A Device to Quantify Sweat in Single Sweat Glands to Diagnose Neuropathy

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1 Background

We devised an objective "Sensitive Sweat Test" (SST) that detects and quantifies early changes in the function of sudomotor nerves that activate sweat glands (SGs). The SST is designed to diagnose peripheral neuropathy early, when the probability for reversal is greatest.

Chemotherapy induced and diabetic neuropathy are very common causes of neuropathy in the USA. Both result in peripheral numbness, pain, decreased sweating, abnormal circulation, and eventual weakness. Early recognition can provide a better opportunity to treat and halt neuropathy than discovery after the onset of nerve degeneration. We contend that early diagnosis can be achieved by sensitive monitoring of sweating. Unfortunately, the changes that first signal impending sweat deficiency escape detection by conventional clinical examination and current tests [1,2]. We previously reported a Dynamic Sweat Test (DST) that greatly improved sensitivity over current methods [3]. The newer SST is designed to quantify the reduced water produced by partial denervation of individual SGs. Partial denervation is possible because each SG receives multiple unmyelinated sudomotor nerve fibers [4]. The SST detects the sweat deficiency by continuous imaging and measuring of secretion rate, volume, number and distribution produced over the course of about a minute by each of >200 activated SGs.

We contracted with several MN small business concerns (SBCs) to construct the SST miniature camera device (Fig. 2) to characterize sweating of control subjects and of patients with chronic and acute peripheral neuropathy.

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2 Methods

Skin sites on the medial calf and foot dorsum, each measuring 2 cm^2 were stimulated to sweat maximally by iontophoresis of 1% pilocarpine (2 ma, 5 min; Fig 1).

Transparent tape thinly coated with starch was attached over the lens of the SST miniature camera. The skin test sites were prepped with a 1% iodine solution. The skin was wiped dry and immediately the camera was pressed against the skin, activating a switch to begin image collection and storage. As sweat water exited from each sweat pore it contacted iodine and starch and formed a tiny dark spot. The tape prevented formation of a drop. Instead, sweat was forced to flow centrifugally to form a flat expanding dark spot. The SST device imaged spots from >200 SGs at 1 frame/sec (area of 2 cm^2) for 60 to 90 seconds, until adjacent spots coalesced. The process was performed twice. Image analysis was done in the Mathworks Software, MATLAB version R2012a. Each individual sweat spot was identified and followed from frame to frame (Fig. 3). The software calculated the rate of expansion and area for each spot. Data was transferred to a database for final calculations and conversions as predetermined by appropriate camera calibrations, to a rate and volume of sweat for each SG in nanoliters/minute, total volume, total number of SGs

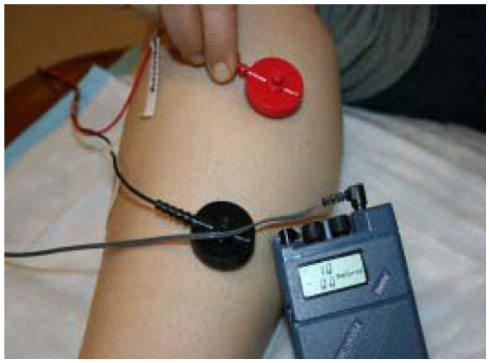

Fig. 1 Iontophoresis

Fig. 2 SST camera

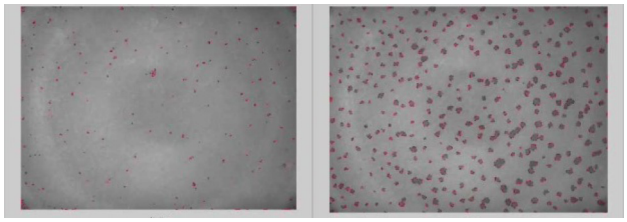

Fig. 3 MATLAB tracks individual sweat spots

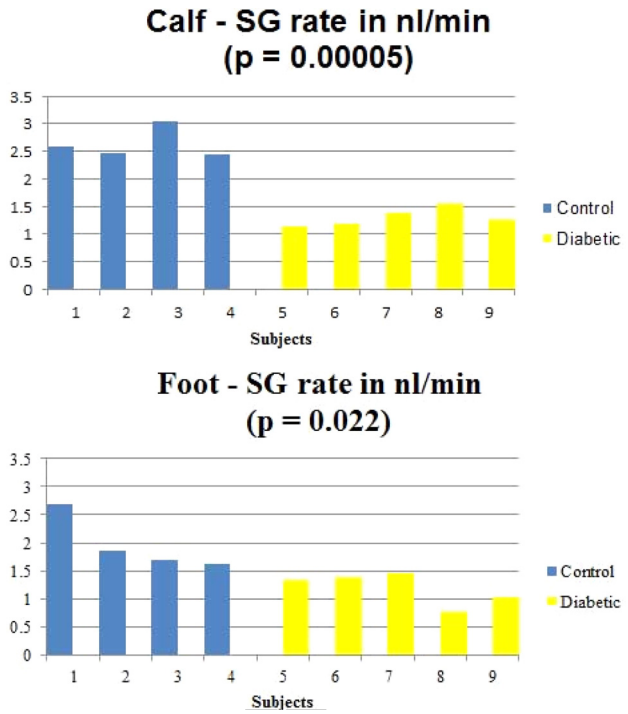

Fig. 4 Sweat rate reduced in diabetic subjects

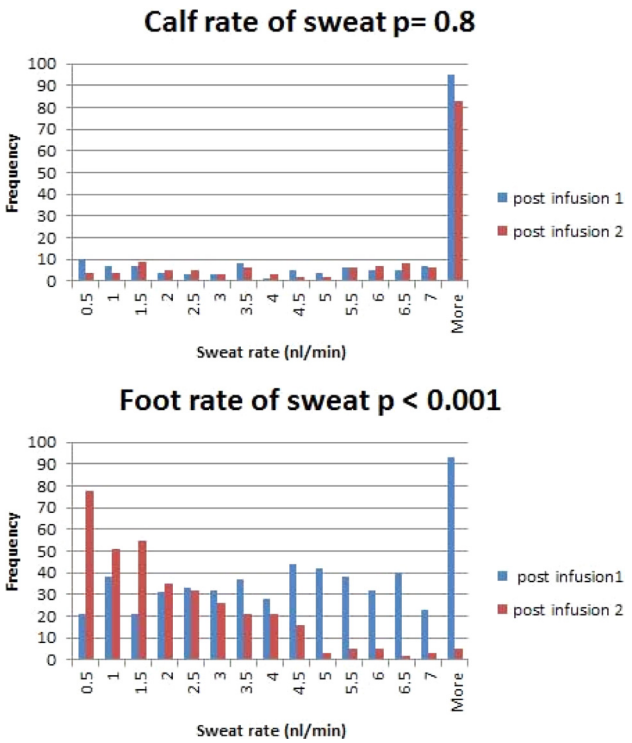

Fig. 5 Foot sweat rate reduced following second infusion

for the area imaged, later converted to density per cm^2, and distribution of active SGs.

3 Results

We used the hand held SST prototype device (Fig. 2) to study patients with chronic chemotherapy and diabetic neuropathy. This showed feasibility of the method to quantify sweating.

The results demonstrated that the secretion rate and volume of each active sweat gland could be measured. There was a significant change in the rate of sweating for the foot and calf of diabetic subjects (Fig. 4; $p < 0.05$); however only the sweat rate on the foot was affected in post chemotherapy subjects. The active SG density was reduced in all neuropathy subjects.

We are currently testing our first breast cancer patient. After two chemotherapy infusions of taxol and carboplatin we found a marked decline of mean SG function in the foot with no change in the calf (Fig. 5). This finding remained unchanged after the third infusion. Other patients will soon be tested in collaboration with UMN oncologists.

4 Interpretation

This new medical device provides dynamic quantification of the individual rate and volume of sweat secretion by a large number of single SGs and the total water secreted per skin area. The distribution pattern shows the location of all secreting SGs, thereby providing the number of active SGs per area (density). Areas in the distribution pattern that are void of sweat spots indicate the location of inactive, probably denervated SGs. Denervated SGs fail to secrete even if exposed to agonist [4]. These test characteristics give a sensitive, more precise indication of SG function than the single measurement of total water per skin area provided by the quantitative sudomotor axon reflex test (QSART) [5]. The SST can be used as a measure of unmyelinated motor nerve innervation to contribute to the early diagnosis of peripheral autonomic neuropathy.

Preliminary testing of our SST device indicates that it is a fast, accurate, inexpensive method to study the function of SGs. We believe that it has potential to diagnose and stage degrees of beginning neuropathy in the medical clinic, at bedside and eventually the home. The device shows promise of being capable to measure the progression of neuropathy. The possibility exists that in serial studies of the same skin areas it will also record recovery by illustrating the appearance of sweat droplets secreted by reinnervated SGs [6].

We began to gather additional control values from healthy persons and from patients with chemotherapy induced peripheral neuropathy, diabetic neuropathy and other neuropathies in Minnesota. We will soon distribute devices to collaborators at M.D. Anderson Cancer Hospital (Houston), Massachusetts General Hospital (Boston), National Hospital Queen's square (London) & Salvatore Maugeri Foundation (Italy).

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