AMERICAN ASSOCIATION OF ELECTRODIAGNOSTIC MEDICINE REVIEW: QUANTITATIVE SENSORY TESTING EQUIPMENT AND REPRODUCIBILITY STUDIES

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INTRODUCTION

This review is provided as a service to the membership of the American Association of Electrodiagnostic Medicine (AAEM). This paper discusses quantitative sensory testing (QST) equipment using the following sensory modalities: 1) light touch, 2) vibration, 3) thermal, and 4) pain. First, is a summary of the different QST equipment and the equipments' specifications as reported in the literature. Second, is a table that summarizes the different reproducibility studies on vibration, thermal, and heat-pain thresholds that have been reported since 1981. Other sensory testing devices such as the current perception test, tactile circumferential discriminator, and two-point esthesiometer are not included in the table. This review was based on searches of MEDLINE, and references from relevant articles published between 1966 and 2001. The following search terms were used quantitative sensory testing," "QST," "sensory threshold"," "thermal threshold," "temperature sense," "vibration," and "vibration threshold." The search for literature included only articles written in English.

No clinical tests or trials were performed by the AAEM or the authors of this review. Neither the AAEM nor the authors of this report reviewed any product literature regarding the pieces of equipment included in the paper nor did the AAEM review the specific equipment. The information included about the equipment and the opinions expressed regarding the reproducibility of each type of equipment are those of the author(s) of the papers cited. The conclusions are not those of the AAEM or the authors of this review. This paper was not created with the intent that it be used as a basis for reimbursement decisions.

A literature review of QST can be found in *Muscle & Nerve* in the May 2004 issue, volume 29, pages 734-747 or on the *Muscle & Nerve* website at: http://www3.interscience.wiley.com/cgi-bin/fulltext/108066505/HTMLSTART.

EQUIPMENT

Light Touch

von Frey Hairs

In 1898, von Frey introduced this method of measuring pressure perception with horsehair.[28] Semmes and Weinstein utilized a set of nylon monofilaments with varying diameter and stiffness or bending pressures. The monofilaments are attached to rods at right angles. The examiner applies the monofilaments on the skin at a right angle, and pressure on the rod is increased slowly until the monofilament buckles or bends. The examiner then asks the patient whether a sensation of pressure was felt. The length and diameter of the monofilaments are standardized and the pressures required to bend the monofilaments are predictable. This device is now called the Weinstein-Semmes pressure aesthesiometer.[28] The markings on the rod (1.65 to 6.65) represent the logarithm of 10 times the bowing force in milligrams. The higher number represents a thicker monofilament, which requires a higher pressure to buckle.[8]

CASE III system

This system was developed by Dyck and colleagues to assess cutaneous light touch perception. The apparatus consists of a stylus tip with a diameter of 0.64 mm that is attached to a galvanometer. The stylus tip rests on the skin at a constant load to allow for accommodation. During stimulation, a known force is applied to indent the skin.[22] The tactile stimuli are applied to a matrix of 9 points 1 mm apart in a 3 x 3 array and the threshold is estimated using the forced-choice algorithm. The stimulus intensity is given in 21 levels with forces that range from 2.9 mg to 12,000 mg. A forced-choice response paradigm is used to obtain the threshold at each point. The mean threshold for the nine sites is also calculated. The most recent CASE IV system no longer includes this apparatus because the galvanometer motor became unavailable and vibration perception testing may be used to assess the large myelinated sensory fibers.[11]

Vibration

Bio-thesiometer (Bio-Medical Instruments, Newbury, OH)

This is a hand-held electromagnetic vibrator with a stimulating probe (12-mm diameter) that vibrates at 100 Hz. It has been in use since 1957. The stimulating probe is placed on the site to be tested, usually the big toe or the finger, and it rests on its own weight (300 g).

The intensity of vibration in increased or decreased by changing the voltage to the stimulator. The vibration threshold is determined by the method of limits and expressed on an arbitrary scale in volts. The operator manually increases the applied voltage until the subject feels the vibration. The voltage is then manually decreased until the sensation disappears.[35,23] Being a hand-held instrument has the following limitations: (1) the movement of the stimulator is in more than one plane; (2) the static load on the probe may affect the amplitude of the vibration; and (3) the rate of increase in stimulation intensity is manually controlled and therefore not constant.[35] Probably the most

important limitation of this device is the effect of tissue damping on the actual amplitude of vibration. Goldberg and Lindblom showed that the actual vibration amplitude varies depending on tissue consistency of the stimulation site and that different tissues have different damping effects on the vibrator.[21]

Vibrameter (Somedic AB, Sweden)

This instrument is a modification improvement of the Bio-Thesiometer. Instead of using the applied voltage as the measure of stimulus intensity, an accelerometer measures the level of vibration in micrometers. This modification overcomes the problem of varying vibration amplitude secondary to different tissue consistency. The application pressure of this hand-held device on the stimulation site may be held constant with the aid of a load-weighing display. The stimulator generates a sinusoidal vibration at a constant 100-Hz frequency.[21] The stimulus intensity or the vibration amplitude is adjusted manually.

CASE IV vibration stimulator

This device is part of the CASE system that was first introduced by Dyck in 1978.[14] It is an automated system that includes a personal computer and software. The system generates the stimuli, cues the patient, records the subject's responses, and determines the sensory threshold according to selected algorithms (WR Medical Electronics Co., Stillwater, MN). Since 1978, the system has undergone modifications of stimulus characteristics, number of stimulus levels, and techniques of finding the sensory threshold. The vibration stimulator is a galvanometer that is mounted on a balance arm to allow the stimulating probe (9 mm diameter) to rest on the base of the nail of the index finger or big toe at a force of 30 grams. The stimulator generates vibration at 125 Hz (previously 250 Hz). The amplitude is controlled by the computer to vary from 0.1 to 576 micrometers in 25 (previously 21 under CASE III) levels or just noticeable difference (JND).[22] A cue device informs the subject of the stimuli and the patient responds by pressing on the button of a response box.

Vibratron II (Sensortek Inc., Clifton, NJ)

This device consists of two identical stimulating posts (1.4-cm diameter) and a controller unit. Only one post vibrates at any one time. The vibration frequency is 120 Hz. The amplitude of vibration varies from 0 to 20 "vibration units." The "vibration units" may be converted to microns of stimulator displacement. The subject is asked to press the digit against each stimulating post for 1 second at a time and identify the probe that is vibrating using the forced-choice protocol. A method of limits protocol has also been used.[18,19,20]

Vibratory sensory analyzer (Medoc Ltd., Israel)

The stimulating probe is mounted on a balance arm that provides a constant weight of 70 grams. The probe faces up against the pulp of the finger or toe. The contact area is 1.2 cm^2 and the vibration frequency is 100 Hz.[30]

Maxivibrometer (Penn State University, University Park, PA)

This device allows sensory loss to be quantilized over a wider range. It measures vibration amplitude from 1 to 1100 mm. The diameter of the stimulating probe is 12.5 mm and the stimulating frequency is 60 Hz. The subject lies prone on the examining table and the device is mounted on a tripod that is not connected to the table to prevent transfer of vibrations through the table.[34]

Thermal

All commercially available thermal stimulators utilize the Peltier principle. The temperature change is made possible by passing a current through two different metals. Cooling occurs at one side of the bimetallic junction while warming occurs on the other side. Kenshalo introduced this method for the study of temperature sense in humans and subhuman species.[27]

Marstock stimulator (Somedic AB, Sweden)

Fruhstorfer, Lindblom, and Schmidt described this device in 1976. It is called the Marstock stimulator because of the collaboration between investigators from the two cities of Marburg and Stockholm.[17] The Peltier device and a thermocouple are placed in the thermode and circulating water cools the device. The thermode is placed over the palmar aspect of the thenar region or the lateral aspect of the dorsum of the foot. The subject is instructed to press a button as soon as a warm sensation is perceived. The direction of temperature change reverses to cool when the button is pressed. The temperature is measured with a thermocouple and plotted by a pen recorder. The warm-cold difference limen is then measured from the temperature recording. This original method evaluates warm and cool sensation together. It is a quick way to assess temperature sensation. Moreover, hypoesthetic and hyperesthetic conditions can be evaluated. Subsequent modifications of this method have been described to measure warm and cool thresholds separately.[6,29,36]

CASE IV thermal testing probe

This instrument is part of the CASE IV automated system (WR Medical Electronics., Stillwater, MN). In contrast to the thermode in CASE III, this thermode is now water-cooled to allow a faster rate of temperature change. The stimulating surface that comes in contact with the skin is a ceramic sheet (10 cm^2) with high conductance. The thermode consists of two thermoelectric units (TEU 1 and TEU 2) and a thermocouple attached to the ceramic sheet. An aluminum block separates the two TEUs. Another aluminum block is mounted on TEU 2 and water circulates around it to dissipate heat. TEU 1 provides the warm or cold temperature ramps and TEU 2 maintains the aluminum block at skin temperature. The patient's skin temperature is used as the baseline. The thermode's temperature is maintained by the computer through the

thermode's temperature ranges from 5ºC to 50ºC, and the stimulus intensity is given in 25 levels or JNDs.

The rate of temperature change is set at 4ºC/s. The maximum temperatures that can be attained are the following: 9ºC x 10 s for cold perception threshold, 45ºC x 10 s for warm perception threshold, and 49ºC x 10 s for heat pain perception.[11,22]

Glasgow system

This is an automated system used to measure warm and cool thresholds. The original thermode was watercooled,[25,26] but a portable system that did not require water cooling became available as the "Triple T" (Thermal Threshold Tester, Medelec).[5] The stimulating thermode has a surface area of 12.5 cm^2. Using a constant rate of temperature change (1ºC/s), the stimulus intensity is graded by changing the duration of stimulus application. The baseline skin temperature is maintained at 34ºC. The thermal threshold is defined as the minimal temperature change from the baseline skin temperature that the subject can reliably perceive.[5]

Middlesex Hospital thermal testing system

This is another computer-driven portable system with no water cooling system. The stimulating surface area is 7.5 cm^2 for the hand and 26 cm^2 for the foot.[16] Similar to the Glasgow system, the rate of temperature change is kept constant at 1ºC/s and the stimulus duration determines the stimuli intensity. The warm and cool thresholds are determined by utilizing the yes-no method to obtain the subject's responses and the staircase algorithm to change the stimulus intensities.[16]

Thermal sensitivity tester (Sensortek, Inc., Clifton, NJ)

This device consists of two 25 cm^2 nickel-coated copper plates connected to different power units and cooled with water. The subject alternately presses on each plate for 2 seconds. The temperature of one plate changes on a series of fixed-step digital controls while the temperature of the other plate is maintained at 25ºC. The temperature difference between the plates is displayed on a meter.[1]

Thermal sensory analyzer TSA-2001 (Medoc Ltd., Israel)

This is also a microprocessor driven automated system. The thermode size is 50 x 25 mm^2 and the temperature range is 0-50ºC. A computer feedback mechanism controls the temperature of the thermode. The yes-no method is used to obtain subject's responses. The stimulus intensities are adjusted with an initial step of 4ºC with subsequent steps reduced in half until step size reached 0.2ºC. Unlike the CASE IV system, no visual or auditory cues are given to signal stimulus onset.[36]

PATH-tester MPI 100 (PHYWE Systeme GmbH, Germany)

This is a microcomputer-driven modified Marstock thermode. The thermode contact surface measures 1.6 x 3.6 cm. The temperature range is 17ºC to 50ºC and it is controlled by a feedback circuit.[6]

REPRODUCIBILITY

The following table summarizes the reproducibility studies on vibration, thermal, and heat-pain thresholds that have reported in the literature since 1981. The conclusions are those of the author(s) of the papers cited and not those of the AAEM or the authors of this article.

REPRODUCIBILITY STUDIES ON QST

REF	SUBJECTS	INTERVAL	MODALITY	EQUIPMENT	METHODOLOGY	MEASURE OF REPRODUCIBILITY	CONCLUSION*
34	7 diabetics with neuropathy and 7 matched non-diabetic controls.	3 times daily on 2 separate days within 3 weeks	Vibration	Maxivibrometer (Penn State University, University Park, PA) Heel probe area: 12.5 mm diameter Frequency: 60 Hz. Amplitude range: 1 to 1100 micrometer	Method of Limits. As the stimulus intensity increased, the subject pressed the button as soon as vibration was perceived. Computer recorded this as appearance threshold. Then, the stimulus intensity decreased and the subject pressed the button as soon as the vibration was no longer felt (disappearance threshold). The procedure was repeated 3 times so that 6measurements were made. The average of these 6 measurements was considered the threshold. Stimulation site: right hallux. 1 examiner only.	**Replication to replication ICC** Controls 0.980 Diabetics 0.956 **Day to day ICC** Controls 0.779 Diabetics 0.940	Excellent reliability
30	101 NS, age 6-17	2-4 weeks	Warm, Cold Vibration	Medoc TSA-2001 (Medoc, Israel) Thermode area: 3 x 3 cm Temperature range: 0-50ºC Rate of change: 1ºC/s Medoc Vibratory Sensory Analyzer (Medoc, Israel) Frequency: 100 Hz Probe area: 1.2 cm^2 Constant weight: 70 g	a. Warm, cold thresholds: Method of Limits. Skin adaptation temperature 32ºC, rate of return 1 C/s, average of 4 readings, 6 s interstimulus interval, rate of return 10ºC/s, average of 3 readings, 10 s interstimulus interval. b. Warm, cold thresholds: Method of Levels. Yes or no response. Initial temperature step of 3ºC. Subsequent step sizes were increased or decreased at one half the initial intensity. Null stimuli included. Test terminates when step size decreased to 0.1ºC. Threshold = average of the last "yes" and "no" response. c. Vibration: Method of Limits. Linearly increasing train of 4 stimuli. Intensity starting at 0 µm amplitude and increased at 0.1 µm/s. Threshold = average of 4 consecutive determinations.	Wilcoxon signed-ranks test with a Bonferroni correction for multiple comparisons. Hand and foot. $p>0.05$	a. No significant session differences b. No significant session differences c. No significant session differences
24	49 children, age 3.3 to 6.8	1 to 58 days (27.3±22.9)	Vibration	Vibrameter (Stockholm, Sweden) Frequency: 120 Hz Probe diameter: 13 mm Constant weight: 650 g	Method of Limits. Vibration threshold is the average of 3 appearance thresholds and 3 disappearance thresholds. Catch trials with no stimulation or steady stimuli were included.	2-sided Wilcoxon signed ranks test: $p>0.1$ 2-tailed Spearman rank test: $r = 0.590$, $p<0.01$	High reproducibility
31	23 diabetics with neuropathy	3 times over 21 days with 1 to 14 day intervals	Vibration	Vibraton II (Clifton, NJ) Probe area 1.5 cm^2	Method of Levels. 2 alternative (spatial) FC. 1 examiner only. 2 identical probes were presented to the subject. The subject is asked to identify which one was actually vibrating. The test began at the highest intensity of 20 vibration units (VU) or at a lower intensity appropriate for the patient. The intensity was decreased by 10% after each correct response and increased by 10% after each wrong response. 5 wrong answers were enough to finish the examination. The lowest and highest value of 10 errors and correct responses were eliminated and the mean of the remaining 8 score was called the VT.	CV%/ SD left hand 17.69/ 11.28 Right hand 17.61/ 14.92 left toe 20.60/ 16.99 right toe 19.46/ 11.40	Reproducible
33	64 diabetics	2 to 4 weeks and Same day	Pressure	Semmes Weinstein monofilaments (sizes 4.17, 5.07, 6.10)	Monofilaments applied on both feet at the first toe, medial surface and base of the third metatarsal bone. Threshold was defined as the total number of times the application of the monofilaments was not felt. This could vary between 0 and18.	intraobserver test-retest mean (SD) 0.39 (0.35), intrasubject SD 0.16, CV 0.41, CC 0.80 interobserver test-retest mean (SD)0.40 (0.37), intrasubject SD 0.18, CV 0.41, CC 0.77	Sufficiently Reproducible Sufficiently Reproducible
13	25 NS	Twice at intervals of more than a day but less than 2 weeks	Heat-Pain	CASE IV (WR Medical Electronics Co. Stillwater, MN)thermode area 10 cm^2 rate of change 4ºC/s.	Non-repeating with null stimuli algorithm (see text for details).	HP:0.5 %- to76% within 1 stimulus step HP:5.0% to 88% within 1 stimulus step	Low variability
37	72-76 NS, age 20-59	2 weeks	Heat-Pain	Medoc TSA-2001 (Medoc, Ramat, Yishai, Israel) thermode area 46 x 30 mm^2	Method of Limits. Skin adaptation temperature 32ºC, rate of temperature change 2ºC/s, average of 3 readings, 20 s interstimulus interval.	**ANOVA**-based model by Techno-Stat **"r" value** Thenar 5.85** Foot 4.47 ** significant intersession bias "r" value- 95% confidence that 2 measurements on the same patient would differ by less than r.	Poor Sufficient

REF	SUBJECTS	INTERVAL	MODALITY	EQUIPMENT	METHODOLOGY	MEASURE OF REPRODUCIBILITY	CONCLUSION*
36	72-76 NS, age 20-59	2 weeks	Warm, Cold	Medoc TSA-2001 (Medoc, Israel) thermode 50 x 25 mm^2 20 Hz feedback, mechanism to maintain linear temperature change	a. Method of Limits. Skin adaptation temperature 32ºC, rate of temperature change 1ºC/s, cold and warm perception thresholds, average of 3 readings, 6 s interstimulus interval. b. Method of Levels: (Modified from Yarnitsky and Ochoa 1990, 1991), yes or no response, initial step of 4^{o0}C, reduced by half until step size reached 0.2ºC. c. Method of Levels: Staircase algorithm (Fowler 1987), yes or no response, initial temperature step of 4ºC, subsequent steps at 1ºC, then 0.2ºC, test terminates after 4 "no" responses.	**ANOVA**-based model by Techno-Stat **"r" value** a. Thenar cold 1.964** Warm 1.587** Foot cold 3.778 warm 4.298 b. Thenar cold 1.040 warm 0.572 Foot cold 3.016 warm 3.758 c. Thenar cold 1.144 warm 0.720 ** significant intersession bias	Poor Good Good Good Good
32	132 diabetics with moderate neuropathy, age 18-66, mean 45.4	4 weeks	Warm, Cold Vibration	Thermal Testing System (London, UK) Bio-Thesiometer (Bio-Medical Instruments, Newbury, OH)	A multicenter study, FC, ascending and descending intensity ramps.	**Total variation coefficient (%)** Warm 64.5 Cold 116.6 Vib mm 35.3 Vib toe 41.0 **Intra-subject variability** (% total variance) Warm 32.8 Cold 15.7 Vib mm 21.0 Vib toe 21.0	Poor Poor Satisfactory Satisfactory
7	30 NS, 12 diabetics	Within 1 week	Vibration Warm Cold	Vibratester 100 (Phyne systeme GmbH, D3400, Gottinger, Germany), frequency 100 Hz, amplitude 0-150µm Warm, Cold, computer-driven modified Marstock thermode-PATH-Tester MPI 100 (Phyne Systeme GmbH, D3400. Gottinger, Germany). thermode size 1.6 x 3.6 cm Ramp rate 1ºC/s Reference temp 35ºC Temperature limits 17 to 50ºC	**Vibration:** a. Method of Limits. The subject is asked to press a button when vibration is perceived with an increasing ramp (perception threshold) and when vibration disappeared with a decreasing ramp (disappearance threshold). Ramp rate- 0.2:m/s threshold is calculated from the mean of 3 vibration perception thresholds and 3 vibration disappearance thresholds. b. 2 alternative (temporal) FC. Up, down transformed rule, amplitude changes are in steps of 25% of the first stimulus. Threshold- the mean of 5 upper and lower reversal values. c. Titration Method. Stimulus starts with a suprathreshold stimulus ($VT + VT^{1/2}$) stimulus amplitude is reduced in small steps until it disappears, catch trials inserted at random, threshold- mean of 5 nonperceived stimuli with reversing effect and their preceding perceived stimuli. **Warm and Cold:** Method of Limits. 7 warm and 7 cold stimuli are applied; the subject presses a button when temperature change is perceived. The 1st stimulus is disregarded and the mean of 6 values represents the threshold.	30 NS **CC (correlation coefficient)** vibration toe Limits 0.92 FC 0.96 Titration 0.89 warm 0.77 cold 0.66 **90th %tile of absolute day-to-day difference** vib toe Limits 0.97 FC 0.75 Titration 1.37 warm 2.3 cold 3.1 **Magnitude of day-to-day differences** (% of mean value) vib toe Limits 2.9 FC 11.0 Titration 6.0 warm 2.0 cold 9.0 12 diabetics, CC vib toe 0.87 warm 0.92 cold 0.78	Good Good Good Good Good Good Good Good
5	39 diabetics without neuropathy, mean age 56.7±8.6	2 weeks	Warm, Cold	Thermal Threshold Tester (Medelec, Woking, UK)	2 alternative (temporal) FC. Initial reference temperature 34ºC, rate of change 1ºC/s, uniform size of steps. Use of varying stimulus duration to change stimulus intensity level with the up-down transformed rule.	**Repeatability coefficient** is twice the SD. SD is calculated from the mean of all differences between measurement 1 and 2 (after 2 weeks). Normal/abnormal Warm hand 0.19/1.17 Cold hand 0.17/1.01 Warm foot 4.34/--- Cold foot 0.60/4.69 --- Insufficient sample size	Acceptable Acceptable Poor/--- Acceptable/poor

REF	SUBJECTS	INTERVAL	MODALITY	EQUIPMENT	METHODOLOGY	MEASURE OF REPRODUCIBILITY	CONCLUSION*
2	49 NS 397 diabetics	Vibration 11 months Thermal 7 months Vibration and thermal 1 month.	Vibration Cold Warm Vibration Cold Warm	Bio-Thesiometer (Bio-Medical Instruments, Newbury, OH) Computer controlled thermal stimulator (reference: Fowler 1987)	A multicenter study (see text- Fowler 1987)	**CV(%)** NS: Vibration Malleolus/ big toe 29.7/ 20.8 Male/female Cool 71.0/61.1 Warm 66.8/60.3 Diabetics: Vibration Malleolus/ big toe 6.1-28.2/ 8.7-29.7 Cool 8.8-129.5 Warm 3.2-108.1	Reproducible Poor Poor Reproducible Poor Poor
12	20 diabetics with and without neuropathy	3 to 5 days	Warm, Cold Vibration	CASE III/IV systems*, thermode 10 cm^2 CASE III/IV systems,** Stimulus frequency 250 Hz in CASE III, and 120 Hz in CASE IV **Modifications were made in the CASE IV system	2 alternative (temporal) FC. Up down transformed rule, algorithm†, thermode‡ †algorithm for obtaining subject's responses and for determination of thresholds were modified in CASE IV. The 4, 2, 1 stepping algorithm was not used in this study. ‡Thermode was modified in CASE IV.	**ICC "r_1" value** Warm >0.8 Cold >0.9 Vibration >0.9 "r_1" value- proportion of this variance attributable to variability among subjects ranging from 0 to 1. 0 = all variability is experimental error. 1 = no error.	High Reproducibility
10	20 NS	"Separate" days	Vibration	CASE IV: vibratory transducer, frequency 120 Hz	a. 2 alternative (temporal) FC. Up down transformed rule. b. Method of Limits. Bekesy algorithm with null stimuli. c. Method of Limits. Linear ramp algorithm with and without null stimuli.	Index finger < 4 JND 75th percentile < 2 JND Great toe < 4 JND 75th percentile < 2 JND At 1 JND/s Index finger 2.1 JND 75th percentile 1.1 JND Great toe <6 JND 75 percentile 2 JND At 4.15µm/s Index finger < 2 JND 75th percentile < 1 JND Great toe 4 JND 75th percentile < 2 JND	Accurate and repeatable Accurate and repeatable Good repeatability but overestimated threshold
6	55 NS, 28 f , 27 m, age 20-79, mean age 41	3 consecutive days	Cold, Warm	Computer-driven modified Marstock- PATH-Tester MPI 100 (PHYNE Systeme GmbH, Germany) Thermode size 1.6 x 3.6 cm Ramp rate 1ºC/s Reference temp 35ºC Temperature limits 17 to 50ºC	2 alternative (temporal) FC. Up and down transform rule. Initial steps of 0.5ºC, then steps of 0.1ºC, after 6 changes in direction, the mean of reversing values represents the threshold. Warm and cold thresholds are measured separately. Method of Limits. 7 warm and 7 cold stimuli are applied; the subject presses a button when temperature change is perceived. The first stimulus is disregarded and the mean of 6 values represents the threshold.	**Retest Reliability coefficient "Rtt"** FC/method of limits Warm threshold: 1st-2nd trial 0.89/0.73 2nd-3rd trial 0.88/0.83 1st to 3rd trial poor Cold threshold: 1st to 2nd trial 0.82/0.71 2nd to 3rd trial 0.78/0.71 1st to 3rd trial poor	Sufficient reproducibility for 1st-2nd and 2nd-3rd trial Vary considerably for1st with the 2nd or the 3rd trial
29	5 NS 131 diabetics	3 occasions over 3 to 6 weeks Twice in 1 to 12 weeks	Thermal	Somedic modification of Marstock method Thermal Sensitivity Tester (Sensorteck, Inc., Clifton, NJ)	Method of Limits. Warm and cool thresholds tested separately. 2 alternative (spatial) FC. 1 plate maintained at 30ºC, up-down-transformed rule, threshold is mean of 6 turnaround points.	**CV** (mean) Normal Subjects Method of Limits Warm 14% Cool 42% Method of Levels 29% Diabetics Method of Levels Mean± SD test 1 1.75 ± 1.51ºC test 2 1.04 ± 0.71ºC	Suitable for clinical use Suitable for clinical use Suitable for clinical us.
9	71 NS, M:F 29:42, age 21 to 92	Twice on "separate" days.	Thermal	2 thermostimulators 3 x 4 cm	2 alternative (spatial) FC: First thermode is maintained at 5ºC above or below skin temperature when evaluating warm or cold thresholds respectively. Second thermode's temperature is varied at a random sequence. Initial temperature difference between the 2 thermodes is 10ºC and is changed according to the up-down transformed rule. Correct answer = CCC, CCWC Wrong answer = CW,CCWW Thermal discrimination threshold is defined as the mean value of the last 6 reversal points.	CV Warm 58.4% Cold 56.0%	Large intraindividual variability

REF	SUBJECTS	INTERVAL	MODALITY	EQUIPMENT	METHODOLOGY	MEASURE OF REPRODUCIBILITY	CONCLUSION*
1	10 NS	10 times at intervals of at least a day.	Thermal	Thermal Sensitivity Tester (Sensorteck, Inc., Clifton, NJ), thermode 25 cm^2	2 alternative (spatial) FC: 1 plate maintained at 25ºC, initial temperature difference 6ºC, steps of 10% up and down	Mean CV, 19% index finger, 26.6% great toe, CV range 8.3% to 47.1%	Reliable
3	25 NS, 60 diabetics (39 with neuropathy, 21 without), M:F 30:30, age 17 to 73, mean age 1.8±2.1	1 week	Vibration	Modified Bio-thesiometer (Bio-Medical Instruments, Newbury, OH)	Vibration perception threshold is the mean of 5.	Pearson CC NS/diabetics 0.82/0.81 Intra-individual variability-change in the mean values of thresholds expressed as a percentage of the first measurement Normal/ diabetics 4.91%/12.85%	Satisfactory in NS and most diabetics
23	M:F 33:21, age 21 to 55, mean age 34.3 18 NS, 20 diabetics (vibration) 18 NS, 18 diabetics (thermal)	4 weeks	Vibration Thermal	Bio-Thesiometer (Biomedical Instruments, Newberry, OH) Marstock thermostimulator (Somedic, Sweden), thermode 2.5 x 5.0 cm, rate of change 1ºC/s	Vibration threshold is the mean of 3 trials. Method of Limits (warm-cold limen)	CC Vibration: NS Hands r = 0.83 p<0.01; Feet r = 0.86 p<0.01 Diabetics Hands r = 0.73 p<0.01; Feet r = 0.91 p<0.01 Thermal: NS Hands r = 0.69 p<0.01; Feet r = 0.79 p<0.01 Diabetics Hands r = 0.91 p<0.01; Feet r = 0.89 p<0.01	No significant differences Reproducible
25	106 NS, age 6 to 73 mean age 33.0, SD 17, M:F 45:61 2NS	Short term: 24 hours Long term: 2 to 8 weeks, 17 times daily	Thermal	Glasgow Thermal System Computer driven thermode current calculated every 100 m/s Thermode 2.5 x 5.0 cm, water cooled	2 alternative (temporal) FC with null stimuli: 1 person performed all tests. Initial skin temperature 34ºC to 35ºC, rate of change 1ºC/s up down transformed rule uniform size of steps use of varying stimulus duration to change the stimulus intensity level. Site of stimulation: mid-forearm.	**Change in mean** (of the group) thermal threshold < 5% **CV** 0% to 6%	Small intra-individual variation Small intra-individual variation
4	30 NS, age 24 to 91, M:F 11:25 20 diabetics with neuropathy, age 22 to 69, M:F 9:11	1 week	Thermal	2 thermostimulators, Thermode size 3 x 4 cm	2 alternative (spatial) FC: First thermode is maintained at skin temperature. Second thermode's temperature is varied at a random sequence. Initial temperature difference between the 2 thermodes is 10ºC and is changed according to the up-down transformed rule. Correct answer = CCC, CCWC Wrong answer = CW,CCWW Thermal discrimination threshold is defined as the mean value of the last 6 reversal points.	**Intra-individual variability** expressed as maximum difference of TDTs between the 1st and second trial. 0.5ºC for the hands and feet of NS and for the hands of diabetics. Note: 3 diabetics were excluded. 1st and 2nd trial TDTs were as follows: 0.4ºC to 3.0ºC 0.6ºC to 7.5ºC 0.5ºC to 4.0ºC	Small intra-individual variability in all NS and in most diabetic patients
15	13 NS, age 25 to 63, mean age 43.7, M:F 5:8 27 patients with neuropathy of various etiologies age 27 to 71, mean age 53.2, M:F 22:5	Short interval Vibration, 5 NS, 4 times within 5 to 10 minutes. Long interval 13 NS, 4 consecutive days in 1 wk. 4 times at intervals of 1, 3, 5 wks. 27 patients, 4 to 5 times in 7 to 13 wks.	Vibration Touch Thermal	Hand-held bioThesiometer Vibrameter (MUAB AB, Sweden) 100 Hz Tactile Stimulator (Lindblom) Marstock Stimulator	Average of at least 2 up and down values. Method of Limits (warm-cold limen)	**% change from first determination.** Short term, vibration only, 8% to 18% Long term, all types of threshold -90% to +256% On average, a change of <60% or >+150% from initial values is required to ensure that a subsequent value will reflect a true change with probability of 95%.	Short term: Limited variation Long term: Pronounced variation

ANOVA = analysis of variance; **C** = Correct; **CC** = Correlation Coefficient; **CCV** = Correlation Coefficient Variation; **CV** = Coefficient of Variation; **FC** = Force Choice; **HP** = Heat Pain; **ICC** = Interclass Correlation Coefficient; **JND** = just noticeable difference; **M:F** = Male:Female; **mm =** medial malleoli**; NS** = Normal Subjects; **s** = second; **SD** = Standard Deviation; **TDT** = Thermal Discriminating Thresholds; **vib**= vibration; **VT** = Vibration Threshold; **VU** = Vibration Units; **W =** Wrong; **wks** = weeks **y** = years.

** The conclusion listed in this column is that of the author(s) of the paper cited in the reference. The conclusion is not the opinion of the AAEM.

Disclaimer: No clinical tests or trials were performed by the AAEM or the authors of this review. Neither the AAEM nor the authors of this report reviewed any product literature regarding the pieces of equipment included in the paper nor did the AAEM review the specific equipment. The information included about the equipment and the opinions expressed regarding the reproducibility of each type of equipment are those of the author(s) of the papers cited. The conclusions are not those of the AAEM or the authors of this review. This paper was not created with the intent that it be used as a basis for reimbursement decisions.

REFERENCES

1. Arezzo JC, Schaumburg HH, Laudadio C. Thermal sensitivity tester. Device for quantitative assessment of thermal sense in diabetic neuropathy. Diabetes 1986;35:590-592.
2. Armstrong FM, Bradbury JE, Ellis SH, Owens DR, Rosen I, Sonksen P, Sundkvist G. A study of peripheral diabetic neuropathy. The application of age-related reference values. Diabet Med 1991;8 Spec No:S94-S99.
3. Bertelsmann FW, Heimans JJ, van Rooy JC, Heine RJ, van der Veen EA. Reproducibility of vibratory perception thresholds in patients with diabetic neuropathy. Diabetes Res 1986;3:463-466.
4. Bertelsmann FW, Heimans JJ, Weber EJ, van der Veen EA, Schouten JA. Thermal discrimination thresholds in normal subjects and in patients with diabetic neuropathy. J Neurol Neurosurg Psychiatry 1985;48:686-690.
5. Bravenboer B, van Dam PS, Hop J, vd Steenhoven J, Erkelens DW. Thermal threshold testing for the assessment of small fibre dysfunction: normal values and reproducibility. Diabet Med 1992;9:546-549.
6. Claus D, Hilz MJ, Neundorfer B. Thermal discrimination thresholds: a comparison of different methods. Acta Neurol Scand 1990;81:533-540.
7. Claus D, Mustafa C, Vogel W, Herz M, Neundorfer B. Assessment of diabetic neuropathy: definition of norm and discrimination of abnormal nerve function. Muscle Nerve 1993;16:757-768.
8. Dellon AL, Mackinnon SE, Brandt KE. The markings of the Semmes-Weinstein nylon monofilaments. J Hand Surg 1993;18:756-757.
9. Doeland HJ, Nauta JJ, van Zandbergen JB, van der Eerden HA, van Diemen NG, Bertelsmann FW, Heimans JJ. The relationship of cold and warmth cutaneous sensation to age and gender. Muscle Nerve 1989;12:712-715.
10. Dyck PJ, Karnes JL, Gillen DA, O'Brien PC, Zimmerman IR, Johnson DM. Comparison of algorithms of testing for use in automated evaluation of sensation. Neurology 1990;40:1607-1613.
11. Dyck PJ, Karnes JL, O'Brien PC, Zimmerman IR. Detection thresholds of cutaneous sensation in humans. In: Dyck PJ, Thomas PK, Griffin J, Low PA, Poduslo JF, editors. Peripheral Neuropathy, Vol 1; Philadelphia: WB Saunders; 1993. pp 706-728.
12. Dyck PJ, Kratz KM, Lehman KA, Karnes JL, Melton LJ, O'Brien PC, Litchy WJ, Windebank AJ, Smith BE, Low PA, Service FJ, Rizza RA, Zimmerman BR. The Rochester diabetic neuropathy study: design, criteria for types of neuropathy, selection bias, and reproducibility of neuropathic tests. Neurology 1991;41:799-807.
13. Dyck PJ, Zimmerman IR, Johnson DM, Gillen D, Hokanson JL, Karnes JL, Gruener G, O'Brien PC. A standard test of heat-pain responses using CASE IV. J Neurol Sci 1996;136:54-63.
14. Dyck PJ, Zimmerman IR, O'Brien PC, Ness A, Caskey PE, Karnes J, Bushek W. Introduction of automated systems to evaluate touch-pressure vibration, and thermal cutaneous sensation in man. Ann Neurol 1978;4:502-510.
15. Fagius J, Wahren LK. Variability of sensory threshold determination in clinical use. J Neurol Sci 1981;51:11-27.
16. Fowler CJ, Carroll MB, Burns D, Howe N, Robinson K. A portable system for measuring cutaneous thresholds for warming and cooling. J Neurol Neurosurg Psychiatry 1987;50:1211-1215.
17. Fruhstorfer H, Lindblom U, Schmidt WG. Method for quantitative estimation of thermal thresholds in patients. J Neurol Neurosurg Psychiatry 1976;39:1071-1075.
18. Gerr FE, Letz R. Reliability of a widely used test of peripheral cutaneous vibration sensitivity and a comparison of two testing protocols. Br J Ind Med 1988;45:635-639.
19. Gerr F, Letz R, Harris-Abbott D, Hopkins LC. Sensitivity and specificity of vibrometry for detection of carpal tunnel syndrome. J Occup Environ Med 1995;37(9):1108-1115.
20. Gerr F, Letz R, Hershman D, Farraye J, Simpson D. Comparison of vibrotactile thresholds with physical examination and electrophysiological assessment. Muscle Nerve 1991;14:1059-1066.
21. Goldberg JM, Lindblom U. Standardised method of determining vibratory perception thresholds for diagnosis and screening in neurological investigation. J Neurol Neurosurg Psychiatry 1979;42:793-803.
22. Gruener G, Dyck PJ. Quantitative sensory testing: methodology, applications and future directions. J Clin Neurophysiol 1994;11:568-583.
23. Guy RJ, Clark CA, Malcolm PN, Watkins PJ. Evaluation of thermal and vibration sensation in diabetic neuropathy. Diabetologia 1985;28:131-137.
24. Hilz MJ, Axelrod FB, Hermann K, Haertl U, Duetsch M, Neundörfer B. Normative values of vibratory perception in 530 children, juveniles and adults aged 3-79 years. J Neurol Sci 1998;159:219-225.
25. Jamal GA, Hansen S, Weir AI, Ballantyne JP. An improved automated method for the measurement of thermal thresholds. I. Normal subjects. J Neurol Neurosurg Psychiatry 1985;48:354-360.
26. Jamal GA, Weir AI, Hansen S, Ballantyne JP. An improved automated method for the measurement of thermal thresholds. II. patients with peripheral neuropathy. J Neurol Neurosurg Psychiatry 1985;48:361-366.
27. Kenshalo DR, Bergen DC. A device to measure cutaneous temperature sensitivity in humans and subhuman species. J Appl Physiol 1975;39:1038-1040.
28. Levin S, Pearsall G, Ruderman RJ. Von Frey's method of measuring pressure sensibility in the hand: an engineering analysis of the Weinstein-Semmes pressure aesthesiometer. J Hand Surg 1978;3:211-216.
29. Levy D, Abraham R, Reid G. A comparison of two methods for measuring thermal thresholds in diabetic neuropathy. J Neurol Neurosurg Psychiatry 1989;52:1072-1077.
30. Meier PM, Berde CB, DiCanzio J, Zurakowski D, Sethna NF. Quantitative assessment of cutaneous thermal and vibration sensation and thermal pain detection thresholds in healthy children and adolescents. Muscle Nerve 2001;24:1339-1345.
31. Nasseri K, Strijers RL, Dekhuijzen LS, Buster M, Bertelsmann FW. Reproducibility of different methods for diagnosing and monitoring diabetic neuropathy. Electromyogr Clin Neurophysiol 1998;38:295-299.
32. Valensi P, Attali JR, Gagant S. French Group for Research and Study of Diabetic Neuropathy. Reproducibility of parameters for assessment of diabetic neuropathy. Diabet Med 1993;10:933-939.
33. Valk GD, de Sonnaville JJ, van Houtum WH, Heine RJ, van Eijk JT, Bouter LM, Bertelsmann FW. The assessment of diabetic polyneuropathy in daily clinical practice: reproducibility and validity of Semmes Weinstein monofilaments examination and clinical neurological examination. Muscle Nerve 1997;20:116-118.
34. van Deursen RW, Sanchez MM, Derr JA, Becker MB, Ulbrecht JS, Cavanagh PR. Vibration perception threshold testing in patients with diabetic neuropathy: ceiling effects and reliability. Diabet Med 2001;18:469-475.
35. Yarnitsky D, Fowler CJ. Quantitative sensory testing. In Binnie CD, Cooper R, Fowler CJ, Mauguiere F, Prior PF, Osselton JW, editors. Clinical neurophysiology- EMG, nerve conduction and evoked potentials. Oxford: Butterworth-Heinemann; 1995. pp 253-270.
36. Yarnitsky D, Sprecher E. Thermal testing: normative data and repeatability for various test algorithms. J Neurol Sci 1994;125:39-45.
37. Yarnitsky D, Sprecher E, Zaslansky R, Hemli JA. Heat pain thresholds. normative data and repeatability. Pain 1995;60:329-332.