Chapter 6

Quantitative Tactile Examination Using Shape Memory Alloy Actuators for the Early Detection of Diabetic Neuropathy

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Additional information is available at the end of the chapter

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Abstract

Diabetic neuropathy (DPN) is asymptomatic in its early phases but can cause serious complications as it progresses. Most DPN tests are cumbersome and produce only qualitative assessments, and simpler approaches that yield quantitative results are needed. Techniques that allow patients to perform examinations themselves would be especially valuable. In this study, we focused on quantifying the decline in tactile sensation associated with DPN and developed a measurement device that used a thin shape memory alloy (SMA) wire as the actuator. An ON/OFF pulse current caused the wire to shrink and expand. This vibration was amplified by a round-headed pin, allowing even DPN patients with reduced tactile sensitivity to detect the stimuli generated when lightly touching the pin with their fingertips. The tactile stimuli were ranked into 30 levels of intensity. A key advantage of the device is that it can be used by patients themselves, returning quantified results within minutes. Although developed for DPN, the method can be applied to the detection of peripheral neuropathy in general.

Keywords: shape memory alloy actuator, neuropathy, tactile application, quantification, quantitative tactile examination, early detection

1. Introduction

In this chapter, we introduce a quantitative tactile examination device using shape memory actuators and discuss previous work by the authors on the use of such a system for the early

detection of diabetic neuropathy (DPN) [1–3]. We consider the range of potential applications and the future potential of this technology.

We have conducted a number of studies on tactile sense-presentation technology that applies micro-vibrations using thin shape memory alloys (SMA) [1–11]. The SMA allows for a compact device that consumes little power and causes no pain to patients.

Tactile-stimulus diagnostic techniques, such as the technique reported in this study, may be possible with other actuators such as small motors [12, 13], piezoelectric actuators [14], or pneumatic actuators [15]. However, each of these technologies requires large electromagnetic devices that require more power than that provided by a portable battery.

Piezoelectric actuators need a driving voltage of the order of several tens of volts, and their inclusion of mechanical parts makes their application in portable devices difficult [14].

Our tactile-stimulus presentation technology that uses a thin SMA avoids the problems of size and power consumption. The present iteration of the device can be driven with a small battery [2, 3, 5–7].

Quantitative diagnosis of DPN at present requires a machine costing at least several million yen and larger than 1 m on a side, such as nerve-conduction studies. Equipment for these tests, in addition to being cumbersome and expensive, requires skilled technicians for its operation.

Some patients refuse a second examination because nerve conduction studies and electromyography studies can be quite painful. Many asymptomatic diabetes patients are left untreated because of the cost, difficulty, and pain caused by the current methods for quantitative diagnosis of the neurological effects of diabetes.

In previous studies [1–3, 5–7], we have developed a range of simple, quantitative, and painless examination methods that use SMA, and the present study summarizes those studies and discusses future prospects.

A wide range of conditions contribute to hypoesthesia and/or peripheral nervous disorders, including the administration of anticancer drugs, DPN, vitamin deficiency, vasculitis, polyneuropathy, depression, alcohol dependence, infection, and uremia. However, the progress of the condition is generally slow, and most sufferers are initially unaware of its presence [16].

Peripheral neuropathy tests can be divided into two main types. The first is qualitative and includes the Achilles tendon reflex/vibration test. The second is nerve conduction studies (NCS), which involve complex and painful invasive examinations but provide quantified diagnoses. Both types require medical expertise and judgment and must be conducted by a healthcare professional. Patients have no access to their test results, making them less likely to seek treatment.

Approximately, half of all patients with diabetes contract asymptomatic neuropathy [17]. As the causes of neuropathy are not limited to diabetes mellitus, it is assumed that there are many more asymptomatic neuropathy sufferers. Currently, patients are unable to perceive the condition themselves, and no simple quantification scale is available. Even patients whose condition is treatable may be unaware of its presence and therefore fail to seek treatment.

A simple method for quantitative detection of the asymptomatic condition is therefore needed. By combining medicine and engineering, we developed a quantitative tactile examination device based on detecting the decline in tactile sensation.

The initial study targeted diabetes patients whose condition was associated with deterioration in sensation. The tactile sensation of diabetic patients was found to be lower than that of normal subjects [1, 2] and that of diabetic patients who were not conscious of the decline to be still lower [3].

2. Tactile sensation and diabetic neuropathy

The sense of touch relies on four main tactile receptors in the skin: the Meissner's corpuscle, Merkel disc, Ruffini ending, and Pacinian corpuscle. As shown in **Figure 1**, Merkel discs are located in the epidermis and are approximately 10 μm in diameter. They are used to sense pressure and texture. Meissner's corpuscles are primarily located immediately below the epidermis and are between 30 and 140 μm in length and 40–60 μm in diameter. They are used to sense stroking and fluttering. Ruffini endings are also located in the dermis, have a length of approximately 0.5–2 mm, and are used for the sense stretching of the skin. Pacini corpuscles are located in the subcutis and are approximately 0.5–2 mm in length and 0.7 mm in diameter. Based on their response speed and size, the receptors are given four labels: fast adapting I and II (FA I and FA II) and slow adapting I and II (SA I and SA II).

The receptors are present at different densities in different regions of the human body. **Figure 2** [13] shows the innervation density in the hand, which is where most human tactile recognition takes place. Receptors are particularly dense in the fingers and especially in the tips. Human fingers are therefore sensitive to a range of stimuli. The response of the receptors is closely related to nervous system activity, and the tips of the fingers are therefore also densely supplied with capillary vessels. When a diabetic condition restricts the blood flow in the capillary

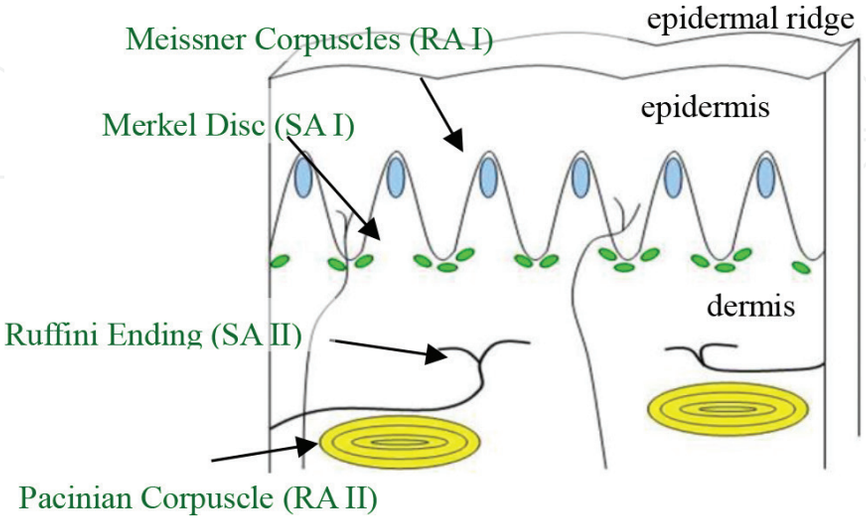

Figure 1. Tactile receptors of the skin [3].

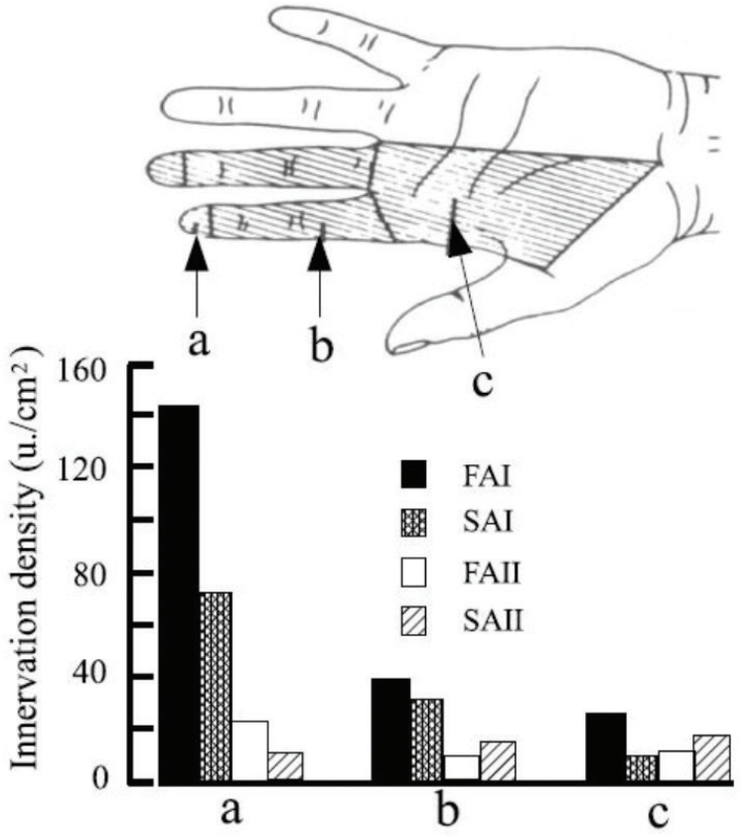

Figure 2. Innervation density of tactile receptors [18].

vessels or destroys them, sensitivity to tactile sensations is restricted. Most diabetes patients, even at an early stage of the disease, have reduced sensitivity to tactile sensations in the fingers and feet. The extent of the decline is a measure of the progress of the condition.

Diabetic neuropathy (DPN) is caused by the degradation of axons in peripheral nerves, which decrease nerve function in slow progression. The rate of degeneration depends on the ability of the patients to control their glycemic index; thus, it varies with each individual. Nerves are distributed throughout the body and vary in function. For that reason, neurological diagnostic methods vary depending on the parts and functions of the nerve distributed, thus making uniform standards difficult to formulate. For example, in the event of dysuria arising from DPN, the patient may consult a urologist. However, a patient who feels discomfort or numbness in the sole of the foot owing to DPN may consult an orthopedist, and both patients may not consult a diabetes specialist until their condition has degraded significantly. DPN presents a variety of symptoms that patients are likely to consult a range of specialists for the same underlying condition. Diagnosis of DPN is so complicated and time-consuming that even many diabetes specialists are not equipped for quantitative studies.

Neuropathy can also be caused by other diseases, but DPN is distinguished by a few symptoms.

DPN presents diffuse neuropathy, with bilateral symmetry. The nerve failure is focused on sensory functions, and DPN tends to progress from peripheral nerves inward.

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While examining patients with multiple neuropathy-causing conditions, the underlying cause of any symptom is very difficult to distinguish, with any diagnostic method; thus, this chapter focuses on tactile anomalies and tactile reduction among the neurological abnormalities that could indicate DPN.

To confirm and diagnose the specific form of neuropathy that a patient has developed, an affected nerve must be biopsied from the patient, but this procedure is generally too invasive for the degree of suffering a patient is experiencing. Instead, clinicians administer a series of tests to collate a program similar to quantitative diagnosis and treatment program.

Our tactile test method stimulates the following four main tactile receptors in the skin: the Meissner's corpuscle, the Merkel disc, the Ruffini ending, and the Pacinian corpuscle. Though it may also stimulate other receptors, this device clearly provides a tactile stimulus that at least stimulates the haptic receptors. Precise diagnostic methods require the application of electric current to a patient's nervous system and measuring response. These tests are painful, while our haptic stimulator causes no pain at all. We have not performed biopsy studies to conclusively demonstrate to diagnoses pathologically confirmed with DPN. But we have shown that the device can quickly, inexpensively, and painlessly assess a patient's tactile response with novel technology in some clinical studies [1–3].

In this study, a tactile device was developed that presented present a range of tactile stimuli to the fingers of a subject and then measured the response from the driving parameters of the tactile actuators.

3. Design of the measurement device

3.1. A compact SMA actuator to generate micro-vibrations

To generate the physical stimuli, an SMA wire was employed. Within the typical operating temperature range, SMA has two phases, each with a different crystal structure and therefore different properties. The first is a high-temperature phase, called the Austenite phase, and the second a low-temperature phase, called the Martensite phase. When the temperature exceeds a critical threshold (70°C), the SMA alternates between the two phases, causing the crystal structure, and therefore the shape of the SMA, to change. SMA has been widely used in actuation and sensing applications and in the aerospace, automotive, and biomedical sectors.

When SMA is formed into a thin wire, its length originally 3 mm at a low-temperature phase will change at a known temperature. In the current study, the SMA wire (Toki Corp., BioMetal, BMF75) was used to create a compact actuator, the characteristics of which are shown in **Figure 3**. When the temperature of an SMA wire passes T1 (68°C), the wire begins to shrink up to 5% lengthwise at the temperature T2, reaching a minimum at T2 (73°C). As the temperature is reduced, the wire gradually returns to its initial length.

As the alloy has an electrical resistance of 0.6 ohms per 1 mm, its length can be controlled by supplying a pulse current. This instantaneously increases the temperature, shrinking the wire.

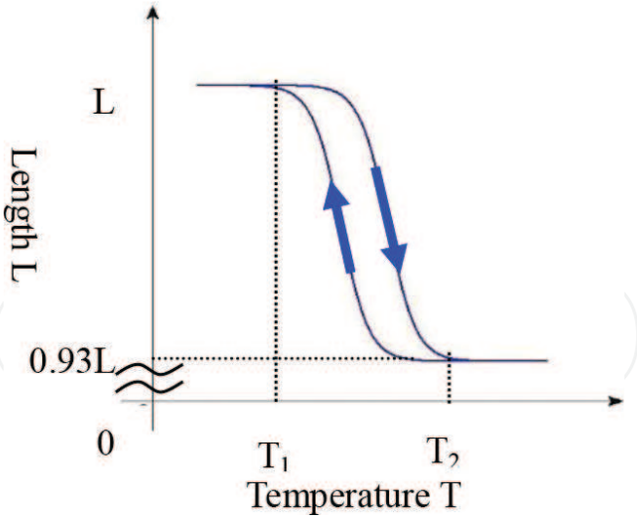

Figure 3. Characteristics of the SMA wire [3].

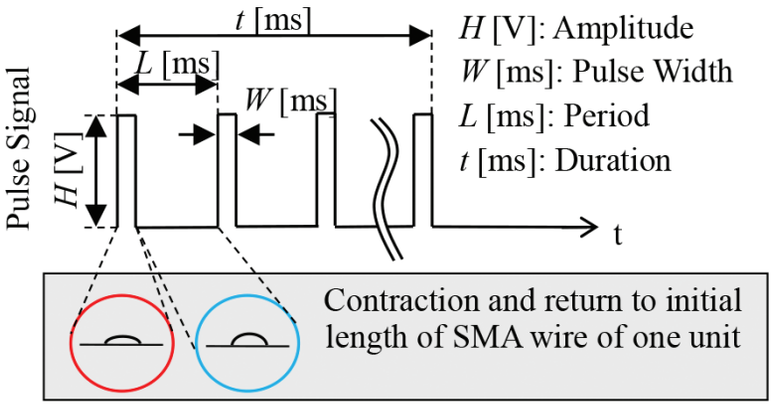

Figure 4. Pulse signal for driving SMA [3].

When the pulse current is halted, the body instantly cools, returning to its initial length. The shrinkage and return are fully synchronized with the ON/OFF pulse current, as shown in **Figure 4**. The magnitude of the vibration created can be precisely controlled by the amplitude of the pulse signal H and the duty ratio W/L. For an efficient operation, the SMA temperature must be maintained within the range T1–T2. In our design, a pulse-width modulated (PWM) rectangular wave signal with an arbitrary frequency, amplitude, and duty ratio is generated by a PC and is then amplified to drive the SMA actuator. The amplifier drives the SMA actuator at frequencies up to 300 Hz. The voltage amplitude is variable and controlled by the current. According to the measurement results of our research so far, the SMA wire shrinks by ~2 μm at the maximum according to the duty ratio of the pulse current. Therefore, according to the duty ratio, the overall length of the SMA wire was observed to be shrinking from 0.1 to 2 μm. The detailed driving pulse signal for each amplitude level of vibration is shown in **Table 1** [3].

While most SMAs have a slow response time, the BMF75 wire with a diameter of 75 μm can respond within less than 1 ms and was used to create the compact vibration actuator.

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Amplitude level	W [ms]	L [ms]	H [V]
1	3	200	1.8
2	4	200	1.8
3	6	200	1.8
4	7	200	1.8
5	9	200	1.8
6	10	200	1.8
7	12	200	1.8
8	13	200	1.8
9	15	200	1.8
10	11	75	1.8
11	13	75	1.8
12	15	75	1.8
13	17	75	1.8
14	19	75	1.8
15	22	75	1.8
16	24	75	1.8
17	26	75	1.8
18	28	75	1.8
19	30	75	1.8
20	12	22	1.8
21	15	22	1.8
22	17	22	1.8
23	20	22	1.8
24	22	22	1.8
25	25	22	1.8
26	27	22	1.8
27	29	22	1.8
28	30	22	1.8
29	30	22	1.8
30	30	22	1.8

Table 1. Driving signal for each amplitude level.

The subject only touches the actuator lightly to eliminate the disturbance of the actuator due to the skin reaction force.

The vibration stimulus generated by the SMA wire is transmitted to the subject through the round-head pin (**Figure 5**) described below. The pin actually touched by the subject is shown

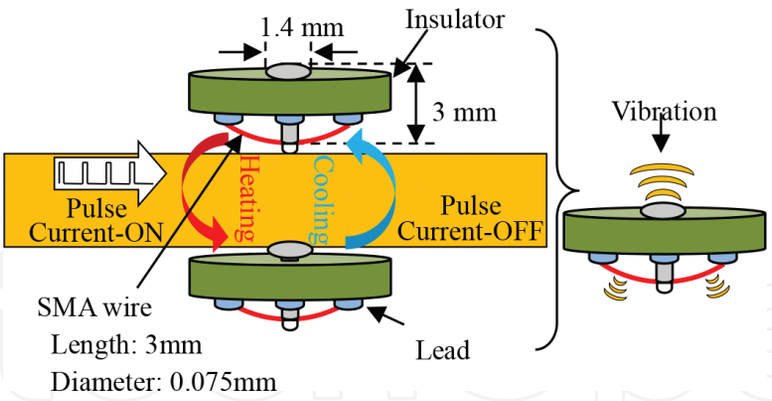

Figure 5. Structure of vibration actuator [3].

in **Figure 6**. As shown in **Figure 6**, the test equipment is shaped in a manner such that the subject can lightly touch the middle and index fingers on the pin array.

Tests were conducted at room temperature, 20–30°C, controlled by air conditioning. We did not use any electromagnetic shielding as the actuator will need to function in unshielded clinical settings.

3.2. Vibration actuator with a round-head pin

To make the actuator usable for tactile screening of diabetes, the micro-vibration generated by the SMA wire required amplification. A round-headed pin was therefore fixed at the center of the SMA wire, transforming the movement of the SMA wire into vibration. As shown in **Figure 5**, the actuator comprised an SMA wire, 75 μm in diameter and 3 mm in length, and a round-headed pin, 1.4 mm in diameter and 3 mm in length.

Shrinking and expansion of the SMA wire was continuously synchronized by the ON/OFF pulse current. This induced vibration in the round-headed pin, allowing even diabetic patients with reduced tactile sensitivity to recognize the tactile stimuli when the vibration pins were brought into light contact with the fingertips.

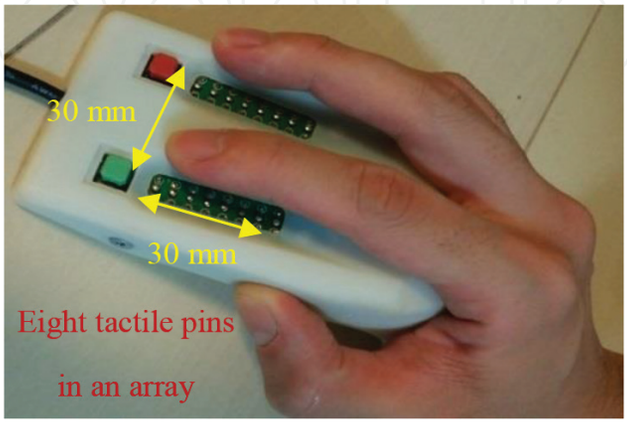

Figure 6. Tactile input for diabetes screening [3].

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3.3. Tactile display for the detection of diabetes mellitus

As shown in **Figure 6**, eight actuators were arranged as arrays. Two of these made up the tactile presentation area. The patient placed the index and middle fingers on these in such a way that the tips of two fingers were in contact with the array.

The presentation of vibratory stimuli makes use of higher-level tactile perceptual processes [21]. The pins in each array were driven by the pulse current signals with a time delay, as shown in **Figure 7**. This was expected to create an apparent perception of movement and the subject to experience a vibrating object moving from Ch. 1 (fingertip) to Ch. 8 (the second finger joint). The apparent movement of the stimuli could be controlled by varying the time delay of the pins.

To confirm that perception of apparent movement could be generated, a pilot study was run, using three healthy subjects, in which the frequencies and the amplitudes were varied using different time delays. Based on the results, the amplitude of the vibrations was divided into 30 levels. The lowest amplitude represented a stimulus that was difficult for healthy people with normal tactile sensitivity to perceive, while the strongest could be perceived even by a diabetic subject with severely compromised tactile sensitivity.

As shown in **Figure 4**, the amplitude of vibration was controlled by selecting the parameters W [ms]: pulse width, L [ms]: period, and H [V]: amplitude. These parameter values were carefully selected to allow the vibration to be increased linearly from level 1 to 30 (**Table 1**).

To examine the lowest threshold of tactile sensitivity of the index and middle fingers, a tactile sensation threshold (TST) score or peripheral neuropathy vibration (PNV) score were used. The subject was asked to place the index and middle fingers on the pin arrays. Tactile stimuli were then presented at different frequencies and amplitudes and in randomized directions. Using "yes" or "no" responses, the system measured the threshold of tactile perception and its relationship to the severity of attenuation. We named our proposed method the finger method.

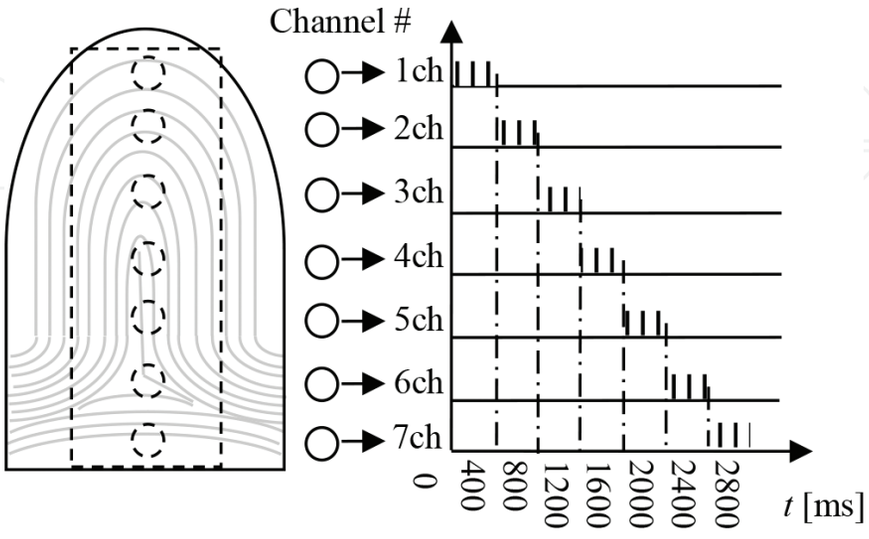

Figure 7. Presentation of tactile vibratory stimuli [3].

3.4. Experimental procedures for detection by diabetes mellitus subjects based on tactile sensation threshold scores

Three different procedures were performed. In the first, tactile stimuli were presented to both fingers simultaneously, in a single direction starting at the fingertips (Pattern 6 in **Figure 8**). Subjects were asked if they had perceived the stimuli. This procedure is known as the tactile sensation threshold 1 direction test (TST-1) or PNV 1 direction test (PNV 1) and was used to investigate the perception of tactile stimuli in two fingers. In the second procedure, a moving stimulus was presented to one of the two fingers in a random direction, and the subject was asked to identify both the finger and the direction of movement. In this procedure, known as the tactile sensation threshold 4 direction test (TST-4) or PNV 4 direction test (PNV 4), the subject was asked to identify the tactile perception as matching one of the four patterns shown in **Figure 8**. In the third procedure, known as the tactile sensation threshold 8 direction test (TST-8) or PNV 8 direction test (PNV 8), stimuli moving in random directions were applied to one or both fingers, and the subject was asked to match the finger(s) and direction of movement with one of the same eight patterns.

In all procedures, the examination began at a stimulus intensity of 15. Based on the accuracy of the answer given, the next round started at an intensity of 22 or 7.

Again, based on the accuracy of the answer given, in the next round, a stimulus intensity of 26, 19, 11, or 4 was presented to the subject. The stimulus intensity was then changed until the subject gave a correct answer 66.7% or more of the time. This TST score or PNV score was defined as the tactile threshold. The value for the tactile threshold was defined as the lowest value among the 30-stage stimulus intensity in which subjects were able to correctly answer more than 66.7%.

To reduce the examination time as much as possible, we applied a protocol to stimuli levels in 30 successive stages.

In our preliminary research on healthy subjects, we gradually increased the stimuli intensity from the weakest stimulus to the strongest. Inspecting patients with obvious neurological

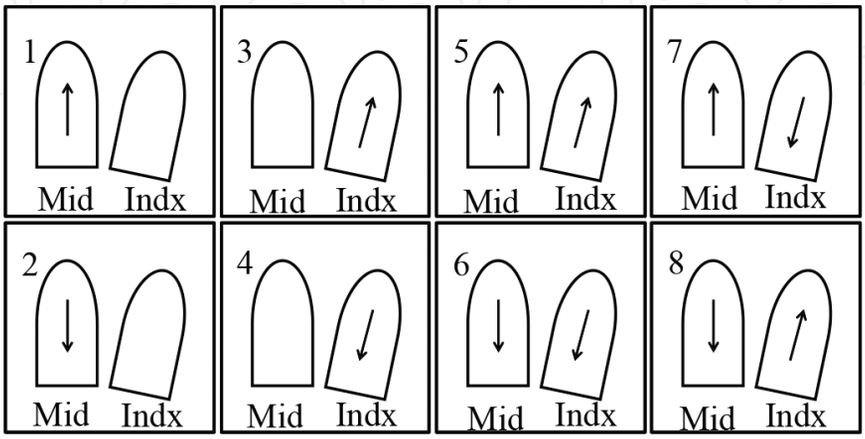

Figure 8. Eight patterns of moving directions of tactile stimuli [3]. Mid = middle finger; Indx = index finger.

disorders in this fashion leads to patient fatigue and boredom, and we cannot expect to see any response for the weakest stimuli. Therefore, we developed a protocol to shorten the inspection time. We began examining all subjects at the middle stimulus intensity of 15. The test stimulus was presented to the subject two or three times. Only subjects who correctly answered 66.7% or more with the test stimulus, that is, examinees who correctly answered at least twice, are next presented with stimulus intensity of 7, which is halfway between the minimum and middle intensities. Subjects who do not detect a stimulus at intensity 15 are presented next with a stimulus intensity of 22. This process significantly reduces the time needed to determine a subject's reaction threshold. Ultimately, the lowest stimulus intensity that was detected more than two-thirds of the presented intensity was defined as the tactile threshold for that subject.

4. Verification of early detection of DPN

4.1. Pilot study to confirm tactile reduction in long-term diabetic patients

The device was first used in a pilot study of 15 diabetic patients with a long history of treatment, and a significant decrease in tactile sensation compared with healthy subjects was confirmed [1].

4.2. Validation of DPN evaluation for diabetic patients

The device was next used to validate the evaluation of DPN in diabetic patients [2]. Based on the criteria [19] for diagnosis of DPN provided by the American Diabetes Association (ADA), tactile sensation was quantified, and a comparison was made of patients with and without DPN. A significant reduction in tactile sensitivity was confirmed in the DPN group.

The goal of this part of the study was to investigate the effectiveness of the proposed method in diagnosing DPN.

A cross-sectional study was conducted of 52 type 2 diabetic outpatients. Patients were evaluated for DPN using the ADA criteria, the Michigan Neuropathy Screening Instrument (MNSI), and our proposed finger method. Patients were assigned to probable DPN or non-DPN groups, based on the ADA criteria. The finger method was used to produce a PNV score from the index and middle fingers, using the three procedures introduced above: PNV 1, PNV 4, and PNV 8. The scores ranged from 1 to 30, and comparisons were made between the two groups.

The PNV scores of the DPN group were significantly higher ($P < 0.01$). The PNV scores for the right fingers of the DPN and non-DPN groups were 10.2 ± 7.4 and 3.4 ± 3.3 in PNV 1, 20 ± 4.9 and 10.7 ± 5.3 in PNV 4, and 23.2 ± 4.9 and 14.6 ± 7.8 in PNV 8, respectively (**Table 2**).

Overall, the tactile threshold of the DPN group was higher than that of the non-DPN group.

The results suggested that the finger method, performed using the proposed device, can be used to evaluate DPN.

	Non-DPN group (N = 21)	DPN group (N = 31)	P-value
Neuropathic symptoms (%)	2 (9.5%)	15 (48.4%)	0.003[†]
MNSI-Q score	1 ± 0.8	2.1 ± 2	0.017[*]
MNSI-E score	1 ± 0.5	2.9 ± 1.3	<0.001[*]
Abnormal MNSI score (%)	0 (0%)	20 (64.5%)	
PNV score			
PNV 1 left	4.1 ± 5	9.7 ± 7.2	<0.001[*]
PNV 1 right	3.4 ± 3.3	10.2 ± 7.4	0.004[*]
PNV 4 left	12.6 ± 6.3	20.4 ± 4.8	<0.001[*]
PNV 4 right	10.7 ± 5.3	20 ± 4.9	<0.001[*]
PNV 8 left	16 ± 7.3 (n = 19)	25.1 ± 3.9 (n = 30)	<0.001[*]
PNV 8 right	14.6 ± 7.8 (n = 19)	23.2 ± 4.9 (n = 30)	<0.001[*]

Data are presented as mean ± standard deviation or as N (%). P-values were calculated using the [*]Mann-Whitney U and [†]χ^2 tests. N = number; DPN = diabetic peripheral neuropathy; MNSI-Q = Michigan neuropathy screening instrument questionnaire; MNSI-E = Michigan neuropathy screening instrument examination; PNV = peripheral neuropathy vibration.

Table 2. Results of neuropathy examinations [2].

4.3. Detection of a decrease in asymptomatic tactile sensation in diabetic patients

Next, a comparison was made of the tactile sensitivity of 31 asymptomatic DPN patients and 32 healthy volunteers. The results confirmed that the asymptomatic DPN patients exhibited a significant reduction in sensitivity [3].

This part of the study focused on the asymptomatic development of decreased sensation, associated with diabetes mellitus. The goals were to investigate the use of the quantitative tactile sensation measurement device to examine diabetic patients who were unaware of abnormal or decreased sensation and to determine whether tactile sensation is reduced in asymptomatic patients. A group of healthy controls was recruited, and the finger method was used to measure the TST score of the index and middle fingers in the three procedures TST-1, TST-4, and TST-8. The TST scores ranged from 1 to 30, and a comparison was made between the two groups. The TST scores of the diabetic patients were significantly higher ($P < 0.05$). The TST scores for the left fingers of the diabetic patients and healthy controls were 5.9 ± 6.2 and 2.7 ± 2.9 in TST-1, 15.3 ± 7.0 and 8.7 ± 6.4 in TST-4, and 19.3 ± 7.8 and 12.7 ± 9.1 in TST-8, respectively (**Table 3**).

Overall, the tactile threshold of the fingers of asymptomatic DPN patients was shown to be higher than that of the healthy controls.

The results suggested that the quantitative tactile sensation measurement device was able to detect a decrease in tactile sensation in diabetic patients who were themselves unaware of abnormal or decreased sensitivity.

Test conditions	Healthy controls (N = 32)	Asymptomatic diabetic patients (N = 31)	P-value
TST-1 for left fingers	2.7 ± 2.9	5.9 ± 6.2	0.025
TST-1 for right fingers	2.9 ± 3.5	4.7 ± 5.2	0.160
TST-4 for left fingers	8.7 ± 6.4	15.3 ± 7.0	<0.001
TST-4 for right fingers	8.4 ± 6.7	13.9 ± 7.2	0.002
TST-8 for left fingers	12.7 ± 9.1	19.3 ± 7.8	0.005
TST-8 for right fingers	12.1 ± 8.9	17.3 ± 7.9	0.009

Data are presented as mean ± standard deviation or as N (%). P-values were calculated using *Mann-Whitney U test. N = number; TST = tactile sensation threshold; TST-1 = TST 1 direction test; TST-4 = TST 4 direction test; TST-8 = TST 8 direction test.

Table 3. Scores on the tactile sensation threshold test [3].

4.4. Summary of the three previous studies

In this section, we summarize the results of the three tests performed on the quantitative tactile examination device. The instrument was demonstrated to be capable of quantitative evaluation of the reduction in tactile sensitivity (or increase in tactile threshold) of patients with DPN. The instrument was also able to distinguish between patients with DPN and non-DPN. Finally, the tactile sensitivity of asymptomatic DPN patients was shown to be lower than that of healthy subjects.

This suggests that the device can be used to distinguish the different stages of DPN.

Although the tests involved a relatively small number of subjects, they suggested that a decrease in tactile sensitivity was present in patients with both severe and mild DPN (**Figure 9**).

4.5. Statistical revalidation using propensity score

To examine whether significance could be added to the TST score by adjusting to reflect the patient's background, a propensity score was derived.

In a cross-sectional study, the novel micro-vibration actuator with shape memory alloy wires was used to measure the tactile sensations of 68 type-2 diabetic outpatients and 89 healthy controls. Patients were again evaluated using the ADA criteria [16], the Michigan Neuropathy Screening Instrument (MNSI) [20], and the TST scores for the index and middle fingers. Patients were classified as probable DPN (n = 31) or non-DPN (n = 37) using the ADA criteria and as symptomatic (n = 26) or asymptomatic (n = 42) using the MNSI. Propensity score weighting was applied to compare the scores of each patient group with that of the control group.

The mean time for determining the TST score was approximately 3 min/patient for all groups. The TST score of every patient group was significantly higher than that of the control group ($P < 0.01$). The right finger scores of the DPN, non-DPN, symptomatic, asymptomatic, and

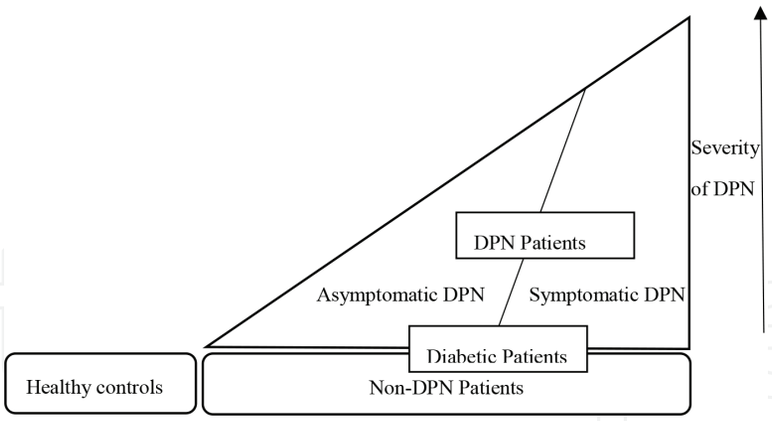

Figure 9. Severity and classification of DPN. DPN = diabetic neuropathy.

control groups were 20.1 ± 4.9, 11.7 ± 5.1, 19.4 ± 4.5, 15.7 ± 6.9, and 6.5 ± 5.7, respectively. This gave P values of 0.00 for DPN, 0.198 for non-DPN, 0.002 for symptomatic, and 0.025 for asymptomatic.

The results confirmed that our novel device provides simple quantitative evaluation of tactile sensation in diabetic patients, facilitating the early detection of asymptomatic DPN.

5. Comparison with other DPN evaluation techniques

In this section, we first describe the diagnostic criteria for DPN and give an outline of representative evaluation methods. Next, we roughly classify these nerve conduction studies as qualitative or quantitative and compare them. Finally, we discuss the difference between these quantitative tests and our proposed method.

5.1. Diagnostic criteria and representative examination methods for diabetic neuropathy

No specific tests for DPN currently exist and nor are diagnostic criteria reflecting an internationally established consensus available. It is therefore necessary to base comprehensive diagnoses of neuropathy on neurological symptoms and the results of examinations. The diagnostic criteria (**Table 4**) [16] of the A DA are used in daily clinical practice.

The tests used include the pain sensation test, vibration sensation test, 10-g monofilament test, and Achilles tendon reflex assessment. By regular application of these tests, it is possible to evaluate the onset and development of neuropathy. They are also effective in the early diagnosis of asymptomatic DPN. Being relatively easy to implement, the tests are useful when applied by a proficient practitioner. However, the results are qualitative.

To confirm the diagnosis, quantitative nerve conduction tests are necessary. These are not widely available, however, as they are time-consuming and require the use of expensive equipment.

Diagnosis	Diagnosis items	Purpose
Possible DSPN	The symptoms or signs of DSPN may include the following. Symptoms: decreased sensation, positive neuropathic sensory symptoms (e.g., "asleep numbness," prickling or stabbing, burning, or aching pain) mainly in the toes, feet, or legs. Signs: symmetric decrease in distal sensation or unequivocally decreased or absent ankle reflexes	Clinical use
Probable DSPN	The combination of any or two or more of the following symptoms and signs: neuropathic symptoms, decreased distal sensation, or unequivocally decreased, or absent ankle reflexes	Clinical use
Confirmed DSPN	The presence of a nerve conduction abnormality and one or more symptoms or one or more signs of neuropathy	Clinical use Clinical research

DSPN: distal symmetric polyneuropathy (used synonymously with DPN in this chapter).

Table 4. Definitions of minimal criteria for DSPN [16].

5.2. Comparison of qualitative methods and the quantitative method

The pain sensation test, made with a sharp object such as a pin, is used to test for hyperalgesia and weakness.

In the vibration sensation test, sensitivity to vibration is investigated by applying a 128 Hz tuning fork to the ankle or the toe of the foot. The ability to sense vibration is compared with that of a healthy person.

In patients with DPN, the Achilles tendon reflex is often attenuated or absent, providing an excellent test that can be performed in a short time if the examiner is proficient.

In the 10-g monofilament test, a thin thread of monofilament nylon is placed on the foot. It is used to investigate the function of the nerve that senses tactile and pressure. In DPN patients, the sensations are dulled.

These tests are representative qualitative examination techniques that can be performed in a short time.

In NCS, the stimulation conductivity of the peripheral nerve is measured. In patients who have developed neuropathy, the speed with which the stimulus is transmitted becomes slower. NCS is able to produce a quantitative measurement of the speed of the peripheral nerves of the human body [21, 22]. However, it requires the patient to be subjected to painful electric shocks. NCS also requires the use of expensive equipment. The examination time is lengthy, and if multiple peripheral nerves on both the left and right side are examined, the procedure may take several hours. NCS is therefore only available at large specialized hospitals.

5.3. Comparison of NCS and quantitative tactile examination methods

The proposed finger method is superior to NCS in some respects. First, the inspection time is short, taking a maximum of approximately 3 min. Second, the patient experiences no

pain, as no electric current is applied to the nerve of the patient. The sensation is experienced only in the nerve being investigated. Third, while medical examination is normally performed by an expert, it is possible for the subject himself/herself to perform the test. This allows the test to be run at a place and time chosen by the patient. If tactile sensation reduces over time, poor glycemic control may be indicated. The test can detect such haptic loss. By making patients aware that their sense of touch is declining, the test may encourage them to seek treatment.

6. Discussion

6.1. Strengths and significance of this device

A key strength of this device is that it can be used by patients themselves, producing quantitative results within minutes. It may be applied not only to DPN but to all forms of peripheral neuropathy. We are currently developing a device for assessing the lower limbs. Applications to diseases other than DPN are also being investigated.

6.2. Limitations

The cross-sectional studies reported here involved outpatients, and the sample sizes were limited. To confirm the effectiveness of the technology, future studies should use larger samples and a wider range of patients.

7. Future work

The tactile test quantification technology introduced in this chapter has a wide range of potential applications. In future studies, we will apply it to other types of peripheral neuropathy.

One such current study is applying the tactile test equipment to the feet. The equipment has already developed to a point where practical application is possible. We plan to conduct further clinical studies of patients with DPN, quantitatively measuring the tactile sensations in the feet as well as the fingers. This will be useful in identifying DPN in different areas of the body.

In further developments, we will use the technology to visualize the severity of peripheral neuropathy in a manner that will be easily understandable by both healthcare professionals and patients. This may prove useful for monitoring the severity of peripheral neuropathy induced by anticancer drugs such as paclitaxel. It may also encourage patients with peripheral neuropathy to seek early treatment.

No currently available examination method can distinguish clearly between nociceptive pain and neuropathic pain, which are treated with standard pain medications and expensive analgesics, respectively. Patients who are misdiagnosed may be prescribed inappropriate analgesics and experience pain over a long period. The prescription of inappropriate pain

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medication may also add unnecessarily to medical expenses. Our tactile test technique may provide a useful tool for distinguishing between nociceptive and neuropathic pain.

By promoting early detection and treatment of asymptomatic peripheral neuropathy, this novel technology may reduce the medical and social resources needed when complications arise or the severity of the condition is unknown. By promoting the use of this technology, the authors hope to make a social contribution.

8. Conclusions

A quantitative tactile examination technique using shape memory alloy actuators was developed. The painless, simple, and quantitative tactile examination technology that can be performed in a short time is an ideal examination technology. A notable feature of this technology is that it succeeded in miniaturization and power saving. This was demonstrated to allow early detection of DPN. Large-scale clinical trials should be conducted, to confirm the effectiveness of this novel technology, which may have applications in the identification of a wider range of neuropathies.

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Conflict of interest

Keiji Uchida holds a patent on the quantitative tactile examination device. The other authors declare that they have no competing interests.

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