Neurometer® CPT

Sensory Nerve Conduction Threshold (sNCT®) Electrodiagnostic Evaluation

Overview and References

NEUROTRON, INCORPORATED
INNOVATIVE MEDICAL TECHNOLOGY
USA
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Prescription Device

All NEUROMETER® neurostimulators are prescription devices. Federal law restricts it to sale by or on the order of a licenced health care provider.

Trademark

Patent

The NEUROMETER® CPT® sNCT® devices and their method of application are covered by one or more of the following United States and foreign patents: U.S.A. No. 5,806,522 and No. 4,503,863, U.K. patent No. 2,052,994, and Canada patent No. 1,157,526, Japan patent No. 3138428. Additionally patents are pending worldwide. This device is licensed for manufacture by Neurotron, Inc., USA.

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Sensory Nerve Conduction Threshold (sNCT) Evaluations

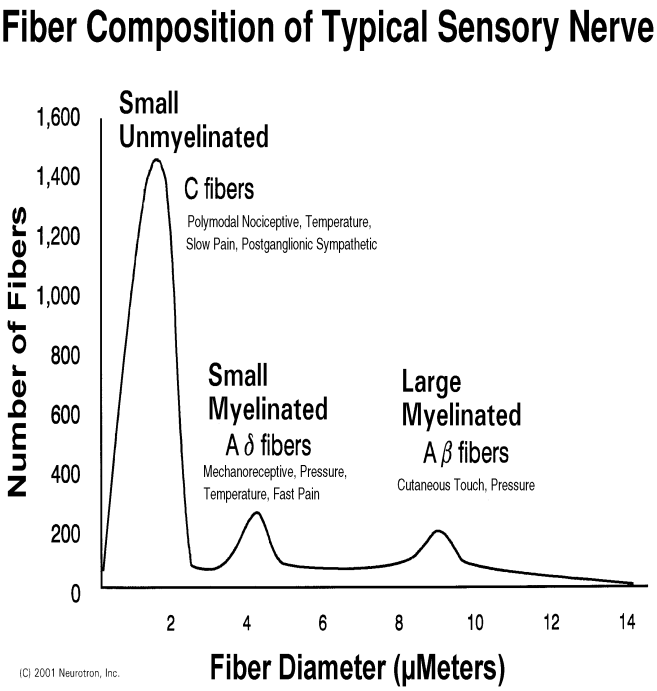
Neurometer® neurostimulators are used to conduct electrodiagnostic neuroselective sensory Nerve Conduction Threshold (sNCT) evaluations. These devices are capable of providing three types of fully automated non-invasive objective measures of sensory nerve function:

1. Current Perception Threshold (CPT) - a painless high resolution diagnostic measure.
2. Rapid-Current Perception Threshold (R-CPT) - a painless low resolution screening measure.
3. Pain Tolerance Threshold (PTT) - an atraumatic painful diagnostic measure.

This overview primarily addresses the clinical utility of the sNCT evaluation CPT measure, which is referred to as "sNCT/CPT". The other two measures, the R-CPT and PTT, are briefly discussed.

Overview of Sensory Nerve Pathology

The typical sensory nerve is comprised of 3 major subpopulations of nerve fibers. The distribution of these fibers is illustrated below[1]. The large myelinated fibers conduct cutaneous touch and pressure sensations, the small myelinated fibers conduct temperature, pressure and fast pain, and the unmyelinated fibers, comprising more than 80% of the total, conduct temperature and slow pain conduct protective sensations that guard against serious injury.



[1]Adapted from: Boyd, IA, Davey MR: Composition of Peripheral Nerves. Edinburgh, Livingston, 1968.

Neuropathological conditions can selectively impair the functioning of specific sub-population(s) of nerve fibers while sparing the others. For example, a loss of pain sensation may be associated with a selective impairment of the small myelinated and unmyelinated sensory fibers without any corresponding impairment of the large myelinated fibers. In this example, the patient would have normal touch sensation but would be unaware that he/she has lost their protective sensation afforded by the smaller fibers.[2] Traditional electrodiagnostic studies only evaluate the large myelinated fibers in a nerve, and are insensitive to impairments effecting the other 90%+ of the fibers. Sensory nerve conduction threshold (sNCT) electrodiagnostic studies, however, independently evaluate all three major subpopulations of sensory nerve fibers in the same evaluation. This feature greatly enhances the neurodiagnostic sensitivity and enables the detection of a much wider range of conditions at an earlier stage of development when intervention may be more effective and treatment less costly.

Progressive Peripheral Neuropathy

Progressive peripheral neuropathies generally begin by impairing the conduction by sensory nerves, with motor nerve conduction becoming impaired only in the more advanced stages. These sensory impairments commonly begin with a hyperesthetic stage (increased sensitivity) and then progresses to a hypoesthetic stage (decreased sensitivity) and ultimately develop into an anesthetic condition (no sensitivity)[3].

Many sensory neuropathological conditions, if detected early enough, will respond to treatment and the sensory nerve fibers will regain function. If the condition is allowed to progress without intervention, however, then motor nerve involvement will occur and weakness will develop. Once the motor nerve loses its connection with the muscle, it generally never re-innervates the muscle. Detecting the early sensory impairments permits earlier intervention and can prevent costly complications. For example, successful treatment of *early* Carpal Tunnel Syndrome (CTS) results in complete recovery and often prevents the need for surgical intervention. In comparison, the treatment of *advanced* carpal tunnel syndrome generally has a full recovery of sensation but there often remains a permanent weakness and disability with impairment of up to 80% of hand function. sNCT/CPT studies are unique in their ability to evaluate both the hyperesthetic and the hypoesthetic conditions of a sensory impairment.[4] The early detection of sensory impairments permitted by sNCT/CPT studies allows for earlier therapeutic intervention which enhances patients prognosis and reduces the cost of their medical management.

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[2] Appendix E, Section 4, includes sNCT studies related to the selective loss of small fiber and/or large fiber function.

[3] A) Adams, R.D., Asbury A.K. Diseases of the Peripheral Nervous System. Harrison's Principals of Internal Medicine, 10th Edition, New York, McGraw-Hill Book Co., Chapter 368, pp. 2156-2169, 1983.
B) Clark, R.G. Manter and Gatz's Essentials of Clinical Neuroanatomy and Neurophysiology, Edition 5, page 28, F.A. Davis Company, Philadelphia, 1975.

[4] Appendix E, Section 9, provides references.

Focal Lesions

Focal peripheral nerve and spinal cord lesions are often the result of traumatic injuries which sever the connection between the peripheral nerve or spinal cord and the brain. When this happens, segments of the nerve or cord may still be able to conduct impulses, but since those impulses can't reach the brain they have lost their sensory function. Purely physiological electrodiagnostic procedures can determine if a short segment of a nerve is operational, but they do not permit determination of whether the signals from that segment are actually reaching the patient's brain and conducting any functional information. Functional physiological procedures such as sNCT/CPT studies, however, evaluate sensory nerve conduction from the periphery to the brain and can determine that a full nerve segment is operational and conducting sensory information to the brain.

Description of the sNCT/CPT Evaluation

Overview

sNCT/CPT studies are performed by applying a mild electrical stimulus through a pair of small disposable surface electrodes placed on the skin. Three painless, neuro-selective electrical stimuli are applied to a peripheral nerve or dermatome innervation field in order to determine, confirm and record sensory threshold responses. Each stimulus evaluates the functioning of one of the three major subpopulations of sensory nerve fibers which together comprise more than 90% of the typical sensory nerve. sNCT/CPT studies can be used to localize or map a sensory nerve dysfunction. The measures can be used to detect and evaluate hyperesthetic conditions that can precede progressive nerve impairment and hypoesthetic conditions that reflect a loss of functioning. The studies are appropriate for any patient capable of indicating when they detect a change of sensation at the site being stimulated.

sNCT/CPT studies follow a standardized, automated procedure to generate objective, sensitive and reliable measures of sensory nerve function. Measures are obtained using microprocessor controlled constant alternating current (AC) sinusoid waveform stimuli presented at intensities ranging from 0.001 mAmperes to 9.99 mAmperes and at frequencies of 5 Hz, 250 Hz and 2000 Hz. The stimulation frequency dependent measures in Current Perception Threshold (CPT) units, each of which represents the minimum intensity of a neuroselective, transcutaneous constant electrical current required to reproducibly evoke a sensation (1 CPT unit equals 0.01 mAmperes).

The electrical stimulus produced by the sNCT equipment is self-calibrating and able to maintain a constant current output regardless of normal variations in skin thickness and impedance. The system monitors the impedance at the skin electrode interface and instantly warns operators when conditions cause excessive impedance that could distort the accuracy of the measures. The system also monitors the consistency of a patient's responses to guard against false CPT readings due to improper procedures or non-compliance. sNCT studies follow a double blind, forced

choice testing paradigm to determine CPT measures with a resolution of +/- 20 μAmperes to a $p<0.006$.[5]

The equipment used for sNCT studies is battery powered and portable and does not require any special electrical shielding for safe and reliable operation. Patients can be evaluated almost anywhere they can be made comfortable and in an environment free from interruptions. Studies have demonstrated the reliability of sNCT evaluations conducted under a wide range of conditions, both in and out of clinical settings.[6]

Summary of the sNCT/CPT Evaluation Procedure

Pre-Service Work: The examiner determines which nerves are to be studied based upon the health care provider's prescription and the available clinical information.

Intra-service Work: The health care provider supervises and/or performs patient preparation including electrode placement, explains the procedure and begins the automated threshold determination study. Each nerve test site is evaluated with the three sNCT neuroselective electrical stimuli to assess both large and small fiber functioning. Additional testing may be prescribed during the course of the study in response to the information obtained.

Post-service Work: Examination data are entered into software that evaluates and grades the sNCT/CPT measures based upon a comparison with standardized, clinically established normative values. These data are subjected to range analyses, intra-site and inter-site comparisons. The health care provider integrates the graded sNCT findings with clinical and other laboratory findings into a report and defines or generates the diagnosis. On occasion, suggestions for additional work-up will be included.

Conducting an sNCT/CPT Study

The patient is placed in a comfortable position - typically sitting - and in a location with minimal interruptions. The examiner connects the electrode cable to the sNCT device, attaches a new set of 1 cm. diameter, disposable gold plated electrodes to the cable, and then powers up the equipment. The examiner then performs a Pre-Exam Cable Test by following the directions displayed on the device's LCD screen. Successful completion of this test confirms the proper functioning of the equipment, electrodes and cables prior to each examination.

The examiner explains the general nature of the test to the patient, tells them what they can expect and answers any questions they may have. The examiner then examines the prescribed skin test sites to confirm that they are free of any signs of

[5]Katims, J.J. Electrodiagnostic Functional Sensory Evaluation of the Patient with Pain: A Review of the Neuroselective Current Perception Threshold (CPT) and Pain Tolerance Threshold (PTT). Pain Digest Volume 8(5), 219-230, 1998.

[6]Appendices D and E, review related publications.

recent trauma which could effect the sNCT measures.[7] Finally, the examiner prepares each test site using a mildly abrasive skin prep paste that cleanses and hydrates the skin and facilitates the testing.

The electrodes are coated with a thin layer of electro conductive gel and then taped to the test site on the patient. Next, the patient is presented with an automated or manual Intensity Alignment procedure that quickly narrows down the threshold level to a range of +/- 50 μAmperes out of a total range of 0 to 9.99 mAmperes. The Auto Test Mode then begins, which is a fully automatic, double-blind, forced choice procedure that determines the actual CPT measures. Patients are presented with randomly generated sets of a real and a placebo or placebo and placebo stimuli and must indicate which of the two - if either - felt stronger. Responses can be made verbally, by pushing a button or any other means through which the patient's intent can be communicated.

Depending upon the patient's response, the sNCT device automatically re-adjusts the output intensity of the stimulus and randomly generates a new testing order for the next pair of tests in the series. Because the sNCT/CPT testing methodology is completely automated, neither the subject nor the operator can influence the testing sequence. The Auto Test Mode follows a testing paradigm similar to that used in standard objective auditory tests and determines the patient's CPT measures with a resolution of +/- 20 μAmperes to a $p<0.006$. When a sufficient number of correct consecutive responses have been obtained to achieve this level of statistical significance, the sNCT device calculates and displays the CPT value for the test series and optionally prints out the results. The device also monitors patient responses for consistency and accuracy, and in the event that there are inconsistent responses, the operator is alerted so that the test may be repeated or discontinued. This testing sequence is repeated for each of the three stimulus frequencies at each site being studied.

The average time required to complete a three-frequency single site electro-diagnostic sNCT/CPT evaluation is approximately 9 minutes. A typical evaluation could involve testing 2, 4 or 6 sites (bilateral evaluation of 1 to 3 peripheral nerves or dermatomes) and require approximately 20-60 minutes to complete plus an additional 5-10 minutes for the initial equipment set-up and patient orientation. Electrodiag-nostic testing is considered dynamic, however, in that one test may indicate that an additional test or tests are indicated or not necessary.

Statistical Evaluation of sNCT Data

sNCT/CPT measures are evaluated by software that compares them to clinically determined ranges of healthy measures that have been established for dozens of different test sites.[8] Both the CPT values and their ratios are considered when determining the degree of sensory nerve impairment and both contribute to the overall neurological diagnosis. The data analysis may include a determination of hyperesthetic

[7] Appendix J reviews physical constraints of sNCT measures.

[8] Appendix E, Section 8 and Appendix H provide related reference information.

and/or hypoesthetic conditions, and a detailed laboratory report and narrative are generated. As with any neurodiagnostic test, a clinician's interpretation including a clinical correlation is essential and necessary for diagnostic purposes.

Interpreting the Clinical Significance of sNCT Findings

A licensed health care provider with appropriate training interprets the results of an sNCT study by using the graded data generated by the computer analysis in conjunction with other laboratory data and clinical impressions of the patient. The location, distribution, neurospecificity and severity of the CPT abnormalities (if present) help the health care provider develop and confirm a diagnosis. Clinical certification courses are available for health care providers which include a review of the neurophysiological basis and clinical use of the sNCT electrodiagnostic evaluation and the interpretation of the test results.[9] Technical certification courses are also offered for technicians operating the sNCT equipment that emphasize examination techniques and use of the evaluation software.

Indications and Clinical Applications of sNCT/CPT Studies in Patient Management

sNCT/CPT studies are performed to evaluate and document a variety of sensory neuropathological conditions that can result from metabolic impairments, compressive or traumatic lesions, toxic exposure, infectious/neoplastic diseases, immunological disorders, digestive impairments, hereditary impairments or environmental exposure. sNCT findings assist in patient management in four primary areas:

1. Identifying abnormal sensory nerve function.
2. Localizing areas of abnormal function.
3. Quantifying the severity of an abnormality.
4. Monitoring the course of a progressive neuropathy or the efficacy of a treatment.

sNCT studies are indicated for patients with a suspected diagnosis of sensory nerve dysfunction in need of confirmation and evaluation.[10] The studies objectively quantify sensory function when the history (sensory symptoms) and physical examination (abnormalities detected with tuning fork, pinwheel, radiating pain reproduced with provocative orthopedic maneuvers etc.) merit further investigation. They are not indicated for routine use with every patient, however. For instance, gross, clearly delineated sensory impairments like hemiplegia or paraplegia generally do not require electrodiagnostic evaluations.

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[9] Sensory Nerve Conduction Threshold (sNCT) Evaluation Neurometer® CPT Certification: Neurology and Clinical Overview, Neurotron, Inc., Balto., MD, USA, 2000. Also Appendix H reviews the evaluation of sNCT measures.

[10] sNCT/CPT study indications and utilization guidelines are presented in Appendices A and B..

Focal, as well as diffuse sensory impairments, often do require electrodiagnostic evaluations such as sNCT/CPT studies to precisely localize the somatic distribution and determine the severity of the impairment. Incorporating clinical findings with the data provided by a sNCT/CPT study can assist the clinician in diagnosing conditions such as a spinal cord disorder, radiculopathy, polyneuropathy and/or compressive/focal neuropathy. sNCT/CPT studies also assist in differentiating axonal from demyelinating and small fiber from large fiber neuropathies.[11]

sNCT/CPT studies may be used to determine if a patient's symptoms are consistent with sensory neuropathy or with a non-neurological impairment. Non-neurological conditions, such as vascular insufficiency, soft tissue lesions, arthritis, ligament sprain or muscular strain, can include symptoms of radiating pain that may mimic neuropathic conditions. Electrodiagnostic studies such as sNCT, are used to confirm or rule out sensory neuropathy, assist in reaching a diagnosis and help in prescribing appropriate treatment.

Identifying Abnormal Nerve Function

Accurate identification of abnormal nerve functioning is *the* basic requirement for any neurodiagnostic procedure. Research using sNCT study CPT measures to evaluate sensory nerve function have demonstrated that the sensitivity and specificity the sNCT studies range from being substantially equivalent to being markedly superior to traditional electrodiagnostic nerve tests like nerve conduction velocity studies.[12] There are four features specific to sNCT/CPT studies that make them highly sensitive and accurate neurodiagnostic tools.

Evaluate Hyperesthesia and Hypoesthesia: sNCT/CPT studies detect and quantify sensory nerve impairments from the early hyperesthetic stage characterized by abnormally low sensory thresholds, through to the advanced or late stage neuropathies with hypoesthesia (elevated sensory thresholds) or anesthesia (complete loss of sensation). The high sensitivity of sNCT/CPT studies enables identification of many progressive neuropathies in the hyperesthetic stage, before the nerves have lost significant functioning. Traditional electrodiagnostic nerve tests are limited to identifying neuropathies only after they have progressed to the hypoesthetic stage and a significant loss of sensory function taken place.

Conditions such as HIV infection, early diabetic neuropathy or radiculopathy and selective small fiber neuropathy can result in hyperesthetic abnormalities. A recently published study of 2360 diabetics evaluated with sNCT/CPT studies clearly demonstrated that hyperesthesia precedes hypoesthesia in the development of diabetic neuropathy.[13]

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[11] Appendix E, cites examples of research demonstrating the clinical utility of the sNCT evaluation for specific pathological conditions.

[12] Statistical analyses conducted for the United States Government, Dept. Health and Human Services, CMS, are available upon request from Neurotron, Inc.

[13] This publication and others related to the ability of the sNCT evaluation CPT measures to evaluate the hyperesthetic condition are cited in Appendix E, Section 9.

Test Any Cutaneous Site: sNCT/CPT studies can be conducted at any cutaneous or mucosal site, a feature which greatly enhances the detection of both proximal and distal impairments and helps localize of the distribution of impairments. Diseases effecting myelin function often initially impair nerve function proximally in the region of the dorsal root ganglia, while the most common diseases effecting nerve fiber function start at the tips of the longest nerve fibers (i.e., toes). sNCT/CPT studies can be conducted at both proximal and distal sites, e.g. the tips of the toes or proximally at a paraspinal site. Traditional electrodiagnostic studies, however, are generally limited to testing over major branches of peripheral nerves in the extremities, a location where neuropathies may not appear until many months or years after they first appear in the more distal sites.[14]

Neuroselective Measures : sNCT studies evaluate all three major sub-populations of sensory nerve fibers at the site of stimulation. A typical sensory nerve is comprised of large myelinated, small myelinated and unmyelinated fibers, however most progressive neuropathies don't effect all the subpopulations of sensory nerve fibers equally or at the same time. sNCT studies evaluate all three major sub-populations of sensory nerve fibers, enabling them to detect a wider range of neuropathies than traditional electrodiagnostic studies that typically evaluate only the large myelinated fibers representing less than 10% of the nerve.[15]

Functional Physiological Evaluation : sNCT studies evaluate the full length of sensory nerve conduction or transmission, from the site of stimulation to the brain where the signals from the nerve are translated into sensations such as heat, cold, touch and vibration.[16] Conditions exist in which a segment of a nerve remains intact and functioning even though it is no longer conducting sensory information to the brain. Consequently, electrodiagnostic procedures that evaluate only a short segment of a nerve can fail to report any abnormality even when the nerve is no longer conducting sensory information to the brain. sNCT electrodiagnostic studies, however, are functional physiological evaluations that can detect an abnormality located anywhere along the length of the nerve transmission to the brain.

Localizing Areas of Abnormal Nerve Function

Areas of abnormal sensory nerve function or conduction can be localized by performing sNCT/CPT studies at multiple cutaneous sites. Localizing these impairments is often an essential element for an accurate diagnosis.[17] Multiple studies

[14] Appendix E reviews supporting research publications.

[15] Appendix E, Section 10, reviews supporting publications.

[16] Bocerra, L., Stojanovic, M., Chang, I., Breiter, H., Tracey, I., Fishman, S., Edwards, A., Gonzalez, R., Borsook, D. fMRI Mapping of CNS Activation Following Noxious Heat and Electrical Stimuli. Fifth Scientific Meeting of the International Society for Magnetic Resonance in Medicine, 1997.

[17] Adams, R.D., Asbury A.K. Diseases of the Peripheral Nervous System. Harrison's Principals of Internal Medicine, 10th Edition, New York, McGraw-Hill Book Co., Chapter 368, pp. 2156-2169, 1983.

can also monitor the progress of a disease or the efficacy of a therapy or procedure.

The sNCT/CPT evaluation of specific pathological conditions reveals the following distributions of sensory impairment:

Spinal Sensory Impairment : Presents with a segmental distribution of impairment. The sNCT/CPT evaluation of syringomyelia, for example, reveals a preferential loss of small fiber function isolated to a segmental distribution involving several adjacent dermatomes.[18]

Radiculopathy : Presents as a sensory impairment confined to a dermatome distribution[19]. For example, a herniated intervertebral disc impinging on a spinal nerve resulting in a sensory impairment confined to a dermatome distribution.[20]

Focal Peripheral Sensory Impairment : Presents with a loss of sensory nerve function distal to the site of the lesion. These impairments include vasculitis related mono-neuropathies which can effect sensory function at any cutaneous site, as well as compressive neuropathies such as Carpal Tunnel Syndrome (CTS).[21]

Polyneuropathy - Distal : Distal axonal neuropathy, the most common type of metabolic/toxic peripheral neuropathy, presents first at the tip of the great toe. sNCT/CPT studies are capable of testing at that site, a feature which allows evaluation of this type of polyneuropathy months or years earlier than other electrodiagnostic studies.[22]

Diffuse Polyneuropathy : Diffuse polyneuropathy generally presents with sensory impairments involving both a proximal and a distal distribution, for example involving toes and legs, fingers and arms and effecting multiple nerves and dermatomes. Inflammatory polyneuropathies are primarily confined to impairments of myelinated fiber function and often result in diffuse polyneuropathies (e.g.. Chronic Inflammatory Demyelinating Polyneuropathy, Guillian-Barré Syndrome).[25]

Nerve Regeneration : sNCT/CPT studies can document a recovery of sensory function in the innervation field of a regenerating nerve. sNCT/CPT studies are able to evaluate nerve regeneration and provide critical information to the health care provider whereas the other electrodiagnostic studies can not.[23]

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[18] Appendix E, Section 1 reviews supporting research publications.

[19] Dermatomal distribution is based on the following:1) Keegan, JJ, Garrett, FD The segmental distribution of the cutaneous nerves in the limbs of man. Anat. Rec. 1948;102:409-437; 2)Kegan, JJ Neurosurgical interpretation of dermatome hypalgesia with herniation of the lumbar intervertebral disc. J. of Bone and Joint Surgery, 1944;26:238-248.; 3) Last, R.J. Innervation of the limbs. J. of Bone and Joint Surgery 1949;31(B)452-464.; 4) Cocchiarella, L., Andersson, G.B. Guides to the evaluation of Permanent Impairment, 5th Ed., page 377 and 381, American Medical Association Press, Chicago, IL USA, 2001.

[20] Appendix E, Section 1 reviews supporting research publications.

[21] Appendix E, Section 6 reviews supporting research publications.

[22] Appendix E, Sections 2-4 review supporting research publications.

[23] Appendix E, Section 5 reviews supporting research publications.

Neuroselective Evaluation of Pain

The sNCT stimulus may be administered at intensities above the painless sensory threshold to evaluate the Pain Tolerance Threshold (PTT). This PTT measure has utility in pain medicine in assessing pathological conditions such as allodynia. Allodynia is defined as a painful response to a normally painless stimulus. Normative PTT values have been established and they assist in the objective and neuroselective diagnostic evaluation of pain any related neurological impairments. The PTT measure also have utility in assessing analgesic interventions.[24]

Quantifying the Severity of an Abnormality

Quantifying the relative severity of a sensory impairment is a very important part of evaluating a disease or condition or for selecting the most appropriate intervention. Unlike other electrodiagnostic tests that only report findings as being "normal" or "abnormal",[25] sNCT/CPT reports grade the severity of the abnormality ranging from hyperesthesia through hypoesthesia.[26] For instance, the information can be used to determine whether or not to increase the duration of hemodialysis therapy for a patient with an equivocal presentation of mild to moderate neuropathy. It can also be used to determine if a low back or neck injury with radiating pain includes spinal nerve impairment, or of the advisability of a surgical referral for the treatment of Carpal Tunnel Syndrome versus more conservative treatment. Post intervention, sNCT studies can help determine if a surgical repair of a nerve injury is healing appropriately. A delay of return of sensation can indicate a neuroma formation which, if undetected, could impair or block recovery.

sNCT measures are compared to standardized, clinically established ranges of healthy measures in order to detect neuropathies and quantify their severity[27]. sNCT/CPT measures falling either above or below the established range of healthy measures are graded to indicate the severity of the abnormality detected. Software analyzes the test data and assigns all measures falling below the minimum - indicating a lower threshold than normal - one of two grades showing the degree of hyperesthesia detected. sNCT/CPT measures above the maximum range - indicating a higher than normal threshold and reflecting a loss of sensory function - are assigned one of 4 grades of severity. The software also analyzes the measures from each major subpopulation of sensory fibers, both independently and collectively, to provide the maximum amount information to the health care provider with the greatest sensitivity and specificity.[28]

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[24] Appendix E, Section 11, discusses related publications.

[25] Dyck, P.J. et al. Use of percentiles and normal deviates to express nerve conduction and other test abnormalities. Muscle & Nerve, Volume 24:307-310, 2001.

[26] Appendix H reviews the evaluation of sNCT study measures.

[27] Appendix E, Section 8 and Appendix H provide related references.

[28] Appendices D and H provide related references.

Monitoring the Course of a Neuropathy or Efficacy of a Treatment

Monitoring the functioning of sensory nerves in order to chart the course of a progressive neuropathy or gauge the efficacy of a treatment are also critical functions of neurodiagnostic procedures. For example, a 1993 NIH Consensus Development Conference titled Morbidity and Mortality of Dialysis, reported on the value of the sNCT/CPT evaluation of uremic neuropathy in assisting in monitoring the adequacy of kidney dialysis therapy. sNCT/CPT studies were reported to be "highly predictive" of 1-year mortality in non-diabetic patients with uremia. These findings were upheld later in a 4-year follow-up study..[29]

Comparison of Electrodiagnostic Sensory Nerve Studies

All electrodiagnostic sensory nerve studies operate by using the application of an electrical stimulus to the nerve (via surface electrodes) and then analyzing responses evoked by the stimulus to quantify the functioning of that nerve or nerve segment. There are numerous types and variations of nerve conduction tests including motor nerve conduction velocity, sensory nerve conduction velocity, F-wave, H-reflex, electromagnetic stimulation evoked responses, somato-sensory evoked potential responses, and auditory brain stem, visual and vestibular evoked potential responses. Different types of nerve conduction tests are used to evaluate nerves because there is no single type of procedure that is both reasonable and necessary for the diagnosis all sensory or motor nerve impairments.

sNCT/CPT studies have three unique features that distinguish them from the other electrodiagnostic nerve tests and make them far more sensitive to a much wider range of diseases and conditions affecting the sensory nervous system. sNCT/CPT studies are the only electrodiagnostic studies able to detect and quantify hyperesthesia which is often the earliest stage of a neuropathy. sNCT/CPTs are the only electrodiagnostic studies able to evaluate more than 90% of the sensory fibers in a nerve bundle as compared to less than 10% of the nerves fibers evaluated by the other studies. sNCT/CPT studies can be performed at the most distal parts of the body where most neuropathies begin instead of more proximally where they won't appear until months later. The following table summarizes some of the key differences between sNCT/CPT, sensory Nerve Conduction Velocity (NCV) and Evoked Response (ER, aka Somato Sensory Evoked Potential) electrodiagnostic studies.

[29] Appendix E, Section 3 provides related references.

Comparison Table

Capabilities and Features	Electrodiagnostic Study		
	sNCT/CPT	ER	NCV
Neuroselective Evaluation of All Major Sensory Fiber Types	✓		
Evaluates Hyperesthesia and Hypoesthesia	✓		
Tests Any Cutaneous Site	✓		
Evaluation of Radiculopathy	✓		
Localizes Abnormal Sensory Function from Periphery to Spinal Cord	✓		
Functional Physiological Measure	✓		
Standardized Automated Objective Examination Procedure	✓		
Painless study	✓		
Unaffected by Skin Thickness, Scar Formation or Edema	✓		
Unaffected by Skin Temperature	✓		
Shielded Room not Required	✓		

Neuroselective Measures : sNCT studies evaluate all three major subpopulations of sensory nerve fibers (large myelinated, small myelinated and unmyelinated) that together comprise more than 90% of the fibers in a sensory nerve bundle in one procedure. Neuropathologic conditions can selectively damage individual subpopulations of nerve fibers at different rates while completely sparing the others. Consequently, the selective evaluation of all major subtypes of fibers is necessary to accurately diagnose neuropathies.[30] ER and NCV studies evaluate less than 10% of the fibers (large myelinated only) and require that other procedures be performed to evaluate the smaller fibers.

The procedures often used in conjunction with ER and NCV studies to evaluate the small myelinated and unmyelinated fibers (which they can not evaluate), are non-electrodiagnostic Quantitative Sensory Tests (QSTs) including vibratory and thermal studies. Due to the physical nature of the stimuli used by these procedures, however, they are far more subjective, unreliable and non-specific than the electrodiagnostic sNCT/CPT, ER and NCV studies.

Hyperesthesia and Hypoesthesia : While ER, NCV and sNCT/CPT evaluations are all capable of detecting and evaluating a loss of nerve function or conduction associated with a pathological condition, only the sNCT/CPT studies can quantify the hyperesthetic stage of a neuropathy that often precedes the loss of function. Detection of this hyperesthetic

[30] Appendix E, Sections 4 and 10, discuss related publications.

condition permits earlier therapeutic intervention, thereby improving the prognosis with the potential of limiting more severe damage and reducing the cost of care.[31]

Test Any Cutaneous Site : sNCT/CPT studies may be performed on any cutaneous or mucosal site in order to localize and map the distribution of proximal or distal sensory nerve impairments.[32] ER and NCV procedures are usually conducted over major branches of peripheral nerves in the extremities and not distally at the tips of the toes or proximally at paraspinal sites, the locations where many neuropathies initially present. In these situations, ER and NCV studies are limited to detecting more advanced conditions and are insensitive to the earlier stages of a neuropathy which can benefit from timely intervention.

Evaluation of Radiculopathy: The sNCT/CPT evaluation is reasonable and necessary in the immediate assessment of suspected sensory spinal cord disorder or radiculopathy. A compressive radiculopathy resulting from a herniated disc can only be detected by needle EMG three to six weeks after the injury occurs, delaying appropriate therapeutic intervention. The sensory NCV evaluation tests only a small segment of a peripheral nerve and is insensitive to all spinal cord disorders and most radiculopathies.[33]

Localization of Abnormal Sensory Function: sNCT studies evaluate sensory impulse transmission from the peripheral nerve to the brain permitting localization along the path. NCV studies evaluate only isolated portions of a peripheral nerve, and while they are effective in localizing focal peripheral nerve lesions, they are insensitive to spinal pathology and most types of radiculopathy. ER studies derive most of their utility from evaluating spinal pathology and are not generally effective for localizing peripheral nerve lesions.

Functional Physiological Measure: sNCT studies provide a functional physiological measure of sensory nerve impulse conduction from the site of stimulation through to the brain. Other electrodiagnostic nerve studies, such as NCV, however, are limited to providing a purely physiological measure of only a small segment of a nerve. An example of the practical difference between these two measures can be illustrated by examining the expected results of tests performed on a paraplegic patient with a transected spinal cord. sNCT studies performed on this patient's lower extremities would fail to obtain any measure of sensory functioning, consistent with the patient's condition. NCV studies from these same extremities in which the patient had lost sensory function, however, would be insensitive to any sensory impairment.

Standardized Procedure: sNCT/CPT studies are performed using a computer controlled double-blind automated procedure that maximizes the objectivity and reliability of the measures. sNCT/CPT measures are statistically analyzed by a computer through comparison to universal clinically established ranges of normative measures to assure reliability independent of the clinic or technician. ER and NCV studies are manually controlled, single-blinded procedures that involve a considerable amount of subjective input from the

[31] Appendix E, Section 9, discusses related publications.

[32] Appendix E, Sections 1, 2 and 4 discuss related publications.

[33] Kimura, J. Electrodiagnosis in Diseases of Nerve and Muscle. Edition 2, page 448, F.A. Davis Co. Philadelphia., PA, 1989 and Goodgold, J. Rehabilitation Medicine. page 53, C.V. Mosby Co. St. Louis, MO, 1988. Appendix B, Section 1, also discusses related publications.

examiner in order to determine the test measures.[34] The measures from these procedures are individually determined by the health care provider and variations in the equipment and examination procedures and interpretation methods have precluded the establishment of universal standards.

Painless Stimulus: sNCT/CPT measures use a painless stimulus to evaluate sensory nerve function, while NCV and ER studies use a much stronger electrical stimulus that is usually characterized as unpleasant or painful. There are numerous reports of poor patient compliance with electrodiagnostic NCV studies because of the discomfort associated with this test.[35] Other studies have shown the successful use of sNCT studies for evaluating children with early diabetic neuropathy - a group for whom traditional NCV studies are generally avoided because of their aversive nature.[36]

Unaffected by Skin Thickness, Scar Formation or Edema: sNCT studies are not affected by the presence of edema, a condition which is a major confounding variable that can prevent ER and NCV studies from being reliably performed. Scarring and calluses, which are also major confounding variables for a variety of neurodiagnostic procedures, don't interfere with sNCT studies, either. The constant current stimulus employed for sNCT studies automatically compensates for differences in skin electrical resistance caused by variations in thickness, dryness or swelling, and produces reliable measures.

Unaffected by Skin Temperature: sNCT studies are not affected by the normal variations in skin temperature that can cause significant variability in other types of neurodiagnostic measures.[37] For example, a one degree change in skin temperature can cause a significant change in NCV, ER and other electrodiagnostic measures, as well as in non-electrodiagnostic QST measures of vibratory or thermal sensation. The insensitivity of sNCT study CPT measures to normal variations in skin temperature contributes to their reliability and clinical utility.

Shielded Room not Required: sNCT studies are not affected by the 60 Hz electro-magnetic fields that can distort results of ER and NCV studies, so expensive, electronically shielded rooms are not needed for reliable operation. sNCT studies can be performed almost anywhere including an unshielded office or a patient's bedside, in order to maximize compliance and minimize expenses and inconvenience. Studies with patients receiving sNCT evaluations while undergoing dialysis therapy - an environment in which 60 Hz shielding is unavailable - demonstrate the utility of sNCT studies afforded by their convenience and painless nature.[38]

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[34] Chaudry, V. et al. inter- and Intraexaminer reliability of nerve conduction measurements in patients with diabetic neuropathy. Neurology. Volume 44;1459-1462, 1994. and Chaudry, V. et al. inter- and Intraexaminer reliability of nerve conduction measurements in normal subjects. Annals of Neurology, Volume 30(6):841-831, 1991.

[35] Mittman, N., Avram, M.M. Management of Uremic Peripheral Neuropathy. Dialysis Therapy, 2nd edition, edited by Nissenson, A.R. & Fine, R.N, pp. 277-279, 1993. Also see references in Appendix B, Part 3.

[36] Appendix E, Section 2 discusses related publications.

[37] Maeda, M., Tsuji, T., Sasaki, U., Yorizumi, K., Oofuchi, S., Nagasawa, H., Shiba, Y. Changes of Current Perception Threshold on Sensory Nerve Fiber in Thermotherapy. Japanese Association of Physical Medicine Balneology. Volume 63(3):143-150, 2000. Additional studies available upon request.

[38] Appendix E, Section 3, discusses related publications.

Cost Savings and Diagnostic Advantages of sNCT Studies

Early intervention in a disease often results in a better prognosis and less expensive treatment, which is why use of sNCT studies can result in greater cost effectiveness for health care and better clinical outcomes for patients. The ability of sNCT/CPT studies to accurately evaluate a wide range of neurological problems often before extensive damage occurs, permits much earlier therapeutic intervention, a better prognosis and considerable cost savings. Limitations of other electrodiagnostic procedures can result in significant and costly delays in developing a timely diagnosis.

Each sNCT/CPT study independently measures the functioning of all three major types of sensory nerve fibers in the same evaluation. Since diseases can effect some types of fibers while sparing the others, a broad spectrum assessment is critical for an early and accurate diagnosis. Other electrodiagnostic procedures evaluate less than 10% of the fiber types in a typical sensory nerve and their use, therefore, requires that two additional types procedures be performed in order to evaluate the same range of fibers examined in each sNCT/CPT study.

sNCT/CPT studies can be performed at the most distal sites on the body where many neuropathies initially appear. Other electrodiagnostic studies are not able to test at these distal sites, and require waiting for a disease or condition to advance in severity until the nerve dies back to a more proximal point before the lesion can be detected. This dying back process can take months or years to occur and can significantly delay effective treatment.

sNCT/CPT studies can detect and quantify hyperesthesia the earliest stage of many neuropathies that generally occurs before significant and irreversible damage takes place. Other electrodiagnostic studies are limited to evaluating only the more advanced hypoesthetic conditions, that may not occur until months or years later and for which treatment may be much more expensive.

sNCT/CPT studies are immediately sensitive to impairments in spinal cord and spinal sensory nerve conduction that are generally not detectable by the NCV. The needle EMG is only sensitive to the related motor components of such impairments weeks or months after they have occurred. The early detection afforded by sNCT/CPT studies can reduce expenses and allow for the optimal medical management of spinal cord disorders and radiculopathy by enabling earlier treatment of the condition.

High patient compliance with the painless and convenient sNCT/CPT procedure combined with its high sensitivity, enhance it's use for the serial monitoring of diseases and therapies. An NIH Consensus Development Conference titled "Morbidity and Mortality of Dialysis" report along with a follow-up report 4 years later, demonstrated that the sNCT/CPT studies provided measures that were "highly predictive" of mortality in non-diabetic hemodialysis patients. The NIH report indicated that the sNCT/CPT measures were a more sensitive marker of mortality than a number routine blood chemistry measures. The study concluded that sNCT/CPT studies for the evaluation of dialysis patients could assist in optimizing therapy which, "would reduce morbidity, mortality, and the cost of the ESRD in the United States."[39]

Finally, when a health care provider examines a patient and discovers a suspected neuropathy, he must typically refer the patient out to be examined at another office that has the electrodiagnostic equipment and shielded environment needed to perform quantitative neurological testing. Then, he must wait for the results of the tests to be returned before he can proceed with

[39] Appendix E, Section 3 reviews supporting research publications.

diagnosing the patient's condition and designing a course of treatment. Besides the inconvenience to the patient and the delay in diagnosing and treating the underlying condition, the patient will be also charged for a second physical exam that is performed just prior to the neurological study by the consultant health care provider as part of the routine preparation for the study. Unlike other electro-diagnostic procedures, however, automated sNCT/CPT studies do not require specially shielded rooms and are not distorted by inter-operator variability so they can easily be performed in the health care provider's office immediately after a suspected neuropathy is discovered. This permits an earlier diagnosis, greater convenience for patients and lowered costs for the health care.

Together, these many different aspects and features of sNCT/CPT studies combine to create an extremely efficient and sensitive diagnostic tool that enables the early and accurate and diagnosis of a wide range of neuropathological conditions. Alternative electrodiagnostic studies, limited by their narrow focus on a single small subpopulation of nerve fibers, their insensitivity to early neuropathies and inability to test at the most distal sites, can significantly delay intervention, adversely effecting the prognosis and significantly increasing the costs of treatment for many conditions.

Conclusion

An early and accurate diagnosis is the cornerstone of effective treatment, patient welfare and cost control. Without adequate diagnostic information, treatment is delayed until symptoms become more severe, the prognosis worsens and costs rise. The sNCT/CPT is a neurodiagnostic tool that objectively evaluates a wider range of sensory nerve impairments from an earlier stage than other types of electrodiagnostic studies. The sNCT/CPT evaluation fills an important gap in health care neurodiagnostic services by permitting the objective assessment of protective and other sensations, studies from any cutaneous site and the evaluation of over 90% of the nerve fibers missed by all the other electrodiagnostic tests. Additionally the painless, automated and 'use anywhere' features of this diagnostic study enhance its clinical utility.