Overview and References

Appendix E. Selected Study References

Section 1. Evaluation of Spinal Nerve/Cord Function ............... E - 2
Section 2. Evaluation of Diabetic Neuropathy ....................... E - 4
Section 3. Evaluation of Uremic Neuropathy ....................... E - 7
Section 4. Evaluation of Large and Small Fiber Polyneuropathies .... E - 8
  Small Fiber Polyneuropathy ..................................... E - 8
  Large Fiber Polyneuropathy ..................................... E - 8
  Axonal and Demyelinating Polyneuropathy ....................... E - 9
  Distal Axonal Polyneuropathy .................................. E - 10
  Hand-Arm Vibration Syndrome Polyneuropathy .................... E - 10
Section 5. Evaluation of Nerve Regeneration and Recovery of Function E - 11
Section 6. Focal Nerve Lesions, Carpal Tunnel Syndrome ............ E - 11
Section 7. Study References for Appendix D ......................... E - 12
Section 8. Selected sNCT/CPT Normative Value References .......... E - 12
Section 9. sNCT/CPT Studies of Hyperesthesia ....................... E - 13
Section 10. Studies related to sNCT/CPT Neuroselectivity ............. E - 13
Section 11. sNCT Studies Related to Pain ........................... E - 15

The following collection of selected references document many different aspects of the clinical utility of sNCT evaluations. Each study reference citation is followed by a brief summary of significant points in the article. A comprehensive
bibliography of sNCT publications appears in Appendix F.

Section 1. Evaluation of Spinal Nerve/Cord Function

The following publications involve the use of the sensory Nerve Conduction Threshold (sNCT) study as it relates to the evaluation of impaired sensory functioning in the spinal cord/nerves. As a functional physiological test, sNCT/CPT studies are able to evaluate the full length of sensory nerve conduction, from the periphery to the brain, so impairments in and around the spine may be evaluated.


This study from the Sapporo Medical University and the Sapporo Kiyota Orthopedic Hospital appears in the official international journal of many spine societies, including those from Asia, Europe, North and South America. This paper documents the ability of the sNCT/CPT evaluation to document sensory nerve dysfunction in dermatomes associated with pain and unequivocal disc dysfunction as shown by magnetic resonance imaging. A total of 48 patients were studied and 11 healthy subjects were used as control subjects. In the control group, there was no significant difference in sNCT/CPT values between the left and right legs. In the patient group, the sNCT/CPT measures in the affected leg dermatome test sites were significantly higher than in the contralateral matched test sites (p<0.01). The authors conclude that the sNCT/CPT evaluation is useful in quantifying sensory dysfunction resulting from radiculopathy.

[Note: The sensory nerve conduction velocity and amplitude evaluation is insensitive to the sensory impairment that results from radiculopathy.]


This publication from Virginia Mason University appears in the official journal of the American Society of Anesthesiology. The paper demonstrates the ability of the sNCT/CPT study CPT measures to document the loss of sensory function resulting from the spinal injection of lidocaine in six healthy individuals. The sNCT/CPT study immediately quantified the loss of sensation in the periphery with this pharmacologically induced spinal neurological impairment. The findings demonstrated the sNCT/CPT evaluation frequency dependent CPT measures providing independent assessments of both large and smaller fiber spinal sensory functioning. The neuroselective longer lasting effect of the lidocaine in impairing smaller diameter sensory nerve fiber transmission while sparing the larger diameter sensory nerve fiber transmission was measured by the sNCT/CPT evaluation 5 Hz and 2000 Hz measures respectively and was also detected clinically by a loss of thermal sensation with intact touch sensation. The p values for the differential
effects of the lidocaine impairment ranged from \( p = 0.02 \) to \( p = 0.04 \).

This study also included measures from an upper cervical test site to demonstrate that the effects of the spinal administration of lidocaine are not systemic but have a segmental distribution with no significant effect at the cervical test site (\( p>0.3 \)).

[Note: Other electrodiagnostic procedures, including somato-sensory evoked response (ER), and nerve conduction velocity (NCV) evaluations could not have been used to document the late effects of the Lidocaine in this study, because both are limited to large fiber evaluation only. Further, the NCV can test only isolated segments of a peripheral nerve is therefore insensitive to spinal sensory impairments. Documentation of this type of functional sensory impairment (local anesthetic block) with standard MRI evaluation is also impossible because it is a physiological and not a structural lesion.]


This study from the University of Texas, Houston was published in the official journal of the International Anesthesia Research Society. This 8 subject crossover controlled study demonstrated the ability of the sNCT study CPT measures to document a neuroselective segmental impairment in spinal function caused by the administration of lumbar epidural lidocaine (\( P<0.05 \)). The clinicians in this study were unable to demonstrate this neuroselective and segmental sensory impairment by standardized clinical evaluations including touch, pin prick and cold evaluations.


This research demonstrates that sNCT study CPT measures are sensitive to nerve damage occurring inside the spinal cord resulting from a condition called syringomyelia. In the early stages of this condition, there is a selective loss of protective sensations such as pain and temperature (small fiber function) with sparing of normal painless sensation such as touch (large fiber function). This study of 10 patients with syringomyelia and 15 age matched normal subjects reports - sNCT/CPT detected sensory abnormalities confined primarily the 5 Hz CPT measures with 71.4% detection sensitivity versus the 2000 Hz CPT measures with a detection sensitivity of 7%, \( p<0.001 \) (i.e a selective loss of small diameter fiber function with a sparing of large fiber function). The sNCT/CPT studies detected abnormalities that correlated with the clinical and MRI findings in locating the
spinal level of abnormality ($r=0.73; p<0.01$. The findings demonstrated the ability of the sNCT/CPT study to neuroselectively evaluate and localize spinal cord pathology.

[Note: Only the most advanced stages of this condition would be detectible by evoked potential response (ER) studies. Sensory nerve conduction velocity (NCV) evaluations are insensitive to all spinal cord pathology.]


This publication from the official journal of the American Society of Pain Management, demonstrates the diagnostic utility of the sNCT/CPT study in a population of 70 patients with clinical signs and symptoms of radiculopathy. Automated CPT measures were obtained from cervical or lumbar/sacral dermatome test sites to evaluate for a distribution of sensory impairment consistent with radiculopathy and differentiate focal and polyneuropathy lesions. The patients were also evaluated with MRI studies. The statistical analysis of the measures demonstrated good agreement between the sNCT/CPT and MRI findings with a “high degree of level specific agreement” (95% confidence interval) when both tests were positive with an 84% sensitivity of the sNCT/CPT studies. The authors conclude that sNCT/CPT measures “may be a useful tool to help the clinician assess the functional significance of MRI disc findings.”


This paper from the Craig Hospital in Denver, Colorado, includes 52 patients. It reports that 5 Hz CPT measures correlated well with neurophysiologic abnormalities as monitored intraoperatively from the substantia gelatinosa (lamina II) area of the spinal dorsal horn innervated by C fiber afferents. The 5 Hz CPT measures were more sensitive in identifying pathologic spinal segments than the intraoperative neurophysiologic measures (approximately 84% for CPT versus 56% for neurophysiologic ). This publication clearly demonstrates the ability of the CPT evaluation to localize the dermatome level of a spinal cord lesion. A previous related publication by these researchers includes:


Section 2. Evaluation of Diabetic Neuropathy

The following publications involve the use of the sensory Nerve Conduction
Threshold (sNCT) study as it relates to the evaluation of impaired sensory functioning in the diabetic patient. sNCT/CPT studies have the unique ability to evaluate hyperesthesia, most often the earliest stage of diabetic polyneuropathy, permitting earlier therapeutic intervention. They can also test at the tip of the great toe where these neuropathies first appear. Earlier intervention improves the prognosis and reduces the cost of care by limiting more severe damage and related complications. sNCT/CPT studies can also detect and quantify small myelinated and unmyelinated fiber pathology in diabetic subjects in the same evaluation. These fibers mediate protective sensation (pain and temperature), and their loss, if undetected, can lead to disastrous complications (e.g. ulceration or amputation). Documenting small fiber neuropathy and a loss of protective sensation at an early stage can allow for interventions (e.g. orthotics) that can decrease the cost of care.


This study of 71 diabetic patients with a combined total of 169 complete evaluations over a 12 month period compares sNCT/CPT measures and sensory nerve conduction velocity (NCV) findings as they correlate with clinical findings by health care providers. The sNCT/CPT study was found to be a more effective predictor of symptoms and physical impairments as determined by clinicians than NCV testing. The correlation coefficients of the symptoms and physical findings were $p<0.001$ and $p<0.001$ for the sNCT/CPT studies $p<0.01$ and $p<0.05$ for NCV studies, respectively.


This study of 44 healthy control subjects and 59 diabetic subjects illustrates that sNCT/CPT measures may be utilized to localize the distribution of diabetic sensory impairment starting at the tip of the great toe. The correlation coefficient with history (symptom score) and physical exam (physical score) was 0.53 and 0.65, respectively (both at $p<0.05$).


A study of 30 healthy control subjects and 90 diabetic patients favorably compares sNCT/CPT measures to other tests of nerve function. The 2000 Hz CPT measures correlated significantly with the NCV (large fiber test) measures ($p<0.005$), and the 5 Hz CPT measure correlated significantly with the thermal threshold (small fiber test) measures ($p<0.001$).

This publication provides normative CPT data for 31 healthy subjects as well.
as the coefficient of variation information for 2000 Hz and 5 Hz CPT measures.


This study of 92 insulin dependent diabetic children and 80 healthy matched controls demonstrates the utility of the sNCT/CPT measures in evaluating diabetic neuropathy in children. The diabetic children had significantly elevated CPTs in comparison to the healthy children (p<0.01). The authors conclude that “evidence of peripheral sensory nerve dysfunction is not rare in children and adolescents with diabetes and can be demonstrated by CPT testing.”

This publications provides normative CPT values for 80 healthy children ages 6 to 18 years as well as the coefficient of variation information for repeated CPT measures.


This publication evaluates 12 diabetic patients and 12 controls. The sNCT/CPT identified diabetic patients with polyneuropathy who displayed a severely impaired cardiovascular adaptation mechanism. This impaired mechanism could be used to identify patients at increased risk of cardiac death. The cardiovascular adaptation mechanisms are mediated by small fibers. The most significant sNCT/CPT sensory abnormalities were detected at the big toe test site with the 250 Hz CPT (p<0.007) and the 5 Hz CPT (p<0.002) measures. These sNCT/CPT detected impairments are consistent with small fiber dysfunction.


This study of 558 non-insulin dependent diabetic subjects compared sNCT study CPT measures to quantitative vibratory and monofilament measures. The averaged CPT measures were greater than three times more sensitive than the other two tests (Sensitivity: sNCT/CPT = 33.9%; monofilament = 10.6% and graduated tuning fork = 8.1%). The averaging of CPT measures, however, statistically prohibited these researchers from taking advantage of the ability of the sNCT/CPT study to quantify both hyperesthetic and hypoesthetic conditions. When notified about this limitation of the analysis a new analysis was conducted which evaluated detected both hyperesthetic and hypoesthetic CPT abnormalities that revealed the detection sensitivity of the sNCT/CPT evaluation to was approximately six times more sensitive than the other tests.

This is a study of 2,074 subjects from Nagoya City University Medical School in Japan. This study included 924 healthy subjects, 1001 patients with insulin resistance and 149 insulin dependent diabetics. This study concluded that there is a hyperesthetic stage precedes the hypoesthetic stage in the development of diabetic neuropathy (p<0.01).


A study of 2,360 type 2 diabetic patients with sNCT/CPT evaluations as well as other sensory neurodiagnostic measures with an analysis of demographic data, metabolic parameters and examinations for chronic diabetic complications. Current Perception Threshold (CPT) measures from this study demonstrated a hyperesthetic stage preceding the hypoesthetic stage in the development of advanced diabetic neuropathy (p<0.001). The study concludes that some intervention may be started earlier in the hyperesthetic stage for prevention of the progression to advanced diabetic neuropathy. This observation is consistent with the findings in study #25 in this Appendix.


This publication demonstrates the diagnostic utility and the neuroselectivity of the sNCT/CPT evaluation as compared with the sympathetic skin response (SSR) and the sensory nerve conduction velocity (NCV) evaluations. The study included 14 diabetic patients, 10 alcoholic patients and 24 age matched controls. The study concludes that there is a significant correlation between only the 5 Hz CPT and the SSR measures, which represent small unmyelinated fiber function. The NCV data did not correlate with the SSR measures. This was expected as the NCV test is insensitive to smaller fiber function.

### Section 3. Evaluation of Uremic Neuropathy

The following publications involve the use of the sensory Nerve Conduction Threshold (sNCT) study as it relates to the evaluation of impaired sensory functioning in the uremic patient. The painless, neuro-selective and highly sensitive nature of the sNCT/CPT procedure assists in the determination of when to commence dialysis therapy and in providing a sensitive marker of the adequacy of dialysis therapy. sNCT/CPT studies have also been used evaluate uremic patients for Carpal Tunnel Syndrome (CTS) superimposed on uremic polyneuropathy.

1993.

This NIH Consensus Development Conference presentation of a sNCT/CPT evaluation study of 95 dialysis patients found neuropathy was highly predictive of one year mortality in non-diabetics (p=0.03). The sNCT study CPT measures were found to be a more sensitive marker of mortality than a number routine blood chemistry measures. The study concludes that periodic sNCT/CPT evaluation of dialysis patients could assist in optimizing therapy which, “would reduce morbidity, mortality, and the cost of the ESRD in the United States.” The same authors later reported in a survival study of 123 non-diabetic hemodialysis patients that the sNCT/CPT evaluated neuropathy was also an independent predictor of four year mortality risk. (Mittman, N., Avram, M.M., Castanares, A., Oo, K., Licht, J., Sreedhara, R. Severe Neuropathy Predicts Mortality in Non-Diabetic Hemodialysis Patients. Journal of the American Society of Nephrology, Volume 6:552, 1995.)


A study of 29 hemodialysis patients evaluating the reproducibility of CPT measures and the diagnostic utility of the measures in detecting dialysis associated Carpal Tunnel Syndrome (CTS). The CPT measures were compared to normative measures from 137 matched controls. The findings documented sensory impairments localized to a median nerve distribution that were consistent with CTS. The sNCT/CPT studies had a detection sensitivity of 92% and the NCV studies had a detection sensitivity of 79%. There was a significant correlation between the findings from these two electrodiagnostic measures, \( r = 0.70, p<0.001 \).

This study reports the coefficients of variation of repeated CPT measures from two different fingers from 7 hemodialysis patients over a 4 week period.


This one year duration prospective study of 23 hemodialysis patients using sNCT/CPT evaluation measures and NCV measures showed a significant correlation between the evaluated measures from both tests. Sensitivity measures are presented for both tests as well as a significant linear relationship was found between the grades obtained from both electrodiagnostic studies for repeated measures, \( r>0.80, p<0.001 \).

**Section 4. Evaluation of Large and Small Fiber Polyneuropathies**

The following publications involve the use of the sensory Nerve Conduction Threshold (sNCT) study as it relates to the evaluation of impaired sensory functioning caused by large and small fiber polyneuropathies. sNCT/CPT studies evaluate more than 90% of the typical sensory nerve fiber, including the large and small myelinated and unmyelinated fibers. Other electrodiagnostic procedures can
evaluate only the large myelinated fibers comprising less than 10% of the nerve, making sNCT/CPT studies uniquely valuable for evaluating a wide range of polyneuropathies.

**Small Fiber Polyneuropathy**


This study included 16 patients with hereditary small fiber neuropathy secondary to Fabry’s disease (an X-linked disorder caused by a deficiency of the lysosomal enzyme alpha-galactosidase A) and 50 healthy matched control subjects. With 100% specificity for selective small fiber impairment the sNCT/CPT study had a detection sensitivity of 50%. Hyperesthetic sNCT/CPT/CPT measures were documented in the patients in this study.

Prior to undergoing sNCT/CPT studies, the patients in this study had all been informed that the pain they reported experiencing was psychological and not physiological in origin. This was based upon results from earlier nerve conduction velocity (NCV, large fiber) studies which had been normal. Consequently, these patients did not receive the appropriate treatment for their painful disease until after their rare condition was detected by sNCT/CPT studies.

This publication from Taiwan also provides CPT measures from fingers and toes of 50 healthy subjects. The healthy measures collected in this study are practically identical to the established healthy measures from the USA.

**Large Fiber Polyneuropathy**


This study from the Ministry of Health of Malaysia included 60 farmers exposed to an organo-phosphate toxin and 19 control subjects. A selective loss of myelinated fibers is known to result from organo-phosphate toxin exposure. sNCT/CPT studies and blood serum cholinesterase activity were determined. The sNCT/CPT measures showed a statistically significant correlation with the cholinesterase activity (r = -0.763, p=0.0001). The only significant sNCT/CPT abnormalities detected were with the 2000 Hz and 250 Hz CPT measures (p=0.0001). There were no significant 5 Hz CPT (unmyelinated fiber) abnormalities, and the 250 Hz and 2000 Hz CPT abnormalities are consistent with a selective loss of myelinated fiber function. The authors conclude that sNCT studies may be, “used as an indicator for detecting the effects of pesticide instead of using cholinesterase...”

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enzyme activity.”

The authors report that the sNCT evaluation, in rural Malaysia, reduces the need to draw blood for detecting toxic exposure levels and the study is easier to manage and more cost effective.

**Axonal and Demyelinating Polyneuropathy**


This study included 10 patients with demyelinating polyneuropathy and 10 patients with an axonal polyneuropathy. The sNCT study CPT measures were evaluated based upon comparison with established CPT normative values. The sNCT/CPT study was reported to have a diagnostic sensitivity similar to that of published electrodiagnostic NCV study criteria for demyelinating and axonal polyneuropathies. Using a specificity of 100%, the sensitivity for demyelinating polyneuropathy was 50% and for axonal neuropathy was 70%. The sNCT/CPT study distinguished the demyelinating from axonal polyneuropathies (p<0.05). This study also replicated earlier findings from the United States Air Force (Menkes DL, Hood DC, Ballesteros RA, Bodnar P: Quantitative sensory testing distinguishes axonal from demyelinating polyneuropathies. *Muscle & Nerve*: 20:1056, 1997. This earlier study is not enclosed but is available upon request.)


This study from Columbia University included 10 patients with anti-myelin-associated glycoprotein antibody polyneuropathy. The sNCT study CPT measures were evaluated based upon comparison with established CPT normative values. All the patients had CPT measure abnormalities consistent with myelinated fiber dysfunction. Improvement in CPT and clinical measures were observed following IVIg therapy. If this type of polyneuropathy is not treated, it can be extremely debilitating and condemn a patient to a wheelchair.

**Distal Axonal Polyneuropathy**


This study included 29 alcoholic patients and 60 healthy control subjects. sNCT study CPT measures documented a significant distal loss of sensory function in the toe (p<0.05). Proximal sensory function from the finger and face fell within the normative CPT parameters. This localization of a distal sensory impairment is consistent with the distal axonopathy associated with alcoholic toxicity.
Hand-Arm Vibration Syndrome Polyneuropathy


This publication from the Health and Safety Policy Branch, Ministry of Labor, Toronto, Ontario, Canada illustrates how the CPT measures correlate with other measures of hand-arm vibration syndrome polyneuropathy. The study included 364 subjects who were independently classified by various established Hand-Arm Vibration Syndrome (HAVS) impairment parameters. Studies included NCV and vascular studies. The sNCT study CPT ranked abnormalities were all confined primarily to the 2000 Hz measure, (p<0.01). There were no significant 5 Hz CPT ranked abnormalities, (p>0.6). The neuroselective sNCT/CPT findings were consistent with the demyelinating neuropathy reported associated with HAVS. The sNCT 2000 Hz CPT abnormalities were also in agreement with NCV studies which had significant ranked abnormalities, (p<0.01) in the same population. This study is limited by the fact that it only included the assessment of hypoesthetic CPT measure abnormalities. These findings were replicated by the following publication. This study was replicated in the following publication:


This research from Tottori University and San-in Rosai Hospital of Yonago, Japan, was of 59 men officially recognized by the Japanese Ministry of Labor with hand-arm vibration syndrome that was documented by clinical and laboratory tests. There were 20 matched control subjects. The sensory nerve conduction velocity evaluation was used to confirm Stage 3 vibration neuropathy. Stage 3 is the most advanced stage based upon the international Stockholm classification system. The sensory nerve conduction velocity evaluation is insensitive to the earlier Stages 1 and 2 of vibration neuropathy when intervention is less expensive and more beneficial. The Neurometer CPT evaluation was able to detect sensory impairments in all 3 stages of vibration neuropathy neuroselectively by showing impairments confined to large and small myelinated fiber function only, a finding consistent with histological studies.

Section 5. Evaluation of Nerve Regeneration and Recovery of Function

The evaluation of both nerve recovery and regeneration permits the assessment of therapeutic intervention and assists in the management of the nerve impairment. A study previously reviewed in this Appendix, study #18, is an example of the clinical use of sNCT/CPT studies for evaluating the recovery of sensory function. The publication listed below provides an example of the clinical utility of the sNCT/CPT evaluation of nerve regeneration in the recovery of function.

A total of 22 patients were studied with toe-to-digit or digit-to-digit replantation. Within subject control studies were obtained from the contralateral corresponding normal finger. Following transplantation, sNCT study CPT measures objectively evaluated the recovery of sensory function ($p = 0.72$ between normal finger and transplanted toe with the CPT measures). The same authors previously reported that the Nerve Conduction Velocity (NCV) and Sensory Evoked Response (ER) studies were unable to evaluate the recovery of sensory function with digit replantation due to scar formation which is recognized to be a significant factor effecting these studies.

Section 6. Focal Nerve Lesions, Carpal Tunnel Syndrome

Focal nerve lesions include a wide variety of conditions including radiculopathy and digit transplantation described in Sections 1 and 5 respectively in this Appendix. Another common focal nerve lesion is Carpal Tunnel Syndrome (CTS) and the diagnosis of this condition is discussed in the reference numbers 13, 20 and the following reference:


A screening protocol including sNCT/CPT evaluations was implemented to identify individual workers experiencing UECTDs in a poultry plant (Tyson Foods) of 1500 workers. Upper extremity worker's compensation costs of over $110,000.00 per year. The was a 95% decrease in the UECTD related surgery from the previous year.

[Note: This appendix is dedicated to the diagnostic applications of the sNCT/CPT evaluation, however, the utilization of this diagnostic test for screening purposes has been proven to result in significant healthcare savings for industry. This information is to demonstrate how the sensitivity and reliability of sNCT/CPT studies have contributed to the prevention of severely debilitating neuropathological impairments in thousands of workers. Tyson Foods, the largest poultry processor in the USA, has used the services of Prevention First, an injury prevention firm in Minneapolis, MN, to supervise screening programs designed to minimize the incidence of Musculo Skeletal Disorders (MSD’s) including CTS among its workers. The Prevention First program used sNCT/CPT studies as part of their program at 5 different Tyson Foods facilities, 4 Justin Industry facilities and Magnetek Inc. and conducted over 30,000 studies of median nerve function to monitor for the development of MSD’s. Workers showing early signs of injury, received work hardening or ergonomic assistance. In one study, millions of man-hours of labor without a single lost time incident were documented and the development of advanced CTS requiring surgery was significantly reduced. In another study, a plant that averaged 20 surgeries for CTS injuries per year, saw that number drop to just one · for a worker who had fallen out of the screening program.]
Section 7. Study References for Appendix D

The statistics presented in Appendix D, “Representative Statistical Data”, are derived from the findings presented in 10 different studies. Seven of the studies are cited in earlier sections of this Appendix. They are study numbers 3, 4, 7, 8, 11, 13 and 15. The three additional studies are listed below.


This is an sNCT/CPT study of 1632 healthy individuals CPT measures from the index finger (median nerve). These Japanese measures were similar to the established normative data from the USA.

This publication also provides CPT intra- and inter-rater reliability data including correlation coefficient, prevalence of the percent difference of repeated measures and the coefficient of variation of repeated measures (presented in Appendix D).

The study concludes that “CPT testing appears to have strong potential to provide useful information in epidemiological or clinical studies because of its comparability and reproducibility.”


This publication reports on sNCT/CPT evaluations of 33 randomly selected diabetic subjects and 54 healthy control subjects. The detection sensitivity of the CPT evaluation was 94% based on a specificity of 100%.


This study includes sNCT/CPT studies of 73 diabetic patients and 47 healthy control subjects. The sNCT/CPT studies had a sensitivity of 60% based on a specificity of 95%. The study findings demonstrated that hyperesthetic CPT measures are associated with the early stages of diabetic neuropathy whereas the hypoesthetic measures were associated with the more advanced diabetes and complications such as foot ulceration.

Section 8. Selected sNCT/CPT Normative Value References

Standardized ranges of healthy sNCT/CPT measures have been established for dozens of body sites through clinical studies conducted at several major institutions. These measures are used to evaluate sNCT/CPT study data as discussed in Appendix H. A number of the studies which contributed to the healthy base measures as well as some that established their own normal base measures
Section 9. sNCT/CPT Studies of Hyperesthesia

Numerous studies document the unique ability of the sNCT/CPT study to evaluate the hyperesthetic condition. Five of those studies #’s 11, 13, 14, 15, and 25 appear earlier in this Appendix. Additionally, the Neurometer CPT 510(k) FDA application includes scatter diagrams from clinical trials that illustrate hyperesthetic and hypoesthetic CPT measures from a population of 86 diabetic, alcoholic and other patients with clinical findings of neuropathy compared to 60 healthy control subjects. The detection sensitivity of the sNCT/CPT studies was greater than 95% based on a specificity of 100% with both hyperesthetic and hypoesthetic abnormalities detected in the patient population.


This is a study of 2,074 subjects from Nagoya City University Medical School in Japan. This study included 924 healthy subjects, 1001 patients with insulin resistance and 149 insulin dependent diabetics. This study demonstrated a hyperesthetic stage precedes the hypoesthetic stage in the development of diabetic neuropathy (P<0.01). These findings were consistent with the National Taiwan University study of 2,360 type 2 diabetic patients discussed in reference 11 earlier in this Appendix.

Section 10. Studies related to sNCT/CPT Neuroselectivity

sNCT/CPT studies evaluate the three major subpopulations of sensory nerve fibers, giving them extreme sensitivity for evaluating a wide range of diseases and conditions. There are a number of publications appearing earlier in this Appendix that explicitly utilize the neuroselectivity of sNCT/CPT measures including #’s 1,
2, 3, 5, 7, 16, 17, 18, 20 and 21. In addition, the following publication summarizes the findings from a wide range of studies demonstrating sNCT/CPT neuroselectivity.


This publication summarizes major research findings through early 1998 addressing the neuroselectivity of the sNCT/CPT measures in both the peripheral and central nervous systems.


This sNCT/CPT study from The University of Texas-Houston Health Science Center Medical School confirms an earlier British report that the 5 Hz CPT measures are unaffected by 30 minutes of tourniquet ischemia, whereas the 2 kHz CPT measures were significantly elevated for the last 25 minutes of this ischemia. This observation obtained from 10 healthy individuals is consistent with the understanding that the smaller diameter sensory fibers are more resistant to the effects of ischemia than the larger diameter fibers.

Additional related studies include the following:


29. Dr. Neil Spielholz, Professor at the University of Miami School of Medicine presented sNCT stimulus neuroselectivity findings at the September, 2000 meeting of the American Association of Electrodiagnostic Medicine, Philadelphia, PA.

Using conventional nerve conduction velocity equipment connected to a specially modified sNCT device his research group was able to demonstrate from the median sensory nerve in 10 healthy subjects that the 2000 Hz stimulus evoked a large diameter fiber response whereas the 5 Hz stimulus did not.
Section 11. sNCT Studies Related to Pain

The previously cited studies numbers 1, 2, 3, 15 and 27, are related to the evaluation of pain. The sNCT stimulus may be administered at intensities above the painless sensory threshold to evaluate the Pain Tolerance Threshold (PTT). Other electrodiagnostic tests are incapable of providing pain related information. The following are selected sNCT/PTT related studies.


A recent multi site study of 36 chronic pain subjects and 37 healthy controls had a detection sensitivity of the painful PTT measure of 78% in the painful symptomatic test sites and a painless CPT measure detection sensitivity of 47%. PTT measures are reported to provide additional valuable information for the assessment of the chronic pain patient.


These researchers from Stanford University Department of Anesthesiology used the PTT to evaluate analgesia associated with different analogs of the analgesic, hydromorphone, in 12 subjects in a double blind cross-over design. The study demonstrated the dose dependent effect of the drugs (p<0.001) and demonstrated that the sustained release hydromorphone has analgesic effects of approximately ten times the duration than the immediate release version of this drug.


This study was awarded the National Pain Society of Austria Award for Scientific Research in 2002. This prospective double blind placebo controlled double-blinded cross-over study, from the University of Vienna, included 17 subjects. Neurometer® Pain Tolerance Threshold (PTT) 250 Hz and 5 Hz measures were used to evaluate constant remifentanil infusion during a 3 hour period. The study concludes that this course of administration does not lead to a rapid development of opiate tolerance.