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## RESEARCH: PATHOPHYSIOLOGY

# Pedobarographic Statistical Parametric Mapping may identify specific plantar pressure patterns in patients with diabetes mellitus among different degrees of peripheral neuropathy: A pilot study

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## Abstract

**Aims:** Peripheral neuropathy (PN) in patients with diabetes can lead to changes in the distribution of plantar pressure during walking, which can be recorded with pedobarography. Compared to traditional spatial data reduction analysis, the pedobarographic Statistical Parametric Mapping (pSPM) allows comparison of the footprints with the advantage that sub-regions do not need to be defined *a priori*. Aim of the study was to test the potential of pSPM in identifying specific distribution of spatial pressure in different stages of PN.

**Methods:** PN was defined according to usual tools (i.e., tendon reflexes and sensory tests). Four groups were compared: patients with diabetes without PN (n = 24; 239 steps); with signs of mild PN (n = 12; 117 steps); with signs of severe PN (n = 6; 52 steps) and a control group without diabetes (n = 12; 124 steps). Traditional spatial data reduction and pSPM were performed to compare plantar pressures in the different groups.

**Results:** In patients with PN, traditional spatial data reduction analysis showed lower plantar pressures with PN severity. pSPM analysis is able to better define the initial changes: mild PN patients presents higher pressures on the anterior side of the metatarsal heads compared to patients without neuropathy. Patients with severe PN are characterised by higher pressures under the medial foot arch compared to other groups.

**Conclusions:** pSPM may identify specific features of plantar pressure distribution during walking in patients with mild PN and may become a useful screening tool for a timely identification of this complication.

## KEYWORDS

arthropathy neurogenic, biomechanical phenomena, foot diseases, forefoot human, gait, muscle strength, polyneuropathies, translation

Antoine Chatrenet, Bruno Beaune, Giorgia Barbara Piccoli, and Baptiste Morel equally contributed to the paper.

### Novelty statement

- Peripheral neuropathy in patients with diabetes induces changes in plantar pressure but this alteration is not detectable with the current diagnostic tools until the more severe stages of the pathology develop.
- The present study found that less pressures is applied under the rearfoot before the first clinically overt signs of peripheral neuropathy. Moreover, after the appearance of the first clinical symptoms, we showed an anteriorisation of the plantar pressures beneath the forefoot.
- Over time, the clinical translation of these findings will help timely identifying patients at risk before the development of symptoms.

## 1 | INTRODUCTION

Diabetes mellitus is characterised by several systemic complications including peripheral neuropathy (PN). This insidious complication, which is chronically under-evaluated by the medical staff, may cause devastating consequences due to neuropathic ulcers, infections and amputations.<sup>1</sup> In the long term, PN patients show sensitivity disorders and impaired muscle function<sup>2</sup> associated with reduced walking speed and loss of dynamic balance.<sup>3</sup> These functional impairments can cause biomechanical alterations in gait (e.g., alteration in the foot landing pattern, lower absorption capacity and propulsion inefficiency)<sup>4,5</sup> leading to pathological changes in the distribution of plantar pressures.<sup>6-9</sup>

In the clinical practice PN is usually assessed by testing patients' sensitivity to a stimulus, because tests such as these are inexpensive and easy to carry out. For instance, standardised cutaneous pressure is applied with a 10 g monofilament on different plantar areas of the foot, while the patient's eyes remain closed. This test makes it possible to assess the severity of the PN, but its time consuming and its sensitivity is operator-dependent.<sup>10</sup> Another method used to diagnose PN is electromyography. However, the intrinsic limitation of this method is that it mainly evaluates the largest nerves, whereas PN damages the smaller nerve fibers in the initial phases of the disease.<sup>11</sup> Consequently, electromyographic evaluation is effective to detect alterations occurring during the later stages of PN, but is not sensitive enough in early PN.<sup>7,12-14</sup>

The biomechanical variations involved during walking can be assessed using the pedobarographic method, which allows a reliable measurement of plantar pressures.<sup>15</sup> Patients with PN present with foot supination,<sup>6,13</sup> higher metatarsal peak pressure and higher pressure-time integral compared to those without PN.<sup>8</sup> Once again, these changes are associated with advanced PN, when clinical diagnosis is usually straightforward.

Previous studies investigated plantar pressures in PN patients during walking using the traditional spatial data reduction analysis, in relation to pre-defined anatomical regions of the foot (e.g., usually between 3 and 10).<sup>7,13,16</sup> Variables such

as peak pressure or mean pressure are then extracted in relation to each foot region. This method is useful but represents an oversimplification and specific information may be lost.<sup>17</sup>

In 1995, Friston et al. (1995) proposed the Statistical Parametric Mapping method, performing a spatially extended statistical analysis to test hypotheses about pixel/voxel effects (smallest functional unit in 2d and 3d analysis respectively), as opposed to discrete regions.<sup>18</sup> This method, initially used to evaluate neuroimaging tests, has been adapted to biomechanics and specifically to pedobarographic data by Pataky et al. (2008; 2010).<sup>15,17,19</sup> With the pedobarographic Statistical Parametric Mapping (pSPM) method, the footprint can be evaluated as a whole, with the advantage that hypotheses relating to differences at specific spatial points do not need to be defined *a priori*. To the best of our knowledge, this promising technique has never been applied in patients with diabetes.

Thus, the aim of this pilot study was to test the advantage of pSPM in identifying the specific patterns of spatial pressure distribution in patients suffering from diabetes without PN and with mild to severe PN compared also to controls without diabetes mellitus.

## 2 | MATERIALS AND METHODS

### 2.1 | Patients and controls

Patients and controls were recruited consecutively from the Endocrinology Outpatients clinic (day hospital) devoted to diabetes foot management at the Centre Hospitalier Le Mans, between December 2018 and March 2019.

All patients with diabetes mellitus were asked by the senior physician to enrol in the study. Control subjects were recruited among patients' accompanying persons, selecting persons without diabetes mellitus. All controls were matched for gender and plantar shape (stratified by the Sztriter-Godunov index, as expressed in Supplementary Figure S1).<sup>20</sup>

Exclusion criteria were i) lower limb amputation, ii) presence of orthoses or prostheses, iii) history of sensory impairment or severe pain, iv) ulcers or disabling foot deformations,

v) PN of origin other than diabetes mellitus, vi) established peripheral vascular disease, and vii) grossly asymmetrical PN at baseline clinical assessment.

## 2.2 | Tests and assessments

All individuals took part in a single experimental session, chronologically composed of 1) assessment of Neuropathy Disability Score (NDS), 2) two 10-meter tests, 3) pedobarographic measurement during gait and 4) maximal voluntary contraction of the left and right ankle dorsiflexor muscles.

### 2.2.1 | Neuropathy disability score

We used a simplified NDS assessment, based on the testing of Achilles and patella tendon reflexes plus sensory examination, which includes the cutaneous pressure perception threshold (assessed using a 10 g monofilament) and the vibration perception threshold (assessed at 128-Hz with a tuning fork). A detailed description of the test is available in Supplementary Figure S2. The temperature and the pain tests were omitted, based upon their strict correlation with pressure perception threshold and in order to reduce discomfort and testing time.<sup>21</sup> The test resulted in a 0 to 14 score, where 0 means no clinical PN signs, 1–3 mild PN and 4 or above severe PN.<sup>8</sup>

### 2.2.2 | 10-meter walking test

The participants were asked to walk in a long hall the defined distance in their outdoor-shoes. Time was recorded with a handheld chronometer and patients were unaware of the registration area.<sup>22</sup> The spontaneous gait speed was calculated as the average of two walking tests.

### 2.2.3 | Maximal voluntary contraction

Participants performed a maximal isometric voluntary contraction of the ankle dorsiflexor muscles for each leg. To do so, they sat in a chair and had their hips, knees and ankles flexed at 90°, their arms hanging and their chest upright.<sup>23</sup> A 1000 N Force gauge (Kern and Sohn GmbH, Germany) was placed at the top of the metatarsophalangeal joint, attached to a height-adjustable table. Subjects were asked to raise up their forefoot as forcefully as they could while keeping their heels on the ground. The examiner provided vigorous vocal encouragement. The mean of the left and right maximal force was calculated and normalized to body mass (%BM).

## 2.2.4 | Dynamic plantar pressures analysis

The analysis was performed in two steps. A first recording was taken in an orthostatic static position on the Zebris FDM-S plantar pressure platform (Zebris Medical GmbH Inc., Germany; L = 69 x W = 40 x H = 2.1 cm; 2560 sensors;  $\pm 5\%$  accuracy;  $<3\%$  hysteresis; sample rate of 120 Hz) equipped with Zebris FDM 1.14 software. Subsequently, a second recording is performed after a familiarisation period, the dynamic pedobarographic test was performed: the participants walked comfortably until they reached the mean spontaneous gait speed, calculated based on the 10-meter tests (tolerance =  $\pm 10\%$ ). At this point, all the subjects performed two walking tests of 30 seconds on the Zebris platform, with a one-minute recovery period between each test.

The Zebris software automatically built the footprint area according to the displacement of the foot's center of pressure. The mean force ( $F_{\text{mean}}$ , [N]) was automatically calculated in forefoot and rearfoot areas, and the maximum force ( $F_{\text{max}}$ , [N]) and peak pressure ( $P_{\text{max}}$ , [N.cm<sup>-2</sup>]) were calculated for forefoot, mid-foot and rearfoot sub-regions. All the values were then normalised according to body mass.

According to Pataky (2010), a second analysis of the footprints by means of pSPM was conducted using the spm1d package v0.4.3 with Matlab v2018a (MathWorks corp., USA).<sup>19</sup> The “normalised foot” was calculated and expressed as the mean plantar pressure of each step, normalised for total pressure, foot size and foot progression angle (Appendix 1).<sup>24</sup> To create the “normalised foot”, the plantar pressure pattern was rotated over the foot progression angle and normalised for the foot size by performing a spline interpolation in order to obtain one value per percentage of length/width, so that in the end each step was a 100 x 100 matrix. Each cell of each step matrix was then divided by the sum of the whole step matrix to obtain the relative pressure distribution. Finally, a vertical symmetry transformation was applied to allow to compare the left and right feet.

## 2.3 | Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics v.14 (IBM corp., USA). Normality of series was tested using the Shapiro-Wilk test and homoscedasticity was tested using the Levene's test.

In accordance with the distribution of the series, one-way analysis of variance (ANOVA) or Kruskal-Wallis tests were used to compare anthropometrics variables. Two-way ANOVA was applied to compare variables of interest (i.e., plantar pressure parameters as  $F_{\text{mean}}$ ,  $F_{\text{max}}$  and  $P_{\text{max}}$ ) for group and left or right side when normality and homoscedasticity hypotheses were confirmed. Alternatively, if the variance was not equally distributed, Brown-Forsythe's homogeneity

correction was applied. The Bonferroni's post-hoc test was used in case of homoscedasticity to compare groups. Otherwise, Tamhane's post-hoc test was used.

Cohen's *d*, which is a quantitative measure of the magnitude of an effect, was calculated for post-hoc comparisons (0.01 = very small; 0.2 = small; 0.5 = medium; 0.8 = large; 1.2 = very large; 2.0 = huge<sup>25,26</sup>). The minimum Cohen's *d* values were calculated with G\*Power v3.1 (Düsseldorf Univ., Germany) to control for the adequate power of the comparisons (i.e., 80% of statistical power and 5% alpha risk). Only the differences which satisfying this minimum power of comparison will be considered in this study.

Fisher's exact test was used to compare categorical data (e.g., foot plantar forms) between groups. See Appendix 2 for additional information about the pSPM analysis. A two-tailed alpha risk was set at 0.05.

## 2.4 | Ethical issues

The study was conducted in accordance with the principles of the declaration of Helsinki and was approved by the Ethics Committee of the Centre Hospitalier Le Mans (June 22th 2020). All individuals gave their written informed consent for their participation.

## 3 | RESULTS

### 3.1 | Baseline data

The study included 42 patients and 12 controls. The study population is relatively old and the majority of individuals included are men (i.e., controls: 83.3%; patients with diabetes: 71.4%; Supplementary Table S1).

Patients with diabetes were scored according to the results of the NDS test and divided into three groups: patients without PN (*n* = 24; 66.7% male), patients with mild PN (*n* = 12; 83.3% male), and patients with severe PN (*n* = 6; 66.7% male). Anthropometric data are shown in Table 1. Patients with an NDS score indicating mild PN exhibited sensitivity deficiency in the toes; patients with an NDS score indicating severe PN exhibited absence of foot sensitivity and absence of Achilles and patella tendon reflexes (Supplementary Figure S2). The study population's body mass index was relatively high and obesity was more frequent in patients with severe PN. The average time since diagnosis of diabetes was about 13 years, with no difference across groups; similarly, glycated haemoglobin level (last available data) was not correlated with PN severity. The minimum Cohen's *d* values were: 1.02 for the comparison of the control or the mild-PN vs. the non-PN group; and 1.20 for the comparison of the control vs. the mild-PN; 1.49

TABLE 1 Baseline data

	No-neuropathy				<i>p</i> -value
	Controls	Non-PN	Mild PN	Severe PN	
<i>n</i>	12	24	12	6	
NDS (a.u), mean [CI]	-	0	1.5 [1.0–1.9]	7.9 [4.0–12.3]	<0.001
Age (years), mean [CI]	69.2 [63.4–74.8]	57.2 [50.6–63.8]	59.8 [52.1–67.5]	65.7 [57.1–74.2]	0.067
Gender (% males)	83.3%	66.7%	83.3%	66.7%	0.587
Body weight (kg), mean [CI]	76.4 [70.1–82.6]	75.6 [70.5–80.6]	90.8 [77.5–104.2]	100.6 [95.0–106.2] <sup>a,b</sup>	<0.001
Height (m), mean [CI]	1.66 [1.61–1.70]	1.67 [1.63–1.71]	1.75 [1.67–1.83]	1.69 [1.59–1.79]	0.115
BMI (kg.m <sup>-2</sup> ), mean [CI]	27.9 [25.6–30.2]	27.2 [25.4–29.0]	29.6 [26.2–33.0]	35.5 [31.7–39.2] <sup>a,b</sup>	0.002
Diabetes duration (years), mean [CI]	-	11.2 [6.6–15.9]	16.8 [5.4–28.2]	17.3 [1.3–33.4]	0.556
HbA <sub>1c</sub> , mean [CI],					
IFCC unit in mmol/mol		77 [65–89]	56 [42–70]	55 [49–62]	0.070
(NGSP unit in %)		(9.2 [8.1–10.3])	(7.3 [6.0–8.6])	(7.2 [6.6–7.8])	
Foot plantar forms, <i>n</i> (%)					0.875
Fallen foot arch	1 (8.3%)	2 (8.3%)	0%	1 (16.6%)	
Normal foot	2 (16.7%)	3 (12.5%)	1 (8.3%)	1 (16.7%)	
High foot arch	4 (33.3%)	7 (29.2%)	5 (41.7%)	3 (50.0%)	
Very high foot arch	5 (41.7%)	12 (50.0%)	6 (50.0%)	1 (16.7%)	

PN, Peripheral neuropathy in patients with diabetes; NDS, Neuropathy disability score; BMI, Body mass index; HbA<sub>1c</sub>, Glycated haemoglobin;<sup>a</sup>: different compared to controls and <sup>b</sup>: different compared to Non-PN for *p* < 0.05.

for the comparison of the control or the mild-PN vs. the severe PN group and 1.33 for the comparison of the non-PN vs. the severe PN one.

### 3.2 | Maximum voluntary contraction

The maximum voluntary contraction adjusted for body mass identified a significant difference between groups, with a reduction in strength as PN worsened ( $p < 0.001$ ; Figure 1). No gender influence was identified. Controls presented greater strength compared to the patients with mild PN ( $p = 0.020$ , Cohen's  $d = 1.41$ ) and compared to patients with severe PN ( $p = 0.002$ , Cohen's  $d = 2.16$ ), while they had no difference compared to patients without PN.

### 3.3 | Traditional spatial data reduction

Plantar pressure measurements expressed according to traditional spatial data reduction are presented in Table 2. No differences were identified between left and right plantar pressure regions. The three main parameters describing force and pressure at rearfoot level ( $F_{\text{mean}}$ ,  $F_{\text{max}}$  and  $P_{\text{max}}$ ) varied across the groups ( $p < 0.001$ ), while parameters for mid- and forefoot did not show any statistical difference between groups.

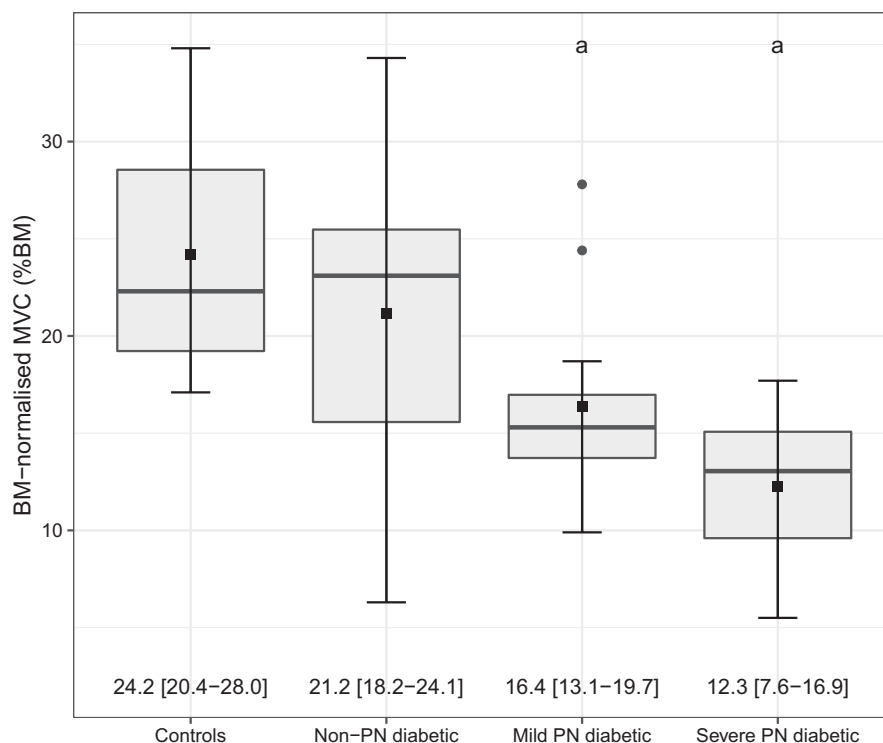
Post-hoc analysis showed that the load under the rearfoot sub-region is inversely related to PN severity. Controls subjects presented higher  $F_{\text{mean}}$  ( $p = 0.004$ , Cohen's  $d = 1.36$ )

and  $F_{\text{max}}$  ( $p = 0.042$ , Cohen's  $d = 1.22$ ) compared to mild PN patients and higher as well in  $F_{\text{mean}}$  ( $p = 0.007$ , Cohen's  $d = 2.36$ ) and  $F_{\text{max}}$  ( $p = 0.002$ , Cohen's  $d = 2.22$ ) compared to severe PN. Non-PN subjects with diabetes showed higher  $F_{\text{max}}$  ( $p = 0.002$ , Cohen's  $d = 1.67$ ) and  $P_{\text{max}}$  ( $p = 0.003$ , Cohen's  $d = 1.75$ ) compared to severe PN.

### 3.4 | pSPM analysis

As shown in Figure 2A, plantar pressure distribution differs between groups. The differences mainly concern the anterior part of the rearfoot, the anterior part of the forefoot and the internal edge of the foot arch. There is no evidence of any differences between left and right plantar pressure distribution in any of the comparisons made.

pSPM post hoc analysis, shown in Figure 2B highlights the following differences: 1) higher plantar pressure distribution at the anterior part of the rearfoot in controls compared to non-PN patients; 2) higher pressure distribution beneath the anterior side of the 1st, 3rd, 4th and 5th metatarsal heads in patients with mild PN compared to non-neuropathy groups, 3) a lower distribution under the posterior forefoot in mild PN compared to non-neuropathy groups, 4) a lower distribution at the anterior part of the rearfoot in patients with mild PN compared to non-neuropathy groups; 5) lower plantar pressure distribution beneath the anterior part of the forefoot in patients with severe PN compared to the other groups; 6) a higher distribution of the pressures beneath the foot arch in patients with severe PN compared to the other groups. The



**FIGURE 1** Maximal voluntary contraction of the ankle dorsiflexor's muscle normalised for body mass according to study groups. Group statistics were expressed as mean [CI 95%]. MVC, Maximal voluntary contraction; %BM, Percentage of body mass; Black squares indicates mean, black circle were outlier patients; "a" was significantly different with the controls



TABLE 2 Ground force parameters recorded with traditional sub-region analysis

	No-neuropathy				<i>p</i> -value
	Controls	Non-PN	Mild PN	Severe PN	
n	12	24	12	6	
Valid footprints, n	124	239	117	52	
Normalised $F_{\text{mean}}$ (%BM), mean [CI]					
Forefoot	101.8 [96.5–107.1]	101.9 [97.2–106.5]	99.1 [93.0–105.1]	93.8 [84.1–103.4]	0.311
Rearfoot	77.4 [74.1–80.8]	74.2 [71.4–76.9]	67.7 [62.1–73.3] <sup>a</sup>	66.0 [62.2–69.8] <sup>a</sup>	<0.001
Normalised $F_{\text{max}}$ (%BM), mean [CI]					
Forefoot	100.4 [95.3–105.4]	100.7 [96.1–105.3]	97.6 [91.9–103.3]	89.5 [82.4–96.5]	0.079
Mid-foot	22.3 [17.6–27.1]	20.8 [16.1–25.4]	19.7 [15.6–23.7]	26.4 [13.9–38.8]	0.510
Rearfoot	72.9 [70.3–75.5]	71.6 [68.3–75.0]	64.4 [58.7–70.2] <sup>a</sup>	58.8 [51.2–66.3] <sup>a,b</sup>	<0.001
Normalised $P_{\text{max}}$ (%BM.cm <sup>-2</sup> ), mean [CI]					
Forefoot	5.4 [4.4–6.4]	6.2 [5.3–7.0]	6.8 [5.2–8.3]	4.8 [3.2–6.5]	0.178
Mid-foot	2.2 [1.9–2.5]	2.3 [2.1–2.5]	2.4 [1.5–3.2]	2.2 [1.4–3.1]	0.974
Rearfoot	4.0 [3.7–4.4]	4.5 [4.2–4.8]	3.6 [3.0–4.2]	3.1 [2.6–3.7] <sup>b</sup>	<0.001

Number of individuals and normalised footprints (n) and the source data for calculating the normalised footprint in each subset (Valid footprints).

$F_{\text{mean}}$ , Mean force;  $F_{\text{max}}$ , Maximal force;  $P_{\text{max}}$ , Maximal pressure; %BM, percentage of body mass; PN, Peripheral neuropathy in patient with diabetes;<sup>a</sup>: different compared to controls and <sup>b</sup>: different compared to Non-PN for  $p < 0.05$ .

highlighted areas in Figure 2 indicate only the statistically significant differences (see Appendix 2 for calculation).

## 4 | DISCUSSION

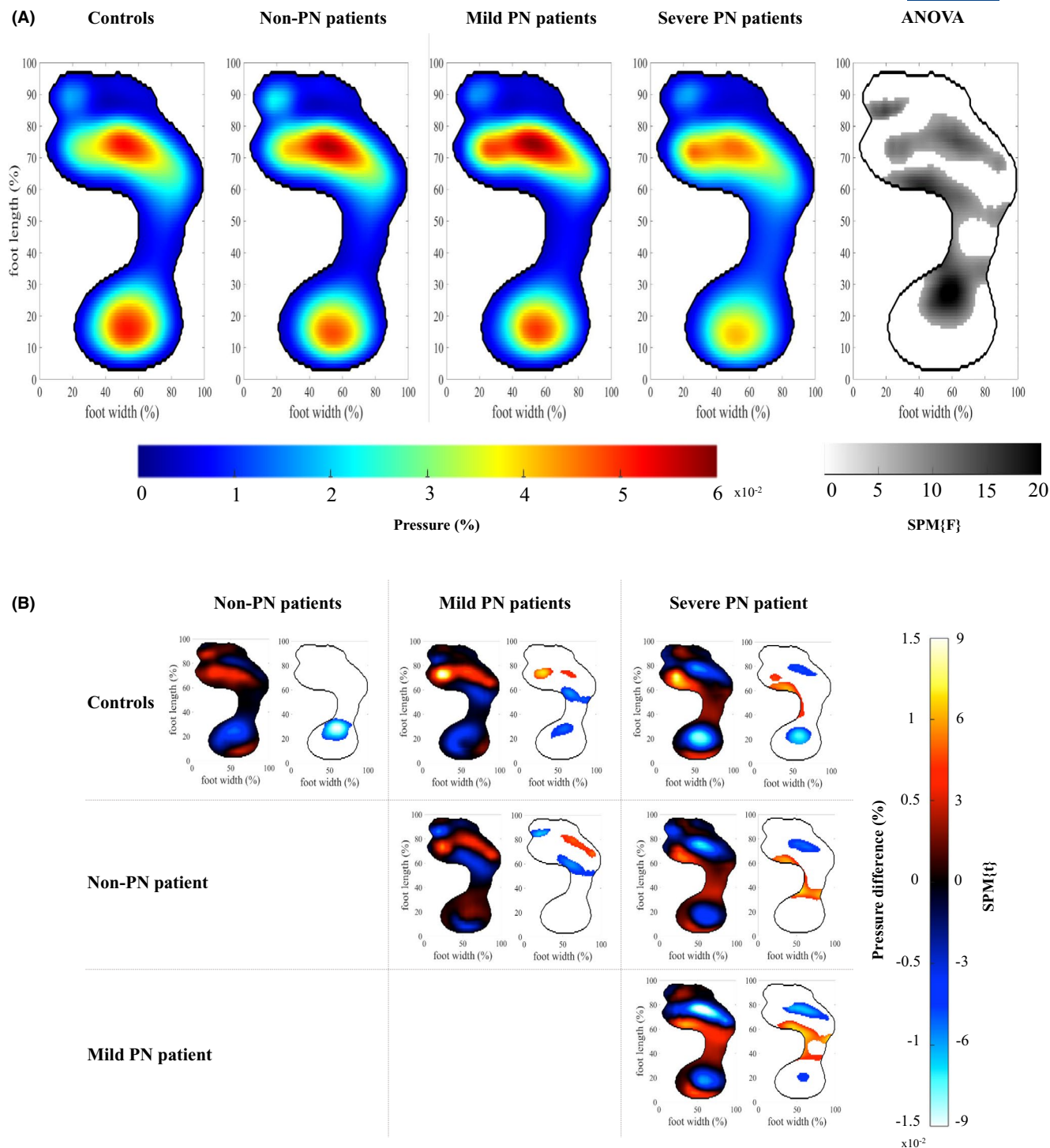
The aim of this study is to highlight pSPM potential in the diabetes foot examination. This new methodology may enable identify different plantar pressure patterns among degrees of PN, making it possible over time, to monitor this complication of diabetes, thus preventing foot ulcerations. Indeed, the future test should be quick and user-friendly and should allow to identify specific plantar pressure patterns in early PN. If validated, this test should lead to an anticipation of the foot cares in patients with diabetes identified at risk. Traditional foot plantar analysis, based upon spatial data reduction, is not effective in the identification of the specific areas at risk in patients with early signs of PN. Conversely, our study suggests that with pSPM analysis it could be possible to identify patients affected by mild PN to differentiate them from patients with no PN or with severe PN. Interestingly, the pSPM analysis demonstrated that patients with mild PN were characterised by shrinkage and anteriorisation of the forefoot area, whereas patients with severe PN were characterised by higher pressure beneath the foot arch.

This method added important information to the traditional spatial data reduction, which demonstrates lower planar pressures in the rearfoot region. This may be explained by a change of the stance phase during gait, associated with a progressive deterioration of the maximal voluntary contraction of dorsiflexor muscles (Figure 1). This observation is in

line with previous studies,<sup>2</sup> which reports alteration of the eccentric force of the dorsiflexor muscles during foot landing, which is manifested in foot slap gait.<sup>4</sup> Previous studies provided evidence of a lateralisation of plantar force due to a marked supination in PN patients.<sup>6,13</sup> Unfortunately, the classical analysis of the footprint does not correspond to the anatomical sites of interest in the diabetes foot cares (e.g., first metatarsal head),<sup>17</sup> which were, on the contrary, clearly highlighted by pSPM analysis.

In this regard, our exploratory analysis suggests that changes begin at an early stage of diabetes, before the first clinically overt signs of PN. The anterior part of the heel appears to be less loaded in the non-PN group compared to the control group. These differences could be due to the thinning of the heel fat pad, reducing the area of support.<sup>27</sup>

In early-stage PN, the pSPM analysis displayed an overloading of the anterior sides of the 1st, 3rd, 4th and 5th metatarsal heads, along with the unloading of the posterior part of the forefoot. This reorganisation of the distribution of plantar pressures suggests a biomechanical gait alteration possibly induced by a reduction of proprioception. In addition, these results show an anteriorisation of the plantar pressures, and possibly shrinkage of the forefoot supporting area. As previously reported, patients with mild PN present altered proprioception and muscle atrophy of the foot, which turn into an imbalance between flexor and extensor metatarsal muscles. This structural change leads to prominent metatarsal heads and clawing of the toes<sup>28</sup> which provide a possible explanation for the shrinkage of the supporting area of the forefoot revealed in the present study. Moreover, this feature is consistent with the thinning



**FIGURE 2** Between-group pedobarographic SPM analysis. (A) Mean relative plantar pressure (% total pressure) for each group; ANOVA SPM{F} values with non-significant clusters being left blank (right), threshold of significance was 6.9. (B) SPM post-hoc analysis (t-test with Bonferroni correction) comparing all groups (intersections between row and column). For each comparison, the left footprint represents the mean difference between the two groups of interest (blue/red colors represent lower/higher values for the group in column compared to the one in row). Right footprint represents the SPM{t} maps, blank being non-significant (threshold of significance was  $\pm 3.0$ ). PN, Peripheral neuropathy; ANOVA, Analysis of variance; SPM, Statistical parametric mapping

of the fat pad, mechanically reducing the supporting area.<sup>27</sup> Additionally, reduction of dorsiflexor muscle strength in patients with PN (Figure 1) may be related to a disturbed foot control during gait which result in foot slapping, and

in anterior over-compression of the forefoot. Finally, as shown by Caselli (2002), an anteriorisation of the center-of-pressure during gait may be observed.<sup>8</sup> This shrinkage and anteriorisation of plantar pressures beneath the



forefoot should prompt specific care of the foot in patient with diabetes, even before the first clinical symptoms. In the case of the French health-system, early identification of PN allows to classify patients with diabetes as with foot stage 1 (i.e., four podiatrists sessions reimbursed per year).

As shown in Figure 2B, severe PN is characterised by reduced distribution of plantar pressures under the anterior forefoot coupled with an overload at the internal side of the mid foot which increases ground contact area. These complex changes are combined with osteoarthropathy, such as Charcot's foot deformities, whose pathophysiology is still not fully explained.<sup>29</sup> The deterioration of the foot architecture causes micro-fractures, non-unions and dislocations which then lead to further deformations.<sup>9,29</sup>

This first exploratory study has limitations: it is a cross-sectional analysis with a limited number of cases and controls, and had no long-term follow-up. The recruitment was easier for cases than controls and the two groups were unevenly balanced. The strength of this study is however the innovation of use of pSPM in this population of patients with diabetes. This test is fast and patient-friendly with low operator dependency. This new promising technique needs to be validated in larger populations of patients with diabetes before being employed in a clinical setting with the aim to allowing a timely detection of gait abnormalities in patients with PN before they became overtly evident. Validation needs also to assess the role of other factors, such as obesity-related postural control alterations.<sup>30</sup>

## 5 | CONCLUSIONS

The present study is the first one to use pSPM method to identify spatial pressure distribution in patients suffering from diabetes with differing degrees of PN who were compared to controls without diabetes. By identifying a shift on pressure towards the anterior part of the forefoot, pSPM analysis made it possible to identify specific features of plantar pressure distribution in early stages of PN, not demonstrated by traditional methods. pSPM analysis also made it possible to identify specific features of patients with severe PN, interesting for targeting care. If validated in larger studies, these findings may enhance our understanding of the biomechanical consequences for the diabetes foot management, allowing early identification of patients at risk, in order to anticipate foot care and reduce the social and economical cost of this complication.

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## CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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## APPENDIX 1.

### Definition of foot characteristics assessed by pSPM technique

Foot progression angle was defined as the average angle of the tangent lines to the medial and lateral side of the foot.

Foot length was defined as the distance between the back of the heel and the forefoot line.

Foot width was defined as the medio-lateral distance between the most medial and most lateral point of the forefoot.

## APPENDIX 2.

### Additional details about the pSPM methodology and statistical analysis.

In addition to the methodology previously described, pSPM analysis was performed according to the following methodology: Zero-variance nodes (i.e., which contain zeros for all observations) were excluded as no statistical values can be computed for these nodes. Maps of plantar pressures

correspond to 2D 1D continuum (matrices), they were flattened in a 1D-1D continuum for the analysis (vectors). A non-parametric permutation tests with 10,000 iterations were performed to determine the threshold corresponding to an alpha risk of 5% (Nichols et al., 20). Firstly, a non-parametric pSPM ANOVA was conducted to test a group effect (i.e., control, non-PN, mild PN, severe PN), and the SPM{F} statistic was computed for each node. Then, non-parametric pSPM t-tests were performed to compare each group to another. A Bonferroni correction was applied to the alpha error threshold to consider the number of comparison (n=6). The SPM{F} and SPM{t} values were reorganised in their original conformation (i.e. matrices) for interpretation. To be considered as a cluster of significant differences, nodes had to reach the threshold determined by the permutation test for both SPM{F} and SPM{t} values.

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