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NC-stat® System, NeuroMetrix® Inc.
(Nerve Conduction Testing System)

Technology Assessment
January 19, 2006

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INTRODUCTION

NC-stat by NeuroMetrix® is an automated nerve conduction testing system marketed as an alternative to conventional nerve conduction testing. It is a diagnostic and screening tool designed to perform nerve conduction studies (NCSs).

NCSs assess the integrity and may aid in diagnosing diseases of the peripheral nervous system by measuring the speed, size and shape of conduction through a nerve in response to a stimulus (AANEM).

The NC-stat system is marketed to "perform non-invasive nerve conduction testing" [http://www.NeuroMetrix®.com/products.htm, May 31, 2005] and consists of 4 components: 1) patented single use sensors, 2) a monitor that connects to the sensors and collects and stores information, 3) a docking station for the monitor and 4) the OnCall® information system to which test data are transmitted for analysis.

According to the manufacturer, results can be analyzed and available within minutes and are transmitted to the physician's office via email, fax or an internet download [http://www.NeuroMetrix®.com/oncall.htm, May 31, 2005]. Personal health information is protected through use of a numeric coding of patient information. Interpretation of test data is performed by a computerized system available online "24/7". As the system is portable and offers rapid turn-around of test results, it is purported to be a useful addition for general practitioners at the "point-of-service".

Marketing information cites benefits of this system to be ease of use and rapid results allowing for confirmation of diagnosis and subsequent treatment decisions. Material available on the NeuroMetrix® website also state the system is "Validated against Gold Standard Diagnostics".

The portable system was originally indicated to evaluate distal motor latency (DML) and F-wave latency in a primary care setting (FDA 510(k), K982359). The original version was designed to assess motor responses in the median and ulnar nerves. As of 2004 design revisions and FDA 510(k) notification allow the device to be used for assessing nerves of the upper and lower extremities as well as sensory responses in the median and ulnar nerves.

Food and Drug Administration Status of NC-stat (NeuroMetrix®)

The FDA determined the original NC-stat to be substantially equivalent to devices marketed prior to May 28, 1976. NeuroMetrix® was permitted to market the device as described in the 510(k) premarket notification provided by the company. Table 1 documents FDA 510(k) information available on NC-stat at the time of this report.

Table 1: FDA 510(k) information on NC-stat.

Date of 510(k) notification	Predicate Device	Biosensors for:	Intended Use from 510(k) Summary
October 1998 original	Neurotron Neurometer and TECA TD-10/TD-20 EMG	Median nerve DML and F-Wave	"intended to measure neuromuscular signals that are useful in diagnosing and evaluating systemic and entrapment neuropathies. The NC-stat is intended to be used as an adjunct to and not a replacement for conventional diagnostic measurements."
June 2000 modified	SE to NC-stat of prior approval	Addition of ulnar DML and F-Wave capability.	"intended to measure neuromuscular signals that are useful in diagnosing and evaluating systemic and entrapment neuropathies. The NC-stat is intended to be used as an adjunct to and not a replacement for conventional diagnostic measurements."
January 2001 modified	SE to original NC-stat and TECA TD-10/TD-20 EMG	Addition of median and ulnar evoked sensory nerve action potential providing DSL (distal sensory latency).	"intended to measure neuromuscular signals that are useful in diagnosing and evaluating systemic and entrapment neuropathies. The NC-stat is intended to be used as an adjunct to and not a replacement for conventional diagnostic measurements."
January 2002 modified	SE to original NC-stat and TECA TD-10/TD-20 EMG	Addition of tibial and peroneal biosensors for lower limb neuropathies.	"intended to measure neuromuscular signals that are useful in diagnosing and evaluating systemic and entrapment neuropathies."
August 2004 modified	SE to prior NC-stat devices and TECA TD-10/TD-20 EMG	Addition of sural nerve biosensor.	"intended to measure neuromuscular signals that are useful in diagnosing and evaluating systemic and entrapment neuropathies."

Objective of this Review

To evaluate the available peer-reviewed literature on the NC-stat nerve conduction testing system following inquires from community physicians and staff within the Department of Labor and Industries. The objective of this review is to assess the evidence of the effectiveness of the device for the intended use.

Search Strategy

Using the terms "NC-stat", "NCStat", "NeuroMetrix® ", PubMed and EMBASE databases were searched for English language, human studies. The NeuroMetrix® website was used as a source of information and to identify appropriate research articles. The search resulted in six peer-reviewed articles for this assessment in May 2005.

Literature Review

Leffler et al., 2000. In this study two groups of 75 patients referred to a hospital electromyography lab for upper extremity or neck symptoms were studied with NC-stat administered by a technician and by conventional neurodiagnostic evaluation supervised and interpreted by neurologists. The objectives were to 1) compare results of NC-stat (DML and F-Wave of **median nerve** measures by a technologist) with conventional neurodiagnostic studies in symptomatic patients referred to an electromyography lab in a general hospital, 2) determine the value of clinical parameters and nerve conduction time provided by NC-stat in diagnosing median neuropathy at the wrist, and 3) evaluate patient acceptance of the NC-stat .

Subjects were enrolled consecutively "from the standpoint of the technician". The initial group went through the study to include NC-stat testing by a technologist followed by clinical and conventional electrodiagnostics performed by a neurologist. The technician was blinded to NC-stat output when performing the studies. The neurologist was blinded to the NC-stat results when performing the clinical exam and electrodiagnostics. Conventional electrodiagnostics included needle electromyography if indicated. All subjects were studied with NC-stat for median neuropathy. Each NC-stat test reported median distal motor latency (DML) and median F-wave latency.

Following the initial study group, modifications were made to processing algorithms in the NC-stat device and a validation group (n=75) was then consecutively enrolled and studied in the same manner as the initial group. Additionally, 95 asymptomatic subjects without diabetes or history of CTS, age 18-75, were tested to determine appropriate physiologic corrections with the final NC-stat device. Subjects in the initial and validation groups completed questionnaires on demographic and medical risk factors and a hand symptom diagram. Each patient received a formal neurodiagnostic evaluation including Phalen's and Tinel's tests.

Analysis included Pearson correlation of NC-stat measures with conventional NCS results as well as the percent of subjects NC-stat was capable of assessing compared to conventional means. Multivariate modeling was performed to evaluate the "utility of supplementing clinical information with" NC-stat measures.

Inclusion and exclusion criteria of 2 study groups:

Inclusion	Exclusion
• Age 18 to 75 • Symptoms for at least 1 month prior to examination and on most days in week prior	• Median nerve injection in previous 30 days

Results:

- Of 150 symptomatic subjects studied the neurologist diagnosed 69 (46%) with isolated MNW, 56 (37%) with normal median nerve function and 25 (17%) either coexisting ulnar neuropathy, cervical radiculopathy, polyneuropathy or contralateral median neuropathy.
- NC-stat detected DML in 97% of hands in the validation group and 92% in the initial group. Correlation between NC-stat with the conventional DML was 0.94 ($P<0.001$) in the validation group and 0.90 ($p<0.001$) in the initial group.
- NC-stat detected F-wave latency in 65% of subjects detected by conventional means in the initial group; 92% in the validation group, with correlations to conventional F-wave measures of 0.84 (retrospective analysis) and 0.86 respectively ($P<0.001$ in each).
- The neurologist diagnosed 117 (47%) of 248 symptomatic hands with MNW. At 90% specificity, the NC-stat had a sensitivity rate of 86% for MNW among those diagnosed with MNW by the neurologist.
- All 150 patients reported that they would be willing to undergo NC-stat again.

Rotman et al., 2004. NC-stat was used to identify predictors and outcome of recovery in subjects with carpal tunnel syndrome (CTS) treated by endoscopic carpal tunnel release surgery.

Subjects without prior hand surgery referred to one hand surgeon were recruited. There were 2 overlapping study groups; one consisted of subjects with pre-surgery NC-stat and conventional NCS studies available to establish diagnostic validity by assessing **median nerve DML** for comparison to traditional EMG tests. NC-stat validity was shown by comparing distal motor latencies (DMLs) obtained prior to surgery with reference DMLs obtained by referral to an electromyography lab (conventional NCS). The second group included subjects with NC-stat DML values available prior to surgery and from at least one test post surgery.

Results

- Forty-eight subjects were enrolled and 46 subjects (88 hands) had referral lab NCS results by conventional electromyography. Median number of days between referral lab results and NC-stat studies was 28.3 and 98% (45/46) subjects had conventional (referral lab) testing before NC-stat studies.
- Pearson correlation coefficient between the two DML measures was 0.94 ($P<0.0001$).
- NC-stat sensitivity was 89% (62 hands of 70 meeting standardized CTS definition) at predetermined specificity of 0.95.

Wells et al., 2002. Case-control study in which NC-stat was used to assess DML and F-wave latencies in **tibial and peroneal nerves** bilaterally in subjects with MRI confirmed L5-S1 nerve root compression (n=35) and a control group (n=35) of asymptomatic individuals with no history of radiculopathy. The objective was to evaluate the diagnostic efficacy of a composite nerve conduction measurement for detection of lumbosacral nerve root compression.

Posterior tibial and deep peroneal nerves were studied bilaterally in all subjects using NC-stat device, consisting of DMLs and F-wave latencies that assess nerve root pathophysiology.

A statistical model was used to define a composite nerve conduction measurement from NC-stat acquired F-wave and DMLs using status in control or compression group (confirmed by MRI) and clinical factors, as the dependent variable.

Results

- NC-stat results were acquired in 100% of control limbs (35 subjects) and 76% of compression group limbs (25 subjects of 33 tested, 2 apparent dropouts). Reasons for incomplete results in compression group included unrecordable responses (4), technical difficulties (2), inability to tolerate stimuli (2). Dropouts not explained.
- Five F-wave latency parameters were predictive of nerve root compression.
- The composite constructed of the 5 predictive parameters yielded a receiver operating characteristic curve of 0.91.
- In retrospective analysis of subjects the composite of parameters assessed with NC-stat resulted in a diagnostic specificity and sensitivity of 84% and 83% respectively.

Vinik et al., 2004. Case-series, seventeen diabetic subjects studied with NC-stat and conventional NCS performed by a neurologist to evaluate the robustness and diagnostic validity of NC-stat for upper extremity nerve abnormalities in subjects with diabetes. **Median and ulnar DML and F-waves** obtained by both methods. Acquisition of NC-stat and conventional NCS measurements was alternated sequentially.

Data were analyzed per hand. Validity of NC-stat was assessed by 1) Pearson correlation between DML as measured by NC-stat and reference method and 2)NC-stat results were compared to a historical control population and defined as having diabetic peripheral neuropathy (DPN) if at least 2 NCS parameters were equal to or greater than the 99th percentile in the control population.

Results

Table 1:DML and F-wave results acquired in study subjects. NC-stat did not return ulnar nerve DML and F-waves results in one subject, and ulnar F-wave in a second subject.

Parameter Median nerve N=17	NeuroMax EMG Mean ms (SD)	NC-stat Mean ms (SD)	Paired t-test	Pearson Correlation
DML N=17	4.6 (1.12)	3.97 (0.76)	<0.001	0.96 (p<0.001)
F-wave N=17	31.1 (2.90)	31.0 (2.8)	NS	0.89 (p<0.001)
Ulnar nerve				
DML N=16	3.10 (0.35)	2.87 (0.38)	<0.05	0.70 (p<0.001)
F-wave N=15	31.1 (2.7)	31.0 (3.0)	NS	0.78 (p<0.001)

Table 2: Comparison of NC-stat results in subjects with diabetes compared to controls.

Parameter	Diabetes	Control		
Median nerve N=17	Mean ms (SD)	Mean ms (SD) abnormality threshold	Paired t-test	Abnormality rate
DML N=17	3.9 (0.76)	3.38 (0.34) 4.17	<0.05	17.7%
F-wave N=17	30.3 (2.8)	27.6 (1.7) 31.6	<0.005	23.5%
Ulnar nerve				
DML N=16	2.82 (0.36)	2.57 (0.24) 3.13	<0.05	25.0%
F-wave N=15	30.0 (3.2)	28.1 (1.7) 32.1	<0.05	26.7%

Reported abnormality rate using normative data by – median DML 17.7%, F-wave 23.5% - ulnar DML 25.0%, F-wave 26.7%. Twenty-five percent of subjects met the case definition for DPN; 50% for median neuropathy of the wrist, defined by median DML greater than 1ms compared to ulnar DML.

Guyette et al., 2004. Fifty-two subjects with complete data from prospective database of 400 subjects between the ages of 20 and 90 who were scheduled for carpal tunnel release were studied. Exclusion criteria were previous CTS surgery, surgery not performed by a Curtis National Hand Center surgeon, current pregnancy or renal dialysis or history of acute peripheral neuropathy from lead exposure. Pre- and post-operative data were examined to identify pre-operative factors determining clinical, functional and symptomatic outcomes. Data were collected through clinical exams, patient questionnaires and electrophysiologic testing with NC-stat (DML and F-wave).

Data analysis included pre- and post-surgery comparison of the presence or absence or Tinel's or Phalen's signs were assessed, grip strength, DML and F-wave changes and symptom severity and functional scores. Also assessed were the time course of symptom severity and functional changes based on open or

endoscopic surgery, age (below or above 60), symptom duration prior to surgery, Workers' Compensation status and symptom severity and functional status prior to surgery.

Results

Baseline characteristics not reported.

NC-stat F-wave latency did not decrease significantly at 6 months, but did at 12 months. DML improved significantly at 6 months and did not change from 6 to 12 months.

Conclusions

Electrophysiologic studies had variable post-operative course. Recognition of differential electrophysiologic changes after surgery will aid in interpretation of postoperative studies.

Study limitations include sample size (13% of 400 subjects in database with complete data) and that subjects were studied at only one site and may not be representative of the population undergoing CTS surgery.

Fisher MA, 2004. Retrospective comparison of NC-stat acquired F-waves recorded from peroneal nerve to evaluate the accuracy and reliability of an automated analysis method. Eighty F-wave sets of data from 2 previously reported studies were used. Comparison of a neurologist's (study author) manual analysis of F-waves acquired by NC-stat were compared with an automatic, computerized analysis of the same data. Exclusion criteria were F-wave sets with obvious A-waves.

Results

Fifty-five subjects were included in analysis, 40 female. Mean age was 57 (25-80), 33% evaluated for sciatica, 25% for diabetic peripheral neuropathy, 24% for leg pain, 18% for a "variety of other reasons".

There was high correlation between the automatic analysis and the manual analysis (100% yield and correlation coefficient of 0.996 for median F-wave measures).

Conclusions

The high yield rate and correlation to manual analysis by an experienced clinical neurologist indicates that a clinically useful automated method should be feasible.

Professional Associations

American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM): No formal policy or assessment of NC-stat. Excerpts from the AANEM "Guidelines for Ethical Behavior Relating to Clinical Practice Issues in Electrodiagnostic Medicine" state:

> From Section 2.4. Professional Fees:
> The consultant should bill for and receive compensation for only those services actually rendered or supervised.
>
> From Section 2.5. Appropriate Electrodiagnostic Services:
> Whenever possible, the NCSs and EMG examination on the same patient should be performed on the same day, by the same EDX consultant, for continuity and consistency.

Other Insurers

Aetna's Clinical Policy Bulletin 0502, Nerve Conduction Velocity testing, describes non-coverage of F-wave measures for carpal tunnel syndrome as this is deemed not medically necessary for CTS diagnosis. Non-coverage of NCS performed using hand-held devices is included in this policy as these devices do not provide waveform analysis. No specific mention is made of NC-stat in Aetna's policy (Aetna 2005).

Wellmark Blue Cross Blue Shield (Iowa) considers use of portable hand-held nerve conduction devices, including NC-stat , as part of the Evaluation and Management or Consultation visit (Wellmark, BlueInk Dec 2004).

Oregon Workers' Compensation does cover NC-stat, separate from evaluation and management code. Oregon Workers' Comp., July 26, 2001, available at:
www.cbs.state.or.us/external/wcd/policy/issues/policyissues.html.

Health Plan of Nevada does not cover nerve conduction studies performed with NC-stat , portable hand-held devices incapable of waveform analysis, studies for screening of polyneuropathy of diabetes or end-stage renal disease or nerve conduction studies for the sole purpose of monitoring disease intensity or treatment effectiveness for polyneuropathy of diabetes or end-stage renal disease. Health Plan of Nevada's policy also states "NCV studies should only be performed and interpreted by a neurologist and/or physiatrist". (Health Plan of Nevada/Sierra Health and Life Insurance Company, 11/18/2004).

Payment Issues

Codes

The following codes may be applicable to testing performed with NC-stat

CPT® Codes*	Description		CPT Modifier	
		Global	-26	-TC
95900		$90.88	$32.38	$57.98
95903		$96.63	$46.48	$50.14
95904		$77.30	$26.64	$50.66

* Fees effective 7/1/2005. Fee schedule is updated annually.

CONCLUSIONS

The NeuroMetrix® NC-stat nerve conduction system is a device approved for marketing by the FDA for assessment of nerve function (median, ulnar, tibeal, peroneal, sural). The intended use was originally cited as an adjunct and not a replacement for traditional nerve conduction testing (the gold standard). Careful review of published scientific literature does not demonstrate that this system is equivalent to the current gold standard for assessing nerve function in a workers' compensation population. Furthermore, the studies reviewed each have methodological issues which must be considered when interpreting the reported results.

Well designed prospective comparison of the NC-stat system, tested by general practitioners to whom the system is marketed for use, are required to adequately assess the effectiveness in a general practice setting.

The effectiveness of the NC-stat nerve conduction system is not demonstrated in peer-reviewed scientific literature. NC-stat is therefore considered experimental and investigational.

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