SUDOSCAN2

EARLY IDENTIFICATION AND FOLLOW-UP OF PERIPHERAL AUTONOMIC NEUROPATHIES

- Establish diagnosis
- Control effectiveness of treatment
- Provide quantitative data to adapt patient care and lifestyle

3 MINUTES

SIMPLE

QUANTITATIVE

NON-INVASIVE

OBJECTIVE

impetomedical

SWEAT GLAND FUNCTION – A RELIABLE INDICATOR FOR PERIPHERAL AUTONOMIC NEUROPATHY

Why test sweat gland function?

Sweat glands are innervated by small sympathetic C-fibers. Sudomotor (sweat) dysfunction can be one of the earliest detectable neurophysiologic 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].

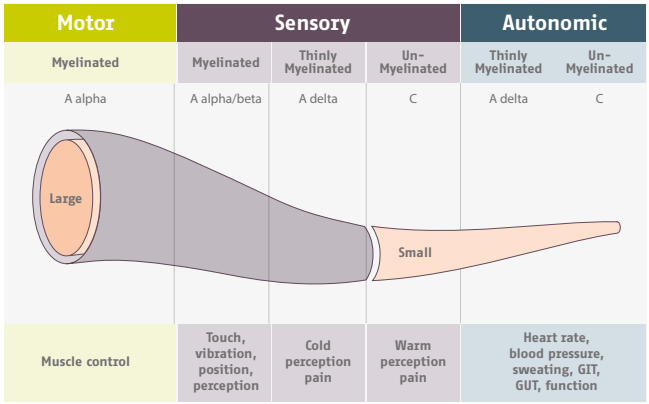


Figure 1: The peripheral nervous system is made of large and small fibers. The small, un-myelinated C-fibres are in charge of autonomic functions such as sweating [5].

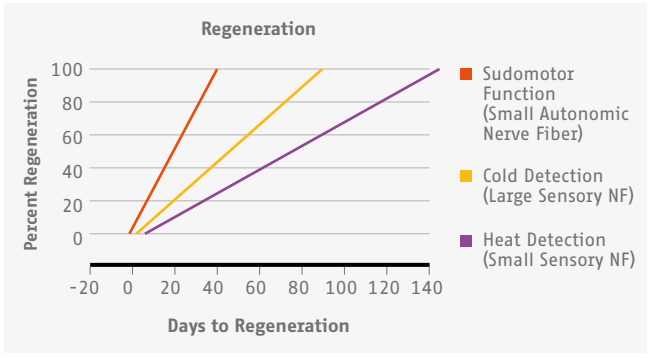


Figure 2: Small fiber autonomic nerves regenerate more quickly than the large fiber nerves upon capsaicin application [adapted from 6].

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 requirs fairly expensive equipment and is available in few centers.

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

How does it work ?

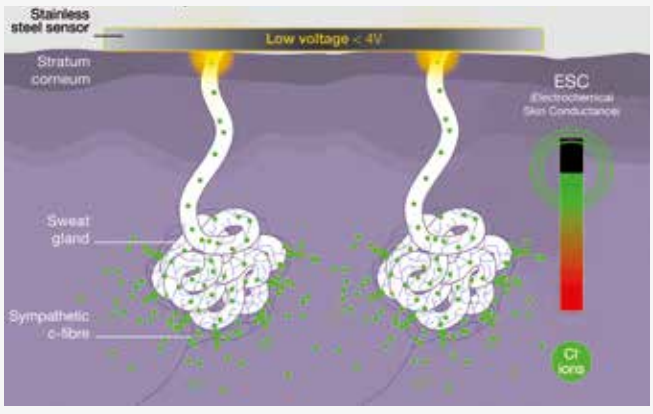
The degeneration of small nerve fibers reduces sweat gland innervation and alters sudomotor function [12]. Sudoscan measures the concentration of chloride ions produced by sweat gland activity.

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

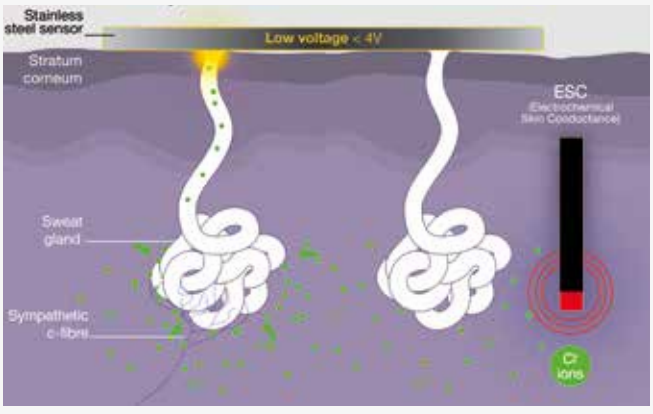


Figure 10: ESC measurement of a subject with normal (left) and abnormal (right) sweat function.

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

Fast testing

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.

Figure 3: Conductance and asymmetry of hand and feet.

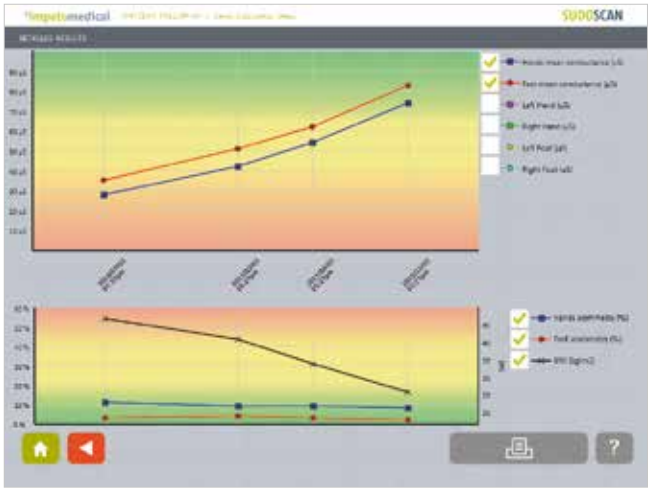


Figure 4: Easy follow-up of the evolution of the neuropathy.

SUDOSCAN FACILITATES PREVENTION, EVALUATION AND FOLLOW-UP OF DIABETES RELATED PERIPHERAL NEUROPATHY

A broad range of diseases

Sudomotor dysfunction is a common finding, and one of the earliest detectable abnormalities in a number of peripheral and autonomic neuropathies.

SUDOSCAN has been tested for small fiber nerve neuropathies in several diseases and compared to guidelines reference tests:

- **Diabetes**
- **Parkinson**
- **Chemotherapy induced polyneuropathy**
- **Familial amyloid polyneuropathy**
- **Fabry disease**

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 diabetes 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].

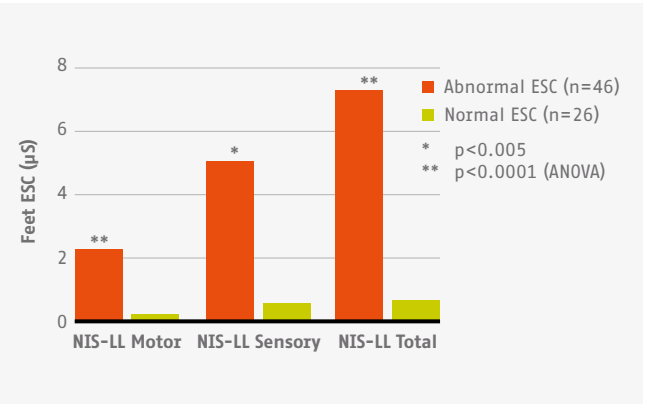


Figure 5: Mean Neuropathy Impairment Score within the Lower Limbs (NIS-LL) in diabetes patients with normal vs abnormal feet Electrochemical Skin Conductance (ESC).

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].

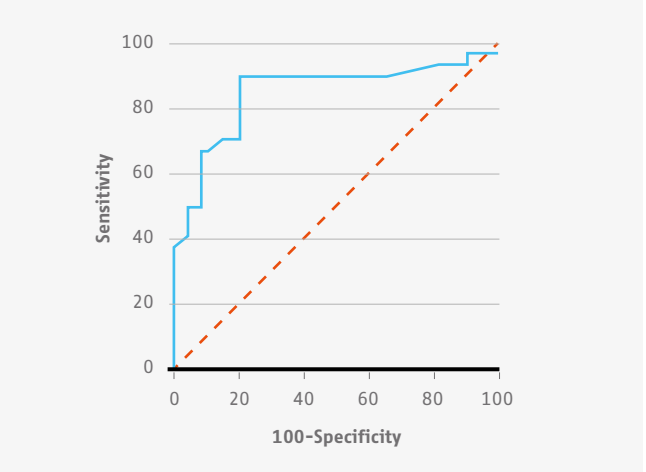


Figure 6: Graphic representation of the diagnostic performance of the SUDOSCAN 2 risk-score, E:I ratio,30:15 ratio and Blood Pressure (BP) change on standing by Receiver Operating Curve (ROC) analysis, using the low-frequency, power component during moderate activity at a threshold of 90 ms² (first quartile).

Follow-up

Diabetes treatment

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

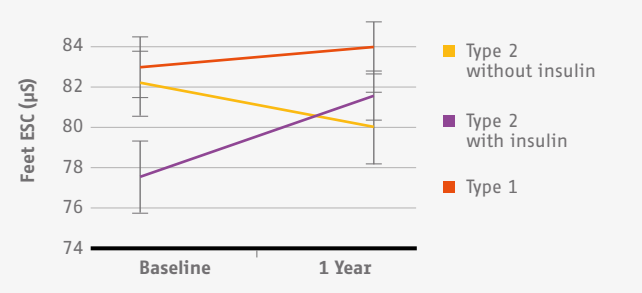


Figure 7: Changes in feet Electrochemical Skin Conductances (ESC) during one-year follow-up in patients with type 2 diabetes receiving insulin or not and patients with type 1 diabetes.

Lifestyle interventions

SUDOSCAN and VO_2-max have parallel evolution in response to lifestyle changes.

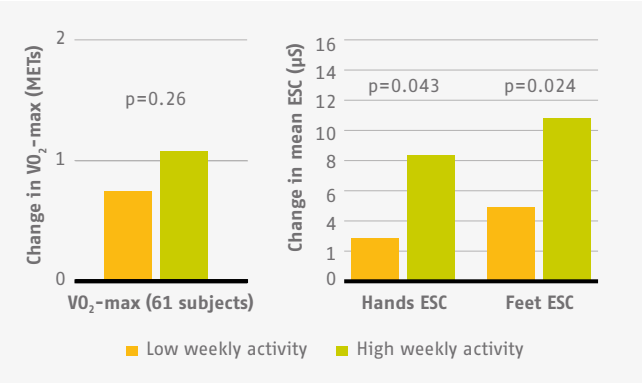


Figure 8: Improvements of VO_2-max and ESC in individuals undergoing a 12 months lifestyle intervention program [11].

Neurology

Positive comparison to IENFD

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

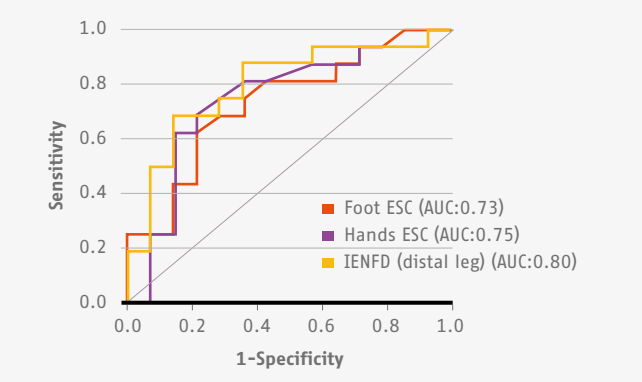


Figure 9: ROC curves for foot and hands ESC and IENFD at the distal leg (using Utah Early Neuropathy Score (UENS) as gold standard).

Oncology

Chemotherapy Induced Polyneuopathy (CIPN)

SUDOSCAN has results parallel to Total Neuropathy Score clinical version (TNSc). SUDOSCAN can easily be performed in the Oncology department, before and after treatment for an optimal follow-up of patients to detect Chemotherapy Induced Polyneuropathy (CIPN) [11].

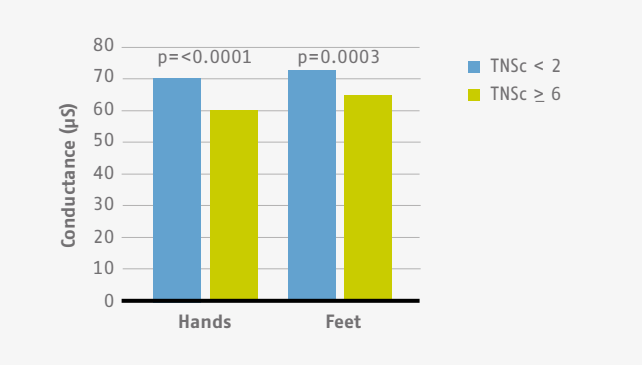


Figure 10: SUDOSCAN scores correlates to TNSc extreme values [11].

Comparison to other technologies

Detection of Small Fiber Polyneuropathy (SFPN)

SUDOSCAN demonstrates to be an easy, rapid and reliable method compared to other tests to detect Small Fiber Polyneuropathy [15].

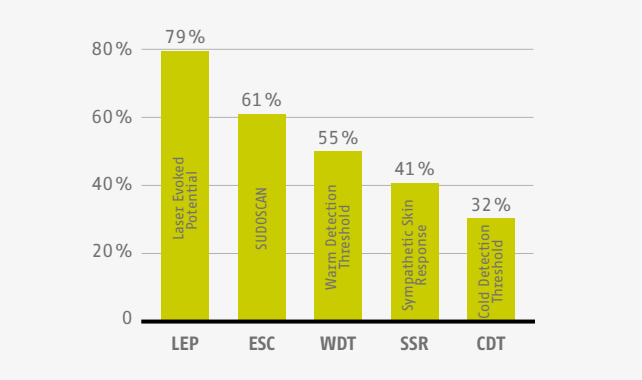


Figure 11: Diagnostic performance of Laser Evoked Potential (LEP), SUDOSCAN, Warm Detection Threshold, Sympathetic Skin Response (SSR) and Cold Detection Threshold for detecting Small Fiber Polyneuropathy (SFPN).

Amyloidosis

Included in the TTR-FAP Guidelines

SUDOSCAN has been included in the testing and management of individual at risk guidelines written by the ATTReuNet Network [17].

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].

Design: bb&b – Photos: Gael Kerbaol - v16-05

About Impeto Medical

Impeto Medical is a privately owned medical device company formed in June 2005. Its corporate headquarters are located in Paris, France. Two subsidaries have been created : Beijing Impeto Medical in China and Impeto Medical Inc. in San Diego, U.S.

Impeto Medical has developed a technology that assesses sudomotor function through sweat gland activity. This technology is protected by over 50 French and localized patents. With devices sold throughout the world and many publications in peer-reviewed journals, Impeto Medical continues to grow.

Class IIa according to the European Medical Device regulation - SGS United Kingdom Ltd, Notified Body 0120

Please read the user manual instructions carefully. Please, contact our office for more information.

impetomedical

Impeto Medical
17, rue Campagne Première
75014 Paris - France
Tel: +33 1 43 20 16 40
Fax: +33 1 43 35 18 33
www.impeto-medical.com

References

[1] **Illigens et al.** Sweat testing to evaluate autonomic function. Clin Auton. Res. 2009:19;79-87

[2] **Low PA.** Evaluation of sudomotor function. Clinical Neurophysiology. 2004:115;1506-1513

[3] **Gibbons et al.** Capsaicin induces degeneration of cutaneous autonomic nerve fibers. Ann Neurol. 2010;68:888-898

[4] **Tesfaye et al.** Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. Diabetes Care. 2010:33;2285-2293

[5] **Vinik et al.** Nature Clinical Practice Endocrinology & Metabolism. 2006;2:269-281

[6] **Joint Task Force of the EFNS and the PNS.** European Federation of Neurological Societies/Peripheral Nerve Society Guideline on the use of skin biopsy in the diagnosis of small fiber neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society. J Peripher Nerv Syst 2010;15:79–92

[7] **Hubert et al.** Abnormal electrochemical skin conductance in cystic fibrosis. Journal of cystic fibrosis. 2010;10(1):15-20

[8] **Vinik et al.** SUDOSCAN, a non-invasive tool for detecting diabetic small fiber neuropathy and autonomic dysfunction. Diabetes technology and therapeutics. 2013;15(11)

[9] **Selvarajah et al.** SUDOSCAN: A Simple, Rapid, and Objective Method with Potential for Screening for Diabetic Peripheral Neuropathy. PLoS One. 2015 Oct 12;10(10):e0138224

[10] **Schwarz et al.** Assessment of Small Fiber Neuropathy through a Quick, Simple and Non Invasive Method in a German Diabetes Outpatient Clinic. Experimental and Clinical Endocrinology & Diabetes. 2013;121(2):80-83

[11] **Raisanen et al.** Sudomotor Function as a tool for Cardiorespiratory Fitness Level Education: Comparison with Maximal Exercice Capacity. Int J. Environ. Res. Public Health. 2014;11:5839-5848

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

[13] **Selvarajah et al.** SUDOSCAN: A simple, rapid and objective method with potential for screening Diabetic Peripheral Neuropathy. PLoS One. 2015 Oct 12; 10(10):e0138224

[14] **Saad et al.** Quick, non-invasive and quantitative assessment of small fiber neuropathy in patients receiving chemotherapy. J Neurooncol. 2015. DOI 10.1007/s11060-015-2049-x

[15] **Lefaucheur et al.** Diagnosis of small fiber neuropathy: a comparative study of five neurophysiological tests. Neurophysiol Clin. 2015 Dec;45(6):445-55

[16] **Ayoub et al.** Electrochemical Characterization of Nickel Electrodes in Phosphate and Carbonate Electrolytes in View of Assessing a Medical Diagnostic Device for the Detection of Early Diabetes. Electroanalysis. 2010;21:2483-2490

[17] **Obici et Al.** Recommendations for presymptomatic genetic testing and management of individuals at risk for hereditary TransThyRetin Amyloidosis. CO Neurology. February 2016; 29:1

[18] **Castro J, Miranda B, Castro I, de Carvalho M, Conceição I.** The diagnostic accuracy of Sudoscan in Transthyretin Familial Amyloid Polyneuropathy. Clin Neurophys. 2016 Feb 27

CE
0120