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Research Article

Further Analysis on the Ultra-Weak Photon Emission of Patients with Type 2 Diabetes: A Potential Non-Invasive Diagnostic Tool

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Abstract

Background: Ultra-weak photon emission (UPE) is a phenomenon of spontaneous emission of visible range photons by biological systems including human subjects. The UPE signal is claimed to possess information about pathological, psychological and physiological condition of human subjects and should, therefore, be a potential non-invasive diagnostic tool. We have demonstrated that there exist significant differences of different parameters of each photon signal spontaneously emitted from five body sites between type 2 diabetes and age-matched non-diabetic subjects, and all the subjects could be roughly clustered into two groups by 1st principal component analysis. However, the discriminating ability of every parameter and everybody site are not involved.

Methods: In this paper, these photon signals were selected for further analyzed, and more new parameters of each signal were calculated. The 2nd principal component analysis (PCA) and cluster analysis are utilized to assess the discriminating ability of the above parameters.

Results and conclusion: The 2nd principal component is different in the signals of diabetic or non-diabetic subjects. Cluster analyses not only segregates diabetic and non-diabetic subjects, but also sub-categorizes them, and have the ability to predict the diabetic condition of a subject from its UPE signals. The paper presents the results of analyses and hopes to pave the way for similar investigations in subjects suffering from other diseases.

Keywords: Ultra-weak photon emission, Type 2 diabetes, Non-invasive diagnostic tool, 2nd principle component analysis, Cluster analysis

Introduction

All living systems could spontaneously and incessantly emit ultra-weak photon emission (UPE), often called biophoton, mainly in the visible region, its spectral range is 200-800 nm, and the intensity is very weak, about a few to hundreds of photons/s•cm^2 [1-3]. There are some indications of the involvement of oxidative metabolic processes in UPE [4-7]. It has been suggested that UPE is connected to life and its signal contains information about ongoing metabolic activities and molecular composite structures implicated in them [8]. The investigations made for showing the existence of this information relied upon signal strength, photon count distribution, and spectral distributions [9-11]. They tried to link these properties to physiological and pathological states. It was noticed that signal strength differed vary different body sites and diseased states [12-14]. The strength of signals from index and middle fingers was found to be lower in patients of hypothyroidism and in patients whose thyroid glands had been removed [15]. Cohen and Popp reported higher signal strength in a patient of multiple sclerosis compared to healthy subjects [16]. The left-right asymmetry of signal strength increased in patients of cold and hemi-paresis [13,17]. Yang, et al. [18] reported significant difference in the maximum spectral peak of spectral distribution from healthy subjects and patients with cold. Spectral peak of some points of patients with essential hypertension showed red-shift at the attack state and returned to normal during the remission state [19]. Significant differences have been observed in spectral parameters, such as frequency, intensity, and band shape of UPE signals of cancer patients and normal people [20]. Chen could distinguish serum samples of patients with acute lymphoblastic leukemia from those of healthy volunteers [21]. The intensity and spectrum of UPE could significantly distinguish the breast cancer-bearing nude mice from healthy controls [22,23].

The findings of above-mentioned studies based on strength of UPE signal, were indicative. Afterwards, attempts were made to discover more parameters of UPE other than strength that carry information. Nearly unchanging signal strength turned out to be a boon for it allowed the study of fluctuations in photon number that led to the discovery of many more parameters of UPE signals. A calculation method has also been developed that is successful in ten parameters of a UPE signal from its time series [24,25]. The parameters of UPE signals emitted from different body sites of same human subject vary and their variation body sites of a subject is also a carrier of some information about the subject. Every one of these parameters contains some aspects of the information about the emitting subject. UPE of four areas of each hand were measured by Zhao et al. [26], signal strength and Fano factor values of photon counts were analyzed, their results suggest that UPE is able to predict one's chronological age. In another studies, the UPE of dorsal and palm of left and right hand from three subtypes of pre-diabetic subjects were detected, ten parameters were calculated from UPE time series and the resulting correlation networks accurately reflected the differences between three subtypes in early-stage type 2 diabetes [27]. Yet, the concerned studies of these parameters are still less compared with that of signal strength, the diagnostic potential of signals parameters for identifying pathological states need to be further analyzed.

In our previous paper, the differences of signal strength, Q value, squeezed state parameters (|α|, θ, ø, r) and SSI between type 2 diabetes and healthy subjects were preliminarily analyzed, and all the subjects could be roughly clustered into two groups utilizing the obtained parameters by 1st principal component analysis [28]. However, the discriminating ability of every parameter and everybody site are not involved, and more new parameters also should be considered. In this paper, the fluctuating UPE signals at five body sites in two groups of diabetic and non-diabetic were selected for further analysis. More new parameters including signal strength, intercept, slope, curvature of Fano factor curve, squeezed state parameters (|α|, θ, ø, r), SSI, and average square of the difference in observed and calculated probabilities using universal values of r, θ, and φ (ASDP) were calculated and analyzed. Then, the 2nd principal component analysis (PCA) and cluster analysis are utilized to assess the discriminating ability of the above parameters and different body sites, with the aim of demonstrating diagnostic potential of UPE signals in identifying diabetic or non-diabetic subjects. The paper presents the results of analyses and hopes to pave the way for similar investigations in subjects suffering from other diseases.

Subjects and Methods

Subjects

46 patients with type 2 diabetes (19 females and 27 males, age 41–75 years) and 49 age-matched healthy volunteers (20 females and 29 males, age 39–73 years) participated in the spontaneous UPE measurement as subjects voluntari-

ly. Healthy subjects were interviewed to exclude physical or emotional disorders. Type 2 diabetes patients were all collected from Diabetes Hospital of Shandong Province, and had been diagnosed as type 2 diabetes. They adequately understood the measurement procedure and gave verbal informed consent for it. They then signed an informed consent agreement before the commencement of experiment as required by the Medical Research Involving Human Subjects Act (2006). Five body sites (named forehead, throat, heart, abdomen, and navel) located on the frontal middle line of human body were selected in order to avoid the influence of left-right symmetry.

UPE detection measurement

The UPE is detected by a highly sensitive and low-noise PMT (Electron Tube 9235QA) in single-photon-counting mode, which is of diameter 51mm and sensitive in the spectral range of 290-630 nm. To increase the sensitivity and decrease the dark current, the PMT was cooled to -23 using FACT50PMT cooling housing (ET Enterprises, Britain). The components of the UPE detection system have been detailed described in our previous paper [28]. Subjects were measured between 15 p.m. and 17 p.m. in order to reduce the influence of diurnal rhythms.

Before the UPE measurement of human body, the background of PMT with the shutter closed was recorded firstly for 10 min at intervals of 50 ms. Subjects remained during this period in the red dim light of the control room. Subjects then walked into the dark room with controlled temperature and humidity and were positioned on the bed for at least 5 min. The photomultiplier tube was placed above the body, the ring at the front port of the photomultiplier barely touching the body. The navel, stomach, heart, neck, and forehead was measured in sequence, respectively. The duration of each recording was 10 min consisting of 12,000 time intervals of 50 ms, and the total measurement time for each person was approximately 1 hour. The temperature in the dark room was maintained at 23 , and the background noise was in the range of 10.8-11.5 counts/s.

Data analysis

Many parameters, including signal strength, slope, intercept and curvature of Fano factor curve, squeezed state parameter $|\alpha|$, squeezed state index (SSI) and ASDP, were statistically analyzed, and the formula and process of computation of all the above parameters can be found in the literatures [24,25]. Statistical analysis of photon signals was performed with SPSS 16.0 software (SPSS, USA).Principal component analysis (PCA) and K-means cluster analysis was used to classify the diabetic subjects and non-diabetic subjects using the obtained data. Calculation and data graphing was made with GraphPad Prism 5.

Results and Discussion

Parameters of UPE signals from diabetic and non-diabetic subjects

The parameters including signal strength, slope, intercept and curvature of Fano factor curve, squeezed state parameter $|\alpha|$, SSI and ASDP of diabetic and non-diabetic group are statistically analyzed and shown in Figure 1. Figure 1 illustrates that signal strength and slope value of navel of diabetic is significantly higher than that of non-diabetic according to independent t test($p=0.012$, $p=0.009$), intercept and SSI value of navel of diabetic group is significantly lower than that of non-diabetic ($p=0.023$, $p=0.019$), slope value of heart and SSI of abdomen of diabetic is significantly lower than that of non-diabetic($p=0.004$, $p=0.028$), curvature value of throat, ASDR value of heart and forehead is significantly higher than that of non-diabetic ($p=0.018$, $p=0.020$, $p=0.007$). Various parameters have different values in diabetic and non-diabetic subjects, which suggest some potentiality of diagnosing diabetic and non-diabetic subjects by various parameters.

Principal component analysis of the properties of UPE signals

The PCA determines two principal components of UPE signals from their two categorical and seven parameters. The categorical properties are site and condition. The site property takes one of the five possible values: naval, abdomen, heart, neck or forehead, and the condition property takes one of the two possible values: diabetic or non-diabetic. The seven parameters are signal strength, intercept, slope, and curvature of Fano Factor curve, SSI, $|\alpha|$ and ASDP. Figure 2 illustrates the standardized biplot of two principal components and each circle depicts a measured signal in 2-dimensional principal component space.

From the Figure 2, most of the circles are clustered in two regions, the upper region depicts signals of diabetic subjects and lower region of non-diabetic subjects. The two regions have nearly thin rectangular shape with the longer side nearly parallel to the axis of 1st principal component. It indicates that the differences between signals of diabetic and non-diabetic subjects

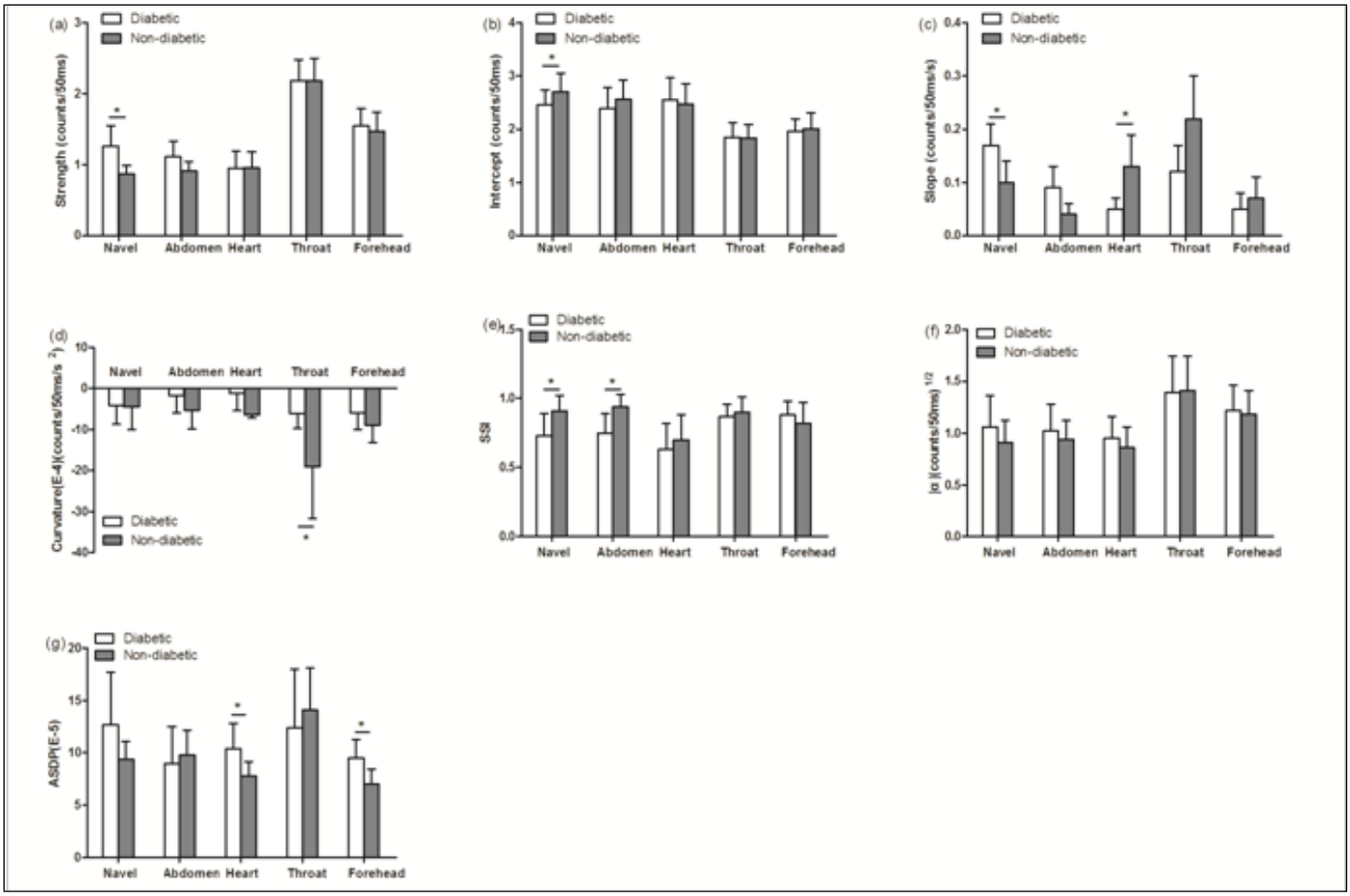

Figure 1: The parameters of UPE signals in diabetic and non-diabetic.(a)-(g) is signal strength, intercept, slope, curvature of Fano factor curve, SSI, |α| and ASDP, respectively.

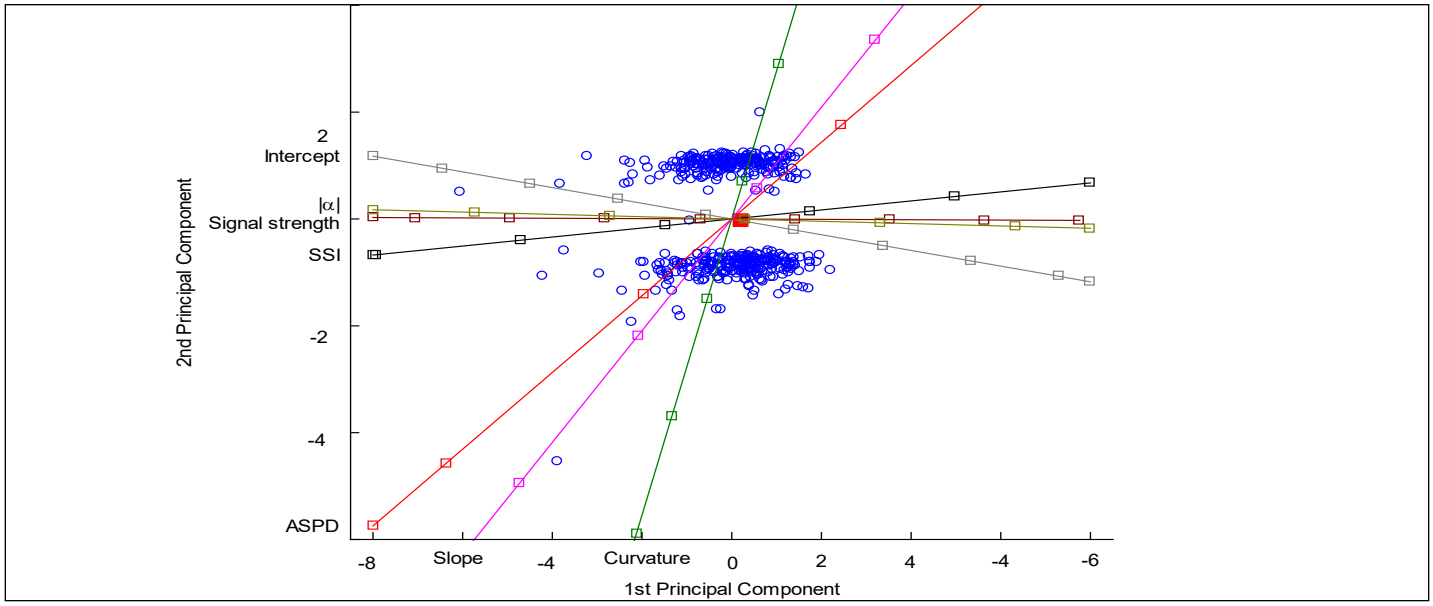

Figure 2: The standardized biplot of two principal components and each circle depicts a measured signal in 2-dimensional principal component space.

are not prominent and still, 2nd principal component can discriminate them. Figure 2 also depicts seven lines intersecting at a point, each line for a parameter. The lines for intercept, |α|, signal strength and SSI make small angles with the axis of 1st principal component and hence, these parameters are not suitable for identifying diabetic and non-diabetic subjects. In contrast, the lines for ASDP, slope and curvature make small angles with the axis of 2nd principal component, which suggest that they are suitable for identifying diabetic and non-diabetic subjects.

Figure 3 depicts 2nd principal component of UPE signals sorted by body site and condition. The signals are numbered after the sorting, which ensures that the first 46 signals are of diabetic subjects at the site navel, followed by the next 49 signals of non-diabetic subjects at the site navel. The numbering continues in the same manner for signals from other sites. The figure depicts signals from different sites by different symbols; unfilled symbols depict signals of diabetic subjects, and filled symbols depict non-diabetic subjects. The figure shows that the component does not exhibit any systematic difference among signals at different sites. It is pointed out that separation of subjects occurred only with respect to one categorical property though both categorical properties were used in PCA. The inability of the 1st principal component to separate subjects suggests that diabetic condition has marginal effect on the UPE signals of five sites.

Cluster analysis of 95 subjects

The roman numerals were used for identifying clusters obtained in analyses. Cluster numbers were assigned different to clusters obtained in analyses without and with the inclusion of the categorical property diabetic condition. In the analyses without the categorical property, the cluster with the highest population was assigned the number I, the cluster next in population was assigned the number II and so on. In the analyses with the categorical property, the cluster containing maximum population of diabetic subjects was assigned the number I, the cluster with maximum population of non-diabetic subjects, the number II, the cluster next in population of diabetic subjects, the number III and the

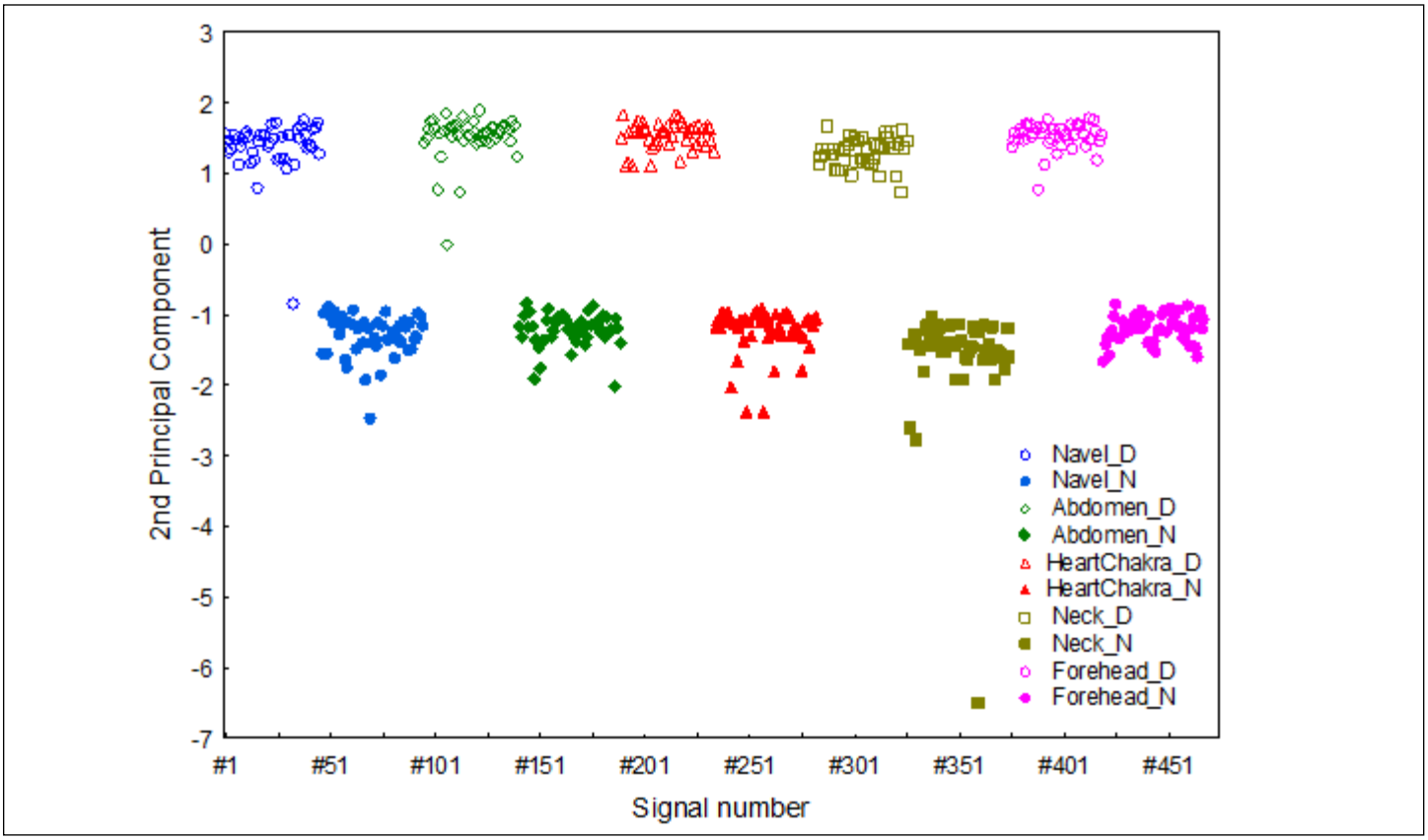

Figure 3: The 2nd principal component of signals from five sites in diabetic and non-diabetic subjects. The letter D and N in the legends depict signals from diabetic and non-diabetic subjects, respectively.

Table 1: Cluster analysis results of subjects based on the parameters of UPE signals. Populations of diabetic and non-diabetic subjects in clusters obtained cluster analyses based on and identified by different properties.

Identity of Analysis	No categorical property diabetic condition		Categorical property diabetic condition	
	Diabetic	Non-Diabetic	Diabetic	Non-Diabetic
ALL	I (25), II (16)	I (34), II (15)	I (23), III (18)	II (44), III (5)
SSI	I (26), II (15)	I (37), II (12)	I (25), III (16)	II (33), IV (9), V (7)
Strength	I (18), II (23)	I (32), II (17)	I (23), III (18)	II (34), IV (15)
|α|	I (15), II (23), III (3)	I (29), II (14), III (6)	I (23), III (15), IV (3)	II (31), IV (18)
Intercept	I (31), II (10)	I (38), II (11)	I (22), III (19)	II (38), IV (11)
Slope	I (37), II (2), III (2)	I (40), II (4), III (5)	I (41)	II (49)
Curvature	I (22), II (19)	I (26), II (23)	I (26), III (15)	II (38), IV (11)
ASDP	I (38), II (3)	I (49)	I (41)	II (49)
Navel	I (33), II (11), III (1), IV (1)	I (35), II (14)	I (45), III (1)	II (49)
Abdomen	I (35), II (10)	I (37), II (12)	I (29), III (16)	II (49)
Heart Chakra	I (17), II (14), III (7), IV (7)	I (27), II (11), III (7), IV (4)	I (29), III16)	II (32), IV (17)
Throat	I (41), II (2)	I (48), II (1)	I (43)	II (48), III (1)
Forehead	I (20), II (11), III (6), IV (7)	I (22), II (13), III (9), IV (5)	I (44)	II (37), III (12)

cluster next in the population of non-diabetic subjects, the number IV. Each subject is endowed with thirty-five continuous parameters-seven of each signal from five body sites-and one categorical property diabetic condition. Cluster analyses are carried out with and without the categorical property diabetic condition and results are presented in the Table 1. It is pointed to that because UPE signals in 5 subjects are recorded at less than five sites(they cannot endure the long UPE measurement), the number of non-diabetic subjects is 49 in all analyses but the number of diabetic subjects varies from 41 to 46. From the Table 1, the analysis ALL without categorical property segregates subjects into two clusters, I containing 59 subjects and II containing 31 subjects. The analysis SSI without categorical property separates subjects in clusters almost similar to those obtained in ALL. Perhaps, both analyses segregate subjects on same or similar basis. The smaller values of SSI of signals of the subjects in cluster II in both analyses indicate some health issues of these subjects. The remaining eleven analyses without categorical property segregates subjects in different cluster but their significance is not so obvious. Future measurements of UPE signals along with pathological and clinical parameters of the subjects might throw some light on their significance.

Table 1 also shows that eleven of thirteen cluster analyses with the categorical property diabetic condition could correctly segregate diabetic and non-diabetic subjects in separate clusters. The segregation in the remaining two analyses-ALL and |α|- is mostly correct: ALL places five non-diabetic subjects in the diabetic cluster III, and |α| places three diabetic subjects in the non-diabetic cluster IV. It is suspected that the incorrectly placed eight subjects were borderline cases of diabetes. Most of these analyses determine two and sometimes three clusters for diabetic or non-diabetic subjects, which suggest two subcategories of diabetic and two subcategories of non-diabetic subjects. The two subcategories of diabetic subjects contains around 25 and 15 subjects, and of non-diabetic subjects around 35 and 15 subjects. The sub-categorization indicates a new aspect of diabetes. One wonders if other systems of health care are aware of it. Perhaps, Traditional Chinese Medicine is aware of it. This system associates diabetes with Qi and Yin deficiency and envisages three categorizes of Qi and Yin deficiency, plain, with dampness and with stagnation [28].

Many cluster analyses segregate diabetic and non-diabetic subjects in different clusters. They all have ability to predict the diabetic nature of a subject from its UPE signals. Cluster analysis may be viewed as a training to garner this ability. The 10 v-fold cross validation tests this ability and uses it to

obtain optimum number of clusters. It selects 10 subjects randomly, obtains clusters from the data base of the parameters of remaining subjects (varied from 80 to 85 in different analyses) using some parameters, checks the placement of randomly selected subjects in different clusters, minimizes the sum of distances of these signals from their respective cluster centers for obtaining optimum number of clusters, adds the data of randomly selected subjects to the data base and obtained the structure of optimum number of clusters. The different analyses of the data base are reading for predicting diabetic condition of new subjects from their UPE signals. The prediction could be made by calculating 35 continuous properties of new subjects and assigning unknown discrete value to their categorical variable health, adding them to the data base and performing different cluster analyses. Different analyses would place unknown subject in clusters and the placement would determine the health or diabetic condition. The prediction of different analyses might not agree in a subject or different analyses might place a subject in a cluster not containing any subject with known value of health. The former would be an example of border line case and later of failure. The border line and failure cases would be few and different analyses would agree in their predictions, so that all analyses need not be performed. Predictions could be made by using the most well determined parameter of signals from all sites or by using all seven parameters of the most well determined signal from a site. The more sites and more parameters enhance the reliability of prediction; so, does the inclusion of UPE signals of more subjects in the data base.

Conclusion

Ultra-weak photon signals emitted from five body sites of diabetic and non-diabetic group were selected, more new parameters are calculated and statistically analyzed, the 2nd principal component analysis (PCA) and cluster analysis are utilized to assess the discriminating ability of the above parameters and five body sites. The 2nd principal component is different in the signals of diabetic or non-diabetic subjects. Cluster analyses not only segregates diabetic and non-diabetic subjects, but also sub-categorizes them, and have the ability to predict the diabetic condition of a subject from its UPE signals. The paper presents the results of analyses and hopes to pave the way for similar investigations in subjects suffering from other diseases.

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Conflict of Interest

The authors declare that they have no competing interests.

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