Human ultra-weak photon emission as non-invasive spectroscopic tool for diagnosis of internal states – A review

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Abstract. In the knowledge that human ultra-weak photon emission (UPE) is mainly due to the metabolic oxidative stress processes that the skin cells undergo in the presence of reactive oxygen species (ROS), external stressors (like UV radiation), but also internal stressors (like diseases or brain activity) might strongly influence the UPE. This manuscript revises the scientific advances focused on the influence of internal factors on the human UPE. According to literature, the UPE seems to be influenced by some diseases (including diabetes, hemiparesis, protoporphyria, or a typical cold), and even by the cerebral intention/relaxation (brain activity/meditation). These allow to consider UPE as a natural and promising non-invasive spectroscopic tool for helping during the diagnosis of a variety of illnesses or stress- / mood-state disorders. Nonetheless, further research is required for answering some still unresolved controversial points.

Keywords: Human biophoton emission or ultra-weak photon emission (UPE); Applications; Bioluminescence; Spectroscopy; Internal states; Diagnosis.

Introduction

Biophoton emission or ultra-weak photon emission (UPE) is the spontaneous emission generated by all living systems without the need of an external excitation [1-6]. According to Pospíšil *et al.* [7-9], UPE has been mainly attributed to the relaxation of electronically excited *reactive oxygen species* (ROS) formed in biological systems during oxidative processes like lipid peroxidation and protein and nucleic acid oxidation. The mechanism of the formation of electronically excited species by an oxidative metabolic process is complex and has been proposed in detail by Pospíšil el al. [7]. The oxidation of these biomolecules leads to the formation of high-energy intermediates, whose decomposition generates electronically excited species that undergo electronic transition to the ground state emitting photons primarily in the visible (VIS) range of wavelength. This visible radiation is not visually detectable because it is 3-6 orders of magnitude lower than the human eye visual threshold [10], but it can be distinguished from the black-body radiation because the intensity of a blackbody radiation is 1/1000 times weaker than the UPE intensity [5].

It is essential **not to confuse UPE with other types of emission processes that can occur in living systems, such as bioluminescence**. Bioluminescence has higher light intensities and is related to specific biochemical reactions, such as the well-known Luciferin-Luciferase bioluminescent system of fireflies, jellyfish, krill, some fungi, etc. [11, 12]. On the contrary, UPE is due to general oxidative stress reactions that are common to all living beings, including human beings [5-9]. Since Gurwitsch discovered UPE a century ago, numerous experimental studies have been published confirming the emission of biophotons from multiple cell types, either prokaryotic or eukaryotic (plant, fungi or animal) [2, 5, 13-16]. In the case of multicellular organisms, multiple cells contribute to UPE. However, the biophotons emitted by internal cells will not normally exit/leave the organism because of the low penetration of VIS radiation. Consequently, the UPE measured from multicellular organisms mainly comes from the cells located in their outermost layers. Regarding humans, the emitting cells responsible for UPE are primarily in the skin, being nowadays accepted that **the origin of human UPE is mainly the human skin [7]**. The skin is the front-line barrier of some external stressors such as the solar radiation and bacteria. Thus, this organ has developed an effective system to react to changes in the external environment [17]. In this respect, the correlation between UPE and the oxidative stress processes in the skin has been deeply studied [18-28]. The skin is exposed to the exogenous oxidative stress by ROS that may result from ultraviolet

(UV) irradiation [19], ozone, air pollutants, etc. [18]. In this respect, several authors evidenced that UPE from the skin strongly increased after being exposed to UV-radiation, concluding that UV-radiation was an important skin stressor [20-28]. In addition, UPE intensity was not only evidenced to increase after exposition to UV radiation, but also a spectral shift was observed in the UV-induced UPE in comparison to the spontaneous UPE. Particularly, irradiation with UVA or UVB led to a UPE peak at approximately 550 nm, whereas the spectral pattern of spontaneous UPE peaked at 600-650 nm as evidenced by Kobayashi *et al.* [27] (Figure 1).

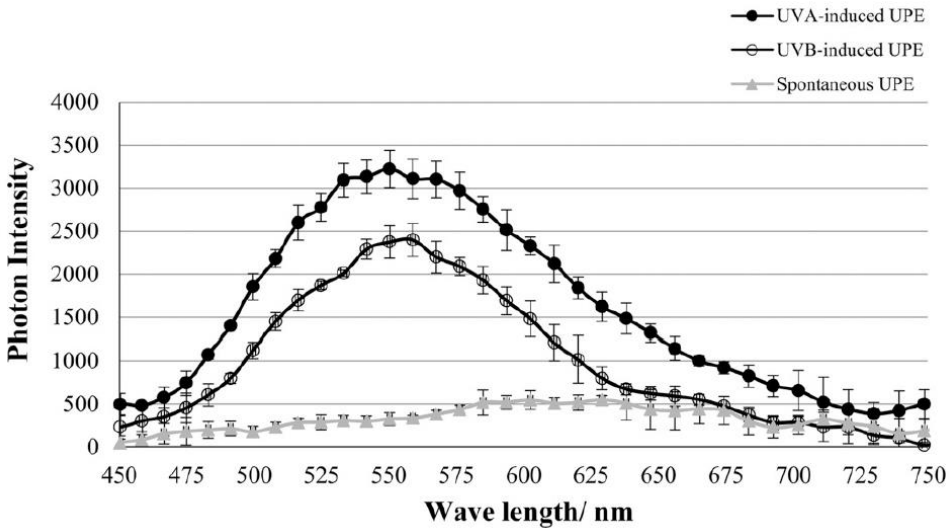

Figure 1. *Spectrum of UV-induced UPE in human skin. UPE spectra were taken for 20 min after irradiating the human skin with UVA (1100 mJ/cm^2) or UVB (234 mJ/cm^2). The black line shows the UPE spectra after the UVA radiation, and the dark-grey line shows the spectra after the UVB radiation. The light-grey line indicates spontaneous UPE from human skin. Data are presented as means ± standard deviations (SD) and N=3 [27]. Reproduced with permissions from [27].*

Besides UV radiation, a significant number of studies have investigated how UPE changes under the influence of other external factors such as temperature, season or time of day (biorhythm). The main milestones achieved over time regarding the analysis of human biophotons is summarized in ***Figure 2***. The figure also indicates, for each measurement, the detector system used, the instrumental parameter measured, the part of the body analysed, and the number of subjects considered. For the interested reader, further information about the UPE phenomenon and the main technical advances regarding the measurement of human UPE are comprehensively and extensively discussed in previous literature [29-34].

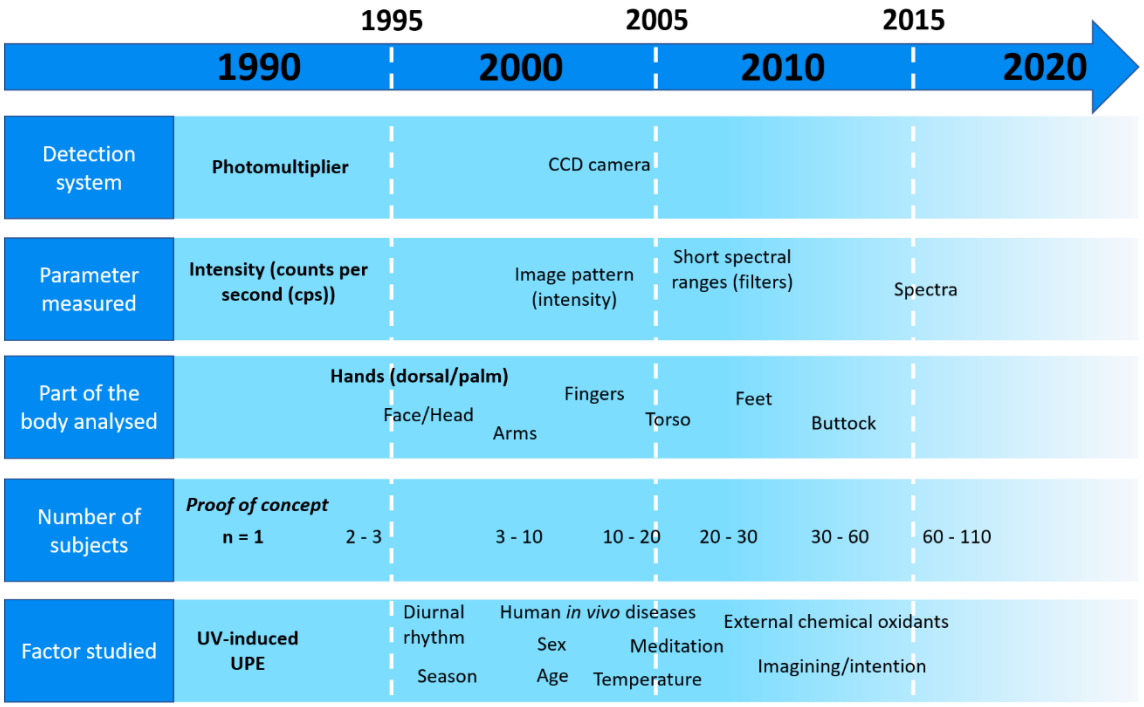

***Figure 2**. Timeline showing the major challenges achieved in the human biophoton field (in black, marking in bold black the most widely studied or employed). Abbreviations: PMT, photomultiplier tube; CCD, charge-coupled device; cps, counts per second; n, number of subjects studied.*

Besides external factors, several studies have researched the influence of internal factors such as age, brain activity, diseases, etc. in human UPE. Particularly, within the last few years there has been an increasing interest on the analysis of human biophotons in relation to internal states, especially diseases, and their possible use as diagnostic tools. Therefore, this revision aims to comprehensively summarize and provide a critical overview of the published works to date about the influence of internal personal states, including disease, brain activity and other states, on the emission of biophotons in humans.

Human biophoton for internal states diagnosis

Regarding the research of UPE in human beings, the factors influencing the UPE intensity might be classified into two types: external (from the ambient and outside the body) and internal (characteristic of the body and its internal state) [34]. The external factors include the diurnal rhythm, the season, the external light (which induce a delayed luminescence emission), and the oxygen concentration [10, 35-39].

The studied internal intrinsic factors include the age, sex, temperature, and body areas [10, 38, 40-43]. However, this review aims to rather make a critical revision of the internal states affecting UPE. These internal states comprise the presence of some diseases (health

state) and the mood (personal state). The use of UPE as a non-invasive tool to diagnose different illnesses and/or evaluate the overall health state of a person has been preliminary proposed and discussed in literature [44-47]. It is presumable that some diseases might influence to a greater or lesser extent the normal UPE emitted by healthy cells or organism. Table 1 summarizes the most relevant studies focused on the influence of internal states on the UPE intensity.

Table 1. Summary of the literature studying the influence of internal factors on human UPE.

Internal states	Part of the body analysed	Number of subjects*	Main milestones	Ref
Health States/Diseases				
Hemiparesis	Hands (Dorsal &Palm)	27 (7D/20H)	Hemiparesis patients emitted **less UPE intensity** in the parts affected by the disease. UPE asymmetry decreased after acupuncture treatment	48
Erythropoietic protoporphyria (EPP)	Buttocks and hands	15 (15D)	A significant **decrease in the UVA-induced UPE intensity** was observed in the patients that had started the treatment	49
Cold	Fingers	30 (10D/20H)	**Higher UPE intensity** in cold patients. And **spectral UPE red-shift** of the maximum UPE peak from 525 nm to 580 nm in cold patients with respect to healthy subjects	50
Diabetes	Hands (Dorsal &Palm)	44 (44D)	**UPE intensity differences** among the three subtypes of diabetes	51, 52
	Forehead, neck, heart, stomach, and navel	110 (50D/60H)	Navel UPE intensity of diabetic group is significantly higher than in the healthy group. Forehead UPE intensity in the diabetic group is significantly lower than in the healthy group. No significant differences for the other three body sites between the D and H groups. Differences between the patients with type 2 diabetes and healthy subjects for several UPE parameters (using PCA**)	53
Spleen-Qi deficiency syndrome	7th cervical vertebra on the midline of the back	45 (30D/15H)	**UPE intensity** in the Spleen-Qi deficient patients was **higher** than that of health subjects. UPE intensity decreased after ginseng treatment	54

Personal States/Mood				
Meditation	Hands and forehead	5	Significant **decrease in UPE intensity** during meditation	60
	12 different areas (including torso, head, neck, and hands)	20*** (10/10) 60*** (20/20/20)	**Weaker UPE intensity emission** in long-term transcendental meditation experienced subjects with respect to non-meditating subjects	61, 62 63
Imagining, intention or cognition (*i.e.* brain activity)	Head	8	Significant **increase in the UPE intensity** from the right brain hemisphere when imagining white light	65, 66
	Head	11		67

* D means diseased subjects; H means healthy subjects. ** PCA is Principal Component Analysis. *** 10/20 subjects who practised transcendental meditation were compared to 10/20 control subjects. An extra group of 20 subjects who practiced other relaxation techniques were included in ref 64.

Various studies measured the spontaneous UPE from human subjects (*i.e.*, *in vivo*) with some diagnosed illnesses. Jung *et al.* [48], compared the UPE from seven patients with hemiparesis against healthy subjects. The subjects differed in their UPE asymmetry, as hemiparesis patients emitted less in the parts affected by the disease. This asymmetry decreased after acupuncture treatment (Table 1). Petersen *et al.* [49], measured the UPE from the buttocks and hands of fifteen patients with Erythropoietic protoporphyria (EPP); a rare inherited disorder that results in acute cutaneous photosensitivity upon light exposure. Specifically, they evaluated the efficacy of taking zinc supplements to treat EPP in those patients. Previous exposure to UVA radiation was also studied. According to the results, lower UPE intensity values were obtained from buttocks than from hands. Lower UPE intensity values were also obtained without previous UVA irradiation than immediately after UVA exposure. Curiously, the UPE from hands in the EPP patients was found to be similar to the UPE of healthy individuals. In addition, a significant decrease in the UVA-induced UPE intensity (-73 %) was observed in those patients that had started the zinc treatment. According to the authors [49], the oxidative stress induced by UVA radiation in the EPP patients seemed to be lower when they took zinc supplements (Table 1). Yang *et al.* [50] measured the spontaneous UPE from 20 control healthy subjects and 10 patients with a cold (previous diagnosis). The individuals wore

gloves for 30 min to eliminate the influence of their fingers delayed luminescence emission. The UPE from each finger was separately recorded. The spectral distribution of the UPE emission was measured by using bandpass filters. Interestingly, for some of the fingers, the ratio between the UPE at 550 and 495 nm showed significant differences between healthy and cold patients (Table 1). Therefore, the comparison of these particular ratios was confirmed as a suitable parameter for diagnostic purposes [50].

Since 2017, several authors focused on investigating the UPE as a diagnosis tool of type 2 diabetes. Sun *et al.* [51] measured the spontaneous UPE from 44 male subjects with type 2 diabetes. They differentiated three subtypes of this disease by comparing the spontaneous UPE from the dorsal and palm sides of both hands with factors related to the symptoms, and with the use of statistical tools. In a second study regarding the three subtypes of diabetes (Table 1), they performed metabolomic analysis in combination with UPE measurements in order to correlate the UPE parameters with specific plasma metabolites. [52]. According to the authors, the UPE could be used as a screening tool to detect this disease in its early stages, before the onset of complications [51, 52]. In addition, Yang *et al.* [53] compared the spontaneous UPE from 50 female and male patients with type 2 diabetes, and from 60 healthy female and male subjects. The UPE was measured from five body parts including forehead, neck, heart, stomach, and navel. In addition, besides the UPE intensity, they used statistical analysis to study several parameters regarding the UPE signal including photon intensity, Q value, and squeezed state parameters. The large dataset allowed using several statistical methods. The results revealed some differences between the patients with type 2 diabetes and healthy subjects for several parameters (Table 1). Interestingly, when performing a Principal Component Analysis (PCA) considering all parameters and subjects, the subjects were clustered into two groups; healthy and diabetes-bearing subjects [53].

The combination of the UPE measurement and metabolomic analysis was also researched by Wang *et al.* [54] in order to diagnose Spleen-Qi deficiency syndrome. This is a syndrome referred by the traditional Chinese medicine characterized by physical weakness, pale, breath shortness, sweating, low voice, etc. In addition, they experimentally evaluated the efficacy of ginseng (*Panax ginseng*), the key herb traditionally taken to treat this syndrome. They measured the UPE at the Dazhui GV14 point, which locates under the 7^{th} cervical vertebra on the midline of the back. According to the results, the UPE intensity at the Dazhui point in the 30 Spleen-Qi deficient patients was higher than that of the 15 health subjects. After the ginseng treatment, the UPE

intensity decreased significantly (Table 1), which indicates that ginseng might reduce the oxidative stress of the Spleen-Qi deficiency subjects. In addition, 15 biomarkers potentially involved in the Spleen-Qi deficiency syndrome were identified using metabolomics and statistical analysis [54].

Curiously, as far as we know, there are no reports of any study proving UPE differences between human patients with or without cancer. Some authors have focused on studying the influence of cancer on UPE but using *in vitro* cell cultures and/or using *in vivo* mice models [55-59]. Amano *et al.* [55] evidenced a slight increase in the UPE intensity from mice with transplanted bladder cancer. The regions of untreated tumour provided higher UPE intensity than normal regions. Takeda *et al.* [56, 57] evidenced characteristic spectral differences in the UPE emission during the cell proliferation of human oesophageal carcinoma cells (TE9 cell line) (*in vitro* studies) [56], and during tumour growth of the TE4, TE9 and AH109A tumours in transplanted mice [57]. Zhao *et al.* [58] studied the entire breast cancer growth process comparing against healthy controls. They tried to find differences in the UPE intensity from the right and left side of the body surface on human breast cancer-bearing nude mice models. Significant differences in the UPE intensity were observed between the tumour-bearing and control mice. Similarly, Murugan *et al.* [59] also differentiated mice with and without tumours based on the differences in their UPE. The UPE from healthy mice remained stable whereas mice with tumours showed different fluctuations in the UPE intensity. Hence, at least in animal models, the measurement of UPE seems to be a promising non-invasive tool for cancer diagnosis. Therefore, there is a research need focused on this approach in order to settle the UPE-measurement as a non-invasive tool for *in vivo* human cancer diagnosis.

In addition to the health state, **some mind/mood states (*i.e.*, personal states) were also evidenced to influence the UPE intensity**. This influence was studied by Wijk *et al.* [60-63] by evaluating the effects of transcendental **meditation** on the UPE intensity. In a first study (Table 1), the UPE intensity was measured from five healthy subjects (two female and three male) experienced in meditation before, during and after meditation in sitting or supine positions [60]. The UPE from hands was recorded when sitting, while the UPE from their foreheads was recorded when lying on their backs. Subjects were hidden away from ambient light for at least one hour before their UPE measurement. The results supported the hypothesis that the human UPE can be influenced by meditation, because a significant decrease in UPE was observed during meditation (Table 1). In a

second study, they recorded the UPE images from 12 different areas (including torso, head, neck, and hands) of 20 healthy men (50 years old) [61]. The measurements were made between 11 am and 2 pm. Ten of the subjects practised transcendental meditation, whereas the remaining ten did not practise any relaxation technique. The authors observed that the UPE was significantly weaker in those long-term transcendental meditation experienced subjects (Table 1) [61, 62]. However, the percent contribution of the UPE emission from different anatomic locations (*i.e.*, relative UPE distribution along the body) was not significantly different for meditation practitioners and control subjects [62]. Afterwards, the authors increased the subject population (n = 60) including an intermediate group of 20 subjects who practised other relaxation techniques other than transcendental meditation. They obtained similar results (Table 1), although transcendental meditation was more efficient than the other techniques [63]. The authors claimed that the results agreed with the other documented investigations that confirmed physiologic changes during meditation, which were observed in the corresponding electrocardiogram, electroencephalogram, and skin-resistance recordings. This observation might be in accordance with the fact that the stress is connected to an increased production of ROS, which could explain the higher UPE in the control subjects. Moreover, the differences in the hands UPE between the control subjects and the meditation practitioners were not noteworthy. However, significant differences were found between the control subjects and the meditation practitioners when comparing their head and torso UPE intensities [61-63].

Besides meditation, some authors focused on the spontaneous UPE intensity changes due to the simple fact of **imagining, intention and/or cognition (*i.e.*, brain activity)** (Table 1) [64-67]. Dotta *et al.* [65] first showed that during brief intervals, when volunteers (n = 8) sat in a dark room and imagined white light, there was a repeatable, reliable and very statistically significant increase in the UPE from the right brain hemisphere while there was no change in the left hemisphere (Table 1). Later, this research group found a quantitative relationship between the deviation from random fluctuations in an electronic device and the brain activity's UPE when comparing "imagining" (intention) *versus* mundane (passive or non-intentional) thinking [66, 67]. When imagining, noticeable and reversible photon UPE intensity increased from the right hemisphere (Table 1). This was strongly correlated to left prefrontal brain activity [67]. Thus, these last discoveries suggest that the subject's intention modified, at least, the brain's UPE.

Conclusions

The UPE in humans is mainly due to the metabolic oxidative stress processes that cells naturally undergo in the presence of ROS. Nowadays it is accepted that the source of external human UPE is human skin. The skin is highly reactive to external stressors like UV radiation, which has been proven to influence UPE, but also to internal stressors such as a disease or brain activity. For the last two decades, there has been a significant increase in the research, and thus, published results, regarding UPE experiments focused on its dependence/correlation to diseases or brain activity. According to the revised literature, the ailing of some diseases in humans (including diabetes, hemiparesis, protoporphyria, or a typical cold) and some traditional Chinese disorders (including Spleen-Qi deficiency syndrome), influences the UPE. The influence of cancer on the spectral UPE emission has also been explored in mice and *in vitro* human cells, making it another field of enormous interest for future explorations of human cancer´s diagnosis. In conclusion, UPE seems to be a natural and promising non-invasive tool for helping during the diagnosis of a variety of illnesses.

In addition, the preliminary results regarding the influence of cerebral intention/relaxation (brain activity/meditation) on the human UPE would open new research lines. This capability might be useful in the future in the diagnosis of stress- / mood-state disorders. For all these reasons, the UPE measurements seems to show and provide a great potential for being explored in practice. Nonetheless, further research is needed in order to answer some still pending controversial points.

Conflicts of interests

Authors declare no conflicts of interests.

Acknowledgements

The authors thank the Spanish Ministry of Science, Innovation and Universities for the CTQ2017-91358-EXP research project, and also the University of Alcalá co-funding for allowing the equipment acquisition (2019 and 2020 calls).

REFERENCES

[1] F.A. Popp, B. Guenther, H.L. Koenig, Photon storage in biological systems. Electromagn. Bio. Inf., Proc. Symp. (1979) 123-149.

[2] H.J. Niggli, Ultraweak photons emitted by cells: biophotons. *J. Photochem. Photobiol. B: Biology* 14 (1992) 144-146. DOI: 10.1016/1011-1344(92)85090-H

[3] B. Devaraj, M. Usa, H. Inaba, Biophotons: ultraweak light emisión from living systems. Current Opinion Solid State Mater. Sci. 2 (1997) 188-193.

[4] Y. Zhu, Z. Zhu, Z. Guo, J. Ma, S. Li, Z. Bao, C. Bao, The spectra distribution properties of ultraweak photon emission from biological system and its applications in 21st century. SPIE 3899 (1999) 417-425.

[5] H.J. Niggli, L.A. Applegate, Biophotons: ultraweak photons in cells, in: F.A. Popp, L. Beloussov, Integrative Biophysics. Biophotonics. Springer. 2003. Pp. 361-386.

[6] H. Schwabl, H. Klima, Spontaneous ultraweak photon emisión from biological systems and the endogenous light field. Forsch Komplementärmed Klass Naturheilkd 12 (2005) 84-89. DOI: 10.1159/000083960.

[7] P. Pospíšil, A. Prasad, M. Rác, Role of reactive oxygen species in ultra-weak photon emission in biological systems. Journal of Photochemistry and Photobiology B: Biology 139 (2014) 11-23. DOI: 10.1016/j.jphotobiol.2014.02.008

[8] P. Pospíšil, A. Prasad, M. Rác, Mechanism of the formation of electronically excited species by oxidative metabolic processes: Role of reactive oxygen species. Biomolecules 9 (2019) 258. DOI: 10.3390/biom9070258

[9] A. Prasad, A. Balukova, P. Pospíšil, Triplet excited carbonyls and singlet oxygen formation during oxidative radical reaction in skin. Frontiers Physiol. 9 (2018) 1109. DOI: 10.3389/fphys.2018.01109

[10] M. Kobayashi, D. Kikuchi, H. Okamura, Imaging of ultraweak spontaneous photon emission from human body displaying diurnal rhythm. PLoS One. 4 (2009) e6256. DOI: 10.1371/journal.pone.0006256

[11] M. Valiadi, D. Iglesias-Rodríguez, Understanding bioluminescence in dinoflagellates – How far have we come? *Microorganisms* 1(1) (2013) 3-25. DOI: 10.3390/microorganisms1010003

[12] G.S. Erzinger, F. Schmoeller L.H. Pinto, L. Américo, R. Hemmersbach, J. Hauslage, D. Häder, Chapter 12. Bioluminescence systems in environmental biosensors, in: Bioassays. Advanced Methods and Applications, (2018) 241-262. DOI: 10.1016/B978-0-12-811861-0.00012-7.

[13] H.J. Niggli, Biophotons: our body produces light, Network 68 (1998) 16-17.

[14] M. Cifra, P. Pospíšil, Ultra-weak photon emission from biological samples: Definition, mechanisms, properties, detection and applications. J. Photochem. Photobiol. B. 139 (2014) 2-10.

[15] M. Kobayashi, Highly sensitive imaging for ultra-weak photon emission from living organisms. J. Photochem. Photobiol. B. 139 (2014) 34-38. DOI: 10.1016/j.jphotobiol.2013.11.011.

[16] I. Volodyaev, L.V. Beloussov, Revisiting the mitogenetic effect of ultra-weak photon emission. Frontiers Physiol. 6 (2015) 241. DOI: 10.3389/fphys.2015.00241

[17] R. Nejati, D. Kovacic, A. Slominski, Neuro-immuneendocrine functions of the skin: an overview, Expert Review of Dermatology, 8(6) (2013) 581-583. DOI: 10.1586/17469872.2013.856690

[18] F. Khabiri, R. Hagens, C. Smuda, A. Soltau, V. Schreiner, H. Wenck, K. Wittern, H. Duchstein, W. Mei, Non-invasive monitoring of oxidative skin stress by ultraweak photon emission (UPE)-measurement. I: mechanisms of UPE of biological materials. Skin Research Technol. 14 (2008) 103-111. DOI: 10.1111/j.1600-0846.2007.00205.x

[19] S. Premi, S. Wallisch, C. M. Mano, A. B. Weiner, A. Bacchiocchi, K. Wakamatsu, E. J. H. Bechara, R. Halaban, T. Douki, D. E. Brash, Chemiexcitation of Melanin Derivatives Induces DNA Photoproducts Long after UV Exposure. Science 347, 6224 (2015) 842-847.

[20] T. Blatt, C. Mundt, C. Mummert, T. Maksiuk, R. Wolber, R. Keyhani, V. Schreiner, U. Hoppe, D.O. Schachtschabel, F. Stäb, Modulation des oxidativen Stresses in der humanen Altershaut. Z Gerontol Geriat 32 (1999) 83-88.

[21] C. Scaletta F.A. Popp H.J. Niggli, L.A. Applegate, Y. Yan, UV-induced DNA damage and ultraweak photon emission in human fibroblastic skin cells: parameters to trigger intra- and extra-cellular photobiostimulation. Trends Photochem. Photobiol. 8 (2001) 53-65.

[22] H.J. Niggli, S. Tudisco, L. Lanzano, L.A. Applegate, A. Scordino, *et al*. Laser-ultraviolet-A-induced ultraweak photon emission in human skin cells: A biophotonic comparison between keratinocytes and fibroblasts. Indian J. Exp. Biol. 46 (2008) 358-363.

[23] F. Khabiri, R. Hagens, C. Smuda, A. Soltau, V. Schreiner, H. Wenck, K. Wittern, H. Duchstein, W. Mei, Non-invasive monitoring of oxidative skin stress by ultraweak photon emission (UPE)-measurement. I: mechanisms of UPE of biological materials. Skin Research Technol. 14 (2008) 103-111. DOI: 10.1111/j.1600-0846.2007.00205.x

[24] R. Hagens, F. Khabiri, V. Schreiner, H. Wenck, K. Wittern, H. Duchstein, W. Mei, Non-invasive monitoring of oxidative skin stress by ultraweak photon emisión (UPE)-measurement. II: biological validation on ultraviolet A-stressed skin. Skin Research Technol. 14 (2008) 112-120. DOI: 10.1111/j.1600-0846.2007.00207.x

[25] E. Van Wijk, R. Van Wijk, S. Bosman, Using ultra-weak photon emission to determine the effect of oligomeric proanthocyanidins on oxidative stress of human skin. J. Photochem. Photobiol. B 98 (2010) 199-206. DOI: 10.1016/j.jphotobiol.2010.01.003

[26] M. Kobayashi, T. Iwasa, M. Tada, Polychromatic spectral pattern analysis of ultra-weak photon emissions from a human body. J. Photochem. Photobiol. B. 159 (2016) 186-190. DOI: 10.1016/j.jphotobiol.2016.03.037

[27] K. Tsuchida, T. Iwasa, M. Kobayashi, Imaging of ultraweak photon emission for evaluating the oxidative stress of human skin. J. Photochem. Photobiol. B 198 (2019) 111562. DOI: 10.1016/j.jphotobiol.2019.111562

[28] K. Tsuchida, M. Kobayashi, Oxidative stress in human facial skin observed by ultraweak photon emission imaging and its correlation with biophysical properties of skin. Scientific Reports 10 (2020) 9626. DOI: 10.1038/s41598-020-66723-1

[29] R. Van Wijk, E. Van Wijk, Ultraweak photon emission from human body. In: Biophotonics, X. Shen, R. Van Wijk, Eds.; Springer, Boston, MA, 2005. pp 173-184.

[30] R. Van Wijk, E. Van Wijk, An introduction to human biophoton emission. Forsch Komplementärmed Klass Naturheilkd 12 (2005) 77-83. DOI: 10.1159/000083763

[31] R. van Wijk, E. van Wijk, H.A. van Wietmarschen, J. Greef, Towards whole-body ultra-weak photon counting and imaging with a focus on human beings: A review. J. Photochem. Photobiol. B. 139 (2014) 39-46. DOI: 10.1016/j.jphotobiol.2013.11.014

[32] M. Cifra, C. Brouder, M. Nerudová, O. Kučera, Biophotons, coherence and photocount statistics: A critical review. J. Luminescence 164 (2015) 38-51. DOI: 10.1016/j.jlumin.2015.03.020

[33] I. Volodyaev, L.V. Beloussov, Revisiting the mitogenetic effect of ultra-weak photon emission. Frontiers Physiol. 6 (2015) 241. DOI: 10.3389/fphys.2015.00241

[34] M. Calcerrada, C. García-Ruiz, Human ultraweak photon emission: Key analytical aspects, results and future trends - A review. *Crit. Rev. Anal. Chem.* 49(4) (2019) 368-381. DOI: 10.1080/10408347.2018.1534199

[35] E. van Wijk, R. van Wijk, Multi-site recording and spectral analysis of spontaneous photon emission from human body. Forsch Komplementärmed Klass Naturheilkd 12 (2005) 96-106. DOI: 10.1159/000083935

[36] H. Jung, J. Yang, W. Woo, C. Choi, J. Yang, K. Soh, Yearlong biophoton measurements: Normalized frequency count analysis and seasonal dependency. J. Photochem. Photobiol. B. 78 (2005) 149-154. DOI: 10.1016/j.jphotobiol.2004.08.002

[37] G. Sauermann, W. Mei, U. Hoppe, F. Stab, Ultraweak photon emission of human skin in vivo: Influence of topically applied antioxidants on human skin. Meth. Enzymol. 300 (1999) 419-428. DOI: 10.1016/S0076-6879(99)00147-0

[38] K. Nakamura, M. Hiramatsu, Ultra-weak photon emission from human hand: Influence of temperature and oxygen concentration on emission. J. Photochem. Photobiol. B. 80 (2005) 156-160. DOI: 10.1016/j.jphotobiol.2005.02.005

[39] A. Prasad, P. Pospíšil, Two-dimensional imaging of spontaneous ultra-weak photon emission from the human skin: Role of reactive oxygen species. J. Biophotonics. 4 (2011) 840-849. DOI: 10.1002/jbio.201100073

[40] X. Zhao, E. van Wijk, Y. Yan, R. van Wijk, H. Yang, Y. Zhang, J. Wang, Ultra-weak photon emission of hands in aging prediction. J. Photochem. Photobiol. B. 162 (2016) 529-534. DOI: 10.1016/j.jphotobiol.2016.07.030

[41] Y. Gabe, O. Osanai, Y. Takema, The relationship between skin aging and steady state ultraweak photon emission as an indicator of skin oxidative stress in vivo. Skin Research Technol. 20 (2014) 315-321. DOI: 10.1111/srt.12121

[42] T. Kim, K. Nam, H. Shin, S. Lee, J. Yang, K. Soh, Biophoton emission from fingernails and fingerprints of living human subjects. Acupunct. Electrother. Res. 27 (2002) 85-94. DOI: 10.3727/036012902816026068

[43] R. van Wijk, M. Kobayashi, E. van Wijk, Anatomic characterization of human ultra-weak photon emission with a moveable photomultiplier and CCD imaging. J. Photochem. Photobiol. B. 83 (2006) 69-76. DOI: 10.1016/j.jphotobiol.2005.12.005

[44] J.A. Ives, E. van Wijk, N. Bat, C. Crawford, A. Walter, W.B. Jonas, R. van Wijk, J. van der Greef, Ultraweak photon emission as a non-invasive health assessment: A systematic review. PLoS One 9(2) (2014) e87401. DOI: 10.1371/journal.pone.0087401

[45] M. He, M. Sun, E. van Wijk, H. van Wietmarschen, R. van Wijk, Z. Wang, M. Wang, T. Hankemeier, J. van der Greef, A Chinese literature overview on ultra-weak photon emission as promising technology for studying system-based diagnostics. Complement. Ther. Med. 25 (2016) 20–26. DOI: 10.1016/j.ctim.2015.12.015

[46] R.C. Rossetto-Burgos, E. van Wijk, R. van Wijk, M. He, J. van der Greef, Crossing the boundaries of our current healthcare system by integrating ultra-weak photn emissions with metabolomics. Frontiers Physiol. 7 (2016) 611. DOI: 10.3389/fphys.2016.00611

[47] M. Yang, E. Van Wijk, J. Pang, Y. Yan, J. van der Greef, R. Van Wijk, J. Han, A Bridge of Light: Toward Chinese and Western Medicine Perspectives Through Ultraweak Photon Emissions. Global Adv. Health Medicine 8 (2019) 1-7. DOI: 10.1177/2164956119855930

[48] H. Jung, W.M. Woo, J.M. Yang, C. Choi, J. Lee, G. Yoon, J.S. Yang, S. Lee, K.S. Soh, Left-right asymmetry of biophoton emission from hemiparesis patients. Indian J. Exp. Biol. 41 (2003) 452-456.

[49] A.B. Petersen, P.A. Philipsen, H.C. Wulf, An explorative study of non-invasive ultra-weak photon emission and the anti-oxidative influence of oral zinc sulphate in light-sensitive

patients with erythropoietic protoporphyria. Skin Research Technol. 0 (2011) 1-8. DOI: 10.1111/j.1600-0846.2011.00586.x

[50] M. Yang, J. Pang, J. Liu, Y. Liu, H. Fan, J. Han, Spectral discrimination between healthy people and cold patients using spontaneous photon emission. Biomed. Opt. Express. 6 (2015) 1331-1339. DOI:10.1364/BOE.6.001331

[51] M. Sun, E. van Wijk, S. Koval, R. van Wijk, M. He, M. Wang, T. Hankemeier, J. van der Greef, Measuring ultra-weak photon emission as a non-invasive diagnostic tool for detecting early-stage type 2 diabetes: A step toward personalized medicine. J. Photochem. Photobiol. B. 166 (2017) 86-93. DOI: 10.1016/j.jphotobiol.2016.11.013

[52] M. He, M. Sun, S. Koval, R. Van Wijk, T. Hankemeier, J Van der Greef, E. Van Wijk, M. Wang, Traditional Chinese Medicine-Based Subtyping of Early-Stage Type 2 Diabetes Using Plasma Metabolomics Combined with Ultra-Weak Photon Emission Engineering 5 (2019) 916-923. DOI: 10.1016/j.eng.2019.03.011

[53] M. Yang, W. Ding, Y. Liu, H. Fan, R.P. Bajpai, J. Fu, J. Pang, X. Zhao, J. Han, Ultra-weak photon emission in healthy subjects and patients with type 2 diabetes: evidence for a non-invasive diagnostic tool. Photochem. Photobiol. Sci. 16 (2017) 736-743. DOI: 10.1039/c6pp00431h

[54] N. Wang, X. Huang, T. Li, M. Wang, H. Yue, C. Chen, S. Liu, Application of RRLC-QTOF-MS-based metabonomics and UPE for investigating Spleen-Qi deficiency syndrome with Panax ginseng treatment. J. Ethnopharmacol. 256 (2020) 112822. DOI: 10.1016/j.jep.2020.112822

[55] T. Amano, M. Kobayashi, B. Devaraj, M. Usa, H. Inaba, Ultraweak Biophoton Emission Imaging of Transplanted Bladder Cancer, *Urol. Res.*, 23 (1995) 315-318.

[56] M. Takeda, Y. Tanno, M. Kobayashi, M. Usa, N. Ohuchi, S. Satomi, H. Inaba, A novel method of assessing carcinoma cell proliferation by biophoton emission. Cancer Lett. 127 (1998) 155-160.

[57] M. Takeda, M. Kobayashi, M. Takayama, S. Suzuki, T. Ishida, K. Ohnuki, T. Moriya, N. Ohuchi, Biophoton detection as a novel technique for cancer imaging. *Cancer Sci*, 95:8, (2004) 656-661.

[58] X. Zhao, J. Pang, J. Fu, Y. Wang, M. Yang, Y. Liu, H. Fan, L. Zhang, J. Han, Spontaneous photon emission: A promising non-invasive diagnostic tool for breast cancer. J. Photochem. Photobiol. B 166 (2017) 232-238. DOI: 10.1016/j.jphotobiol.2016.12.009

[59] N.J. Murugan, M.A. Persinger, L.M. Karbowski, B.T. Dotta, Ultraweak photon emissions as a non-invasive, early-malignancy detection tool: An in vitro and in vivo study. Cancers 12 (2020) 1001. DOI: 10.3390/cancers12041001

[60] E. van Wijk, J. Ackerman, R. van Wijk, Effect of meditation on ultraweak photon emission from hands and forehead. Forsch Komplementärmed Klass Naturheilkd 12 (2005) 107-112. DOI: 10.1159/000084028

[61] E. van Wijk, H. Koch, S. Bosman, R. van Wijk, Anatomic characterization of human ultra-weak photon emission in practitioners of transcendental meditation (TM) and control subjects. J. Altern. Complement. Med. 12 (2006) 31-38.

[62] E. Van Wijk, R. Van Wijk, R. Bajpai, Quantum squeezed state analysis of spontaneous ultra weak light photon emission of practitioners of meditation and control subjects. Indian J. Exp. Biol. 46(5) (2008) 345-352.

[63] E. Van Wijk, R. Lüdtke, R. Van Wijk, Differential effects of relaxation techniques on ultraweak photon emission. J. Alt. Complemnt. Medicine, 14(3) (2008) 241-250. DOI: 10.1089/acm.2007.7185

[64] V. Salari, J. Tuszynski, I. Bokkon, M. Rahnama, M. Cifra, On the photonic celular interaction and the electric activity of neurons in the human brain. J. Physics: Conf. Series 329 (2011) 012006. DOI: 10.1088/1742-6596/329/1/012006.

[65] B.T. Dotta, M.A. Persinger, Increased photon emissions from the right but not the left hemisphere while imagining White light in the dark: The potential connection between consciousness and cerebral light. J. Consciousness Expl. Res. 2 (2011) 1463–1473.

[66] B.T. Dotta, K.S. Saroka, M.A. Persinger, Increased photon emission from the head while imagining light in the dark is correlated with changes in electroencephalographic power: Support for Bokkon's biophoton hypothesis. Neurosci. Lett. 513 (2012) 151–154.

[67] J.M. Caswell, B.T. Dotta, M.A. Persinger, Cerebral biophoton emission as a potential factor in non-local human-machine interaction. Neuroquantology 12 (2014) 1-11.