EARLY IDENTIFICATION AND FOLLOW-UP OF PERIPHERAL AUTONOMIC NEUROPATHIES

- Establish diagnosis
- Control effectiveness of treatment
- Provide quantitative data to adapt patient care and lifestyle
How does it work?

The degeneration of small nerve fibers reduces sweat gland innervation and alters sudomotor function [12]. Sudoscan measures the concentration of chloride ions produced by sweat gland activity.

A low-voltage current (<4V) is applied to the hands and feet through stainless steel sensor electrodes. The applied tension extracts chloride ions from the sweat glands which are densely concentrated on the palms and soles. Since the stratum corneum acts as an isolator, the ions can only pass via the sweat ducts. This ensures that the findings correspond solely to sweat gland function. The chloride ions create a detectable electrochemical reaction with the sensor plates which is measured.

What is measured

SUDOSCAN records the Electrochemical Skin Conductances (ESC) of the hands and feet generated from the current associated with the applied voltage. Loss of sweat glands or loss of their innervations results in reduced ESC [16].

Why test sweat gland function?

Sweat glands are innervated by small sympathetic C-fibers. Sudomotor (sweat) dysfunction can be one of the earliest detectable neuropathologic abnormalities in distal small fiber neuropathies. Quantitative assessment of sweat response has been proposed as an index of the severity of autonomic failure as well as an early indicator for regeneration of small fibers [1,2,3]. Diabetes has been shown to be the most common identifiable cause of small fiber neuropathy. The American Diabetes Association (ADA) has identified sudomotor (sweat) dysfunction as one of the major clinical manifestations of diabetic autonomic neuropathy. Furthermore, the assessment of autonomic dysfunction may identify patients at high risk for cardiac autonomic neuropathy, which carries a very high rate of morbidity and mortality [4].

Diabetes has been shown to be the most common identifiable cause of small fiber neuropathy. The American Diabetes Association (ADA) has identified sudomotor (sweat) dysfunction as one of the major clinical manifestations of diabetic autonomic neuropathy. Furthermore, the assessment of autonomic dysfunction may identify patients at high risk for cardiac autonomic neuropathy, which carries a very high rate of morbidity and mortality [4].

What are the alternatives?

The use of skin biopsy to measure Intraepidermal Nerve Fiber Density (IENFD) or Sweat Gland Nerve Fiber Density (SGNFD) is an accepted surrogate measure of small fiber neuropathy. While skin biopsy is well accepted by the medical community, it has certain limitations as: invasiveness, risk of infection, bleeding, and a limited number of labs that can process the sample [7]. The Quantitative Sudomotor Axon Reflex Testing (QSART) measures sweat response under controlled humidity and temperature conditions. It requires fairly expensive equipment and is available in few centers.

Figure 1: The peripheral nervous system is made of large and small fibers. The small, un-myelinated C-fibers are in charge of autonomic functions such as sweating [5].

Figure 2: Small fiber autonomic nerves regenerate more quickly than the large fiber nerves upon capsaicin application [adapted from 6].

SUDOSCAN MEASURES THE CONCENTRATION OF CHLORIDE IONS PRODUCED BY SWEAT GLAND ACTIVITY

How does it work?

The degeneration of small nerve fibers reduces sweat gland innervation and alters sudomotor function [12]. Sudoscan measures the concentration of chloride ions produced by sweat gland activity.

A low-voltage current (<4V) is applied to the hands and feet through stainless steel sensor electrodes. The applied tension extracts chloride ions from the sweat glands which are densely concentrated on the palms and soles. Since the stratum corneum acts as an isolator, the ions can only pass via the sweat ducts. This ensures that the findings correspond solely to sweat gland function. The chloride ions create a detectable electrochemical reaction with the sensor plates which is measured.

What is measured

SUDOSCAN records the Electrochemical Skin Conductances (ESC) of the hands and feet generated from the current associated with the applied voltage. Loss of sweat glands or loss of their innervations results in reduced ESC [16].

Subject with normal sweat function

Subject with abnormal sweat function

Figure 10: ESC measurement of a subject with normal (left) and abnormal (right) sweat function.
THE SOLUTION

SUDOSCAN PROVIDES AN ACCURATE EVALUATION OF SUDOMOTOR FUNCTION BY MEASURING THE ABILITY OF SWEAT GLANDS TO RELEASE CHLORIDE IONS IN RESPONSE TO AN ELECTROCHEMICAL ACTIVATION ON THE PALM OF THE HANDS AND SOLES OF THE FEET, AREAS WITH THE HIGHEST SWEAT GLAND DENSITY [7].

Clear results

1. Simple
   - Ergonomic touch screen operation and detailed graphics allow for visual representation of the results. An immediate quality check ensures reliable results. Results are easy to interpret: Green suggests no neuropathy, Yellow a moderate neuropathy and Orange a more severe neuropathy.

2. Quantitative
   - Actual numerical values of the Electrochemical Skin Conductance (ESC) on the hands and feet are displayed. The level of ESC indicates the severity of the neuropathy. This measure can be compared with later test results to assess the patient’s response to treatment or other prescribed interventions.

3. Symmetry
   - Measure of symmetry between right and left sides help identify the type of peripheral neuropathy.

Fast testing

SUDOSCAN ENABLES FAST AND EASY QUANTIFICATION OF SUDOMOTOR FUNCTION.

SUDOSCAN at a glance

Fast
- No patient preparation
- Results in 3 minutes
- Automatic reports

Simple
- Non-invasive
- No fasting necessary
- Easy training
- Touch screen operation

Accurate
- Quantitative results
- Proven clinical results
- Operator independent
- Four hands and feet electrodes
- Automatic quality check

Figure 3: Conductance and asymmetry of hand and feet.

Figure 4: Easy follow-up of the evolution of the neuropathy.
Diabetes

Diagnosing diabetic neuropathy

Diabetes is the primary identifiable cause of small fiber neuropathy. Early identification of small fiber neuropathy, which may be asymptomatic in up to 50% of diabetic patients, can reduce or delay diabetes complications by timely preventative treatment [4]. The sensitivity and specificity of SUDOSCAN scores to detect diabetic neuropathy were 78 and 92% when compared to NIS-LL [8].

![Image of Foot ESC (µS) comparison](image)

**Figure 5: Mean Neuropathy Impairment Score within the Lower Limbs (NIS-LL) in diabetes patients with normal vs abnormal feet Electrochemical Skin Conductance (ESC).**

Evaluate cardiac autonomic neuropathy

Cardiovascular Autonomic Neuropathy (CAN) is a common but often overlooked complication of diabetes. Studies have shown that SUDOSCAN may be used for early screening of CAN in everyday clinical practice before resorting to the more sophisticated and specific, but ultimately more time-consuming, Ewing tests [9].

![Image of Fig 6: Graphic representation of the diagnostic performance](image)

**Figure 6: Graphic representation of the diagnostic performance of the SUDOSCAN test score, E1 ratio, 30-15 ratio and Blood Pressure (BP) change on standing by Receiver Operating Curve (ROC) analysis, using the low-frequency, power component during moderate activity at a threshold of 90 ms² (first quartile).**

Follow-up

Diabetes treatment

In type 2 diabetes, sweat function improves with insulin therapy [10]. Improvement is reflected by increasing ESC values.

![Image of Fig 7: Changes in feet Electrochemical Skin Conductances (ESC) during one-year follow-up in patients with type 2 diabetes receiving insulin or not and patients with type 1 diabetes](image)

**Figure 7: Changes in feet Electrochemical Skin Conductances (ESC) during one-year follow-up in patients with type 2 diabetes receiving insulin or not and patients with type 1 diabetes.**

Lifestyle interventions

SUDOSCAN and VO2-max have parallel evolution in response to lifestyle changes.

![Image of Fig 8: Improvements of VO2-max and ESC in individuals undergoing a 12 months lifestyle intervention program](image)

**Figure 8: Improvements of VO2-max and ESC in individuals undergoing a 12 months lifestyle intervention program [11].**

Neurology

Positive comparison to IENFD

SUDOSCAN has demonstrated a diagnostic performance similar to Intra Epidermal Nerve Fiber Density (IENFD) [11].

Amyloidosis

Included in the TTR-FAP Guidelines

SUDOSCAN has been included in the testing and management of individual at risk guidelines written by the ATTRNeuNet Network [12].

SUDOSCAN is a sensitive test to assess early autonomic dysfunction in TTR-FAP subjects and can easily be introduced as a routine assessment in this population [18].
References

[12] Smith et al. SUDOSCAN as a Diagnostic Tool for Peripheral Neuropathy Peripheral Nerve Society poster, Saint-Malo, June 2013