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PAPER **Micro-Vibration Patterns Generated from Shape Memory Alloy Actuators and the Detection of an Asymptomatic Tactile Sensation Decrease in Diabetic Patients**

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SUMMARY Diabetes mellitus is a group of metabolic diseases that cause high blood sugar due to functional problems with the pancreas or metabolism. Diabetic patients have few subjective symptoms and may experience decreased sensation without being aware of it. The commonly performed tests for sensory disorders are qualitative in nature. The authors pay attention to the decline of the sensitivity of tactile sensations, and develop a non-invasive method to detect the level of tactile sensation using a novel micro-vibration actuator that employs shape-memory alloy wires. Previously, we performed a pilot study that applied the device to 15 diabetic patients and confirmed a significant reduction in the tactile sensation in diabetic patients when compared to healthy subjects. In this study, we focus on the asymptomatic development of decreased sensation associated with diabetes mellitus. The objectives are to examine diabetic patients who are unaware of abnormal or decreased sensation using the quantitative tactile sensation measurement device and to determine whether tactile sensation is decreased in patients compared to healthy controls. The finger method is used to measure the Tactile Sensation Threshold (TST) score of the index and middle fingers using the new device and the following three procedures: TST-1, TST-4, and TST-8. TST scores ranged from 1 to 30 were compared between the two groups. The TST scores were significantly higher for the diabetic patients ($P < 0.05$). The TST scores for the left fingers of diabetic patients and healthy controls were 5.9 ± 6.2 and 2.7 \pm 2.9 for TST-1, 15.3 \pm 7.0 and 8.7 \pm 6.4 for TST-4, and 19.3 \pm 7.8 and 12.7 ± 9.1 for TST-8. Our data suggest that the use of the new quantitative tactile sensation measurement device enables the detection of decreased tactile sensation in diabetic patients who are unaware of abnormal or decreased sensation compared to controls.

key words: shape-memory alloy wires, micro-vibration patterns, diabetes mellitus, tactile sensation, sensory threshold

1. Introduction

Diabetes mellitus is a group of metabolic disorders that is characterized by a chronic hyperglycemic condition resulting from insufficient insulin action and is known to cause various symptoms and complications. The pancreas normally produces insulin, which is a kind of hormone, to control the level of glucose in the blood, however for a person with diabetes, glucose is not used properly in the metabolic

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cycle, which causes health problems, such as polyphagia, polyuria and polydipsia, since glucose is the main source of energy for the body cells. An estimated 350 million people in the world had diabetes in 2014, and the number is estimated to almost double by 2030. An estimated 1.5 million deaths were directly caused by diabetes in 2012, and the symptoms are more common in the more developed countries. These facts mean that the changes of lifestyle and eating habits might effect to the increase of diabetes mellitus, and in fact the greatest increase in prevalence of symptoms is expected to occur in Asia and Africa.

When the metabolic disorder resulting from insufficient insulin action is mil[d, p](#page-6-0)atients may not be aware of the majority of symptoms $[1]$. Thus, they may remain untreated for a long period of time or lose motivation for treatment. However, when even mild metabolic disorders persist for a long period of time, the risk of developing chronic complications characteristic of diabetes mellitus, [such](#page-6-1) [as](#page-6-2) retinopathy, nephropathy, and neuropathy, is high $\lceil 2 \rceil - 6$. In particular, diabetic neuropathy, which causes a decrease in vibratory and tactile sensation, is a serious complication that occurs without subjective symptoms and leads to fo[ot ul](#page-6-3)ceration or lower-extremity amputation as it progresses[7].

Commonly performed tests for sensory disorders are qualitative, and include the monofilament test, Achilles tendon reflex test, and vibration perception test using a 128-Hz tuning fork. Simple and quantitative methods of sensory testing are needed. The authors pay attention to the different sensitivity of tactile perception of Diabetes patients, and develop a non-invasive screening method of the level of diabetes using a novel micro-vibration actuator that employs a shape-memory alloy (SMA) wire for the [pre](#page-6-4)sentation of various tactile sensations to a human skin $[8]$. The characteristics of a SMA formed into a thin wire were firstly examined in our previous study, and a micro-vibration actuator, which changed its length according to the heat given to the body, was inventively developed. The actuator is electrically driven by pulse signals generated by current control circuits, and generates micro-vibrations with different frequencies synchronized with the pulse frequencies up to 300 Hz to be perceived as different tactile sensations. For the tactile stimuli to a human body, the psychological effects of the higher-level perceptual processes s[uch](#page-6-5) as the phantom sensation and the apparent movement [9] of the tactile

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sensations were also introduced in our study [\[10\],](#page-6-6) [\[11\].](#page-6-7) By using multiple actuators, a tactile display was constructed for transmitting physical stimuli into human skin to present novel and various tactile sensations.

Previously, we performed a pilot study using the device in 15 diabetic patients and confirmed a significant reduction in the tactile sensa[tion i](#page-6-8)n diabetic patients when compared to healthy subjects $[12]$. At this time, the pathogenesis of diabetic neuropathy was complicated and had not been fully elucidated, but the polyol pathway was considered the most likely mechanism underlying the development of diabetic neuropathy. There was aldose reductase inhibitor (ARI) as a drug for diabetic neuropathy. ARI, however, exhibited efficacy only in the early stage of diabetic neuropathy, and its efficacy was weak. Given the current la[ck o](#page-6-3)f diseasemodifying therapies for diabetic neuropathy [7], we consider diabetic patients with an asymptomatic tactile sensation decrease to be important study subjects because it might be possible to motivate these patients to attempt aggressive treatment of diabetes mellitus for the prevention of its complications from the early phase of diabetic neuropathy, prior to the onset of subjective symptoms. Such motivation is conveyed by objectively demonstrating asymptomatic tactile sensation decrease to these patients.

In this study, we focus on the asymptomatic development of decreased sensation associated with diabetes mellitus, and a novel device that quantifies finger tactile sensation thresholds using micro-vibration has been developed by presenting further variety of tactile sensations employing the shape-memory alloy wires. Using the developed device, we investigate whether diabetic patients who are unaware of abnormal or decreased sensation would also show decreased tactile sensation, i.e., higher tactile sensation thresholds, compared to healthy volunteers.

2. Tactile Receptors

In order to facilitate the sense of touch, the skin includes four main tactile receptors: Meissner corpuscle, Merkel disc, Ruffini ending and Pacinian corpuscle. As shown in Fig. 1, Merkel discs are located in the epidermis approximately $10 \mu m$ in diameter, and they can sense pressure and

Fig. 1 Tactile receptors under skin

texture. Meissner corpuscles are primarily located just beneath the epidermis within the dermis between $30 - 140 \mu m$ in length and 40 - $60 \mu m$ in diameter. They can sense stroking and fluttering. Ruffini endings are also located in the dermis around 0.5 - 2 mm in the length, and they can sense skin stretch. Pacini corpuscles are located in the subcutis, and they are about 0.5 - 2 mm in the length and approximately 0.7 mm in the diameter. According to the response speed and size of the receptors, the four receptors can be classified into four categories: fast adapting I and II (FA I and FA II) and slow adapting I and II (SA I and SA II).

The receptors are distributed with different density in different region of a human body. Since most tactile sensation is obtained by human hands, innervati[on de](#page-6-9)nsity in human hands is discussed and shown in Fig. 2 [13]. It is known that the receptors are densely distributed in human fingers, especially in the tip of fingers, and the fingers are sensitive to various kinds of stimuli. The response of tactile receptors is closely related with the activity of the nerve system, and capillary vessels are also densely distributed in the tip of fingers. If the blood flow in capillary vessels is restricted by sugar, or capillary vessels are destroyed by blood sugar caused by the diabetic problem, the sensitivity of tactile sensation will decrease. Most of the diabetes patients, even in the early stage of diabetes, have problems of low sensitivity of tactile sensations in fingers and feet, and the declining degree of the sensitivity proceeds according to the progress of diabetic stage.

In this research, the developed tactile device is employed to present various tactile stimuli to subject's fingers, and the sensitivity of tactile sensations is quantitatively measured by referring to the driving parameters of tactile actuators.

Fig. 2 Innervation density of tactile receptors [\[13\]](#page-6-9)

3. Design of the Quantitative Tactile Sensation Measurement Device

3.1 Compact SMA Actuator for Generating Microvibration

In order to generate physical stimuli give to human skin, a shape memory alloy wire is employed in this study. Within typical operating temperature range, SMA has two phases, each with a different crystal structure and therefore different properties. One is the high temperature phase called Austenite phase and the other is the low temperature phase called Martensite phase. When the body temperature of SMA increases beyond critical value, the phase of SMA will be varied from Martensite phase to Austenite phase and vice versa. Since the crystal structure of SMA is changed corresponding to different phase, the shape of SMA is changed simultaneously. This unique behavior of SMA has made it popular for actuation and sensing, and be applied in many industrial sectors such as aerospace, automotive, biomedical, etc.

By forming SMA into a thin wire, the SMA also presents a unique characteristic to shrink in the length direction at a certain temperature. In this study, a SMA wire (Toki Corp., BioMetal, BMF75) is selected to make a compact actuator for tactile presentation, and its characteristic is shown in Fig. 3. When the temperature of a SMA wire arises beyond T1, the wire begins to shrink till the temperature is over T2. When the temperature of the SMA wire reduces back to T2, the wire begins to expand back to the initial length till the temperature is below T1.

This means that the shrinkage and the return to the initial length of a SMA wire can be controlled by the pulse current, since the alloy has electrical resistance of 0.6 ohms per 1 mm, and accepts electrical current to heat its body. By applying a pulse current to the SMA wire, the body temperature instantly rises due to the generated heat inside the body, and shrinks from its initial length. When the pulse current stops, the body instantly cools down, and recovers its initial length. The process of shrinkage and return to the initial length of the SMA wire synchronizes completely with the ON/OFF pulse current as shown in Fig. 4. To control the magnitude of the vibration, the amplitude of pulse signals H

Fig. 3 Characteristics of SMA wire

and the duty ratio W/L should be properly determined based on the calories exchanged. At the same time, the SMA temperature needs to be maintained between T1 and T2 so as to contract and return to the initial length most efficiently. A pulse-width modulated (PWM) rectangular wave signal with arbitrary frequency, amplitude and duty-ratio is generated in a PC, which is amplified to drive the SMA actuators. The current amplifier was specially designed by the authors for driving SMA actuators in variable frequencies up to 300 Hz and variable voltage amplitude with suitable current control.

As known well, the general SMA have quite slow timeresponse, however, the SMA wire BMF75 with the diameter of 75 $\lceil \mu m \rceil$ can respond instantly, and shrink within less than millisecond. That is the reason that we adapted BMF75 to make a compact vibration actuator.

3.2 Vibration Actuator with a Round-Head Pin

In order to amplify the micro vibration generated by a SMA wire to make it usable as a tactile actuator for the screening of diabetes symptoms, we employ a round-head pin, which is fixed at the middle of the SMA wire to transform the movement of the SMA wire to the vibration of the pin. Figure 5 illustrates the structure of the vibration actuator consisting of a 75 [μ m] (diameter) \times 3 [mm] (length) SMA wire and a 1.4 [mm] (diameter) \times 3 [mm] (length) roundhead pin.

The SMA wire generates continuous synchronization with the state of the ON/OFF pulse current, causing the pro-

Fig. 4 Pulse Signal for Driving SMA

Table 1 Driving signal for each amplitude level

Fig. 6 Tactile display for screening diabetes

Fig. 7 Presentation of tactile vibratory stimuli

cess of SMA wire to shrink and return to its initial length. This vibration is transmitted to the round-head pin. With this structure, the round-head pin successfully amplifies the vibration of a SMA wire, so that even diabetic patients with lower tactile sensitivity can recognize the tactile stimuli generated by the vibration of the pin, when they lightly touches the vibration pins with their fingertips.

3.3 Structure of Tactile Display for the Detection of Diabetes Mellitus Patients

By arranging eight tactile-pin actuators in an array, a screening system of diabetes is constructed. As shown in Fig. 6, two tactile arrays are settled in a tactile display part, on which a patient places his index and middle fingers along with the indicators, so that the tips of the two fingers touch to the arrays.

The presentation of vibratory stimuli generated by the tactile pins is [mad](#page-6-5)e by utilizing tactile higher-level perceptual processes $[9]$. When the pins in an array are driven by pulse current signals with time delays as shown in Fig. 7, a subject is expected to perceive that a vibratory object continuously moves from Ch. 1 (fingertip) to Ch. 8 (second joint of a finger), due to the effects of tactile apparent movement perception. In this manner, moving tactile stimuli can be presented to different directions, according to the time delay among tactile pins.

For verifying the validity of the tactile presentation using apparent movement perception, we preliminarily tested

the vibratory movement by changing the frequencies and the amplitudes with different time delays. Based on this test, the amplitude of the vibration was divided into 30 steps from 1, with the lowest amplitude being difficult for healthy people with normal tactile sensitivity to perceive the movement, to 30, which has the greatest amplitude and is perceived even by a diabetic subject with severely damaged tactile sensation.

The driving pulse signal for each amplitude level of vibration is shown in Table 1. As presented in Fig. 4, the amplitude of vibration is controlled by selecting the parameters W, L, and V. We carefully examined the parameter values and determined them such that the intensity of vibration continuously increases from level 1 to 30, based on an experiment of tactile perception by employing three health subjects.

To examine the lowest threshold of tactile sensitivity of the index and middle fingers, we propose the Tactile Sensation Threshold (TST) score. The subject places his or her index and middle fingers on the pin arrays and is presented with tactile stimuli at different vibration frequencies and amplitudes in random directions. Through "yes" or "no" responses to questions about tactile perception, the system measures the threshold of tactile presentation, which is related to the severity of decreased sensation. This tactile sensation threshold measurement method is defined as the finger method.

4. Experiment for the Detection of Diabetes Mellitus Subjects Based on TST Scores

4.1 Experimental Procedures Using the Finger Method

We performed three different procedures using the finger method to examine the device's ability to reflect the level of decreased sensation. The first procedure presented tactile stimuli simultaneously to both fingers in one direction starting at the fingertips (Pattern 6 in Fig. 8) and asked subjects if they perceived the presented stimuli. This procedure, known as the Tactile Sensation Threshold 1 direction test (TST-1), examined the perception of tactile stimuli in two fingers. The second procedures were to present one moving stimulus to one of the two fingers in a random direction and require the subject to identify the finger and direction. This procedure, known as the TST 4 directions test (TST-4), required the subject to identify the tactile perception as one of four patterns (Patterns 1, 2, 3, and 4 in Fig. 8). The third procedure, known as the TST 8 directions test (TST-8), stimulated one or both fingers with moving stimuli in random directions. The subject was required to identify the finger(s) and the direction of movement from the eight patterns presented in Fig. 8.

4.2 Subjects and Data Collection

This cross-sectional study included 31 consecutive type 2 diabetic outpatients and 32 healthy control subjects presenting at Takamatsu Heiwa Hospital and Kagawa University Hospital between 2013 and 2014. Only diabetic patients who were unaware of abnormal or decreased sensation were included. Subjects were excluded from the study if they met any of the following criteria: peripheral arterial occlusive disease, chronic alcohol abuse, lumbar spine disorders, severe renal failure, critical liver disease, or any other cause of peripheral neuropathy. The study was approved by the institutional ethics committee, and written informed consent was obtained from all subjects.

Subject characteristics, including age, sex, smoking status, and blood pressure, were recorded for all subjects. Low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), HbA1c, and duration of

Fig. 8 Eight patterns of moving directions of tactile stimuli

diabetes were recorded only for diabetic patients.

4.3 Reproducibility

In each procedure, the examination started with the lowest vibratory amplitude and it was increased in a stepwise manner until the subject recognized the tactile stimulus. If the subject answered correctly for at least two of the three stimuli of the same amplitude, the amplitude was decreased one step. This was continued until the subject failed to correctly answer twice, then the previous step stimulus, which was the lowest threshold of tactile sensitivity, was recorded as the TST score.

To assess TST score reproducibility, intra- and interexaminer agreement tests were performed with 10 healthy volunteers. To evaluate the inter-examiner reproducibility, the volunteers underwent the three finger method procedures twice on the same day, with the tests administered by two separate examiners. To evaluate the intra-examiner reproducibility, the volunteers underwent the three finger method procedures twice with the same examiner at a 4-week interval. Intra- and inter-rater agreement values were determined using Spearman's rank correlation coefficient between tests.

4.4 Subjects and Data Collection

The statistical methods used to compare groups included χ^2 tests for nominal variables and Mann-Whitney U tests for ordered categorical variables. All statistical analyses were performed using SPSS version 22.0 (Tokyo, Japan). A P value of <0.05 was considered statistically significant. Missing results were excluded from analyses.

5. Results and Analysis

The diabetic patients and healthy controls showed no significant differences in their clinical characteristics between the two groups (Table 2). Significant differences in TST scores were detected by all test procedures except for TST-1 for the right fingers (Table 3). No significant laterality was observed in the TST score for any of the three procedures.

In the diabetic patients, TST score measured by the finger method using the new device was significantly higher than in the healthy controls in the TST-1 left, TST-4 left, TST-4 right, TST-8 left, and TST-8 right conditions.

In the TST-1 right test, the scores tended to be higher for the diabetic patients than the healthy controls, but no significant difference was observed.

To determine the inter-examiner reproducibility between two examiners, Spearman's rank correlation coefficients for TST-1 left, TST-1 right, TST-4 left, TST-4 right, TST-8 left, and TST-8 right were 0.80, 0.92, 0.89, 0.99, 0.98, and 0.98, respectively. Similarly, in the evaluation of intraexaminer reproducibility between the tests, Spearman's rank correlation coefficients for each test procedure were 0.99, 0.81, 0.99, 0.99, 0.99, and 0.98, respectively.

Table 2 Characteristics of healthy controls and diabetic patients

	Healthy controls	Diabetic patients	P-value
	$(N = 32)$	$(N = 31)$	
Age (years)	58.5 \pm 16.7	63.8 ± 9.3	$0.221*$
Sex (male/female)	15/17	8/23	$0.082 \dagger$
Current smokers $[N (%)]$	$5(15.6\%)$	$6(18.8\%)$	0.697 †
Blood pressure (mmHg)			
Systolic	126 ± 13	128 ± 18	$0.762*$
Diastolic	79 ± 8	75 ± 12	$0.159*$
$LDL-C$ (mg/dL)		104 ± 28	
$HDL-C$ (mg/dL)		57 ± 13	
$HbA1c$ $(\%)$		7.1 \pm 0.9	
Duration diabetes of		10.7 ± 7.5	
(vears)			

Data are presented as mean \pm standard deviation or as N $(%)$. P-values were calculated using the *Mann-Whitney U test, $\uparrow \chi 2$ test. N: number.

Data are presented as mean \pm 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 directions test; TST-8, TST 8 directions test.

The TST scores measured by the tactile sensation measurement device that we developed were higher in the diabetic patients than in the healthy controls for all test procedures. This indicates that diabetic patients who are unaware of abnormal or decreased sensation have higher tactile sensation thresholds, i.e., decreased tactile sensation, compared to healthy controls.

While we performed 3 different tactile sensation test procedures each with the left and right fingers, for a total of 6 procedures, the TST scores of the diabetic patients were significantly higher than those of the healthy controls in the TST-1 left, TST-4 left, TST-4 right, TST-8 left, and TST-8 right conditions. However, in the TST-1 right test, the scores tended to be higher for the diabetic patients than the healthy controls, but no significant difference was observed. Moreover, although the P value of 0.025 for TST-1 left indicates a significant difference, it is greater than the P values for the TST-4 and TST-8 conditions. We believe that this indicates the limitation of the TST-1 as a test procedure. This greater P value may be attributable to the fact that TST-1 scores are based on self-reporting by subjects on whether they have perceived a certain intensity of tactile stimulation. Examiners cannot know whether subjects have perceived the pre-

sented tactile stimuli. Because it is human nature to wish to be more normal and healthier, there may be subjects who report that they have perceived lower levels of vibration than the levels that they can actually perceive. This limitation is also applicable to the conventional vibration perception test using a tuning fork. Meanwhile, because the TST-4 and TST-8 require subjects to not only perceive the tactile stimuli but also identify the direction of stimulation in order to answer correctly, the effects of self-reporting by subjects is eliminated. Thus, among the 3 different test procedures used in the present study, the TST-4 and TST-8 are more useful for detecting decreased tactile sensation than TST-1.

The subjects showed differences in the perception of each tactile stimulus, as exemplified by the eight patterns shown in Fig. 8. Tactile stimuli presented to both the index and the middle fingers in the same direction, as in Patterns 5 and 6, appeared to be the easiest for the subjects to perceive. The second easiest tactile stimuli to perceive were apparently those presented to one of the two fingers as in Patterns 1, 2, 3, and 4. Patterns 7 and 8 are associated with the lowest perception rate. When tactile stimuli of these patterns were presented, some subjects became confused. Although Patterns 7 and 8 are tactile stimuli presented to both the index and the middle fingers as with Patterns 5 and 6, a major difference is that the directions of the tactile stimuli cross each other in the former. This might have caused differences in perception among the subjects. Most notably, because it is uncommon for humans to receive tactile stimuli at the index and middle fingers from different directions, such stimulation patterns may be difficult to perceive. The low perception rates for Patterns 7 and 8 might be associated with the TST-8 scores being higher than the TST-4 scores, as shown in Table 3. Further detailed studies are needed on the differences in perception rates for stimulation patterns.

A nerve conduction (NC) study, which is a quantitative method of sensory testing apart from our tactile sensation measurement device, could be performed. However, a NC study requires a significant time commitment and is very expensive. In addition, assessment of NC abnormality is difficult because NC values vary dependi[ng on](#page-6-10) patient characteristics such as age, height, and weight [14]. For instance, one criterion for NC [norm](#page-6-11)[ality i](#page-6-12)s Σ 5 NC normal deviate score \leq 95th percentile [15], [16]. It is difficult to set normal NC values based on patient characteristics and normal deviate scores.

In contrast to NC study, the finger method using the tactile sensation measurement device is simple and can be performed in a few minutes, similar to the commonly performed tests for sensory disorders, such as the vibration perception test using a tuning fork. In addition, this method has several advantages compared to the current tests. First, the method can be performed by subjects themselves without the help of an examiner. Second, it is a quantitative, rather than qualitative, test that can provide test results with numerical values. Given that many diabetic patients have few subjective symptoms, explicitly stated tactile sensation thresholds may contribute to enhanced motivation for treat-

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ment.

The present study has several limitations. First, there was no significant difference in the TST scores on the TST-1 right between the healthy controls and diabetic patients. When the device is used to examine tactile sensation thresholds, TST-4 and TST-8, which are more objective than TST-1, seem to be more appropriate procedures. Second, although the assessment of TST score reproducibility yielded relatively high correlation coefficients, the reproducibility was confirmed in a small sample. In the future, the reproducibility needs to be confirmed in a larger sample.

6. Conclusions

In this study, we focused on the asymptomatic development of decreased sensation associated with diabetes mellitus, and developed a quantitative and non-invasive detection method of the level of tactile sensation using a novel micro-vibration actuator that employs shape-memory alloy wires. We showed that the sensory threshold of index and middle fingers was significantly higher in diabetic patients who were unaware of abnormal or decreased sensation than in healthy subjects. These results indicated that tactile sensation is decreased in diabetic patients compared to healthy subjects. Our data suggest that the use of the new quantitative tactile sensation measurement device may enable the detection of decreased tactile sensation in diabetic patients.

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References

- [1] [American Diabetes Association, "Diagnosis and classification of di](http://dx.doi.org/10.2337/dc14-S081)abetes mellitus," Diabetes Care, vol.37, Supplement 1, pp.81–90, Jan. 2014.
- [2] Diabetes Control and Complications Trial Research Group, "The ef[fect of intensive treatment of diabetes on the development and pro](http://dx.doi.org/10.1056/NEJM199309303291401)gression of long-term complications in insulin-dependent diabetes mellitus," N. Engl. J. Med., vol.329, no.14, pp.977–986, Sept. 1993.
- [3] Diabetes Control and Complications Trial Research Group, "The effect of intensive diabetes therapy on the development and progres[sion of neuropathy," Ann. Intern. Med., vol.122, no.8, pp.561–568,](http://dx.doi.org/10.7326/0003-4819-122-8-199504150-00001) April 1995.
- [4] C.L. Martin, J.W. Albers, and R. Pop-Busui, DCCT/EDIC Research [Group, "Neuropathy and related findings in the diabetes control and](http://dx.doi.org/10.2337/dc13-2114) complications trial/epidemiology of diabetes interventions and complications study," Diabetes Care, vol.37, no.1, pp.31–38, Jan. 2014.
- [5] Y. Ohkubo, H. Kishikawa, E. Araki, T. Miyata, S. Isami, S. [Motoyoshi, Y. Kojima, N. Furuyoshi, and M. Shichiri, "Intensive](http://dx.doi.org/10.1016/0168-8227(95)01064-k) insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study," Diabetes

[Res.](http://dx.doi.org/10.1016/0168-8227(95)01064-k) [Clin.](http://dx.doi.org/10.1016/0168-8227(95)01064-k) [Pract.,](http://dx.doi.org/10.1016/0168-8227(95)01064-k) [vol.28,](http://dx.doi.org/10.1016/0168-8227(95)01064-k) [no.2,](http://dx.doi.org/10.1016/0168-8227(95)01064-k) [pp.103–117,](http://dx.doi.org/10.1016/0168-8227(95)01064-k) [May](http://dx.doi.org/10.1016/0168-8227(95)01064-k) [1995.](http://dx.doi.org/10.1016/0168-8227(95)01064-k)

- [6] [P. Reichard, B. Berglund, A. Britz, I. Cars, B.Y. Nilsson, and U.](http://dx.doi.org/10.1111/j.1365-2796.1991.tb00415.x) Rosenqvist, "Intensified conventional insulin treatment retards the microvascular complications of insulin-dependent diabetes mellitus (IDDM): the Stockholm Diabetes Intervention Study (SDIS) after 5 years," J. Intern. Med., vol.230, no.2, pp.101–108, Aug. 1991.
- [7] B.C. Callaghan, H.T. Cheng, C.L. Stables, A.L. Smith, and E.L. [Feldman, "Diabetic neuropathy: clinical manifestations and current](http://dx.doi.org/10.1016/S1474-4422(12)70065-0) treatments," Lancet Neurol, vol.11, no.6, pp.521–34, June 2012.
- [8] Y. Mizukami and H. Sawada, "Tactile Information Transmission by [Apparent Movement Phenomenon Using Shape-memory Alloy De](http://dx.doi.org/10.1515/IJDHD.2006.5.3.277)vice," International Journal on Disability and Human Development, vol.5, no.3, pp.277–284, 2006.
- [9] G.V. Békésy, "Sensations on the Skin Similar to Directional Hear[ing, Beats, and Harmonics of the Ear," Journal of Acoustic Society](http://dx.doi.org/10.1121/1.1908938) of America, vol.29, no.4, pp.489–502, 1957.
- [10] [K. Fukuyama, N. Takahashi, F. Zhao, and H. Sawada, "Tactile Dis](http://dx.doi.org/10.1109/hsi.2009.5091060)play Using the Vibration of SMA Wires and the Evaluation of Perceived Sensations," IEEE International Conference on Human System Interaction, pp.685–690, 2009.
- [11] C. Jiang, K. Uchida, and H. Sawada, "Research and Development of Vison Based Tactile Display System Using Shape Memory Alloys," International Journal of Innovative Computing, Information and Control, vol.10, no.3, pp.837–850, 2014.
- [12] H. Sawada, Y. Nakamura, Y. Takeda, and K. Uchida, "Micro-vibration array using SMA actuators for the screening of diabetes," Proc. [6th International Conference on Human System Interaction, Sopot,](http://dx.doi.org/10.1109/HSI.2013.6577889) Poland, pp.620–625, June 2013.
- [13] A.B. Vallbo and R.S. Johansson, "Properties of cutaneous mechanoreceptors in the human hand related to touch sensation," Human Neurobiology, vol.3, no.1, pp.3–14, 1984.
- [14] P.J. Dyck, W.J. Litchy, K.A. Lehman, J.L. Hokanson, P.A. Low, [and P.C. O'Brien, "Variables influencing neuropathic endpoints: the](http://dx.doi.org/10.1212/wnl.45.6.1115) Rochester Diabetic Neuropathy Study of Healthy Subjects," Neurology, vol.45, no.6, pp.1115–1121, June 1995.
- [15] S. Tesfaye, A.J. Boulton, P.J. Dyck, R. Freeman, M. Horowitz, P. Kempler, et al, "Diabetic neuropathies: update on definitions, di[agnostic criteria, estimation of severity, and treatments," Diabetes](http://dx.doi.org/10.2337/dc10-1303) Care, vol.33, no.10, pp.2285–2293, Oct. 2010.
- [16] P.J. Dyck, "Detection, characterization, and staging of polyneuropa[thy: assessed in diabetics," Muscle Nerve, vol.11, no.1, pp.21–32,](http://dx.doi.org/10.1002/mus.880110106) Jan. 1988.

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