incorrect response. Von-Bekesy: amplitude testing rate of 5 dB/sec and initial rate of 3 dB/sec.

MOL = method of limit.

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inspired this field.[24,31,39,85] The stimulus was delivered in the early devices by shakers, and amplifiers remained common for both vibrometric and audiometric devices. The Brüel & Kjær vibration exciter and power amplifiers were used in later (but still relatively early) commercial VT testing devices.[6,32] Sensortek Inc., Somedic Sales, HVLab developed and marketed other more recent commercially available VT testing equipment.

It is evident from this literature review that VT evaluation techniques are still not completely standardized although international standards exist (ISO-13091-1 and ISO-13091-2).[34,35] The relevant recommendations are summarized in Table 5.

Variations in testing protocols, contact conditions, hardware, and several other parameters make it very difficult to directly compare results from different studies. To compare devices and their specifications, Table 6 shows a detailed summary of the equipment parameters of existing devices used for VT testing. Systems in use have many variations in the type of hardware geometry, testing protocol, and testing frequency used. Certain devices offer more range of testing frequencies than others. The probe size and geometry also differ greatly from device to device as does the way in which the probe is interfaced with the subjects' fingers. In addition, probes differ not only in size, but also in the presence or absence of a firm surround.

LIMITATIONS OF VT TESTING

Advancement of a scientific technique is aimed toward not just a better understanding of the fundamental science behind it, but also acknowledging the associated limitations, and this review would not be complete without a thorough discussion of the limitations of VT testing. It is important to note that because the gold standard (for diagnosing CTS) NCV testing measures electrophysiological health of a nerve while the VT testing evaluates the sensory function the results from such tests cannot be directly compared. Other challenges, discussed in more detail in this section, include the challenge in selectively exciting and in fully understanding MR responses, the expense of available VT equipment, and the broad variety of features and lack of standardization in existing devices.

Although the classification of MRs in Table 1 describes the response from a particular type of MRs for VT testing, MRs may be stimulated at a frequency above or below the frequency range associated with it as long as the amplitude is appropriately adjusted. Early theories on the mechanism of perception of touch by neurophysiologists such as Ernst Weber, Max von Frey, Johannes Miller, Alfred Goldscheider, Magnus Blix, and Henry Donaldson, to name a few, were faced with criticism based on lack of anatomical evidence and assigning a receptor only one specific function. For instance, Max von Frey initially suggested the model of skin to be similar to a "mosaic of sensory spots" for touch, cold, warmth, and pain. It was later found that that there are several types of receptors that work together rather than in isolation.[86] Thus, it appears that the simultaneous excitation of several types of MRs may affect VT testing results depending on the testing parameters used. In addition, some MRs have been characterized in great detail at lower frequencies, not all MRs have been explored completely, and work remains to complete investigating MR response at high frequencies (>250 Hz). The classification of MRs based on frequency of excitation should be used as a reference while keeping in mind the relative and approximate nature of the information.

Although current units for VT testing have costs similar to NCV units, this is mainly due to development costs vs. capital costs and operating costs of a commercially available unit. As VT testing moves from the laboratory into the clinic, economies of scale

Q10 ***TABLE 5.* Relevant ISO Recommendations, Adapted from Table 1 in Ref. 34**

		Frequency	*Intermittent*	*Continuous*
	Desired Mechanoreceptor	*Primary; Others*	*Burst; Quiescent*	*Duration; Rest*
Testing frequency	Merkel discs	4.0; 3.15 or 5.0 Hz	<10 sec; ≥0.6 sec	≤50 sec; ≥30 sec
	Meissner's corpuscles	31.5; 20 or 25 Hz	<10 sec; ≥0.6 sec	≤50 sec; ≥30 sec
	Pacinian corpuscles	125; 100 or 160 Hz	0.6–10 sec; ≥0.6 sec	≤50 sec; ≥30 sec
Probe* and Surround†	Edge Radii	Diameter	Gap	Surround Force
	0.2 mm ≤ r ≤ 0.7 mm	4.0 ± 2.1 mm	1.5 ± 0.6 mm	0.7–2.3 N
Subject	Room Temperature	Skin Temperature	Support	
	20–30°C	27–35°C	Forearm, hand, finger, seat with back rest	
Psychophysical Algorithm		An up-down variant‡ or Von-Bekesy		

*Probe: a smooth flat-ended cylinder.
†Surround: may be omitted.
‡Both method of limit and forced-choice method can be implemented as a variation of up down (i.e., amplitude decreased or increased corresponding to correct or incorrect answers).

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TABLE 6. **Comparison of Equipment Parameters Used for VT Testing**

Reference	*Yr*	*Authors*	*Device Used*	*Probe*	*Use of surround, temperature maintained, contact force, etc.*
130	2010	Brammer et al.	Tachometer	3 mm	No surround, skin temperature maintained at 27°C, contact force 0.05 N
131	2009	Wu et al.	PVC polymer probe with computer-aided displacement-controlled protocol	4 mm	No surround, different probe-skin contact angles used
61,132	2007 and 2009	Duke et al. and Temlett	Biothesiometer (Cleveland, OH)	13 mm	No surround, essentially an improved electronic tuning fork
122	2008	Seah and Griffin	HVLab Tactile Vibrometer (HVLab, UK)	6 mm	Surround, skin temperature maintained between 27 and 35.2°C, contact force 2 N
113	2007	Brammer et al.	Tachometer	3 mm	No surround, skin temperature maintained at 27°C, contact force 0.05 N
55	2007	Sesek et al.	VT tester	1 mm	Surround (2 cm), hemispherical cover for testing different finger locations
42	2007	Deshpande et al.	Medoc VSA 3000 (Advance Med. Systems, MN)	1.25 cm	Tested on feet, temperature maintained at 32°C, amplitude 0.5 μm
76	2006	Mahns et al.	Perspex probe with feedback-controlled mechanical stimulator	4 mm	Index finger secured with plasticine, forearm secured in plastic chamber
75	2006	Blakemore et al.	Model 101 (Ling Dynamic Systems, UK)	N/A	Waveform amplified by Stereo Amp (Marantz PM520DC)
74	2006	Laursen et al.	Vibrameter (Somedic, Sweden)	13 mm	At room temperature 22–23°C, hand rested on rice pillow, 650 g pressure
37	2006	Whitehouse et al.	HVLab Tactile Vibrometer (HVLab, UK)	1 mm 6 mm	At room temperature 23 ± 2°C, mean finger temperature 32.8°C, 2 N force maintained, subjects exposed to 70 dB white noise, 5 different test sites, 1-mm gap for 1-mm probe, 2-mm gap for 6-mm probe.
111	2006	Cherniack et al.	Laboratory tachometer (meets ISO-13091-1)	3 mm	Static force of 0.05 N, calibrated using reference signal
49	2006	Neely and Burstrom	Modified version of Von-Bekesy audiometer (Briel & Kjær 1800/WH 1763, Denmark)	N/A	No surround, arm abduction 0° and arm flexion 180° (ISO 5349-1), frequencies generated by Ling Dynamic System 406 vibrator
83	2005	Harazin et al.	P8 Pallestheisometer (EMSON-MAT, Poland) Vibrotactile meter MCW 2K (Poland)	5 mm 10 mm	No surround, contact force: 0.1 N Surround: 16 mm, contact force: 2 N
51	2005	Miscio et al.	Medoc TSA ii-2001 and VSA 3000 (Advance Med. Systems, MN)	N/A	Amplitude 0.1 and 130 μm, temperature maintained at 32°C
123	2005	Pilegaard and Jensen	Vibrameter (Somedic, Sweden)	13 mm	Constant probe pressure 650 g
84	2005	Tannan et al.	Two CS-525 vertical displacement stimulators (CantekMetatron Corp., Canonsburg, PA)	N/A	Two-point stimulators with range of separation 0–40 mm (each independently controlled)
69	2005	Tommerdahl et al.	CS-525 vertical displacement stimulator (CantekMetatron Corp., Canonsburg, PA)	8 mm	Surround
112	2005	Sanden et al.	Vibrameter (Somedic, Sweden)	13 mm	Pressure display: 8.1 N/cm², 0.4 N maintained by subjects
80	2004	Daud et al.	HVLab Tactile Vibrometer (HVLab, UK)	6 mm	Surround: 10 mm

41	2003	Lindsell and Griffin	HVLab Tactile Vibrometer (3/5 locations)	6 mm	Contact force: 1 N, push force: 2 N
			Self built system (1 location)	1.26 mm	Contact force: 0.2 N, no surround
			Brüel & Kjær shaker (1 location)	6 mm	Contact force unspecified, no surround
47	2003	Roberston et al.	Acrylic probe (Ling Dynamic Systems, UK), Frequency gen. E326A (Grason-Stadler, WI)	2 mm	Forces monitored by force transducer (Brüel & Kjær Model 8001, Denmark)
116	2002	Sakakibara et al.	Vibrometer AU-02B (Rion, Japan)	N/A	Contact force: 0.5 N
62	2002	Hillstrom et al.	Oticon-A bone-conductors (hearing aids)	1.6 cm	Tactors covered in foam, plus pink noise via headphones
56	2002	Jensen et al.	Vibrameter (Somedic, Sweden)	13 mm	Contact force: 650 g wt.
73	2001	Wild et al.	HVLab Tactile Vibrometer (HVLab, UK)	6 mm	Surround: 10 mm
44	1998	Verrillo et al.	Shaker beneath a rigid surface as in ref. 16	3.7 mm	Skin temperature monitored by thermistor embedded in rigid surface
120	1998	Greening and Lynn	Vibrameter (Somedic, Sweden)	1 cm	Contact force: 50 g wt.
45	1997	Espritt et al.	Vibratron-II (Physitemp Inc., Clifton, NJ)	N/A	Contact force: 0.1 N, tests conducted at room temperature
119	1995	Gerr et al.	Vibratron-II (Physitemp Inc., Clifton, NJ)	1.4 cm	Calibrated using GY-125-10 accelerometer (Kulite Corp., NJ)
128	1995	LaCourse and Miles	Two speakers mounted axially and back to back in closed chamber	2.54 mm	Probe: blunt pin, amplitude ±20 μm resolution
43	1994	Gerr and Letz	A prototype of Vibratron-II (Physitemp Inc., Clifton, NJ)	N/A	Probe: hardened rubber postprotruding through a plexiglass plate
59	1992	Virokannas	Modified equipment from Brüel & Kjær (Denmark)	2.6 mm	Contact force: 0.2 N, temperature monitored by thermocouple (YSI 400-series probe, Yellow Springs Instrument, USA) to above 28°C
46,82	1992	Lundborg et al. and Lundstrom et al.	Refinement of system in ref. 30 and ref. 6	2.5 mm	Contact pressure: 3.5 N/cm^2
133	1987	Brammer and Pyykko	Custom equipment with accelerometer, device shielded by Faraday cage	N/A	Amplitude: 35 dB, finger restraint used, finger motion calibrated
6,32	1987 and 1986	Lundborg et al.	Modified Von-Bekesy audiometer (Brüel & Kjær 2850, Denmark	2.5 mm	Probe had a 5 mm^2 tip
124	1985	Lundstrom	Vibrations from a shaker driven by power amp and controlled by computer	2.5 mm	Contact pressure: 0.8 N/m^2, accelerometer mounted between shaker and probe
77	1985	Hamalainen et al.	Brüel & Kjær 4810 minishaker (Denmark)	2 mm	Calibrated by piezoelectric accelerometer (Brüel & Kjær 4339)
78	1981	Rhodes and Schwartz	Pallometer head and vibratable probe as in ref. 134	6 mm	Surround: 8 mm, contact force: 100 g
81	1977	Verrillo and Ecker	Von-Bekesy attenuator driving a Goodman's V-47 vibrator	9.6 mm	Calibrated by an accelerometer, subject and device inside a sound- and vibration-isolated booth

VT = vibrotactile threshold.

will drive costs for the VT units down. Operating costs for the VT are very low with no consumable components and the ability to conduct the tests on-site very quickly and with immediate results that require little interpretation. These aspects make the VT an attractive means of workplace surveillance. Although an agreed upon standard has not yet been determined, relative comparisons can be made within individuals. Once a baseline threshold has been determined for an individual, patients can be routinely evaluated and compared against their personal baselines.

The comparison of existing VT testing devices (Table 6) makes it clear that there are large variations used in testing parameters and hardware. This variation makes it difficult to identify one device over another as optimal, and is further complicated by many devices lacking or having poor force control or other inherent inaccuracy of hardware.[87] The importance of force control in sensory testing is necessary for the reliability and repeatability of results.[87–90] Methods to quantify sensory function exist without a general consensus and efforts have been made to develop a well-rounded set of tests to assess clinically relevant aspects of somatosensory function.[91] A study conducted by Bell-Krotoski and Buford to quantitatively measure and simulate force applied by the most commonly used sensory testing instruments (Semmes Weinstein monofilaments were simulated as a paper clip and vibration instruments were simulated as a tuning fork; customized strain gauges were used to measure the applied force) demonstrated that the paper clip had higher reliability than the tuning fork.[88] A wide range of force signals, such as were produced by the hand-held tuning fork, are incapable of selective stimulation of just one type of MR.[92] Although these are certainly drawbacks of the VT test, it is important to recall that two-point discrimination tests have also been critiqued by Lundborg and Rosen[93] for the lack of standardized testing protocol for how much pressure should be applied for testing. Providing an elaborate description of testing protocol for evaluating studies including the starting distance used, number of times the test was performed, use of blunted end needle, and the amount of pressure applied has been emphasized.[93,94] In summary, because most devices currently in use for sensory testing provide a unique set of hardware, software, and testing protocol, it important to conduct dedicated studies to compare results from different devices and algorithms.[95]

To address these challenges, three laws of measurement have been described by Buford[92] for improved objective measurement of sensory function in clinical setting. The first law (law of perturbation) describes that care should be taken to not affect the signal of interest while it is being measured. As discussed above, because the dynamics of hand-held devices are likely to be affected by the user, stationary devices should be used. The second law (law of selectivity) states that the method of measurement should selectively measure and respond to only to the desired signal. Many existing VT testers are likely to excite numerous MRs although it is generally desired that only one type of MR be stimulated. The third law (law of precision and variance) emphasizes the importance of knowing the extent of variance of the function being measured to determine the precision of the device measuring it. As described above, a complete understanding of MR response at frequencies greater than 250 Hz remains a research topic. Dyck et al. have provided comprehensive and controlled data on human sensory function that has been used for the evaluation of variance in human sensory function for clinical testing of tactile function. Attention to these laws of measurement can benefit the hand therapist in evaluating the results of VT testing.

CLINICAL APPLICATIONS

The VT test has many relevant applications for clinical hand therapy practice. Longitudinal studies are recommended to prospectively study the VT in environments that have relatively high rates of hand/wrist disorders. Such studies would help elucidate how well the VT correlates over time with the development of hand/wrist disorders. These studies should include and account for occupational exposures and personal characteristics. Multiple VT protocols with varying frequencies, forces, presence or absence of a surround, etc. should be compared to determine the most optimal and cost-effective protocols for VT surveillance. Until the limitations described previously have been addressed, of course, the VT should be thought of as a compliment to NCV and MRI, rather than as a replacement for them.

It is understood that the VT, NCV, MRI, and other evaluation methods are not measuring the same thing. However, each can be used independently to monitor for changes that might be indicative of the development of a hand/wrist disorder. In this respect, the VT has the advantage of portability and a simpler testing protocol with less need for medical expertize for interpretation (as is needed with NCV and MRI). When changes are detected, referral to a medical expert would be appropriate. Medical professionals would determine the need for further testing, which could include more sophisticated means of evaluation such as NCV or MRI. Although multiple tests could be used to provide medical experts with a more complete view of a patient's condition, only the VT represents a simple means of workplace surveillance that could be used noninvasively and with minimal interruption to work flow.

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As these limitations are resolved, there are many applications in which VT testing can be implemented in the hand therapy clinic. First, when compared with conduction velocity measurement, the VT test is quick, does not require electrode placement, and in addition because it is noninvasive and non-noxious, patients will not mind being retested as often as necessary. The only costs are for the equipment and there are no disposable costs. When used under physician supervision (especially certified hand and/or microsurgeon), reimbursement is often possible. Secondly, because the result of a VT test is a quantitative assessment, there are many areas in which the VT test could be used to improve the treatment of patients. For instance, the VT test can be used to compare baseline pretreatment or presurgery with posttreatment outcomes, and thus it can be used to compare efficacy of different treatment outcomes to determine which treatment is best. Similarly, it can be used in outcomes-based management to quantitatively document results following a therapy protocol. Thirdly, for hand therapy clinicians who see patients with nerve issues related to employment, VT tests have several workplace applications. Quantitative assessment of sensory threshold can help in making return-to-work decisions and in providing a justification of those decisions. Because elevated sensory threshold can be linked to job function, it can help justify worker compensation or disability claims. Repeated testing using appropriate, randomized protocols can help in distinguishing malingering scenarios. Quantitative assessment can help in making therapy decisions such as what form of therapy seems to work best for specific patients with specific injuries or in specific work environments such as choosing between the use of nonsteroidal anti-inflammatory drugs, physiotherapy, and splints.

Use of VT testing for evaluation, screening, and diagnosis of a wide range of conditions has been reported in the literature. Specific examples include detection of neurotoxicity to peripheral nervous system by Gerr et al. with high reliability using Vibratron-II (Sensortek Inc., Clifton, NJ).[96] Identifying changes in threshold by a change in the shape of a ''normal'' vibrogram by Lundstrom et al.[82] has showed the clinical utility of VT testing. More recently, Sesek et al.[55] described the use of VT testing by establishing a baseline for normal threshold for an individual and comparing subsequent changes in the threshold after wrist bending, and observing that the change in VT before and after wrist bending provocation is more significant in subjects showing signs of CTS than in normal subjects. Although further research is needed, this result suggests that the wrist bending provocation in conjunction with VT testing may provide a rapid method of identifying patients in the early stages of CTS.

CONCLUSION

The existing equipment for testing the VT has progressed from a very primitive form of testing based on protocols intended for conducting hearing tests to commercially available products with varying degrees of portability and versatility. Immense variation in probe sizes, equipment geometries, and testing protocols are evident in the literature. The biggest weakness of both the literature in this area and the commercially available equipment is the lack of standardization of these features. It is very difficult if not impossible to compare a VT obtained from two different probe sizes, stimulus protocols, and types of equipment. Although it has been shown that the effect of a surround is appreciable, the use of surround with the probe is not consistent across studies. Although the effects of limb temperature and surrounding environmental conditions are well documented, studies often do not report limb temperature, or whether a fixed limb temperature was maintained. In addition, decibels (dB) were used to characterize sinusoidal stimuli in early devices, but have been replaced by micrometers in recent devices, an improvement that allows direct analysis of results. Further research is required for a complete understanding of MR response, particularly at high frequencies above 250 Hz.

The literature does provide strong evidence that VT evaluation is an important and useful tool for investigating early nerve damage. For maximum flexibility in evaluating changes in nerve health, VT equipment should provide the ability to adjust probe size, firm surround, and testing frequency. More thorough research is required to determine the most appropriate protocols for the evaluation conducted; ideally VT equipment should provide a choice of protocols. Further development of VT techniques—such as the wrist bending provocation proposed by Sesek et al.—could provide improved methods of evaluating nerve damage at a very early stage. This will enhance new applications including investigation of neuropathies resulting from neurotoxic drug treatments or diabetes, and use of vibration in feedback devices for rehabilitation and treatment. Once the limitations of equipment variation and high cost (due to limited availability rather than inherent components) are overcome, there are many ways in which VT equipment can enhance a hand therapy equipment, including providing a quantitative method of regular evaluation, which can be used throughout therapy, to investigate alternative therapies or pre- and postintervention, and to assist in a variety of work-related issues such as justifying worker claims or return-to-work decisions.

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CHAPTER 4

VALIDATION STUDY OF A NOVEL DEVICE TO EVALUATE THE VIBROTACTILE THRESHOLD

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4.1 Abstract

A novel device for testing the vibrotactile threshold is presented. This paper presents the initial prototype design of a vibrotactile threshold evaluator for the workplace (VTEW), which is portable and configurable in terms of the probe diameter (2-10 mm), applied frequency (1-500 Hz), angle of probe (0-120^0), and displacement of probe (1-1500 μm), and is operated with a customizable LabView interface. The vibrotactile threshold (VT) at 50 Hz was evaluated using VTEW and an established device, the Vibrotactile Tester (VTT). These results were compared for validation of VTEW. The results were statistically similar and the age corrections developed for both devices from this study were similar to the previously conducted studies on VTT. Each subject underwent Phalen's and Tinel's test, and the results of these clinical evaluations for carpal tunnel syndrome (CTS) were used to classify subjects as symptomatic and asymptomatic. The mean VT values of all subjects based on this classification showed an increased VT for symptomatic subjects. The low frequency range of the VTEW was used to evaluate the VT at 4 Hz, and a comparison of VT at 4 Hz and 50 Hz showed a higher sensitivity of subjects to 50 Hz as compared to 4 Hz. The gender effect on VT was also studied and discussed, along with recommendation for further investigation.

4.2 Introduction

The word 'vibrotactile' combines vibration and tactile, which can be interpreted as perceiving vibration through touch. The minimum amplitude of vibration that is perceived at a particular frequency by a subject tested using a vibrotactile device is called the vibrotactile threshold (VT). Two international standards, ISO 13092-1 and ISO 13092-2, for measuring vibration and using VT for assessment of peripheral neuropathies

have been developed for standardizing the testing parameters, equipment, and analysis of data collected [1-2].

Carpal tunnel syndrome (CTS) has been well recognized in the literature as a debilitating condition that is a result of median nerve compression in the human hand leading to pain, tingling, and numbness in thumb, index finger, and middle finger. These symptoms are often more pronounced nocturnally [3]. CTS has been reported to cost over $20 billion in workers' compensation annually with an average of over 31 days of lost work per case. Surgeries related to CTS cost over $1 billion annually and have been reported as the most common cause of surgeries for hand and wrist [4-5]. Use of small electric impulses to determine the nerve conduction velocity and compare it to normative values provides a standardized method for diagnosing CTS. However, this method is expensive, requires specialized training, and has been reported to cause discomfort to the subjects being tested.

Efforts since the 1920s have resulted in producing tools that evaluate the condition of the median nerve by assessing sense of touch using vibration stimuli applied directly to the hand [6]. Mechanism of tactile perception, via sensory receptors known as mechanoreceptors, has been well studied and demonstrated to be of use in evaluation of peripheral neuropathies [7-11]. Analogous to tests conducted for evaluating hearing ability (audiometry), tests conducted for evaluating sensory conduction (vibrometry) aid in screening subjects with an altered nerve conduction response, such as that associated with CTS. Vibrometry can be used as a tool for periodically screening employees for CTS at the workplace [12-15]. In addition, evaluating other peripheral neuropathies, dying-back neuropathy, vibration-induced and chemotherapy-induced neuropathy are

other conditions that have been assessed using various VT measuring devices [16-19]. The need for a device that features portability, reasonable price, high repeatability, and accuracy has been emphasized in the literature. Existing devices have large variations in hardware, units of measurement, type of testing protocol, and frequency of testing used in the existing devices [8].

This paper presents a newly designed vibrotactile testing device, called the Vibrotactile Threshold Evaluator for the Workplace (VTEW) for quick and reliable screening for CTS. The design of this device is discussed in Section 4.3, results and discussion of the human study are presented in Section 4.4 followed by concluding remarks in Section 4.5.

4.3 Materials and methods

A vibrotactile device has three essential components: a *stimulator*, a *probe*, and a *surround*. A *stimulator* generates a vibration stimulus and is connected to a *probe*. The subject places his/her finger on the *probe*, which transmits the vibration stimulus directly to the skin. The *probe* may or may not be located within a *surround*, which provides a way of limiting the area of stimulation (the *surround* and the *probe* are typically cylindrical in shape, and are located coaxially) [8]. A typical VT measurement involves testing subjects by providing a vibration stimulus and changing the amplitude following a *testing protocol*; results are typically not comparable between two different tests if different *testing protocols* are used [20].

This section discusses the requirements of these components of the design as well as other desired features, the details of the resulting design, and the human study that was carried out in order to evaluate the design.

4.3.1 Design requirements

The design requirements of the VTEW were motivated by the intended use of this device, namely to evaluate employees (e.g., assembly-line workers) at work on a periodic basis. The design requirements are summarized in Table 4.1 and discussed in detail below.

4.3.1.1 Stimulator. The choice of testing frequency is an important factor in VT testing. With a careful choice of the frequency (or frequencies) used for testing, selective activation of different types of mechanoreceptors can be achieved. For instance, a frequency below 6 Hz allows the activation of slowly adapting mechanoreceptors, whereas the use of the frequency range 16-100 Hz activates the rapidly adapting mechanoreceptors. Nearly all existing VT testing devices provide a finite number of frequencies, often with three or fewer choices (many devices utilize 50, 60, 100, or 120 Hz as a convenience related to the operating frequency of the supply voltage) [8, 21-24]. However, there are many reasons to evaluate at both low (below 10 Hz) and high (above 200 Hz) frequencies, both of which have yet to be studied thoroughly. For instance, testing in the low frequency range is necessary for subjects with decreased sensitivity including older adults or patients receiving chemotherapy. Response of the slowly adapting type I mechanoreceptor has been shown to be acutely and chronically modified by application of neurotoxic chemotherapy agents [25]. It is also exclusively activated by a 4 Hz vibratory stimulus in glabrous skin. Therefore, investigating peripheral neuropathy at very low frequencies (below 4 Hz) is expected to understand the mechanisms of neuropathy produced by chemotherapy drugs such as Taxol and Cisplatin

and provide crucial information to improve the quality of life of cancer patients undergoing treatment.

Displacements for typical frequencies (50-200 Hz) are on the order of tens of μm. However, providing a wide range for displacement of the probe is necessary to permit testing in the low frequency range (where displacements must be larger to be felt) as well as for subjects with lower sensitivity such as patients receiving chemotherapy, and the older adult population

4.3.1.2 Probe. The *probe* diameter translates to the area of direct contact for stimulation of mechanoreceptor population. The vibration stimulus delivered by a smaller *probe* can focus on a smaller mechanoreceptor population to prohibit the activation of receptors located on the entire fingertip. According to the ISO 13091-1 standard, ideal *probe* size should be 2-6 mm in diameter and 0-2 mm in height, and should have smooth surface. However, existing literature demonstrates an inclination towards smaller probe sizes, in the range of 1-4 mm in diameter, in order to maintain a limited area of stimulation [8].

4.3.1.3 Surround. The presence of a 10 mm diameter *surround* offers further control on the effective area of stimulation. The internal diameter of the *surround* typically depends on the size of the *probe.* The recommended gap between the *probe* and the *surround* is 1.5 $\pm$ 0.6 mm [1, 8]. It has been well documented in the literature that activation of the Pacinian system, a mechanoreceptor channel, can cause a decrease in threshold. With experiments conducted specifically in an attempt to activate different mechanoreceptive channels, researchers have found that the use of a *surround* activates non-Pacinian channels and increases the sensitivity to edges (created by use of a

surround with a *probe*) and at higher frequencies, the threshold is elevated since a *surround* reduces the sensitivity of Pacinian receptors [26]. By introducing an additional edge, the travelling waves produced by a vibrating *probe* are effectively reduced or eliminated [26-27].

4.3.1.4 Testing protocol. Determination of VT relies on the different steps involved in the psychophysical testing protocol. These steps include presentation of stimulus, detection of stimulus, and calculation of sensory threshold. For this study, a forced-choice algorithm was used. The subject was presented with a pair of timed intervals in which only one interval contained the vibration stimulus. If the subject chose the interval with stimulus correctly, the amplitude was decreased, while an incorrect answer resulted in an increased amplitude. It was intended that the presentation of the stimulus and the response of subject follow a well-established method, so the forced-choice method was considered to be a suitable protocol.

4.3.1.5 Other considerations. The intended use of this device is in the workplace or in clinical settings, where portability of the set up is desirable. The materials for the housing and the support block were chosen with this requirement in consideration. Also, the stimulator is a lightweight voice coil to keep the overall weight of this device lower. An ergonomic design of this device for comfortable testing of employees at a workplace was essential since the device is intended to be used periodically to maintain and compare the records of VT. The full arm rest allows the subject to be tested in various simulated work postures and for testing the effects of median nerve provocation test.

The testing process should be quick and easy to learn, while keeping the device customizable for experienced investigators to allow versatility in the applications of this

device. A user-friendly interface for changing frequency and amplitude along with the testing protocol offer options for comparing results from different set of testing parameters.

4.3.2 Design details

Solidworks model of the voice coil holding carriage for VTEW is shown in Figure 4.1 a) and b). For portability, the outer housing was entirely manufactured from PVC plastic. The outer housing was ergonomically designed and contoured to provide complete forearm support during the entire testing procedure.

A solidworks model of VTEW has been shown in Figure 4.2 a) to highlight the pivoting mechanism of VTEW voice coil assembly. This type of pivoting can be useful to adjust the *probe* position for comfortable posture during the test. A prototype developed based on the solidworks models in Figure 4.2 a) has been shown in Figure 4.2 b). The prototype features an angle measurement on the side as well as an adjustment string to pull the voice coil assembly up or down.

4.3.2.1 Stimulator. A voice coil manufactured by H2WTech (NCC03-15-050-2X) was used to provide the sinusoidal stimulus. The voice coil drove the *probe* according to the specified sinusoidal waveform. The carriage and shafts used to hold and pivot the voice coil were manufactured using aluminum. The *probe* was made of stainless steel and was in direct contact with the subject's middle finger to provide the vibratory stimulus. A flexure made of annealed spring steel was designed to provide a mechanism for both suspending the voice coil for achieving appropriate displacement and to provide a means of preventing the voice coil from falling out of the holding carriage when pivoted (Figure

4.1 b)). The actuator and probe assembly was assembled such that the probe had a 1 mm offset while at rest.

A computer fan was used to cool the voice coil and to provide a source of white noise during testing. A one-dimensional optical position sensor (Part S3932, Hamamatsu Corp., Bridgewater, NJ,) was used to determine the *probe* location in order to implement closed-loop control of its displacement. The light source, an LED, was attached to the moving *probe* using a specially designed clamp made of aluminum. LabView (National Instruments) was used to provide an interface for the hardware. The LabView program performed the closed loop feedback control, and the software interface allowed customization of frequency, amplitude, and duration of vibration stimulus for each test as desired. A National Instruments data acquisition system (NIDAQ USB-6259) was used to acquire data from the position sensor, and provide the control signal to an amplifier (Copley Controls Inc., Model 422 CE).

4.3.2.2 Probe and surround. For the validation study in this paper, a *probe* diameter of 2 mm was used for two reasons. First, this allowed the closest comparison with the results of the other hardware (the VTT, as described in Section 4.3.1.2), which has a fixed probe of diameter 1 mm. Second, the smaller size improves the control over the area of stimulation, as underscored by preliminary testing with a 6 mm diameter probe (following the ISO 13092-1 standard recommendation for a probe [8]: smooth to touch, 4 $\pm$ 2 mm diameter). At a low frequency of 4 Hz, subjects could not feel the vibration due to the large area of stimulation (1 mm diameter stimulation area: π (0.5 mm)^2 = 0.79 mm^2, 2 mm diameter stimulation area: π (1 mm)^2 = 3.14 mm^2, 6 mm diameter stimulation area: π (3 mm)^2= 28.29 mm^2). A larger area of stimulation may

dampen the vibration stimulus and thus increases the chances of entirely missing the lower frequency spectrum for a subject. Further control of the area of stimulation was achieved by using a *surround* of 10 mm diameter. The s*urround* was built in the top cover for the carriage containing the voice coil and the *probe* was connected using a connector made of aluminum. The top cover also housed the position sensor (Section 4.3.2.1). The *probe* and connector assembly was held in place on top of the voice coil by a custom designed flexure made of spring steel to allow translation of the *probe* once voice coil was activated (Figure 4.1b)). The *probe-surround* gap was 1 mm.

4.3.2.3 Testing protocol. A LabView interface (see Section 4.3.2.5) was designed and implemented to control the frequency and displacement of the oscillation. Using LabView will readily allow a variety of testing protocols to be used with the VTEW hardware. For this validation study, a two-interval forced choice (2IFC) method was implemented as shown in Figure 4.3.

Each subject was presented with a pair of timed intervals to choose from in order to respond to the test. The timed intervals were 1 sec long and were followed by 0.5 sec pauses. The vibration stimulus was present only in one interval for every test and the subject was asked to respond each time. Each set of two pauses and two intervals constituted a cycle followed by a variable response time. The next cycle began only after the subject responded by choosing the interval they thought had the vibration stimulus. The duration of this waiting period was variable.

The pauses and intervals were indicated by LEDs of different colors (Interval 1- Red, Interval 2- Green, Pause- Yellow). The LEDs corresponding to each interval and pause lit up to indicate which part of the cycle was in progress currently. Since a subject

always had only two alternatives for a response, namely interval 1 or interval 2, two buttons were provided. The subject was asked to push one button after each cycle in order to respond. The set up for the LEDs and buttons along with the labels are shown in Figure 4.4.VT testing was performed at 4 and 50 Hz using VTEW and a higher starting amplitude was picked for 4 Hz testing to enable the subjects to get accustomed to the lower frequency. The initial starting amplitude of vibration was 1mm for 4 Hz testing and 0.5 mm for 50 Hz testing. The amplitude was increased each time the subject responded incorrectly and decreased each time the subject responded correctly. The step size for increasing or decreasing amplitude was dependent on the current amplitude presented. For this study the step sizes chosen were 0.5, 0.005, and 0.001 mm. If the amplitude was in the range 1 - 0.024 mm, step size was 0.5 mm, from 0.025 - 0.01 mm, step size 0.005 mm was used, and for amplitude range 0.019 - 0.001, step size 0.001 mm was used. Three different step sizes were chosen to make the algorithm time efficient. Higher amplitudes were associated with a higher step size and lower amplitudes were associated with a lower step size (as shown in Figure 4.5). The idea was to allow the subject to feel higher amplitude in the beginning of the test to get familiarized with the testing process.

If the subject answered correctly, the amplitude was lowered with each correct answer with the same higher step size until the amplitude was in the second range and the step size was changed. The same process was followed until the lowest step size was triggered by the correct answer in the lowest amplitude range. In any amplitude range, if the subject answered incorrectly, the step size was increased to a value that was selected based on the current amplitude. If subjects stated that they did not know when the stimulus appeared, they were told to guess or randomly choose an interval. The change

from a correct to an incorrect answer or vice versa is called a reversal. VT was estimated by averaging the amplitude during 10 reversals in the amplitude range when step size 3 was used.

4.3.2.4 Other considerations. VTEW can accommodate individual differences in hand shape and sizes by pivoting mechanism with a 120° range to enable provocative flexion in the wrist during an entire test. Flexion can effectively reduce the area of carpal tunnel and produce an increased pressure on the median nerve. For a subject showing no symptoms of CTS, flexion of wrist should not affect the VT measurement significantly for short duration (<5 mins). However, for a subject with distinct signs of CTS, flexion of the wrist will increase the discomfort and VT will be significantly increased [28].

For testing with VTEW, the setup involves setting the testing frequency, starting amplitude, and selecting a file to save all the testing data. The testing takes less than 5 min for any given frequency. The device is light weight and easy to set up for right and left hand testing. Since the *probe-surround* assembly is pivoted, a subject of any hand size can rest their forearm comfortably in a neutral posture.

4.3.2.5 LabView interface. The LabView interface was designed to produce the sinusoidal input for the voice coil motor and customize amplitude and frequency. As described in Section 4.3.2.3, the protocol used for this initial study was two-interval forced choice (2IFC) method. The LabView program stored all the data in a file designated by the investigator. shows the LabView interface for the testing program. The LabView program drives the voice coil motor and receives the feedback from the position sensing device (Section 4.3.2.1) as shown in Figure 4.6. The interface also

allows the investigator to run the 2IFC protocol by choosing which interval will contain the vibration stimulus.

4.3.3 Calibration of VTEW

Accuracy in estimation of VT requires maintaining precise displacement of *probe* during testing. This was achieved by using a position sensor controlled and monitored using a LabView interface. The position sensor was calibrated by attaching the sensor on a Computer Numerical Control (CNC) machine stage and comparing the displacements recorded by both CNC machine and the position sensor.

CNC machine stage was used to mount and move the PSD, and for mounting the LED perpendicular to the surface of the PSD. The resolution of position sensor was kept in consideration and a step size 0.01 inch was selected for the movement of CNC stage and position measurement was repeated 10 times for each point and averaged. Six such points of measurement were chosen over the total length of the sensor (0.6 in).

Voltage obtained from the two electrodes on the position sensor was used to find the location of LED source on the sensor using Equation 1 where V_1 and V_2 are the voltages obtained at the two electrodes, L is the length of the sensor, and x denotes the distance between the location of LED and midpoint of the sensor's active region.

$$\frac{V_2 - V_1}{V_1 + V_2} = \frac{2x}{L} \tag{1}$$

Figure 4.7 shows the layout of position sensor with the active area and the distance of light source and the voltage outputs from the two anodes.

4.3.4 VTEW validation study

4.3.4.1 Validation study procedure. For this study, all subjects underwent several tests designed to evaluate the physiological health of the median nerve. An identical sequence of testing was followed for each subject to maintain similar conditions. Since maintaining limb temperature (30-40°C) for accuracy in VT measurement has been emphasized in the literature [13, 29], the temperature of the middle finger was measured before and once during the testing process to ensure that the finger temperature was at least 30°C. The temperature was measured using a portable temperature measurement unit with an infrared sensor.

Two clinical tests were done prior to the vibrotactile testing: Phalen's test and Tinel's test. Phalen's test involves flexing the wrist of the subject for 1 min. This forced flexion causes pinching of the median nerve and an increased pressure in the carpal canal. The result is considered positive for CTS if the subject experiences an aggravation of symptoms (pain, numbness or tingling) within the area innervated by the median nerve. Tinel's test is performed by gently tapping the wrist above the median nerve. This tapping action can be used to spot an irritation in the median nerve by eliciting a tingling sensation, confirming CTS. For this study, a subject was defined positive on Phalen's test if they reported any pain, numbness or tingling. Similarly, any tingling caused by tapping on the median nerve during Tinel's test was considered a positive result.

Following the clinical tests, the subjects were evaluated using an established vibrotactile instrument called the Vibrotactile Threshold Tester (VTT), based on the Automated Tactile Tester, ATT [30-31]. The VTT has been evaluated in the past to be an efficient and reliable tool for compression peripheral neuropathy at 50 Hz (lower testing

frequencies are not available; the VTT can be set to 50, 150, or 250 Hz) [30]. The VTT has a fixed probe size of 1 mm in diameter, with a 20 mm surround. The VTT was set to provide constant starting amplitude for each subject, and the method of limits psychophysical testing protocol was used. This meant that the subjects pushed the button each time they felt a vibration. The initial offset of the probe was set at 100 μm for the subjects to be able to feel the probe and was advanced by the computer another 200 μm to ensure constant contact with the subject's middle finger.

Next, subjects were evaluated on the VTEW at 50 Hz and then 4 Hz, both with neutral hand posture. The 50 Hz frequency allowed comparison to the VTT result, while the 4 Hz frequency provided preliminary data for low frequency applications. As mentioned above, the VTEW probe was 2 mm in diameter, with a 10 mm surround. The *probe* for the VTEW was mounted such that it had a constant offset of 1 mm for the entire study. The psychophysical testing protocol used for VTEW was 2 interval forced-choice method (2IFC), described above in Section 4.3.2.3. Each subject was presented with an initial training stimulus at 50 Hz with a large (0.5 mm or larger) displacement to familiarize him/her with the process; the training stimulus was repeated until the subjects pushed the button for correct interval. The starting displacements were 0.5 mm for 50 Hz and 1.0 mm for 4 Hz.

4.3.4.2 Human subjects. This study, which was approved by the Institutional Review Board at the University of Utah (#42165), recruited 55 adult subjects (31 males and 24 females) with characteristics as listed in Table 4.2. Each subject was required to sign an informed consent form before participating in the study. The participants were allowed to refuse to participate at any point during the study. Subjects were recruited by

circulation of a recruitment email, posted fliers, and through word of mouth from the University of Utah population at large; most subjects were staff or students. The dominant hand was tested for all subjects except one subject who was ambidextrous and had both hands tested (resulting in 56 data points).

For this study, no inclusion criterion was chosen with an intention to have a diverse group of subjects with both genders, different age groups and with no particular preferred profession. Subjects with CTS-like symptoms and no symptoms at all were allowed to participate. Minimum age was restricted to 18 years with no restriction on maximum age. The subjects were excluded from the study if they reported any history of diabetes, peripheral neuropathy, and injury to hand being tested. The dominant hand was tested for all subjects.

For analysis of this validation study, subjects were identified as symptomatic if they had a positive result on either Phalen's test or Tinel's test or both. The symptomatic and asymptomatic subjects were categorized in two different groups for data analysis performed using Minitab® 16.1.1 and Microsoft Excel 2007.

4.4 Results and discussion

4.4.1 VTT and VTEW Comparison

In order to compare the results obtained by VTT and VTEW, a 2-sample t-test was performed on the VT data obtained for each subject (at 50 Hz) using both devices. The p-value for this test was 0.15 ($> \alpha = 0.05$) for data collected from these two devices. The p-value was greater than the chosen α level at 95% confidence interval, suggesting no statistical difference between the data sets. A boxplot displaying the distribution of VT for both VTT and VTEW at 50 Hz is shown in Figure 4.8.

The statistical similarity of the data obtained at 50 Hz from both VTT and VTEW suggest that VTEW is successfully measuring a similar VT to the VTT. The mean value of VT obtained from VTEW is lower than the mean value of VT obtained using VTT as observed in Table 4.3 and Figure 4.8. This can be attributed to the use of forced-choice algorithm for testing with VTEW as compared to the method of limits used for VTT, as was also described in a previous study by Morioka and Griffin [20].

The observations in Figure 4.8 showing unusually high VT were investigated further. For this study, a data point that was greater than 1.5 times the interquartile range (denoted by the top and the bottom edges of the box in a boxplot), were denoted by a * and identified as an outlier. For VTT, the outliers were greater than 5.4 μm and for VTEW the observations greater than 6.3 μm were considered to be outliers.

The highest observation seen with VTT testing was by a subject (VT = 25.8 μm) who has no symptoms in the hand being tested but had nerve damage in the hand that was used to push the button to respond. The response time may have been greater than 2 sec time limit set for this device, which may have caused the results to show a significantly higher threshold. When the same subject was tested on VTEW, no unusual observation was recorded since VTEW uses a forced choice method and the subject is given time to respond by choosing interval 1 or 2 without a time restriction. The other two observations are both in the older age group (65 and 85 years). One subject reported difficulty in perceiving the vibration and maintaining constant focus to recognize the stimulus. The other subject is a piano teacher and reports constant tingling and significant hand discomfort in both hands. For VTEW, both outliers were subjects that indicated difficulty

in differentiating between the noise of the system and the stimulus even for higher amplitudes.

Thus, by investigating the outliers we found that unusually higher VT may indicate device related issues since the subjects corresponding to the outlier observations were not the same for both of these devices.

4.4.2 VT and Age

The VT obtained for the subjects using the VTT at 50 Hz and the VTEW at 50 Hz, are plotted against each subject's age in Figure 4.9. An increasing trend for VT versus age was observed, as shown by the linear fitted lines similar to previous studies conducted using VTT [28]. Mean threshold for VTT was 8 μm and for VTEW was 6.9 μm.

Best subsets regression analysis was performed on the data obtained from this study, with the following variables under consideration: age, height, BMI, and finger temperature. It was found that age was the most significant factor affecting the VT of subjects. An age correction equation was inferred from this analysis for both VTT and VTEW at 50 Hz (Equation 2 and 3).

$$VTT_{50\ Hz} = 0.12 * (age) + 3.38 \quad (2)$$

$$VTEW_{50\ Hz} = 0.12 * (age) + 2.22 \quad (3)$$

As evident in Figure 4.9, the age correlation for both devices has a nearly identical slope, but the offset is higher in the VTEW measurement than the VT measurement. This type of age correction has been used previously to account for the

covariance of age and VT. Previous studies conducted on VTT provide a similar age regression (Equation 4) suggesting the population in this study is reasonably representative of a larger population [28, 32-33].

$$VTT_{50\ Hz} = 0.085 * (age) + 3.32 \quad (4)$$

The age-corrected VT can be found by subtracting the age correction from the VT measured by VTT and VTEW.

4.4.3 VT at 50 Hz vs. 4 Hz using VTEW

In addition to the VTEW test at 50 Hz for comparison to the VTT, subjects were also tested using VTEW at 4 Hz. The p-value for this test was 0.00 ($< \alpha = 0.05$) for data collected from these two devices. The p-value was lower than the chosen α level at 95% confidence interval, suggesting a significant statistical difference between the data sets. A boxplot displaying the distribution of VT at 4 Hz and 50 Hz using VTEW is shown in Figure 4.10.

The dissimilarity between VT at 4 Hz and 50 Hz is to be expected since testing at a lower frequency in glabrous skin exclusively activates non-Pacinian mechanoreceptive channels (i.e., the slowly adapting type I mechanoreceptor) that are edge sensitive, whereas 50 Hz appears to activate both Pacinian and non-Pacinian channels [28]. It has been shown that higher frequencies tend to be associated with lower thresholds [11]. Our results show this trend. Although it is not possible to determine precisely which mechanoreceptive channel was activated by a particular frequency, a comparison at

multiple frequencies (similar to Figure 4.10) will likely be useful for determining future testing protocols.

The mean VT values were higher at 4 Hz as compared to 50 Hz as shown in Table 4.4. The outliers, or unusually higher observations, were identified and investigated in Figure 4.10. For testing at 4 Hz, the outliers were identified as observations that were greater than 1.5 times the interquartile range (denoted by top and bottom edges of the box in the boxplot) to be 23.1 μm. Similarly, at 50 Hz, the outliers were identified as observations greater than 6.3 μm. At 4 Hz, three out of the five such observations were associated with subjects who reported severe hand discomfort and tingling. One of these three subjects had a history of taking corticosteroids in the last 2 years to reduce inflammation related to CTS. Out of the remaining two subjects, one subject was 86 years old and reported being involved in gardening constantly for the 2 days before testing with discomfort arising from holding the tools. The fifth subject reported hand discomfort from typing and lifting a baby frequently. Thus, almost all observations can be attributed to the preexisting hand discomfort for these subjects.

Figure 4.10 includes all symptomatic and asymptomatic subjects. On conducting 2-sample t-tests for VT obtained for symptomatic and asymptomatic subjects at both 4 Hz and 50 Hz, the p-values obtained were 0.255 and 0.802, respectively (α =0.05, 95 % CI). Since there was no statistically significant difference, in order to observe the effect of presence of symptoms on VT, main effect plots were generated. Figure 4.11 a) depicts the mean VT trends for symptomatic and asymptomatic subjects at 4 Hz, and Figure 4.11 b) depicts the mean VT trends for symptomatic and asymptomatic subjects 50 Hz.

At 4 Hz, the mean VT for asymptomatic subjects was 37.1 μm (std. dev = 20.8 μm) and the mean VT for symptomatic was 49.7 (std. dev = 44.3 μm). Similarly, at 50 Hz, the mean VT for asymptomatic subjects was 6.86 μm (std. dev = 3.64 μm) and the mean VT for symptomatic was 7.08 (std. dev = 2.81 μm). The effect of presence of symptoms was observed for both frequencies. It is however, important to note the difference between the number of symptomatic (n= 19) and asymptomatic subjects (n=37) tested for this study. Elevated VT for symptomatic subjects indicates that a study with a higher number of subjects (with equal distribution of symptomatic and asymptomatic subjects could be useful in determining the effect of presence of symptoms of VT.

4.4.4 VT and gender

Two-sample t-tests conducted for VT obtained using VTT at 50 Hz for female and male populations yielded a p-value of 0.236 (α =0.05, 95 % CI). Similar 2-sample t-tests for VT obtained using VTEW at 50 Hz and 4 Hz yielded p-values of 0.702 and 0.103, respectively. All three of these tests indicate no statistically significant effect of gender on VT.

To further investigate the effect of gender on VT, main effect plots were generated for VTT at 50 Hz, VTEW at 50 Hz, and VTEW at 4 Hz, for both genders as shown in Figure 4.12 a), b), and c). It appears that the trends of VT value for both males and females for both devices and both frequencies behave in a similar manner. The mean VT for female subjects was higher than the mean of the total population as compared to the male subjects. The mean values of VT in Figure 4.12 have been summarized in Table 4.5.

The similarity in the observed trends further supports the statistical similarity of the results obtained using the two devices. The effect of gender on VT has been studied but the data have not been conclusive since the average height of males and females tends to differ. Height adjustment may need to be accounted for in order to clearly show gender as a covariate for VT [13]. It is also important to note that the number of symptomatic females (n=11) and asymptomatic females (n=14) was not equal. Similarly, the number of symptomatic males (n=8) was not equal to asymptomatic males (n=23). On comparing the symptomatic and asymptomatic populations based on gender, it appears that since a larger number of male subjects recruited for the study were in fact asymptomatic, the average VT for males was lower than females. It is also important to mention that the average male subject was younger than the average female subject (average male age = 35.3 years, average female age = 40 years), and the oldest female subject was 86 years old while the oldest male subject was only 68 years old.

Females appear to have a higher VT mean value than male subjects for the tests performed at 50 Hz (Figure 4.12) using both VTT and VTEW. Even though the trend at 4 Hz for gender remains the same, with females showing higher mean VT than male subjects, both mean VT values are significantly higher at 4 Hz as compared to 50 Hz. Again, these results support the theory of activation of non-Pacinian channel at 4 Hz and activation of more than one mechanoreceptive channel at 50 Hz [10, 28].

4.5 Conclusion

This paper explores the validity of the results obtained using a novel device, VTEW at two different frequencies, 4 and 50 Hz. An existing device, the VTT, was used to compare the sensory thresholds evaluated by both devices at 50 Hz. No statistically

significant difference in the results from VTT and VTEW was observed. The effects of age, change in testing frequency, and gender on VT were investigated. An age correction was generated to account for the different age of subjects that participated in this study. Even though the age correction follows closely with a previously published study, a future study recruiting more subjects in different age groups would be recommended. Equal numbers of male and female symptomatic and asymptomatic subjects should be recruited and investigators should adjust for the age of male and female subjects to acquire reliable gender effect on VT.

Customizable testing frequencies and testing protocol of VTEW could be exploited for future studies involving low frequency testing for chemotherapy-induced neuropathies and high frequency testing to screen employees at workplace for occupational diseases.

4.6 References

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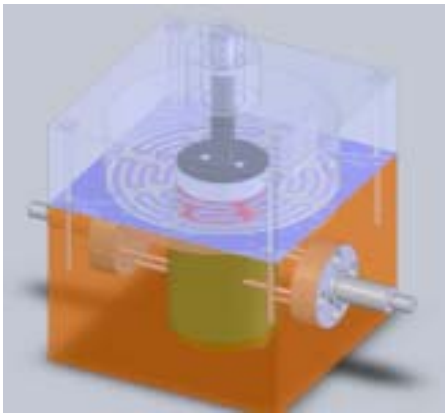
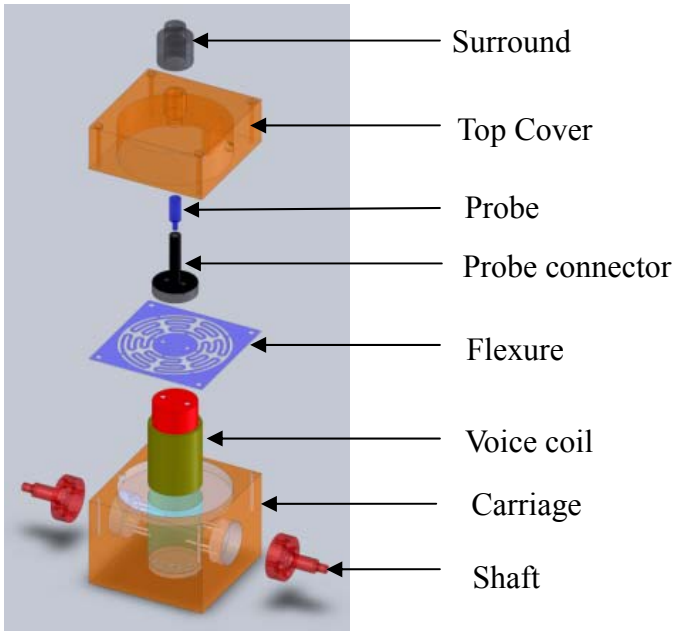
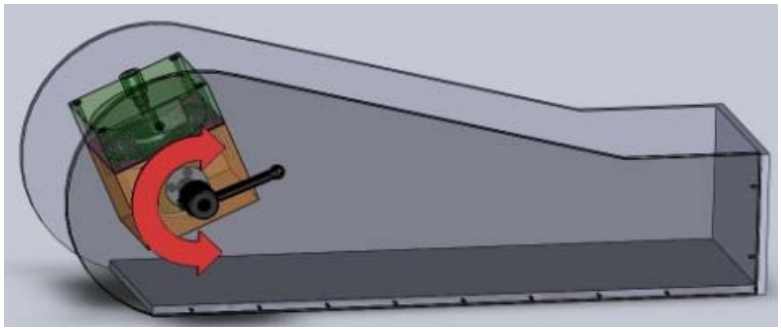


a)

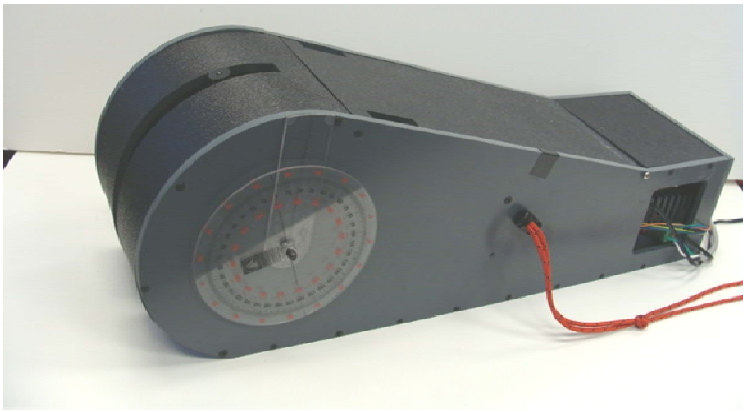


b)

Figure 4.1: Solidworks model of voice coil housed in the carriage supported by a shaft at either end. a) Assembled view of all components and b) exploded view of all components. A probe connector was secured at the top of the voice coil. The *probe* was attached to the probe connector and suspended on the translating voice coil by a flexure. Top cover acted as the *surround* encircling the *probe* and housed the position sensor.



a)



b)

Figure 4.2: Solidworks model and prototype of VTEW. a) Solidworks models of VTEW demonstrating the pivoting mechanism by an arrow. The range of motion achieved by this pivoting was 120^{o}, b) VTEW prototype with angle measurement and adjustment string for supporting and pivoting voice coil assembly.

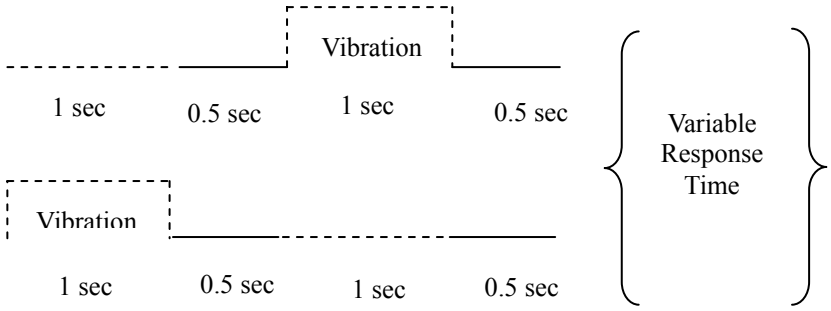


Figure 4.3: 2 interval forced choice testing protocol with vibration stimulus duration 1 sec long. The solid lines represent the pauses and dotted lines represent the two intervals. The upper schematic shows the scenario with vibration stimulus in interval 2. The subject was presented with no vibration for the first 1 sec, followed by a pause 0.5 sec long, 1 sec long vibration stimulus, and another 0.5 sec long pause. The lower schematic shows the scenario for vibration stimulus in interval 1. The subject was presented with a vibration stimulus for 1 sec, followed by a 0.5 sec long pause, no vibration for 1 sec followed by another pause. The last pause was followed by a variable response time during which the subject was instructed to choose interval 1 or 2 as their response. The next cycle began only after the subject had responded.

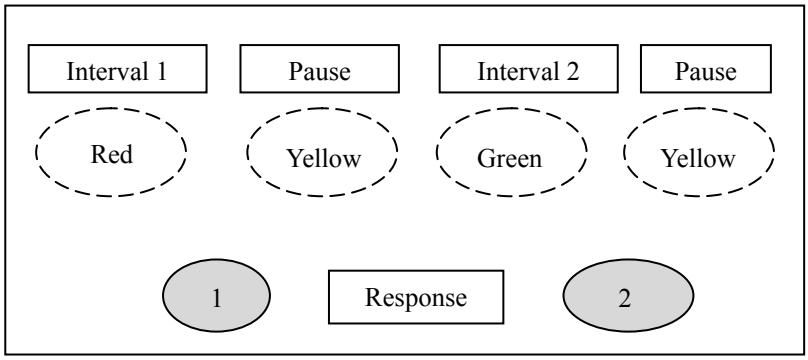


Figure 4.4: Set up for VT testing and response. The top row of boxes represents the labels for LED lights to indicate current interval or pause in progress. The second row represents LEDs with different colors to differentiate intervals and pauses. The LEDs are activated according to the interval or pause in progress. The third row shows the response buttons in gray color. If the subject decided that interval 1 contained the vibration stimulus, button 1 was pushed. If the subject decided interval 2 contained the vibration stimulus, button 2 was pushed.

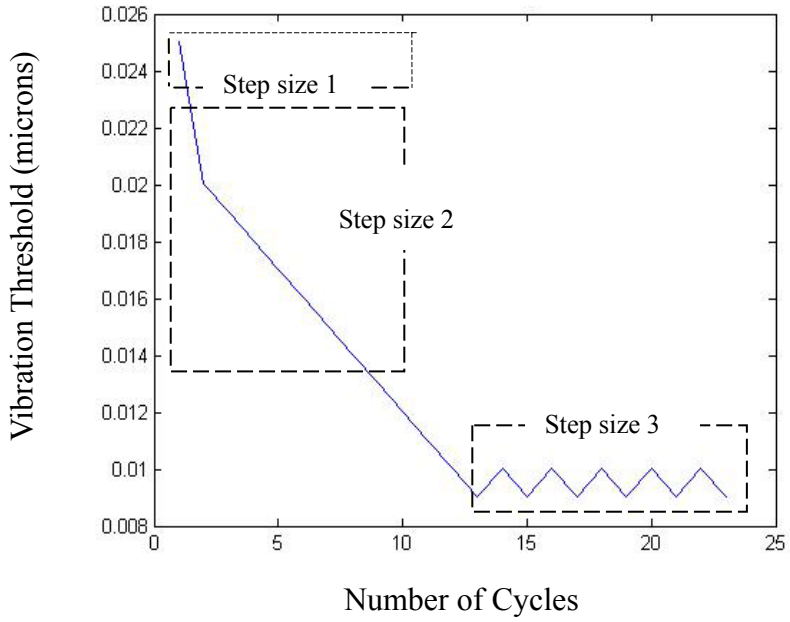


Figure 4.5: VT measurement and demonstration of changing step size used for this study. A correct response resulted in decrease in amplitude by a step size and an incorrect response resulted in an increase in amplitude by a step size. The current amplitude of vibrations stimulus determined the setp size. Step size 1 corresponded to amplitude range 1-0.024 mm. Step size 2 corresponded to amplitude range 0.025-0.01 mm, and step size 3 corresponded to amplitude range 0.019- 0.001 mm.

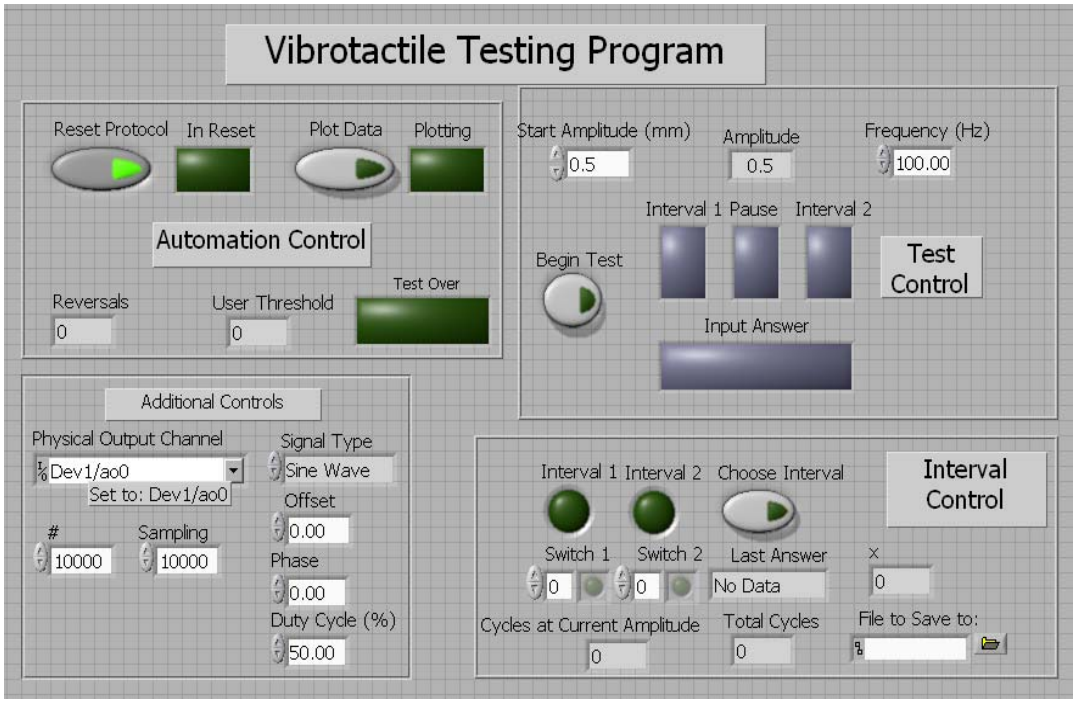


Figure 4.6: Screenshot of LabView interface for VT. Top left box shows the reset button for starting a test from 0.5 mm amplitude. The plot data button provides an instant plot of VT as a function of number of cycles. Starting amplitude can be modified in the top right box along with testing frequency. Interval control is provided in bottom right box to randomly assign the vibration stimulus to Interval 1 or Interval 2.

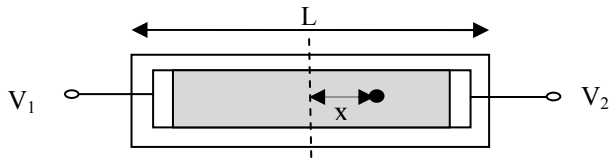


Figure 4.7: Position sensor for measurement of *probe* position with active region shaded and denoted by L. Two anodes output voltages V_1 and V_2. The location of light source on the position sensor is denoted by x. S 3932 position sensor manufactured by Hamamatsu Corp. was used.

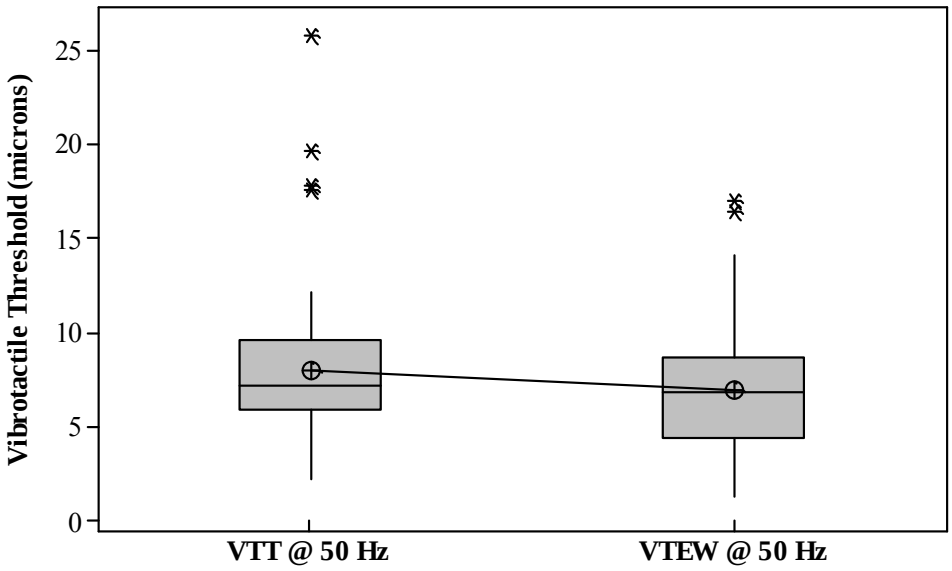


Figure 4.8: Boxplot of VT distribution data obtained from VTT and VTEW at 50Hz. The boxplot shows observations that are unusually higher or lower as outliers (indicated by *). The top and bottom whiskers (vertical lines above and below the boxes) extend to the highest and lowest data points. The lower and upper lines of the box represent the first and third quartile of the data points. The middle line shows the median of the distribution. The p-value was 0.15 ($\alpha = 0.05$, 95 % CI). Sample size was n=56.

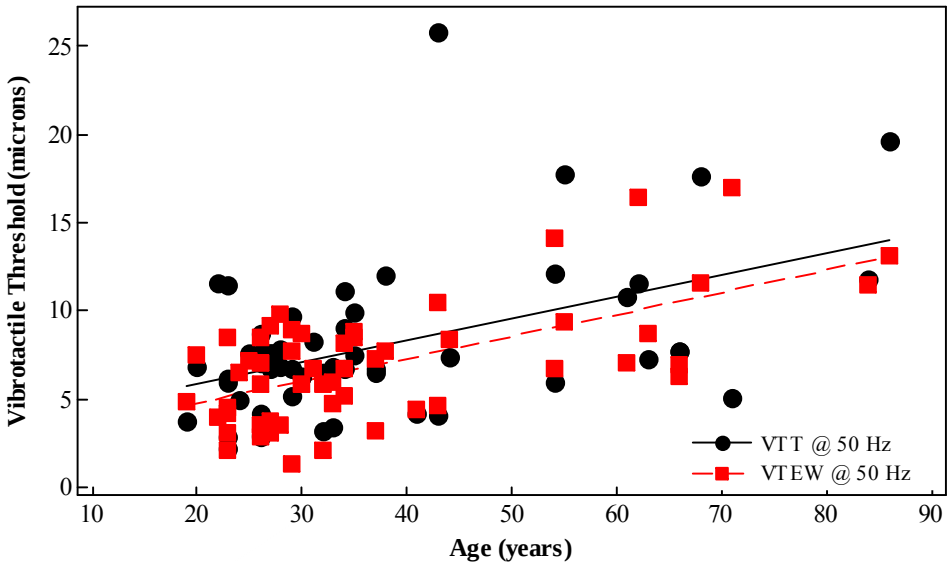


Figure 4.9: VT as a function of age for all subjects evaluated by VTT and VTEW at 50 Hz. The trend lines are shown for VT obtained by both devices. For VTT, the age regression slope was 0.12 and Y-intercept was 3.38. For VTEW, the age regression slope was 0.12 and the Y-intercept was 2.22. The sample size was n= 56.

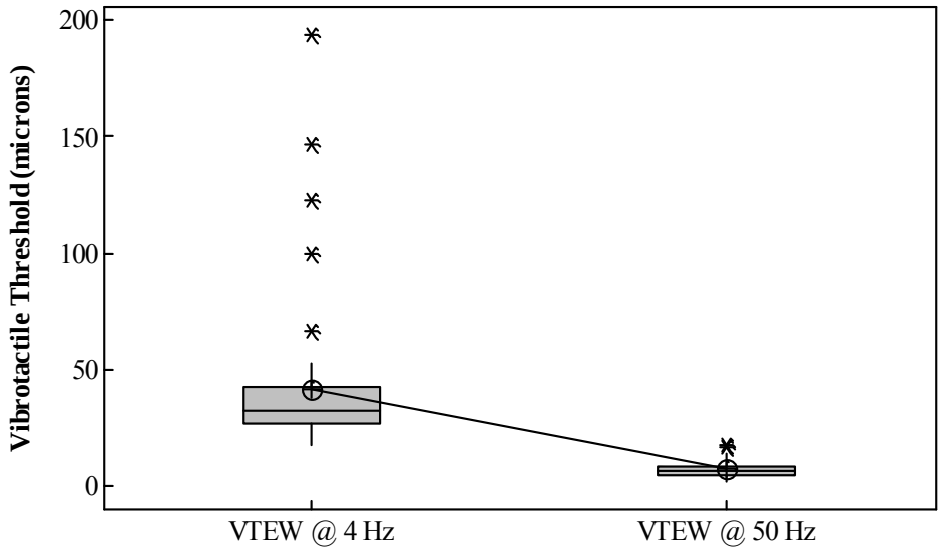
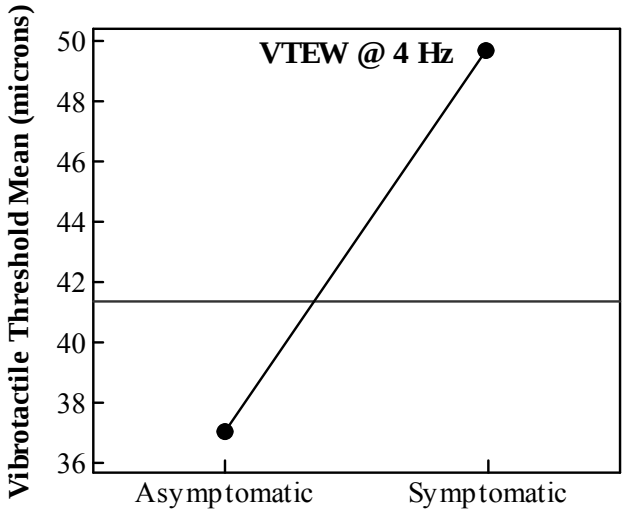
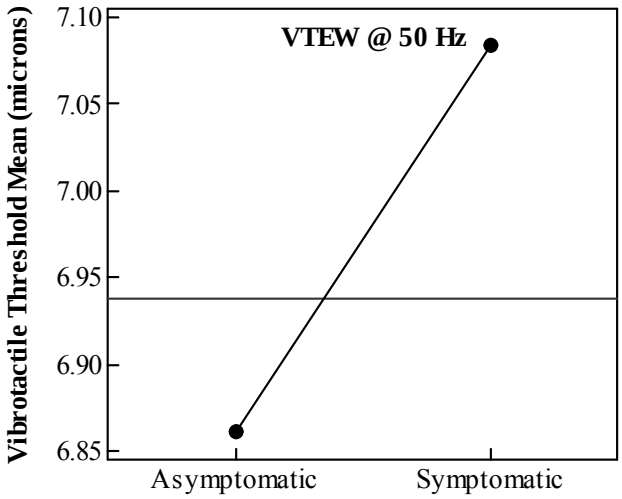


Figure 4.10: Boxplot of VT distribution data obtained at 4 Hz and 50 Hz using VTEW. The top and bottom whiskers (vertical lines above and below the boxes) extend to the highest and lowest data points. The lower and upper lines of the box represent the first and third quartile of the data points. Unusually higher observations are marked as outliers by *. No overlap was observed between the data obtained at 4 Hz and 50 Hz showing statistically significant difference. The p-value was 0.00 ((α = 0.05, 95 % CI). Sample size was n=56.

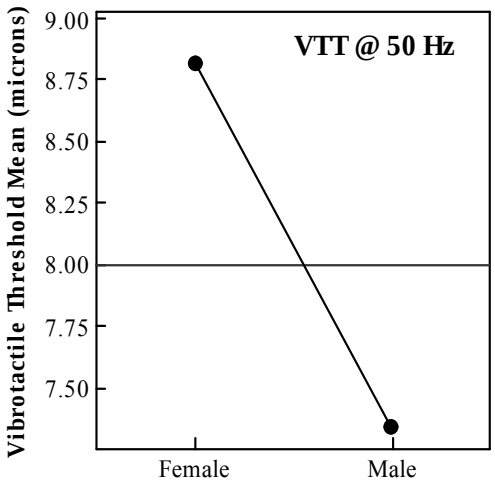


a)

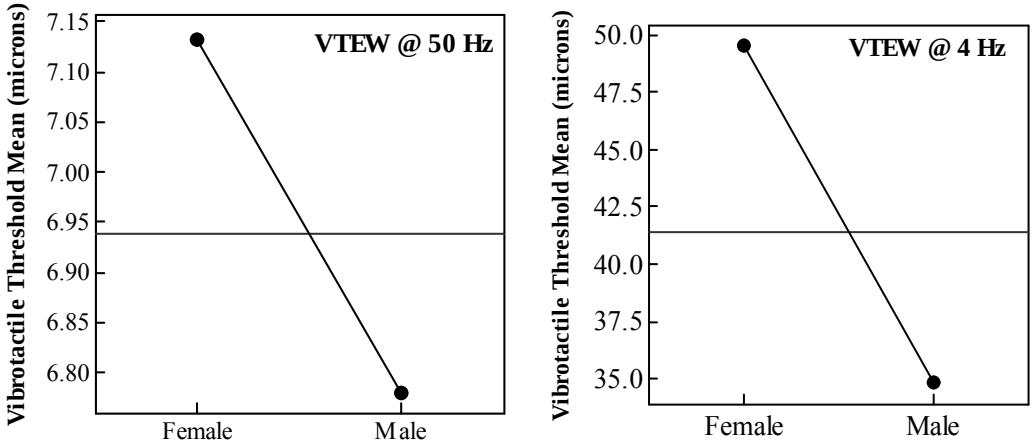


b)

Figure 4.11: VT mean value trends for symptomatic and asymptomatic subjects, a) at 4 Hz and b) at 50 Hz on the VTEW. The main effect plot shows that presence or absence of symptoms affects the mean VT obatined at both 4 Hz and 50 Hz. The symptomatic subjects show elevated mean VT as compared to the asymptomatic subjects at both frequencies. The horizontal line shows the mean VT (41.37 μm at 4 Hz and 6. 94 μm at 50 Hz) for total population as a reference. Mean VT of symptomatic subjects lie above the mean VT of entire subject population. The sample size for asymptomatic (n=37) and symptomatic (n=19) subjects is the same at both frequencies.



a)



b) c)

Figure 4.12: VT mean value trends for all subjects (n=56) using a) VTT at 50 Hz, b) VTEW at 50 Hz, and c) VTEW at 4 Hz. Main effects plot shows that gender affects the VT. Females tend to have higher mean VT as compared to males at both 4 Hz and 50 Hz using VTEW. The horizontal line shows the mean VT for total population as a reference. The sample size for asymptomatic females (n= 14) and males (n=23), symptomatic females (n= 11) and males (n=8) was same at both frequencies and for both devices.

Table 4.1: Requirements for the VTEW

Design Requirements	**VTEW Specifications**
Adjustable frequency range of stimulator	1-500 Hz
Broad amplitude range of probe	1-1500 μm
Multiple probe sizes supported	2-10 mm
Multiple surround sizes supported	6-10 mm
Support for neutral and flexed positions of arm and wrist	120º range
Fast testing time at a given frequency	<5 min
Portable	<0.01 m^3, <5 kg
Support for standard psychophysical testing protocol	Forced-choice method

Table 4.2: Characteristics of study population

Variable	Mean	Std. Dev	Min	Max
Age	37.5	16.6	19	86
Finger temp(deg C)	31.8	1.4	26.0	34.8
Height (in)	67.6	3.0	60	75
Weight (lbs)	172.3	38.5	106	275
Body Mass Index (BMI)	26.4	5.3	18.8	39.5

Table 4.3: Distribution of VT (μm) obtained from VTT and VTEW at 50 Hz

VT @ 50 Hz	Mean	Std Dev	Min	Max
VTT	8	4.3	2.2	25.8
VTEW	6.9	3.4	1.3	17

Table 4.4: Distribution of VT (μm) obtained at 4 Hz and 50 Hz using VTEW

VT at	Mean	Std Dev	Min	Max
4 Hz	41.37	31.01	17.2	194.5
50 Hz	7.863	3.559	2	17.2

Table 4.5: Mean VT values for female, male and total population

Device	Freq. (Hz)	Mean Female VT (µm)	Mean Male VT (µm)	Total Mean VT (µm)
VTT	50	8.82	7.32	8
VTEW	50	7.13	6.78	6.94
VTEW	4	49.52	34.79	41.37

CHAPTER 5

USE OF PROVOCATIVE WRIST FLEXION TEST AND A SELF-REPORTED PAIN AND DISCOMFORT SURVEY FORM FOR CARPAL TUNNEL SYNDROME SCREENING AT WORKPLACE

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5.1 Introduction

Vibrotactile threshold (VT) evaluation has been used for detecting peripheral neuropathy. A frequent application of VT evaluation is for screening for carpal tunnel syndrome (CTS) [1-6]. Typical CTS symptoms are pain, tingling, paresthesia, nocturnal pain, and aggravation of these symptoms in certain hand postures.

CTS is a compressive neuropathy resulting from a pinching of the median nerve at the wrist level [7-9]. Clinical tests for CTS diagnosis (e.g., Phalen's and Tinel's tests) rely on observation of change or aggravation of symptoms on median nerve provocation. Phalen's test relies on aggravated symptoms within 1 min of wrist flexion [10]. Wrist flexion has been used previously for observation of changes in pre- and post- flexion VT for both symptomatic and asymptomatic populations. Tendon loading, wrist flexion with direct pressure application (using a Durkan gauge), and wrist flexion with venous occlusion (decreased blood flow using a pressure cuff) have been examined as alternative forms of provocation in combination with VT [11]. The time taken for the subjects to return within a certain level of the preprovocation VT after flexion, also known as recovery time, has also been investigated [10, 12]. Several other types of methods already exist for diagnosis of CTS; however using VT in combination with a provocation maneuver may offer a low-cost quantitative measure for screening for CTS that could be implemented for regular use in the workplace.

VT evaluation is not intended to be a replacement for the nerve conduction velocity (NCV) testing method, which is considered to be the 'gold standard' for diagnosing CTS. Use of the VT method (e.g., periodic testing at workplace) as a means of screening the population that does not have CTS symptoms, followed by referring the

population that does have symptoms to a more advanced method and level of CTS testing could reduce the cost of compensation and treatment through early detection [13].

The purpose of this study was to examine VT during wrist provocation and compare it to the VT obtained prior to the provocation for symptomatic and asymptomatic subjects. A novel device, the Vibrotactile Threshold Evaluator for Workplace (VTEW), was used for this study [14]. The design of this device allows the examiner to test a subject with different wrist angles for median nerve provocation by pivoting the entire probe and stimulator assembly.

5.2 Materials and methods

5.2.1 Hardware

Subjects were tested using VTEW (Figure 5.1), controlled with a custom designed LabView program, and described in further detail by Gandhi et al. [14]. The configurable features of the VTEW are the probe diameter (2-6 mm), applied frequency (1-500 Hz), probe displacement (1-1500 μm), and angle of probe and stimulus assembly can pivot with a range between 0-120º. The LabView program can support various testing protocols, and the housing supports the arm and wrist, while the probe and stimulus assembly can be adjusted across a range of 0-120°.

For this study, a flat cylindrical probe made of stainless steel with 2 mm diameter and a surround made of plastic with 10 mm diameter was used, and the subjects were tested at 50 Hz. The *probe-surround* gap was 1 mm. Subjects were evaluated in both a neutral and flexed position. The two-interval forced choice testing protocol was used, with an initial amplitude of 0.5 mm in both neutral and flexed postures. The orientation of the probe and stimulus assembly was recorded for each subject at the neutral and

flexed positions. A voice coil manufactured by H2WTech (NCC03-15-050-2X) was used to provide the sinusoidal stimulus. The voice coil drove the *probe* according to a specified sinusoidal waveform. A one-dimensional optical position sensor (Part S3932, Hamamatsu Corp., Bridgewater, NJ) was used to determine the *probe* location in order to implement closed-loop control of its displacement. The light source, an LED, was attached to the moving *probe* using a specially designed clamp made of aluminum [14].

5.2.2 Study description

5.2.2.1 Human subjects. This study was approved by the Institution Review Board (IRB) at the University of Utah (as study #42165) and each subject signed a consent form before participating in the study. Fifty-five subjects (24 female, 31 male, age range 19-86 years, mean age 37.4 years) were tested for this study from the general University of Utah population. Each subject was allowed to refuse participation at any point during the study. Age, height, weight, and dominant hand were also recorded for each subject. The dominant hand was used for testing, except for one female subject who was ambidextrous and for whom both hands were tested, resulting in n=56 data points.

For this study, no inclusion criterion was chosen with an intention to have a diverse group of subjects with both genders, different age groups and with no particular preferred profession. Subjects with CTS-like symptoms and no symptoms at all were allowed to participate. Minimum age was restricted to 18 years with no restriction on maximum age. The subjects were excluded from the study if they reported any history of diabetes, peripheral neuropathy, and injury to hand being tested. The dominant hand was tested for all subjects.

5.2.2.2 Testing procedure. A short survey (Appendix) was filled out by the subjects about their age, gender, handedness, presence of hand discomfort, and type of profession. The subjects were also asked to report and rate the hand discomfort during day and night as well as the frequency of hand discomfort.

Phalen's test was conducted by asking the subject to allow their forearms to be vertical with the wrists assuming a completely flexed posture, and then pushing the backs of the hands together. Numbness or tingling sensation reported within 30-60 sec was considered a positive result for CTS. Tinel's test was performed by tapping gently on the wrist of the subject along the median nerve location. Tingling sensation reported by the subject was considered a positive result for CTS [15]. Subjects were asked to place the forearm of their dominant hand on the VTEW with their middle finger placed directly in contact with the probe, with a neutral hand posture for the first test at 50 Hz frequency [14]. Subsequently, the subjects were asked to place their dominant hand on the device such that their wrist was fully flexed. The angle of flexion was recorded for the neutral and the flexed hand posture. The VT was recorded for both hand postures at 50 Hz. The subjects took about 5 min to complete the test in each posture.

5.2.3 CTS screening criteria

Several criteria were developed for evaluating whether the study subjects were symptomatic or asymptomatic. For each criterion, symptomatic and asymptomatic subjects were abbreviated as C (criterion #) _sym and C (criterion #) _asym, respectively.

5.2.3.1 Clinical tests (Criterion 1). Two tests, Phalen's and Tinel's test, for CTS diagnosis were performed on each subject to detect the presence of CTS symptoms. For Criterion 1, a subject was considered symptomatic (C1_sym) if the result of either or both

Phalen's and Tinel's test was positive. A subject testing negative on both tests was classified as asymptomatic (C1_asym).

5.2.3.2 Limited survey responses (Criterion 2). For Criterion 2, a subject reporting hand discomfort or pain, was classified as symptomatic (C2_sym). If no hand pain or discomfort was reported, the subject was classified as asymptomatic (C2_asym).

5.2.3.3 Rated survey responses (Criterion 3). Each question on the survey related to a risk factor and pain or discomfort rating was given a score. If the risk factor was present, the response scored as 1 and if it was absent, it was scored as 0. The ratings by subjects were used as reported. The subjects were given a composite score by adding all the individual survey question points and could score in the range of 0-32 points. The cut-off score to determine where to classify subjects as symptomatic (equal to or greater than the cut-off) or asymptomatic (less than the cut-off) is discussed below in Section 5.2.

5.2.3.4 Change from pre- to during- flexion VT (Criterion 4). The effect of provocative flexion on VT using VTEW was investigated at 50 Hz, since an increase in VT has been shown to be more pronounced in symptomatic subjects as compared to asymptomatic subjects [7, 11-12]. Each subject was tested in neutral hand posture and fully flexed hand posture. The difference in the preflexion and during-flexion VT values was calculated by subtracting the preflexion value form the during-flexion value. The cut-off change in μm to determine where to classify subjects as symptomatic (equal to or greater than the cut-off) or asymptomatic (less than the cut-off) is discussed below in Section 5.2.

5.3 Results and discussion

Statistical analysis on the data for this study was performed using Microsoft Excel 2007 and Minitab® 16.1.1. First, the cut-off values for two of the criteria were determined as described in Section 5.3.1. Next, the four different criteria defined for classification of symptomatic and asymptomatic subjects were evaluated individually and in combination for screening in Sections 5.3.2 and 5.3.3. The effect of flexion on VT was interpreted based on gender in Section 5.3.4.

5.3.1 Cut-off values for Criterion 3 and Criterion 4

To determine where to set the cut-off values for Criterion 3 and Criterion 4, the spread of values for each criterion were investigated as classified by Criterion 1. While the clinical tests used in Criterion 1 are not a 'gold standards' for diagnosing CTS, they are established clinical tests for screening. Since the purpose of both Criterion 3 and 4 are to improve screening for CTS, this approach provides a reasonable way to investigate where to set the cut-offs since a 'gold standard' diagnosis (such as with nerve conduction velocity testing) was not available for the study population.

5.3.1.1 Cut-off value for Criterion 3. Figure 5.2 shows a boxplot for subjects classified as symptomatic and asymptomatic based on Criterion 1. Three subjects who were classified as asymptomatic by Criterion 1 had unusually higher rated survey score (indicated by * in Figure 5.2). This was investigated by looking at the specific survey responses. Two of the three subjects were musicians who played an instrument at least 6 hours a day and complained of hand discomfort. The remaining subject complained of intermittent pain in index finger and difficulty in gripping objects. The mean rated survey score for symptomatic individuals was 10, which is one option for the cut-off.

However, that would increase the chances of screening out individuals who underestimate their pain and discomfort rating, even though they may have CTS like symptoms. Thus, the cut-off value for rated survey scores was chosen as 6, which corresponds to the top of the box for the results of asymptomatic subjects. This means that subjects who scored 5 points or lower will be classified as asymptomatic and subjects who scored 6 points or higher will be classified as symptomatic when Criterion 2 is applied. Using Criterion 1 to classify the subjects, Table 5.1 shows the range of rated survey scores for the asymptomatic and symptomatic subjects.

5.3.1.2 Cut-off value for Criterion 4. Using Criterion 1 to classify the subjects, Figure 5.3 displays the change in VT pre- and during- provocative flexion (Delta VT). The largest change in Delta VT for symptomatic subjects was 3.2 μm, while for asymptomatic subjects it was 2.3 μm. A cut-off of 2 μm was chosen to include most of the symptomatic subjects while excluding most of the asymptomatic subjects. Table 5.2 shows the distribution of Delta VT for symptomatic and asymptomatic subjects based on Criterion 1.

5.3.2 Evaluation using individual criterion

5.3.2.1 Study population. Understanding the distribution of a studied population is crucial to determine the usefulness of a test. Table 5.3 shows the number of symptomatic and asymptomatic subjects by gender based on all the criteria (Criterion 1, 2, 3 and 4). Criterion 1 has the largest asymptomatic population when compared to the three other criteria. The differences in classification are further explored in Section 5.3.3.

5.3.2.2 Statistical change in classification for each criterion. Since an increase in VT in persons with CTS has been well-documented in the literature, it was of interest to

determine whether a statistical change existed for the populations classified by the four criteria (detailed in Table 5.3).

The results of 2-sample t-tests performed on the VT at the neutral position and at the flexed position for symptomatic and asymptomatic subjects are shown in Table 5.4, followed by an asterisk (*) if the results are statistically significant. A p-value less than the chosen α level at 95% confidence interval (CI) indicates that a significant statistical difference exists between the symptomatic and asymptomatic population for that score. The p-values for all criteria have been summarized in Table 5.4.

None of the criteria show any significant difference between their groups of asymptomatic and symptomatic subjects at the neutral posture. However, at the flexed posture, Criterion 1 (the clinical tests) has p= 0.023, indicating the asymptomatic subjects have a significantly different VT than the symptomatic subjects. Criterion 4 has p= 0.001, which also indicates a statistical difference, although it must be noted that the VT at the flexed position is related to the definition for Criterion 4.

5.3.3 Evaluation using combinations of criteria

Criterion 2, Criterion 3, and Criterion 4 described in Section 5.2.3 were compared with Criterion 1 to assess the differences between the classification of symptomatic and asymptomatic subjects in terms of overall subjects by gender, as well as the VT results pre- and during- provocative flexion. The shaded boxes in the tables and interval plots in this section indicate agreement between both criteria. The white boxes along the opposite diagonal indicate disagreement between the two criteria, with subjects classified as asymptomatic by Criterion 1 but symptomatic by other criteria (Criterion 2, 3, and 4) in the upper right, and subjects classified as symptomatic by Criterion 1 but asymptomatic

by the other criterion (Criterion 2, 3, and 4) in the lower left. Note that there are 25 data points for females and 31 for males.

By combining two criteria at once, it is possible to evaluate the benefit of using a new criterion for classification compared to Criterion 1.

5.3.3.1 Criterion 1 and Criterion 2 subject populations. In Table 5.5, the results of the classifications for Criterion 1 and Criterion 2 are shown separated by gender. Overall, 17 females and 20 males were classified identically by both criteria. The remaining 8 females (32%) and 11 (35%) males were classified as symptomatic based on Criterion 2 but not by Criterion 1. Since Criterion 2 classifies subjects as symptomatic if they report the presence of hand discomfort or pain, these differences indicate subjects who reported pain or discomfort in the hands but did not test positive on Phalen's or Tinel's tests.

To further explore the differences between the subject classifications for Criterion 1 and 2, the VT in the neutral and flexed positions is shown for each classified group of subjects in Figure 5.4. In Figure 5.4, it is evident that for the subjects that Criterion 1 and Criterion 2 agree are asymptomatic (22 subjects), there is no noticeable shift in the VT from the neutral to flexed position. However, for the subjects that Criterion 1 and Criterion 2 agree are symptomatic (16 subjects), the VT increases noticeably from the neutral to flexed position, as expected in symptomatic subjects. Notably, the subjects who are identified as symptomatic in Criterion 2 due to reporting the presence of discomfort or pain in the hand (but not due to a positive result on the clinical tests, resulting in being identified as asymptomatic by Criterion 1) do not have any noticeable increase in the VT from the neutral to the flexed position.

Subjects reporting pain and discomfort on the survey with a negative result for

both clinical tests indicates that the use of a diagnostic test (such as nerve conduction velocity testing, commonly considered a 'gold standard') is needed to further interpret these results.

5.3.3.2 Criterion 1 and Criterion 3 subject populations. In Table 5.6, the results of the classifications for Criterion 1 and Criterion 3 are shown separated by gender. Using Criterion 1 and 3 resulted in more identical classifications of asymptomatic subjects (28 as compared to 22 with Criterion 1 and 2), but fewer identical classifications of symptomatic subjects (12 as compared with 18 for Criterion 1 and 2). 4 females (16%) and 3 males (10%) had scores of 10 or higher on their surveys, in the absence of a positive result on the clinical tests, while 2 females (8%) and 5 males (16%) had a positive result on the clinical tests but a low score on their surveys.

To further explore the differences between the subject classifications for Criterion 1 and 2, the VT in the neutral and flexed positions is shown for each classified group of subjects in Figure 5.5. For subjects where there is agreement on classifications, the results follow those seen in the previous section, with no noticeable shift in the VT pre- and during- flexion for the 28 asymptomatic subjects, but an increase in the VT for the 12 symptomatic subjects. However, the subjects whom Criterion 3 identifies as symptomatic but Criterion 1 identifies as asymptomatic (in the lower left plot) also appear to have an increase in the VT, while the subjects whom Criterion 3 identifies as asymptomatic but Criterion 1 identifies as symptomatic (in the lower left plot) do not have a noticeable change in the VT. This may suggest that Criterion 3 is failing to identify some subjects who are truly symptomatic, but should be further investigated with the use of a diagnostic test.

5.3.3.3 Criterion 1 and Criterion 4 subject populations. In Table 5.7, the results of the classification for Criterion 1 and Criterion 4 are shown separated by gender. Using Criterion 1 and 4 resulted in 25 identical classifications of asymptomatic and 13 identical classifications of symptomatic subjects. Three females (12%) and 3 males (10%) had a positive result on the clinical tests but a change in VT from pre- to during- flexion that was smaller than 2 μm. However, 6 females (24%) and 6 males (19%) had a change in VT larger than 2 μm but had a negative result on the clinical tests. For Criterion 1 and 4, the VT in neutral and flexed positions is shown for each classified group of subjects in Table 5.7.

By definition of Criterion 4, all subjects identified as asymptomatic on Criterion 4 will have a change in VT pre-and during-flexion that is less than 2 μm, while those identified as symptomatic will have a change greater than 2 μm. Thus, it is not surprising that in Figure 5.6, the 6 subjects classified as asymptomatic by Criterion 4 but symptomatic by Criterion 1 (in the lower left) do not have a noticeable change in the VT. The 12 subjects classified as symptomatic by Criterion 4 but asymptomatic by Criterion 1 (in the upper right) have a mean increase in VT of 3.2 μm, which is more than the threshold of 2 μm. Overall, Criterion 4, which uses the change in VT pre- and during-provocation, is identifying nearly a third of all subjects (18, or 32%) differently than the clinical tests. This may indicate that an increase in VT may be a better indication of early symptoms of CTS; however, the use of a diagnostic test (such as nerve conduction velocity testing, commonly considered a 'gold standard') is needed to further interpret these results.

Another interesting result in Figure 5.6 is that there is a decrease in VT pre- and

during- flexion for the subjects that are classified as asymptomatic by both Criterion 1 and 4. Finally, the clear increase in VT pre- and during- flexion for the subjects that are classified as symptomatic by both Criterion 1 and 4 is 3.3 μm, which is again more than the threshold of 2 μm and similar to that of the subjects in the upper right plot.

5.3.4 Gender differences in study population

To investigate whether there were gender-based differences in the change in VT pre and during provocative flexion, these changes ("Delta VT") for symptomatic and asymptomatic subjects, as classified by Criterion 1, are shown in Figure 5.7. The overall increase in change in VT (seen in previous sections) between asymptomatic and symptomatic subjects is evident for both females and males. However, there is not a significant change within each group of subjects by gender, though the females have a slightly wider range in values for the asymptomatic group of subjects and slightly smaller range for symptomatic subjects.

To investigate whether there were gender-based differences in the survey answers, the rated survey scores for symptomatic and asymptomatic subjects, as classified by Criterion 1, are shown in Figure 5.8. As expected, symptomatic females have higher survey scores than asymptomatic females, with little overlap between the ranges. While symptomatic males have a higher mean survey score than asymptomatic males, there is a larger variation in the survey score of the males, with the range of asymptomatic male responses falling within that of the symptomatic male responses. Also, the overall female responses are higher for both groups than the overall male responses. These results point towards a difference in prevalence of symptoms in different genders for this particular study. In addition, the male population was younger

than the female population recruited for this study. This age difference may contribute towards a lower VT for male population as compared to the female population.

5.4 Conclusion

Effect of flexion on VT was studied for the purpose of using it as a screening technique for CTS. Comparison of different criteria based on clinical tests and survey responses against results from provocative flexion testing was conducted. The study was limited in terms of distinguishing symptomatic and asymptomatic subjects without the use of NCV. However, the results show that use of flexion testing along with clinical tests to screen subjects that are clearly not CTS and definitely CTS is reasonable. This could result in reducing the costs of testing and achieve the goal of periodic testing efficiently and inexpensively. Future study with change in outcome parameters and more extensive survey forms for subjects is recommended.

5.5 Acknowledgement

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5.6 References

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Figure 5.1: The Vibrotactile Threshold Evaluator for Workplace Screening (VTEW) device with a subject's arm (cover removed to show the surround and the probe).

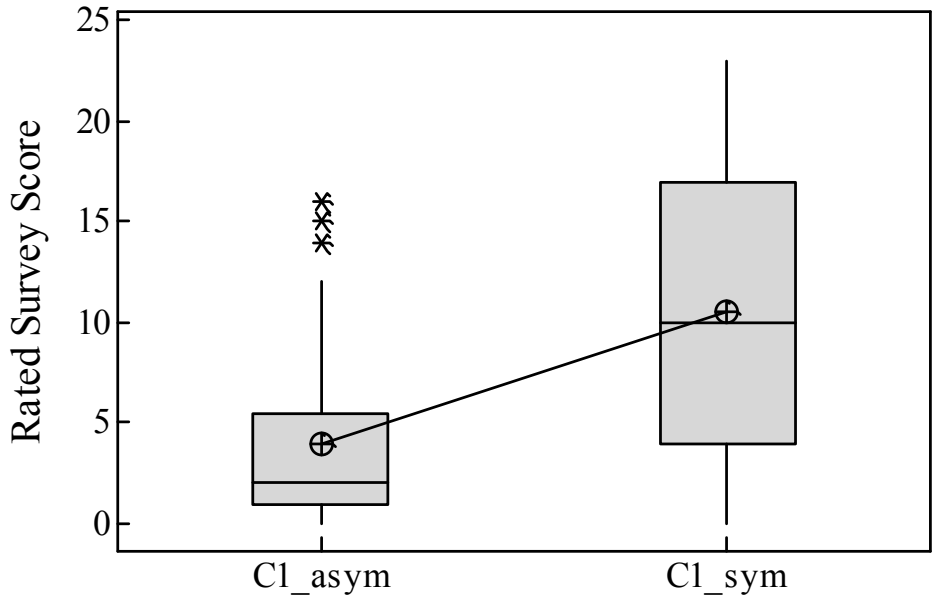

Figure 5.2: Boxplot distribution of rated survey scores of symptomatic and asymptomatic subjects based on Criterion 1. Unusually high observations, outliers, are shown as *. The lower, middle and upper line of the box shows the first quartile, median, and third quartile. Symptomatic subjects (n=19) are labeled as C1_sym and asymptomatic subjects (n=37) are labeled as C1_asym. The classification of subjects is done on the basis of results of Phalen's and Tinel's test (Criterion 1). P-value is 0.002 ($\alpha = 0.05$, 95 % CI). The symptomatic subjects had a maximum survey score of 23 as compared to asymptomatic subjects with a maximum score of 16. On an average the symptomatic subjects had a score higher than 10 as compared to an average score of 4 for asymptomatic subjects.

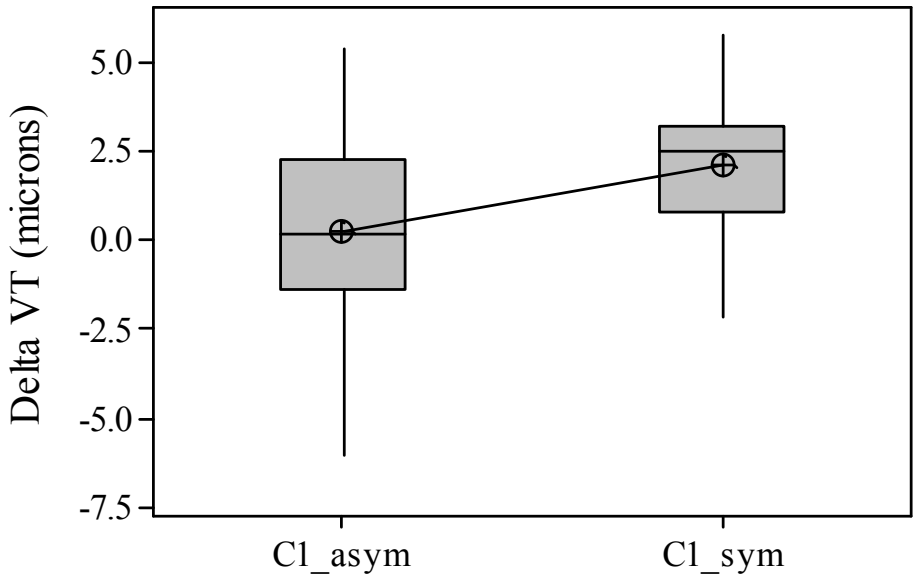

Figure 5.3: Boxplot distribution data of the change in VT for symptomatic and asymptomatic subjects based on Criterion 1. The plot shows the difference between flexed posture and normal posture for asymptomatic (C1_asym) and symptomatic (C1_sym) subjects. Based on Criterion 1, n= 37 for asymptomatic subjects and n=19 for symptomatic subjects. P-value is 0.004 ($\alpha = 0.05$, 95 % CI).

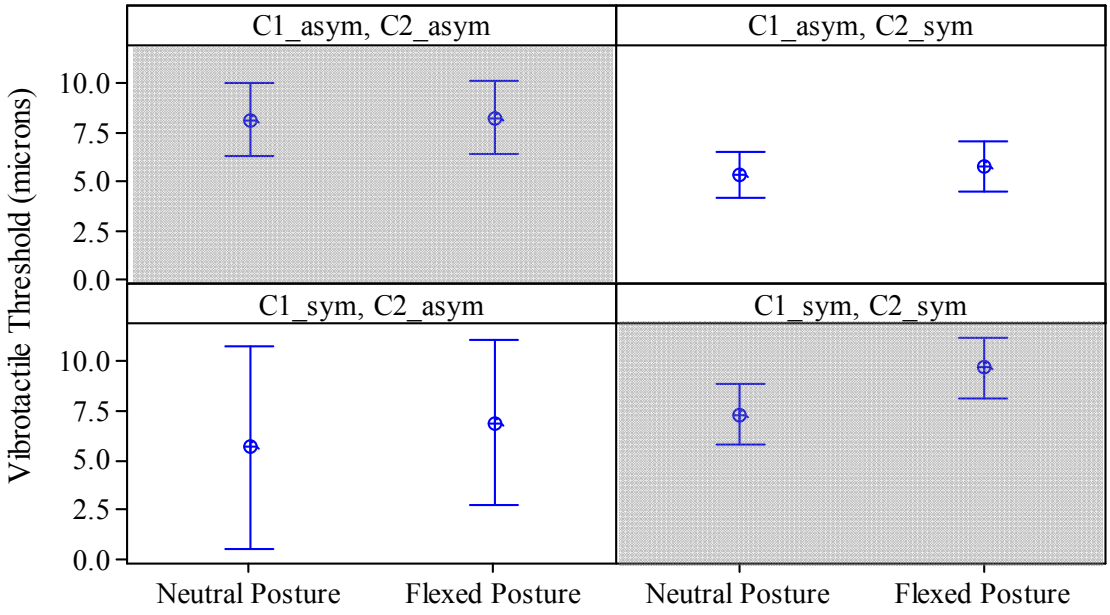

Figure 5.4: Interval plot for VT for neutral and flexed posture based on Criterion 1 and Criterion 2 combined. Shaded panels show the agreement between Criterion 1 and Criterion 2. The remaining panels show disagreement between the two criteria. The largest difference between VT in neutral and flexed posture was seen in agreement panel for both criteria classifying the subjects as sym (n=16) (mean VT in neutral posture was 7.34 µm and mean VT in flexed posture was 9.7 µm).

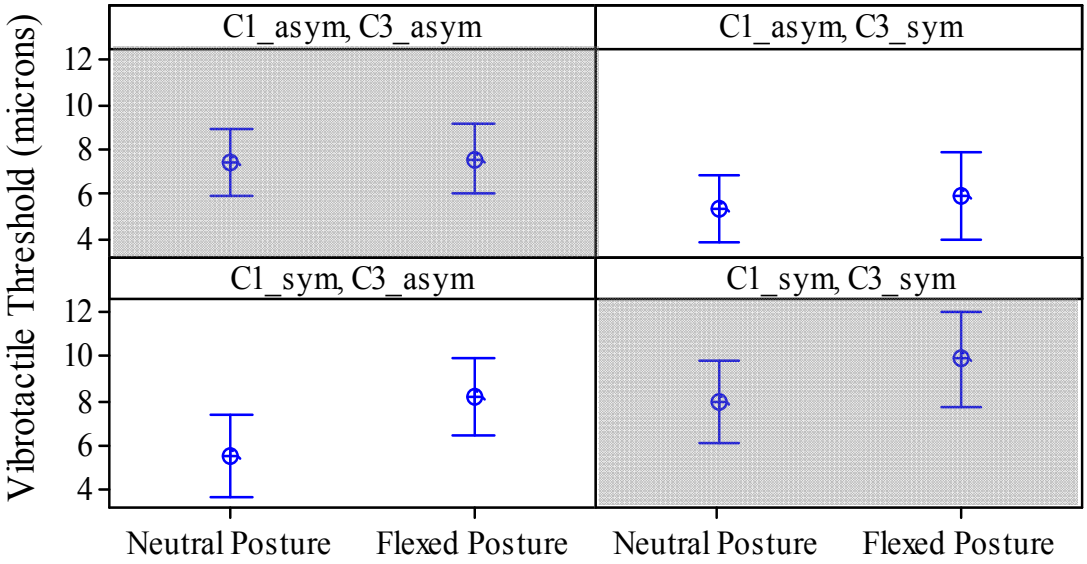

Figure 5.5: Interval plot for VT for pre and during flexion based on Criterion 1 and Criterion 3. Shaded panels show the agreement between Criterion 1 and Criterion 3. The remaining panels show disagreement between the two criteria. Largest difference in mean VT between neutral and flexed posture is observed in left and right bottom panels. For subjects classified as(C1 sym, C3, asym) (n=7), mean VT value went from 5.6 µm in neutral posture to 8.2 µm in flexed posture. For subjects classified as sym by both C1 and C3 (n=12), mean VT, mean VT value went from 8 µm in neutral posture to 9.8 µm in flexed posture.

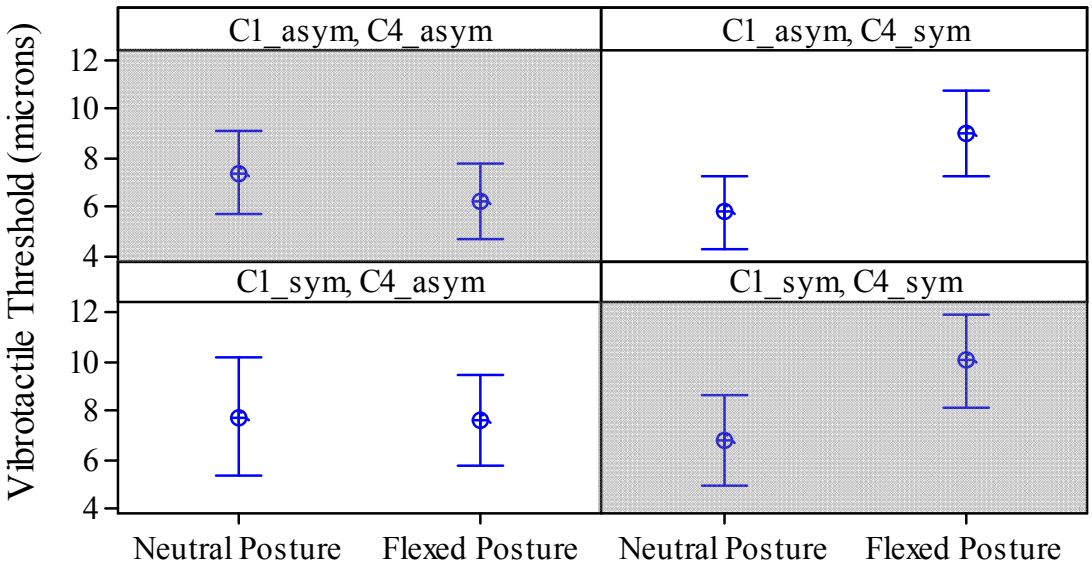

Figure 5.6: Interval plot for VT for pre and during flexion based on Criterion 1 and Criterion 4. Shaded panels show the agreement between Criterion 1 and Criterion 4. The remaining panels show disagreement between the two criteria. For subjects classified asym by both criteria (n=25), mean VT was 7.3 µm in neutral posture and was decreased to 6.2 µm in flexed posture. For subjects classified sym by both criteria (n=13), mean VT was 6.8 µm in neutral posture and 10 µm in flexed posture. For the subjects classified as sym by C3 and asym by C1 (n=12), an increase in mean VT was observed between neutral (5.8 µm) and flexed posture (9 µm).

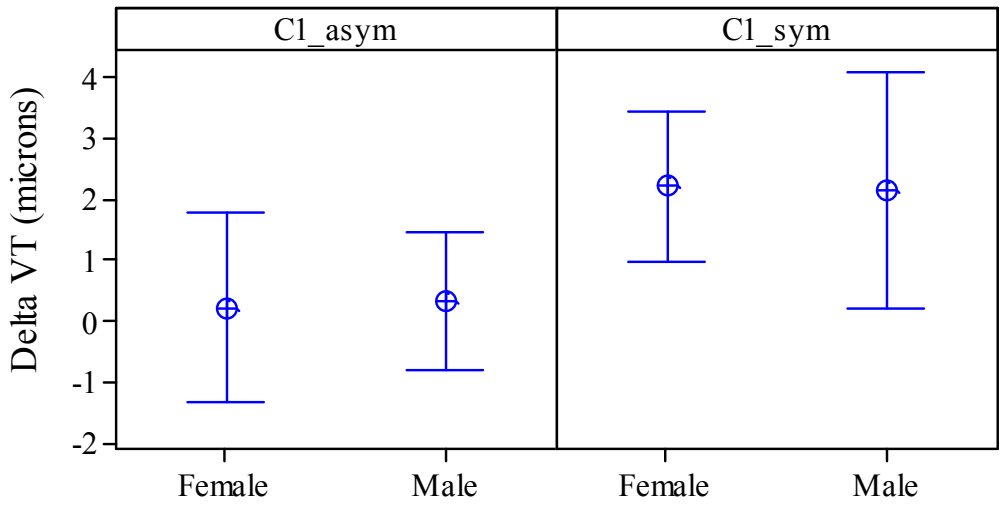

Figure 5.7: Difference between pre and during flexion VT for symptomatic and asymptomatic males and females based on Criterion 1. The mean Delta VT for female asym subjects (n=14) was 0.21 µm and for female sym subjects (n=11) was 2.2 µm. The mean Delta VT for male asym subjects (n=23) was 0.3 µm and for male sym subjects (n=8) was 2.15 µm.

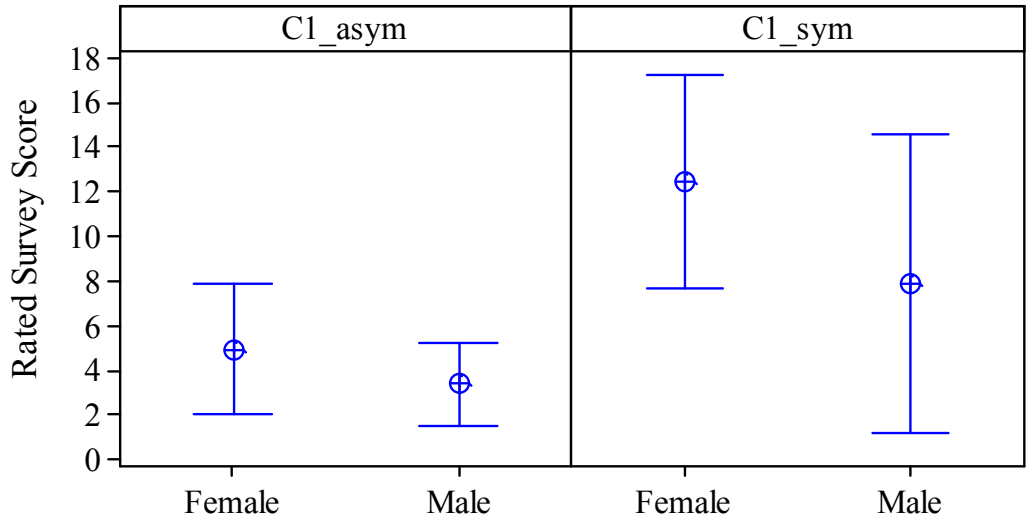

Figure 5.8: Rated survey scores for male and female symptomatic and asymptomatic subjects based on Criterion 1. Mean rated survey score for asym female subjects was 4.9 and for sym female subjects was 12.5. Mean rated survey score for asym male subjects was 3.3, while for sym male subjects was 7.8.

Table 5.1: Distribution of rated survey score for symptomatic and asymptomatic subjects based on Criterion 1

Rated Survey Score	n	Mean	Std Dev	Min.	Max.
C1_asym	37	3.95	4.55	0	16
C1_sym	19	10.53	7.64	0	23

Table 5.2: Distribution of Delta VT for symptomatic and asymptomatic subjects based on Criterion 1

Delta VT	n	Mean	Std Dev	Min.	Max.
C1_asym	37	0.278	2.598	-6	5.4
C1_sym	19	2.184	1.996	-2.1	5.8

Table 5.3: Study population distribution for each individual criterion

	Asymptomatic			**Symptomatic**		
	Male	Female	**Total**	Male	Female	**Total**
Criterion 1	23	14	**37**	8	11	**19**
Criterion 2	16	8	**24**	15	17	**32**
Criterion 3	23	12	**35**	8	13	**21**
Criterion 4	20	11	**31**	11	14	**25**

Table 5.4: Two-sample t-test results (p value with $\alpha = 0.05$, 95% CI) for VT in neutral and flexed hand postures for symptomatic and asymptomatic subjects at 50 Hz

	Neutral Posture	**Flexed Posture**
Criterion 1	0.802	0.023*
Criterion 2	0.127	0.759
Criterion 3	0.823	0.625
Criterion 4	0.182	0.001*

Table 5.5: Subject classification for (Criterion 1, Criterion 2)

(C1_asym, C2_asym)		**(C1_asym, C2_sym)**	
Female 7	Male 14	Female 7	Male 9
(C1_sym, C2_asym)		**(C1_sym, C2_sym)**	
Female 1	Male 2	Female 10	Male 6

Table 5.6: Subject classification for (Criterion 1, Criterion 3)

(C1_asym, C3_asym)		**(C1_asym, C3_sym)**	
Female 10	Male 18	Female 4	Male 5
(C1_sym, C3_asym)		**(C1_sym, C3_sym)**	
Female 2	Male 5	Female 9	Male 3

Table 5.7: Subject classification for (Criterion 1, Criterion 4)

(C1_asym, C4_asym)		**(C1_asym, C4_sym)**	
Female 8	Male 17	Female 6	Male 6
(C1_sym, C4_asym)		**(C1_sym, C4_sym)**	
Female 3	Male 3	Female 8	Male 6

CHAPTER 6

CONCLUSIONS AND FUTURE WORK

6.1 Conclusions

This dissertation has resulted in a major literature review paper (accepted for publication in Jan 2011 with the Journal of Hand Therapy), a Vibrotactile Threshold Evaluator for the Workplace that is highly configurable, including the probe diameter (2- 6 mm), applied frequency (1-500 Hz), probe displacement (1-500 μm), and angle of probe and stimulus assembly (120º range). In addition, four hypotheses were tested:

- *Hypothesis 1 stated that there is a correlation between the VT data obtained from VTT and VTEW*. As shown in Chapter 4, the data obtained from VTT and VTEW were statistically similar.
- *Hypothesis 2 stated that that a subject will have a lower sensitivity to a low frequency (here, 4 Hz) as compared to a higher frequency (here, 50 Hz).* As shown in Chapter 4, the VT of subjects (symptomatic and asymptomatic) at 4 Hz was higher than the VT of subjects at 50 Hz and the difference between VT at 4 Hz and VT at 50 Hz was statistically significant ($p = 0.00$ ($\alpha = 0.05$, 95 % CI)).
- *Hypothesis 3 stated that if a test subject is positive for Phalen's and/or Tinel's test, his/her sensory threshold will be elevated*. As shown in Chapter 4, the mean VT for symptomatic subjects (defined as symptomatic if they tested positive for Phalen's and/or

Tinel's) were higher than asymptomatic subjects. The difference between the VT was not statistically significant at both 4 Hz and 50 Hz (p- value 0.255 and 0.802, respectively (α =0.05, 95 % CI)).

- *Hypothesis 4 stated that a comparison of pre and during- provocation VT will show a larger difference for symptomatic subjects as compared to asymptomatic subjects*. As shown in Chapter 5, the symptomatic subjects (defined as symptomatic if they tested positive for Phalen's and/or Tinel's) had a statistically significant (p=0.023) change in VT during provocation when compared to the asymptomatic subjects. In addition, the change in VT increased in the symptomatic subjects, with p=0.001 with provocative flexion.

Other factors investigated in the manuscripts include the age adjustment for the VT measurement, gender effects on VT, and the use of a survey as a screening tool.

In conclusion, the VTEW is a highly configurable tool that addresses many of the issues facing other equipment for evaluating the vibrotactile threshold available today. Its applicability to clinical practice and evaluation in the workplace were demonstrated through the validation study that supported the hypotheses described above, and for which over 50 subjects were recruited and evaluated.

6.2 Suggestions for future work

In implementing the validation study, it became clear that there are several areas in which future studies should improve. These are detailed below.

- Improvised testing protocol: The testing protocol used for this study was identical for both low and high frequency (4 Hz and 50 Hz) other than the starting

amplitude. It could be useful to choose different step sizes and amplitude values for the lower frequency to see if there is an effect of step size on the VT estimation.

- Subject recruitment: To gain insightful data for the effect of age on VT, it could be useful to recruit the same number of subjects in specified age range groups. This would prevent the bias in data from a particular age group on VT regression with age.
- Statistical design of study: The statistical design for this study was based on the number of subjects who volunteered to participate in the study. Future studies can benefit from a power analysis and recruitment of symptomatic and asymptomatic subjects of similar ages. Multiple recordings of the VT for an individual could be useful to report the repeatability of the measurements by VTEW. It could also be useful to study the effect of various testing protocol such as changing the step size and changing the duration of stimulus for different frequencies.
- Gold standard comparison: It would be useful to test subjects with the VT and an established "gold standard" such as nerve conduction velocity testing so that the predictive values along with sensitivity and specificity could be reported.
- Temperature control for voice coil: The *probe* was connected to the voice coil via a connector made of aluminum. The increase in voice coil temperature translated into an increase in *probe* temperature, causing slight discomfort to the subject. It would be useful to invest some effort in providing cooling by the use of additional ventilation on the sides of the device, liquid circulation cooling system, and/or additional cooling fans installed within the device housing.
- Additional frequencies test: It would have been beneficial to evaluate VT for a much higher frequency for a comparison between lower and higher frequency. The use of

either 125 Hz or 250 Hz could provide a better understanding of the activation of different mechanoreceptive channels.

Implementation of this validation study also resulted in many ideas for other topics to study using the VTEW. For instance, future studies could include a more sophisticated study on the effect of neurotoxin drugs on VT for cancer patients. However, pre- and postchemotherapy VT evaluation would require a substantial commitment on the part of participants. This could be very beneficial in developing screening criteria to detect changes in VT associated with CTS at an early stage.

A larger cross-sectional study to understand the change of VT with age would be useful. Subjects could be tested periodically (e.g., every first Monday of the month) over a year which would provide useful information about changes in VT for a symptomatic versus an asymptomatic individual. This kind of study can provide data for VT for different frequencies, testing protocols for asymptomatic and symptomatic populations.

Use of different frequencies low and high could be useful for future studies to show the versatility of application of VTEW. Comparison of VT with frequency could be used to plot a vibrogram for each subject and compared for asymptomatic and symptomatic individuals.

The VT for the big toe could be evaluated with this device for diabetic patients. The correlation between blood sugar level and VT could also be investigated in future studies.

For this study the temperature was maintained in the range of 30-36^0 C. The change in VT with temperature could be investigated for VTEW.

A study dedicated to change of VT with gender and BMI could be useful. The literature review shows that there is a significant lack of conclusive data on how gender affects VT in symptomatic and asymptomatic populations. It could be useful to recruit a similar number of symptomatic and asymptomatic subjects of each gender.

While the study of the effect of flexion on VT is useful and serves as a quick method for producing CTS-like symptoms, fully flexed postures are not encountered in industry. It would be useful to investigate the change in VT for different deviations and postures of hand that could be more realistic simulation of postures at workplace.

Vibrotactile cues for the visually impaired have become popular in providing assistance in daily activities like walking. Vibrotactile cues could be useful for any individual in a situation with high background noise such as in industrial settings or sports arenas. Investigation of the frequencies and amplitudes that would be most likely to be noticed could be useful for such applications.

APPENDIX

VTEW SUBJECT EVALUATION FORM

VTEW Subject Evaluation Form

Subject ID #:

Age:

Sex (Circle one): Male Female

Height:

Weight:

Result for Tinel's test:

Result for Phalen's Test:

Please answer the following questions by encircling the right answer. If you do not understand any question, please feel free to ask for help.

1. Does your occupation involve repetitive motion of the hand, wrist and/or fingers? Yes No

2. Is your posture at work comfortable? Yes No

3. Have you experienced any pain in your wrist and/or hand (other than when you have been lying with your arms in awkward position) in the past 6 months? Yes No

4. Do you feel any weakness in your hand while grasping objects with your hands? Yes No

5. Do you experience tingling sensation in your hand during the night time or in the early hours of morning? Yes No

6. How long does the episode of pain last during daytime?
   - No pain
   - <10mins
   - 10-60 mins
   - constant pain throughout the day

   If the answer to any or all of questions 3, 4, and 5 is yes, then please answer the following questions.

If the answer to questions 3, 4, and 5 was no, please leave the following questions blank.

	Question (Severity score: 0-None; 4-Severe)	**0**	**1**	**2**	**3**	**4**
1	How severe is the pain in your hand?					
2	How severe is this pain at night?					
3	How severe is the pain in your hand/wrist during daytime?					
4	How severe is the numbness (loss of sensation) in your hand?					
5	How severe is the tingling sensation in your hand?					
6	How painful is it to grab objects with your hands?					

Additional comments:

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