

1 **Effect of Joint Limitation and Balance Control for Gait Changes in Diabetic Peripheral**

2 **Neuropathy**

3

4 **Author** Hiroyuki Yamasaki ^{1*}, Yoshiro Abe ¹, Shunsuke Mima ¹, Mayu Bando ¹, Shinji Nagasaka ¹,

5 Yutaro Yamashita ¹, Kazuhide Mineda ¹, Akio Kuroda ², Munehide Matsuhisa ², Masahiro Takaiwa ³,

6 Ichiro Hashimoto ¹

7

8 ¹Department of Plastic and Reconstructive Surgery, Tokushima University Graduate School of

9 Medical Science, Japan

10 ²Diabetes Therapeutics and Research Center, Institute of Advanced Medical Sciences, Tokushima

11 University, Japan

12 ³Division of Science and Technology, Graduate School of Technology, Industrial and Social Sciences,

13 Tokushima University

14

15 **Abstract**

16 **Background:** Foot ulcers are the most physically disabling chronic complications of diabetes.
17 Prevention and management of foot ulcers are related to the quality of life and prognosis of diabetic
18 patients. The purpose of this study was to analyze the gait patterns of patients with diabetic peripheral
19 neuropathy and changes in their center of mass sway due to peripheral neuropathy to help prevent the
20 formation of foot ulcers and their recurrence after ulcer healing.

21 **Methods:** Forty-two subjects with diagnosis of DM consisted of three groups which were DM group
22 (neither neuropathy nor foot ulcer history), DPN group (with neuropathy and without foot ulcer
23 history), and DFU group (with neuropathy and foot ulcer history). We measured range of motion
24 (ROM) of the lower limb joints at resting position and center of mass sway at standing position. By
25 using 3-D gait analysis, lower limb joint angles in each walking phase and ROM during the during
26 walking, distance factors (step length and step width) were evaluated.

27 **Results:** Concerning the knee joint of the DFU group, function limitation at rest was not observed but
28 ROM limitation during walking was detected. Both of the function and ROM limitations were found
29 regarding the ankle joint of the DFU group. The step length ratio and the step width in the DFU group
30 were significantly lower and higher than the DM group, respectively. The sway distances in the DFU
31 group were higher than the DM and DPN group.

32 **Conclusions:** It is assumed in DFU group that there is a mixture of functional limitation of the
33 joints themselves and changes in gait due to decreased ability to maintain center of gravity.
34 As diabetic peripheral neuropathy progresses, the gait becomes small, wide and shuffle. Because this

35 gait pattern can induce increased planter pressure and shear forces, supporting joint movement during
36 walking will be able to reduce the incidence and recurrence of foot ulcers.

37

38 **Keywords: Type 2 diabetes mellitus, Foot ulcer, Diabetic neuropathy, Gait analysis, Center of**

39 **Mass Sway, Balance**

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41

42

43 **Introduction**

44 The prevalence of diabetic foot ulcers in the world is 1.5-10% and the incidence is 2.2-5.9% (1:Abbott
45 et al 1998, 2:Ramsey et al 1999, 3:Abbott et al 2002). Because foot ulcers precede 80-85% of diabetes
46 mellitus (DM)-related lower extremity amputations (4:Frykberg RG et al 2006), preventing and
47 managing foot ulcers is closely related to the quality of life and prognosis of diabetic patients
48 (5:Raspovic 2013). There are two main causes of diabetic foot ulcers, peripheral arterial disease and
49 peripheral neuropathy. It is reported that patients with foot ulcers caused by the peripheral neuropathy
50 are more common than the peripheral arterial disease (6:Moulik PK et al 2003). Because neuropathic
51 foot ulcers are mainly caused by sensory and motor neuropathy which is difficult to be treated, it is
52 very important to suppress ulcer development and prevent recurrence after healing. To prevent the
53 occurrence and recurrence of foot ulcers, footwears and insoles with high decompression performance
54 is reported to be effective, but the recurrence rate of foot ulcers is still as high as 40% (7:Bus SA et al
55 2013).

56 In addition to plantar dysesthesia caused by sensory neuropathy, DM patients are known to suffer
57 from muscle atrophy and limited range of motion (ROM) of joints due to glycosylation to proteins and
58 lipids and motor neuropathy (8:Wrobel J et al 2010). It has been pointed out that foot ulcers develop
59 as a result of morphological changes in gait due to the combined effects of these factors (9:Andersen
60 H 2012, 10:Giacomozzi C et al 2005, 11:Mueller MJ et al 1989). Although there have been some
61 studies in which detailed dynamic measurements and analyses of speed, pace, stride length, and pattern
62 about gait have been performed in DM patients, the mechanism of foot ulcer development has not

63 been elucidated (8:Wrobel J et al 2010). Furthermore, effect of body mass sway has been less
64 considered in relation to their gait.

65 The purpose of this study was to examine how the DM peripheral neuropathy affects gait changes
66 through analyzing joint movement at rest and during walking and evaluating center of mass sway in
67 patients with DM peripheral neuropathy. These analyses will be able to contribute to the elucidation
68 of the pathogenesis of foot ulcers and the probability of preventive strategies.

69

70 **Methods**

71 **1. Study participants**

72 Subjects were recruited from patients diagnosed with DM (type I and type II) at Tokushima University
73 Hospital between September 2017 and May 2019. All participants were classified into three groups
74 which were DM group (neither diabetic peripheral neuropathy nor foot ulcer history) for control, DPN
75 (diabetic peripheral neuropathy) group (with diabetic peripheral neuropathy and without foot ulcer
76 history), and DFU (diabetic foot ulcer) group (with diabetic peripheral neuropathy and foot ulcer
77 history). Exclusion criteria were subjects who require any assisting apparatus to walk, suffer from
78 peripheral arterial disease in which skin perfusion pressure less than 40 mmHg at any one location,
79 and could not give consent for this study. Subjects with two of the symptoms that are loss of Achilles
80 tendon reflex, decreased vibration perception or decreased plantar perception were considered to have
81 diabetic peripheral neuropathy. This study was approved by the Clinical Research Ethics Review
82 Committee of Tokushima University Hospital, and informed consent was obtained for all subjects

83 prior to the study.

84

85 **2. Range of Motion of Lower Leg at Resting Position (ROM-Rest)**

86 The ROM of the hip joint, knee joint, ankle joint, and metatarsophalangeal (MTP) joint of the first toe
87 were measured at a supine position on a bed. Active and passive ROM for flexion and extension were
88 measured at each joint. We defined Range of Motion at Resting Position (ROM-Rest) as the sum of
89 the ROM for flexion and the ROM for extension of each joint (Table 1).

90

91 **3. Gait analysis**

92 Nine reference points were set up on the floor at every 1m in length and 0.5m in width on a rectangle
93 floor of 2m in length and 1m in width. Five points were set up at every 0.28m in height vertically from
94 each reference point. Therefore, total of 45 points were placed for the measuring area. The subjects
95 walked on a 2m walking path with a 2m approaching path, wearing sneakers at their own comfortable
96 speed for gait analysis. Their walking was recorded with a video camera (EX-100F CASIO, Japan) at
97 120 frame per second (fps) from front and side directions. The captured video images were analyzed
98 offline with Frame-DIAS 6 2D version (DKH, Q'sfix, Japan). The gait process was separated into 7
99 phases and analyzed in these phases which are Loading Response phase, Mid Stance phase, Terminal
100 Stance phase, Pre Swing phase, Initial Swing phase, Mid Swing phase, and Terminal Swing phase
101 (12:Perry J 2010).

102 Reflective markers were placed on the anterior superior iliac spine, greater trochanter, lateral

103 epicondyle of femoral, lateral malleolus, lateral heel, lateral fifth toe MTP joint, and second toe
104 phalanges. The angles of the hip, knee, ankle, and toe MTP joints were measured by analyzing the
105 lateral-image gait movies. The angle of the hip joint was measured by connecting the three points of
106 the anterior superior iliac spine, the greater trochanter, and the lateral epicondyle of femoral. Similarly,
107 the angles of the knee joint, the ankle joint, the toe MTP joint were measured.

108 The joint angles measured at the middle of each walking phase were compared among the 3
109 groups. Then the difference between the maximum and minimum points of each joint angle in a
110 walking cycle was defined as "Range of Motion during walk (ROM-walk)" (Figure 1, Table 1).

111 The distance between the bilateral heel markers in a walking cycle were measured from the lateral
112 video and defined as step length. The distance between the bilateral heel markers in a walking cycle
113 was measured from the frontal video and defined as step width. Because there was a significant
114 difference in height between the groups, the measurements of the distant factors were divided by each
115 height. Ratio of the step length and step width to each height were calculated (Table 1).

116

117 **4. Center of Mass Sway at Standing Position**

118 While the subjects were standing on a measuring device (Wii Fit, Nintendo, Japan), movement of
119 their center of mass was recorded. Measurements were performed with eyes open and closed at 2 kinds
120 of foot width of 0 cm and 10 cm. Distance between the center of the device and the recorded center of
121 mass of the subject was measured continuously for 30 seconds. Then the average sway distance was
122 calculated (Table 1).

123

124 **5. Statistical analysis**

125 IBM SPSS Statistics 25.0 (2017, Stats Guild Inc. Japan) was used to carry out statistical tests.

126 The Kruskal-Wallis test with a significance level of 0.05 was performed on all of the mean values to
127 reveal any differences among the three groups.

128

129 **Results**

130 **1. Study participants**

131 Forty-two subjects (man /woman: 25 /17, mean age \pm SD: 58.9 \pm 14.8 years) participated in the study
132 (Table 2). Among the three groups, age, weight, and BMI were not significantly different by Kruskal-
133 Wallis test. The height in the DFU group was significantly higher than it in the DM group, because all
134 participants in the DFU group were men.

135

136 **2. ROM at Resting Position (ROM-Rest)**

137 As the diabetic peripheral neuropathy progress, tendency of decrease in ROM-Rest of each joint was
138 observed among the 3 groups (Figure 2). There was no significant difference in the ROM-Rest for
139 both the hip and knee joints. In the ankle joint, both of the active and passive ROM-Rest of the DFU
140 group were significantly smaller than these of the DM group ($p < 0.01$). In the MTP joint, both of the
141 active and passive ROMs-Rest of the DFU group were significantly smaller than these of the DM
142 group ($p < 0.01$) and the DPN group ($p < 0.05$).

143

144 **3. Gait analysis**

145 **3-1. Joint angle in each frame during walk**

146 As results of comparing joint angles in each walking phase among 3 groups (Figure 3), angles of hip
147 joint in the DM group are smaller than these in the DPN and DFU groups during almost all walking
148 phases, and the hip joint angle in the DPN group was significantly larger than in DM group at the
149 Initial Swing phase. Concerning the knee joint, the decrease of the joint angle of the DFU group was
150 characteristic at the swing phase. Limitations of the ankle joint angle were observed in the DFU group
151 in the stance and swing phase although no significant difference was observed. Significant limitations
152 of the MTP joint angle in the DPN and DFU groups at the stance phase. Focusing on the DPN group,
153 the angle of the hip joint was greater than it in the DM group and the joint angle of the knee joint was
154 greater than it in the DFU group in the Initial Swing phase but the angle of the MTP joint was
155 significantly lower than in the DM group in the Pre swing phase.

156

157 **3-2. ROM during walk (ROM-Walk)**

158 Regarding angles of ROM-walk of hip joint, no significant difference was observed among 3
159 groups (Figure 4). The angles of ROM-walk in the DFU group were significantly smaller than it in the
160 DM group in the knee joint, the ankle joint, and the MTP joint. The angles of ROM-walk in the DPN
161 group were significantly smaller than it in the control group in the MTP joint.

162

163 **3-3. Distance factor**

164 The step length ratio in the DFU group was significantly smaller than the DM group and DPN
165 groups (Figure 5). The step width ratio in the DFU group was significantly larger than the DM group.

166

167 **4. The Center of Mass Sway**

168 The average sway distances in the DFU group were larger than the DM and DPN group (Figure 6).
169 Significant difference was observed in the measurements in the condition of foot width 10cm with
170 closed eyes and in the condition of foot width 0cm with open and closed eyes.

171

172 **Discussion**

173 In the present study, ROMs of the 4 joints in leg were measured in 2 ways which were the ROM-Rest
174 and the ROM-Walk. Decrease in the ROM-Rest and in the ROM-Walk shows joint function limitation
175 at rest and joint ROM limitation during walking, respectively. The angles in the ROM-Rest and the
176 ROM-Walk in both the ankle and MTP joints tended to decrease as diabetic peripheral neuropathy
177 progressed. The limitations of these ROMs were found to be more advanced at the MTP joint than at
178 the ankle joint among the 3 groups. This finding is consistent with distal axonal degeneration in which
179 diabetic peripheral neuropathy emerges from the periphery (13:Cashman CR 2015). On the other
180 hand, significant difference was not detected in the ROM-Rest of the hip and knee joint. However, we
181 found significant difference in the ROM-Walk of the knee joint in the DFU group. These results
182 revealed that the DFU patients don't have functional limitations of the knee joint at the resting position

183 but have the limitations of the ROM in the knee joint in their walking behavior. Interestingly,
184 significant limitation of ankle joint motion was not found in each walking phase although the
185 significant difference was observed in the ROM-Rest and ROM-Walk between the DM group and the
186 DFU group. Previous studies in clinical population have yielded conflicting results, particularly at
187 ankle joint motion (14:Rao S, Saltzman, 15:Yavuzer G, 16:Sacco IC). It is thought that the joint
188 function limitation and joint ROM limitation in the ankle joint of DFU patients was able to be
189 measured in the present study.

190

191 To observe the results of the joint angles in each phase, characteristics of gait in each group can be
192 revealed. The joint angles at the ankle and MTP joint in the DM group tended to be more than these
193 in DPN and DFU groups, however, concerning the hip joint, flexion in the swing phase of the DM
194 group were less than that of the DPN group, especially at the initial swing phase. The effect of diabetic
195 neuropathy on the motion at the hip has been unclear. Two studies found a decrease in the range of hip
196 flexion in DPN patients when compared with non-diabetic participants (5:Raspovic, 15:Yavuzer G).
197 However, Gomes et al. (17:Gomes AA) found an increase in flexion at the hip in patients with DPN,
198 which they believed was due to a compensatory effect for the loss of motion at distal joints. Our results
199 support the complementary motion of the hip joint observed in the DPN group.

200

201 Our analysis for distance factors revealed decreased step length and increased step width in the DFU
202 group. The significant difference in the distance factors and in the joint ROM limitation observed

203 between the DM and DFU groups in the present study are suggesting that these changes are manifested
204 after the appearance of foot ulcers. However, similar changes have been reported even in DM patients
205 without neuropathy compared to participants without DM (15:Yavuzer G 2006). Few researches have
206 simultaneously measured these distant factors among patient groups with/without DM and
207 with/without neuropathy, and further research is needed to determine how advanced diabetes
208 progresses to abnormalities related to the step length and width.

209

210 Results of our 4 measurements in the sway distance showed significant increase in the DFU group. It
211 is pointed out that damage to vestibular, autonomic, and somatic nerves with DM peripheral
212 neuropathy affects to gait stability (18:Resnick HE et al 2000, 19:Petrofsky J 2005). The vestibular
213 neuropathy often precedes the loss of sensation in the feet (20:Di Nardo W et al 1999). The group II
214 afferent fibers, which are sensory nerves from muscle spindles, play an important role in feedback
215 control under static and dynamic conditions including the stance phase of walking. It is assumed that
216 the conduction velocity of II fibers is reduced in patients with DM peripheral neuropathy (21:Nardone
217 A 2006, 22:Nardone A 2014). The increase in the sway distance found in the present study is thought
218 to be related with these kinds of peripheral neuropathy and to be associated with the increase of step-
219 width ratio. We believe that dynamic control of balance during gait is impaired with the progression
220 of DM peripheral neuropathy and that compensating for the instability by increasing of the step width
221 prevents falls during gait (23:Allet L et al 2008). The primary measurements on previous articles
222 were gait speed and step length but the importance of step width has often been underestimated

223 (24:Lamola et al 2015). Furthermore, mass sway has been studied in relation to fall risk, but its
224 association with gait style has been less frequently reported. We think that the body mass sway
225 potentially affects their gait, especially step width. After joining the results of the distant factors, joint
226 ROM limitations, and joint function limitation, it can be assumed that as diabetic peripheral
227 neuropathy progresses, the gait becomes "shuffle walking" with small step length, wide step width,
228 and little movement below the knee joint. As results of the present study, it is assumed in DFU group
229 that there is a mixture of functional limitation of the joints themselves and changes in gait due to
230 decreased ability to maintain center of gravity. In this study, we measured center of mass sway using
231 the Wii Fit, which has been reported to be as accurate as a force platform (25:Clark et al 2010).
232 Because it is portable, widely available, and less expensive than a force platform, we believe it is a
233 suitable tool for standing balance assessment in general clinical practice.

234

235 Although the shuffle walking and the enlarged step width leads to a stable gait to avoid falling during
236 walking, the increase of pressure and shear force in plantar possibly induce callositas formation and
237 lead to foot ulceration. A limitation of this study is that no measurement of plantar pressure, which is
238 affected by changes in gait, was performed. Future study should be performed in relation between gait
239 changes and planter pressure. In the present study, joint restrictions, distance factor and mass sway
240 abnormalities were not significantly different in the DPN group compared to the DM group, but were
241 significantly more pronounced in the DFU group. It is thought to be important to detect DPN in early
242 stage of DM condition and to delay or stop the transition to DFU by controlling blood glucose and

243 using walking aids such as insole or orthopedic shoes.

244

245 **References**

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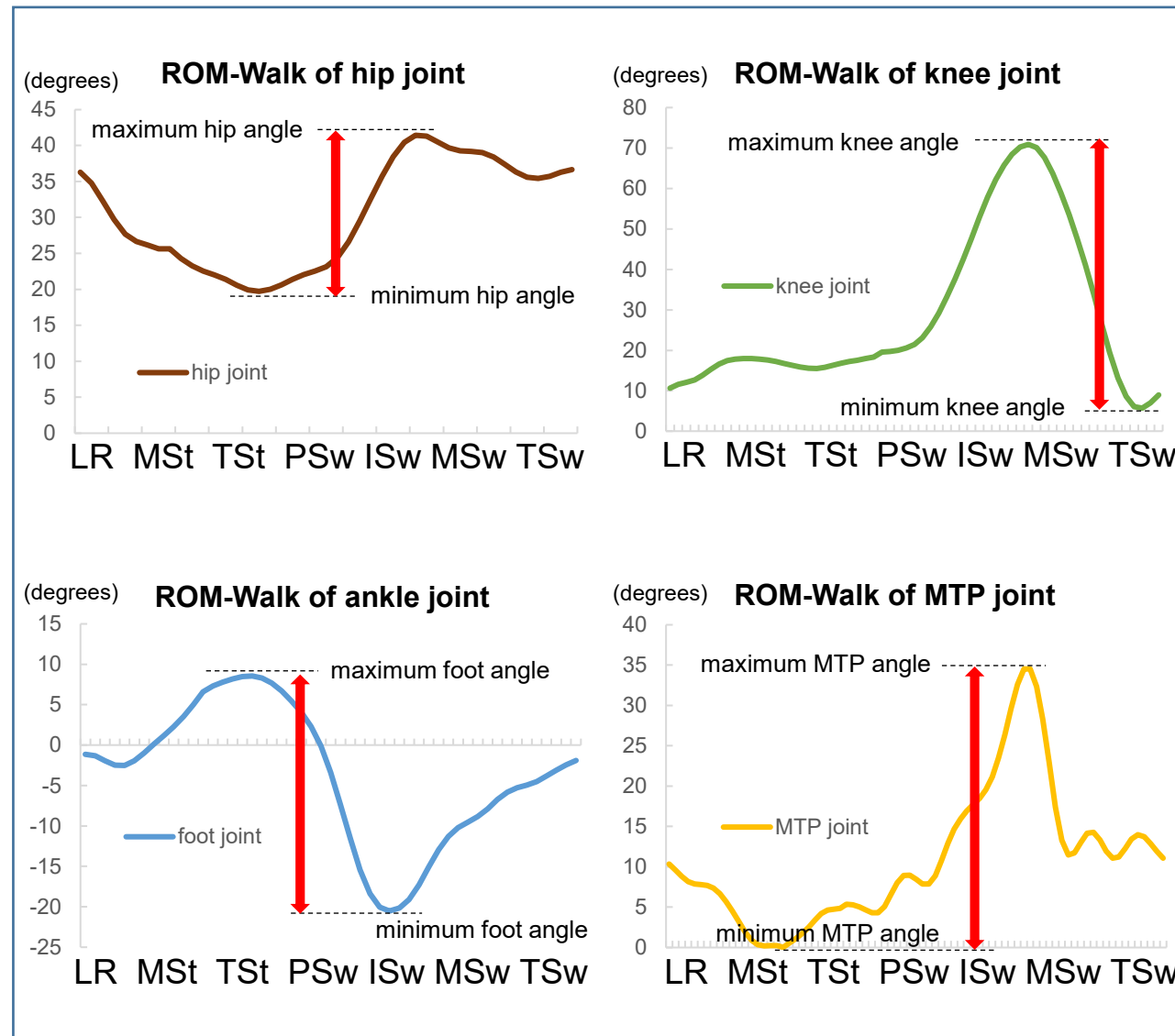


Fig. 1

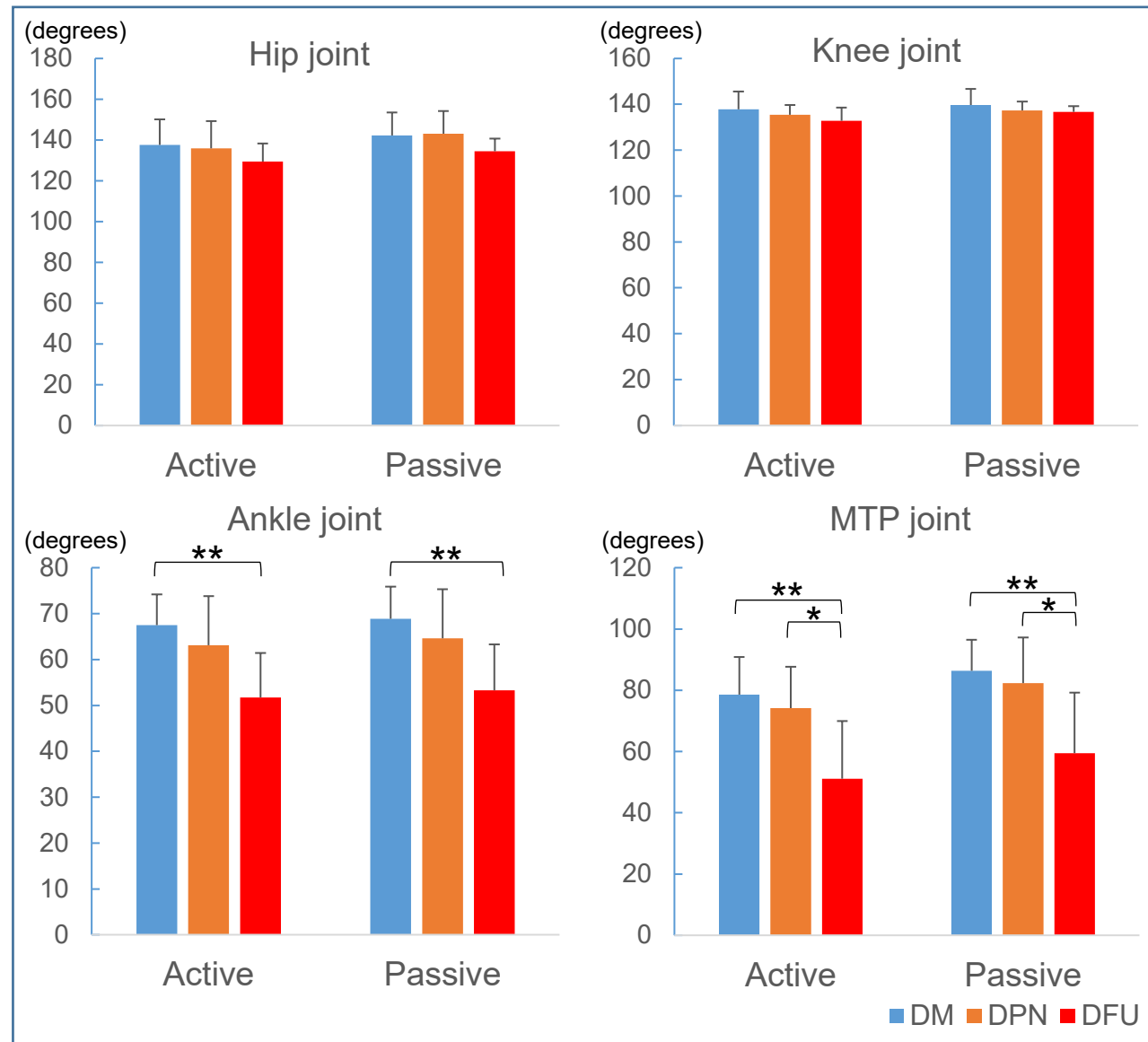


Fig. 2

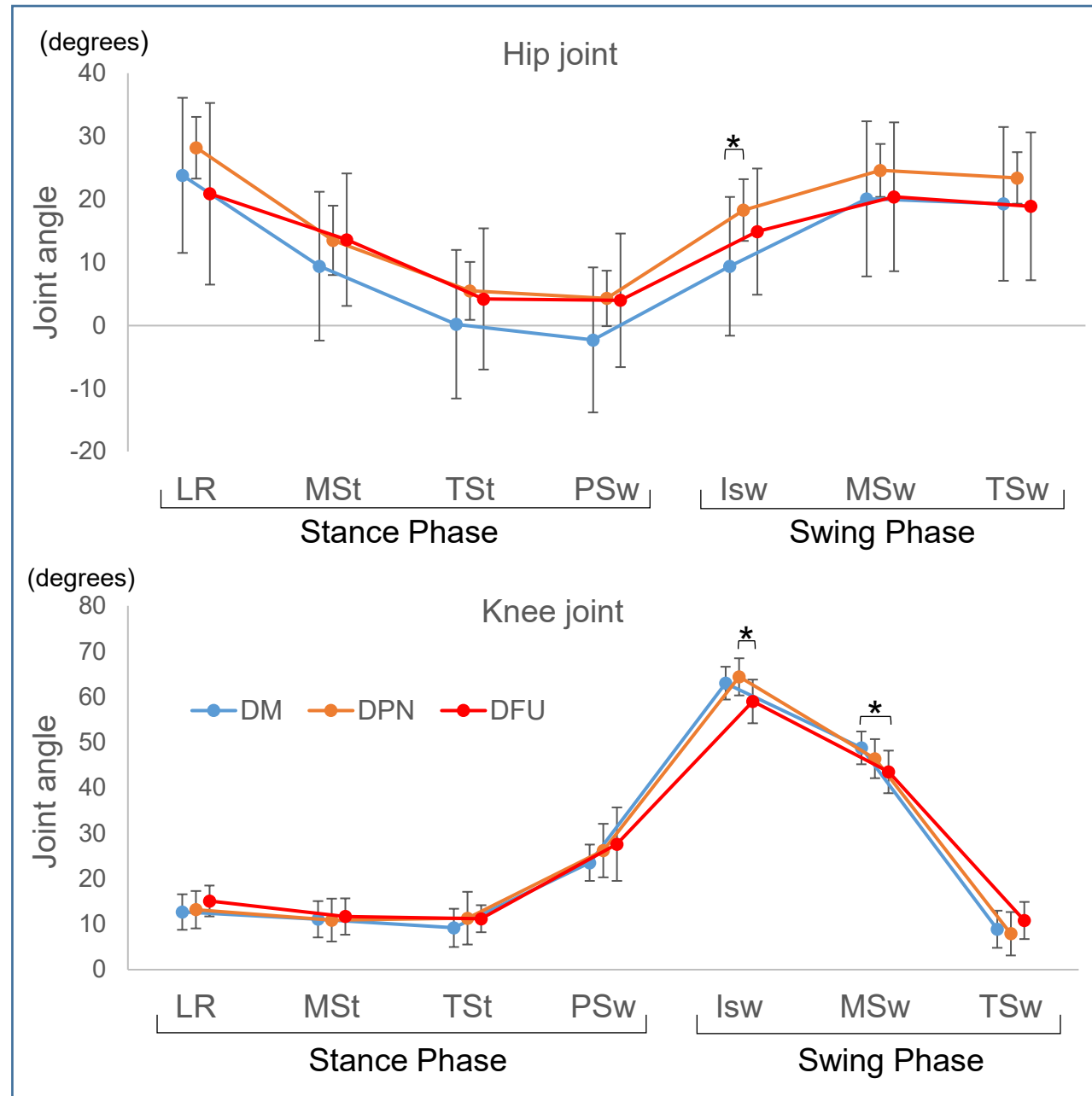


Fig. 3A

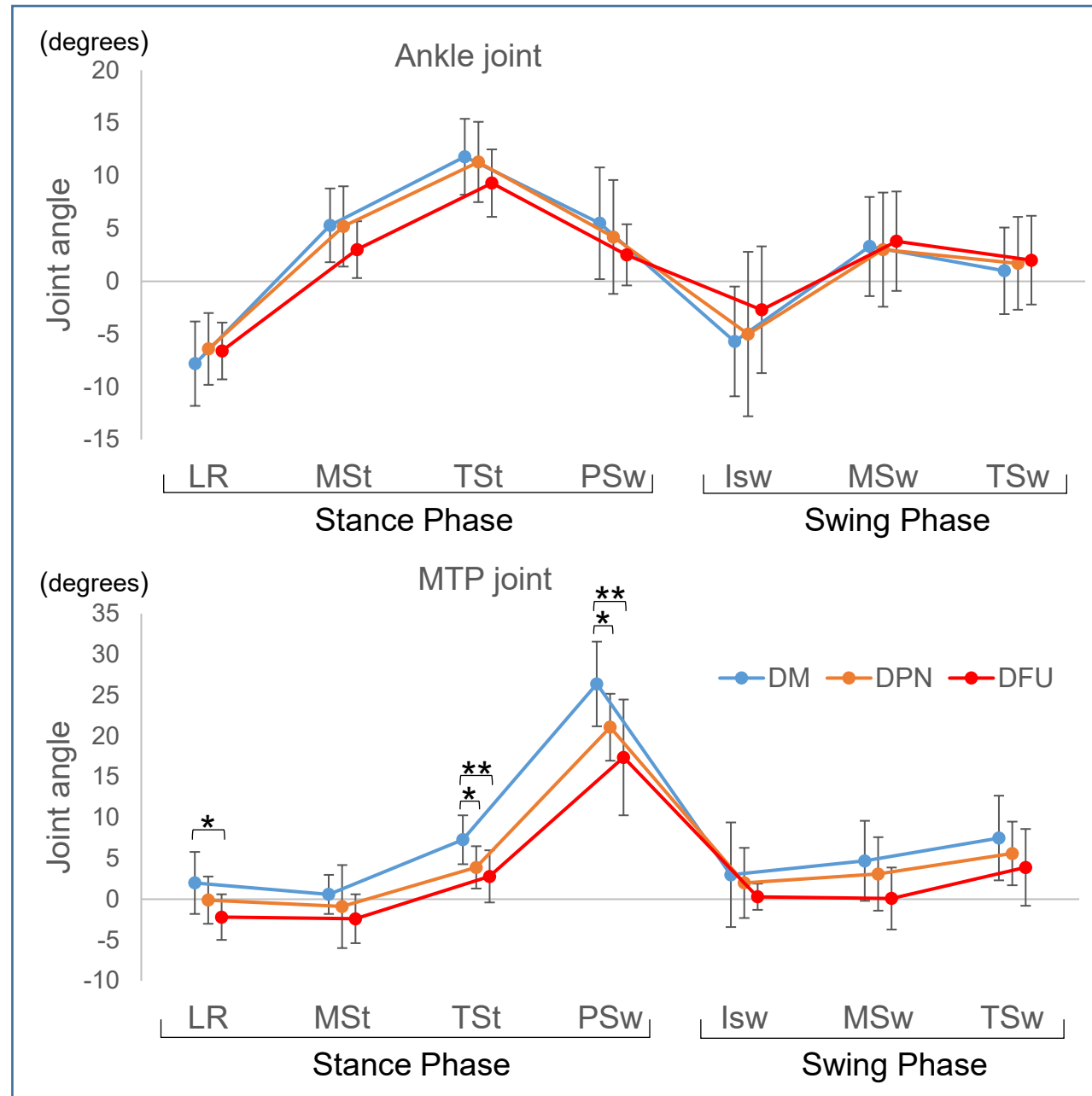


Fig. 3B

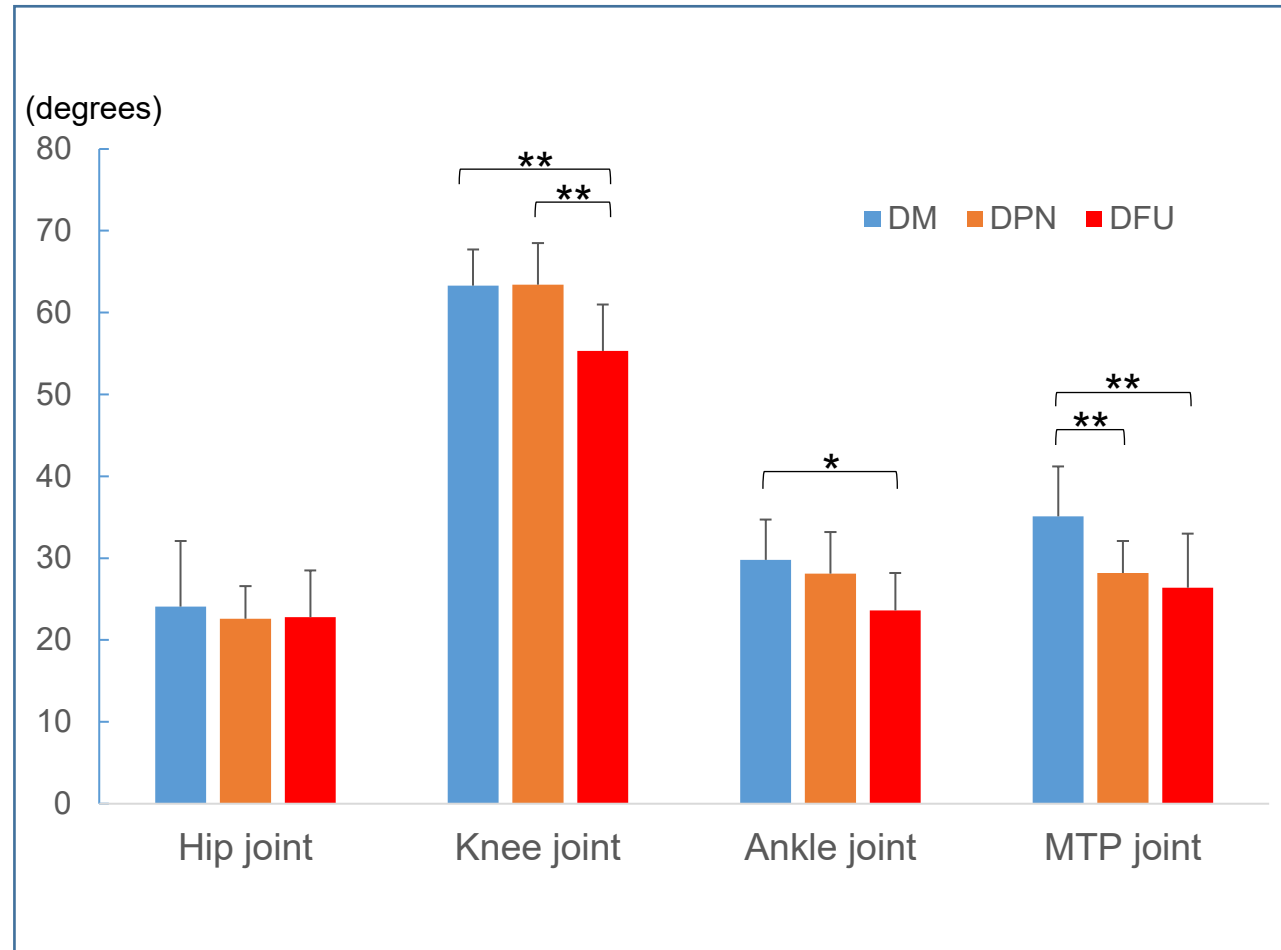


Fig. 4

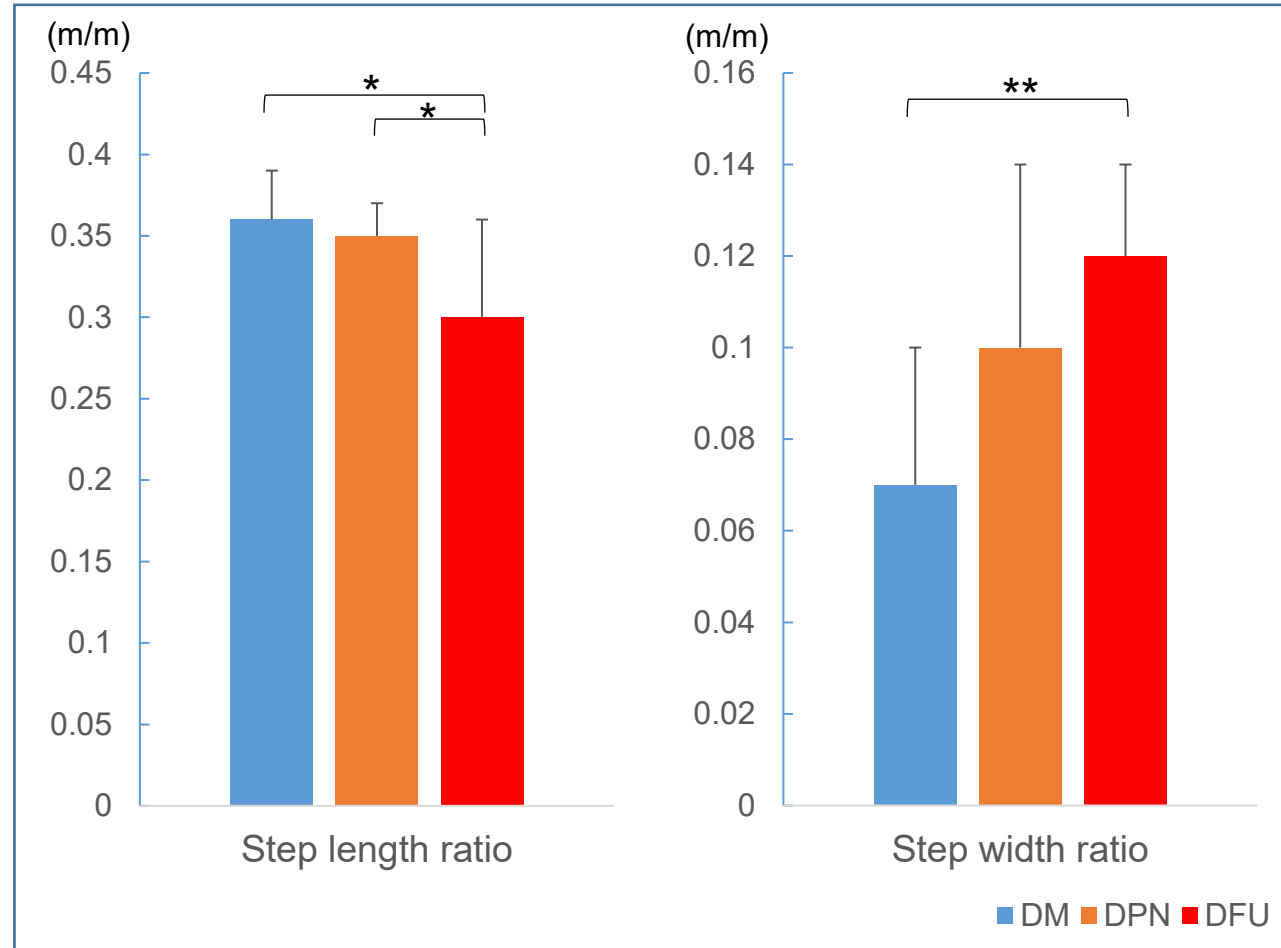


Fig. 5

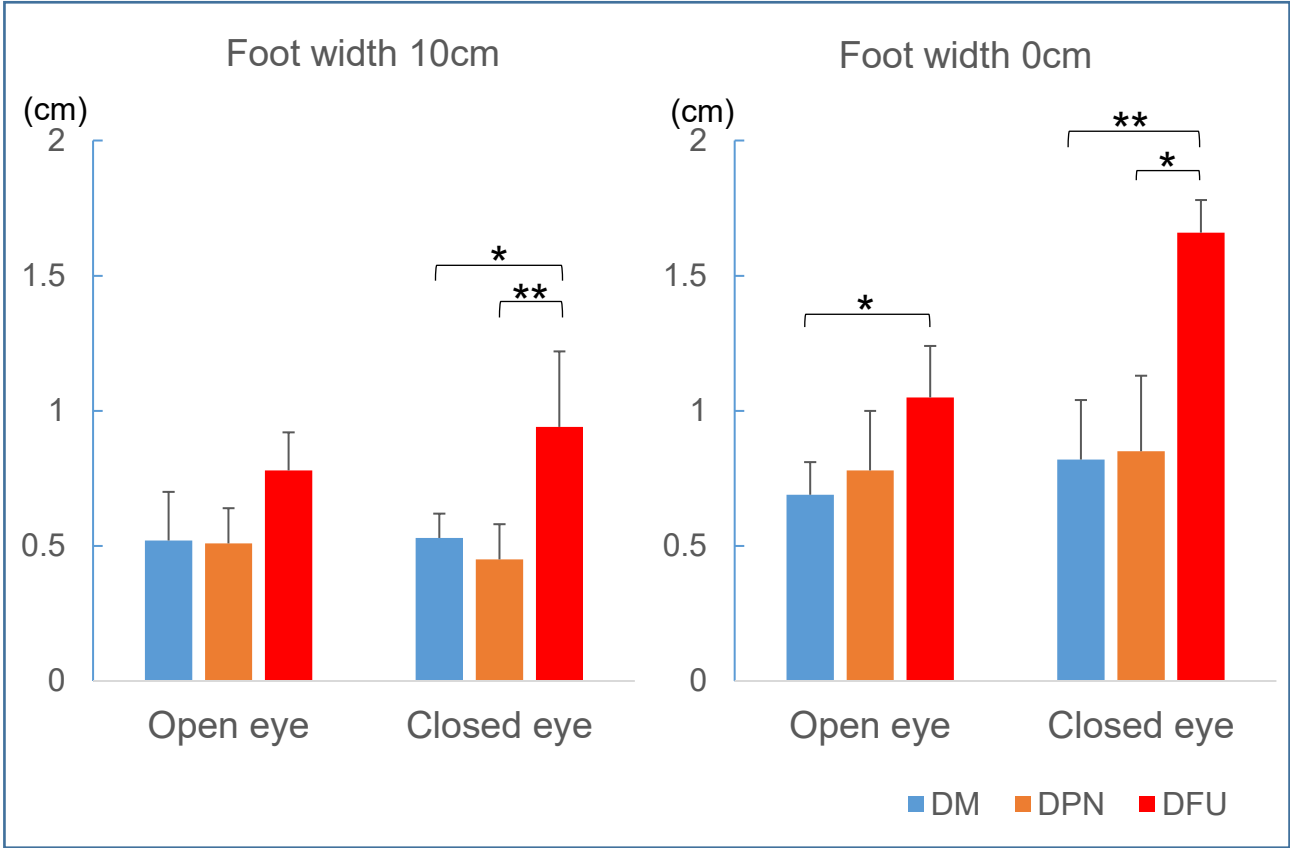


Fig. 6

Table 1. List of measurements in the study

Measurements	Definition/ Method
1. Range of Motion (ROM)	
1-1. ROM at Resting Position (ROM-Rest)	Active and passive ROM measured at resting position
1-2. Joint angle in each frame during walk	Analyzing joint angle through 3 reflective markers in each walking phase during walking
1-3. ROM during walk (ROM-Walk)	Difference between the maximum and minimum angle on each joint in a walking cycle
2. Distant factors	
2-1. Step length ratio	Distance between bilateral heel markers measured from the side in a walking cycle divided by height.
2-2. Step width ratio	Distance between bilateral heel markers measured from the front in a walking cycle divided by height.
3. Center of mass sway	
3-1. Average sway distance	Average distance between the center of the device and the center of mass of the subject

Table 2. Clinical characteristics of the subject groups

Group	DM	DPN	DFU	p-value
n (man/woman)	20 (8/12)	15 (10/5)	11 (7/0)	
Age (years)	59.2 ± 13.9	57.8 ± 17.3	60.3 ± 13.8	0.943
Body weight (kg)	63.2 ± 16.4	65.1 ± 10.7	77.5 ± 18.2	0.058
Height (cm)	158.3 ± 8.9	163.1 ± 8.6	172.8 ± 9.2	0.007
BMI (kg/m ²)	25.1 ± 5.0	24.4 ± 2.7	25.7 ± 4.2	0.690

Values are shown as mean ± SD.

DM: diabetes mellitus without diabetic peripheral neuropathy, DPN: diabetic peripheral neuropathy without foot ulcer history,

DFU: diabetic peripheral neuropathy with foot ulcer history, BMI: body mass index