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Towards whole-body ultra-weak photon counting and imaging with a focus on human beings: A review

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ABSTRACT

For decades, the relationship between ultra-weak photon emission (UPE) and the health state of the body is being studied. With the advent of systems biology, attention shifted from the association between UPE and reactive oxygen species towards UPE as a reflection of changed metabolic networks. Essential for this shift in thinking is the development of novel photon count statistical methods that more reflect the dynamics of the systems organization. Additionally, efforts to combine and correlate UPE data with other types of measurements such as metabolomics be key to understand the complexity of the human body. This review describes the history and developments in the area of human UPE research from a technical – methodological perspective, an experimental perspective and a theoretical perspective. There is ample evidence that human UPE research will allow a better understanding of the body as a complex dynamical system. The future lies in the further development of an integrated UPE and metabolomics platform for a personalized monitoring of changes of the system towards health or disease.

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1. Introduction

1.1. Early history: Body light points to health and the field of medicine

The utilization in the early 1960s in biology of the photomultiplier tube (PMT) provided a research tool that could demonstrate the existence of the ubiquitous ultra-weak photon emission (UPE) from organisms. The earliest work addressing UPE was primarily accomplished in the USSR, and partially translated into English [1]. It established that weak photon emission could occur during oxidation providing information about radical reactions [2,3]. However, outside the USSR, the existence of such radiation was only a subject of dispute [4]. In the 1970s, its existence was finally confirmed by researchers in Japan [5], Australia [6], Poland [7], Germany [8], USA [9], and China [10]. Emissions were in the order of $10–10^3$ photons/s cm^2 demonstrating UPE presence in all of the organisms evaluated including the cells and homogenates of those organisms. In the 1980s and 1990s, the idea that light emanating from bodies could highlight both health and disease increasingly received the attention of mainstream biomedicine. Inaba and coworkers documented observations that the blood of patients suffering from conditions such as cancer, diabetes, and jaundice emits more light than that of healthy people. In 1986, those researchers launched a biophoton project with the intention to improve the technology by adding spatial resolution in order to apply additional knowledge to medical situations [11]. The reactivity of free oxygen radical species then became implicated in numerous disease conditions such as diabetes mellitus, liver and lung diseases, atherosclerosis, cancer, neurodegenerative diseases, rheumatoid arthritis, ischemia/reperfusion injury, and other medical conditions [12–14]. The biomedical future of UPE has recently been less productive as it focuses on the unraveling of the complexity of *in vivo* photon production, absorption and emission.

1.2. From reductionism to a systems approach

Recently, other avenues to stimulate UPE research in biomedicine have opened up including system based rather than a reductionist orientation. The question regarding what type of reaction is responsible for UPE is perhaps less important than the type of metabolism associated with UPE. Rather, it is the change from the search for the molecular basis of UPE towards a search for the metabolic interplay. It parallels the change from reductionism

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to systems biology. The landscape of systems thinking about biology in medicine has been shaped by many contributors advancing key concepts regarding life's complexity pyramid from individual molecules to interacting subsystems [15] including the importance of biological rhythms [16,17]. The basic research approach addresses the survival of the organism. This needs crucial, fault-intolerant biological processes for which multiple parallel metabolic control systems exist [18]. Redox regulation is included. That means that each system, in order to survive, may show a particular metabolic pattern (out of many possibilities). A redox regulation system offers the possibility to categorize into subgroups. The rapid evolution of novel "omics" tools, biostatistics and bioinformatics during the past decade has created the possibility to study, *in vivo*, physiology and pathology systems [19]. Photon emission is then part of the dataset of both radiation and molecular properties of the state of the system that is referred to as a "system response profile". The system's response is environmentally dependent. Within a particular environment, it also depends on a system's history.

1.3. Towards integrating metabolomics and UPE

System-response profiles are commonly generated by applying particular techniques in order to analyze samples that may represent an *in vivo* system [20,21]. It includes the overall chemical composition of body fluids as well as physical whole body UPE radiation. The radiation and chemical approaches both follow a flow chart that represents (1) sampling, (2) analysis, and (3) sub-grouping (Fig. 1). The *sampling* of the radiation approach emphasizes a search for *in vivo* representative anatomical locations. The *analysis* of whole body UPE signals utilizes both the emission spectrum and photon count distribution properties. The many properties of a photon signal require different mathematical techniques for the various types of photon count distribution analyses both for the temporal aspect of the signal and different anatomical locations for the spatial aspect of UPE. In the chemical approach, sampling identifies body fluid (blood, urine, saliva) representing the *in vivo* state. The *analysis* of individual molecules within broad metabolomics technology is utilized with analytical platforms for different types of metabolites: NMR spectra (for high-abundance metabolites); GC–MS and LC–MS spectra (for polar and non-polar metabolites). The third step includes the *subgrouping* of both the UPE and metabolite datasets using correlation network and cluster analysis. Ultimately, the data from both approaches are utilized to correlate systems UPE and metabolic profiles within subjects. The dynamic changes in a subject's system state may then be used for novel individual diagnostic purposes [22].

1.4. Overview of the paper

The present review will be limited to the progress that has been made in human body photon counting and imaging. It discusses the practical choices that must be made for reliable recording of human photon emission (Section 2), the anatomical emission pattern (Section 3), the time scale of spontaneous changes in photon emission (Section 4), induced changes of UPE in studies using adaptogens and UV (Section 5), the application of studies evaluating relaxation/meditation (Section 6). The review finally points to recent and future developments in signal analysis (Section 7) plus the comparison with progress in human UPE research with respect to time-integrated metabolomics (Section 8).

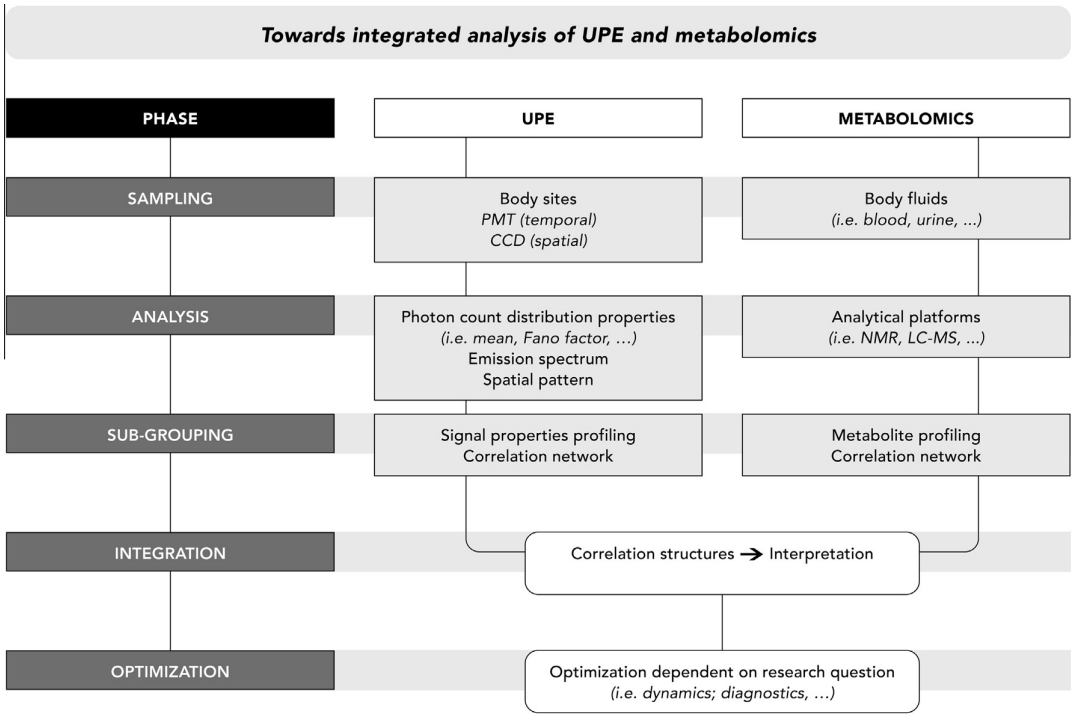

Fig. 1. Developmental phases towards integrated analysis of UPE and metabolomics as part of the systems biology platform. The developmental phases include sampling the system, analysis of data, sub-grouping by profiling and correlation network analysis. Types of sampling, data-analysis and sub-grouping are presented as example. In experiments using the integrated approach the extended correlation structures are used for the interpretation of data with respect to the association of UPE with the type of metabolism.

2. Reliable recording of human photon emission

2.1. Dark room and PMT

Whole-body photomultiplier technology (PMT) achieved a breakthrough by investigations on the influence of thermal and stray radiation that is superimposed on ultra-weak biological radiation [23]. A research room was constructed including (a) only a low background (count rate of less than 0.1 photons s^{-1} cm^{-2}) and (b) a photomultiplier hanging from the ceiling that facilitated manipulation in three directions over a human body. The PMT with a sensitivity in the UV and visible part of the spectrum (300–650 nm) was selected. Under the above working conditions, the low background value averaged 5.4 ± 0.3 cps. The darkroom included a temperature of 20 °C. The subjects were recorded in a supine or sitting position. For positioning of the PMT at specific body locations, a cone shaped extender was fixed at the front of the photomultiplier tube allowing recording of emission from a 9 cm diameter anatomic area at a fixed distance of 7 cm [24,25].

2.2. Scanning mode

The movable photomultiplier should, theoretically, allow systematic scanning of the photon strength over the body. The time slots for recording emission is important in order to obtain reliable data facilitating sufficient types of data analysis. A duration of recording was selected that permitted, on the one hand, registration of the subject over as many skin locations as possible within a reasonable time, and, on the other hand, a high accuracy to reliably distinguish between intensity of different locations. These two variables act in an opposite manner. High accuracy is obtained with longer recording periods whereas the subject's time in the dark room must be limited. For instance, the mean can become stable in measurements of approximately 100 s [26–28]. For photon count distribution analysis a minimal bin size of 50 ms is used. It must be noted that such conditions must be established for each new photon emission attribute.

2.3. Subject's dark adaptation

A disturbing phenomenon called delayed luminescence can easily occur if the potential subject is exposed to light prior to the experimental recording. The time of dark adaptation in the research facility depends on the intensity and wavelength of the previous environmental light exposure. UV (daylight) exposure induces delayed luminescence of skin [26–31]. In contrast, delayed luminescence can also be induced after exposure to visible wavelengths in the range of seconds. This means that "dark-adaptation" of subjects should be done in low visible or red light. Sufficient time of dark-adaptation is advisable after exposure to UV. In most experimental settings, a subject is dark adapted for at least 30 min.

2.4. Emission spectrum

A difference between spectra of emission of different body locations makes it difficult to compare the photon count data from these locations. This is related to the shape of the curve representing the spectral dependency of quantum efficiency of the PMT. For spectral analysis, a series of cut-off filters have usually been utilized. In one study, the UPE spectrum of low, intermediate and high emitting body locations (i.e., leg, forehead and the palms of both hands, respectively) were estimated. The emission spectra are, within the detection limits, rather similar with a major emission between 420 nm and 550 nm [26–28]. However, more studies and more body locations are needed to estimate whether the emission spectrum over the entire body is identical or not.

2.5. Stability of signal

Since photon emission of multiple body locations is consecutively measured, a comparison between body locations will be unreliable if the emission at a particular location is rapidly changing. Especially in long term experiments, such a problem will arise. For this reason, preliminary long term measurements are suggested to estimate the stability of emission. Our data have indicated that subjects in a stable situation, physically and psychologically, demonstrate a photon emission that changes not more than 15% in 1 h. This temporal factor will be further discussed in Section 4.

2.6. Psychological aspects of measurement

Psychological aspects must be considered for ethical reasons. Subjects (non-scientists) not familiar with the long period of lying on a bed in a completely dark room must be given sufficient explanation about the measurement. It must be sure that the tested person will not be stressed. The subject is advised to relax and remain in the relaxed state. However, such state cannot be kept continuously. Also, there is the possibility of falling asleep. Others have learned to relax in a special manner using meditation techniques. In all cases, the advice is to relax and not to meditate.

3. The anatomical emission pattern and studies on symmetry

3.1. A protocol for studying symmetry

With the data presented in Section 2, it can be calculated that a full scanning of an adult human with a skin surface of 2 m^2 (i.e., a subject of 80 kg and 1.83 m) requires more than 300 measurements and would take more than 10 h. This makes it necessary to limit the number of anatomical locations depending on the research question. The first protocol was aimed at studying right-left and dorsal–ventral symmetry of whole-body emission utilizing 29 body locations. During a 1.5 h measurement period, the front of the body (ventral) was recorded first, beginning at the forehead and then moving downwards towards the feet, at each level from left to right. Subsequently, the subject turned and the dorsal part of the body was recorded, beginning with the legs and moving upwards toward the head [26–28]. It was experienced by subjects (in a supine position) as rather exhausting. Therefore, it was only applied in cooperation with 4 colleague researchers.

3.2. Symmetry in research

UPE was not evenly distributed over the body. There were definite areas with relatively low and relatively high UPE. Although the four subjects differed in average UPE, the specific high and low UPE areas were anatomically similar. The thorax/abdomen region had the lowest intensity. In contrast, the extremities and the head region revealed the highest levels. Repetition of these measurements with an intermediate period of 3 h suggested that overall emission could change but the anatomical intensity pattern remained with the high degree of left–right and ventral-dorsal symmetry (Fig. 2) [26–28]. Ventral-dorsal symmetry was slightly less than the left–right symmetry. This may be explained by the fact that emission could change in time. Left–right locations were measured directly one after the other, whereas the corresponding ventral-dorsal locations were more separated in time.

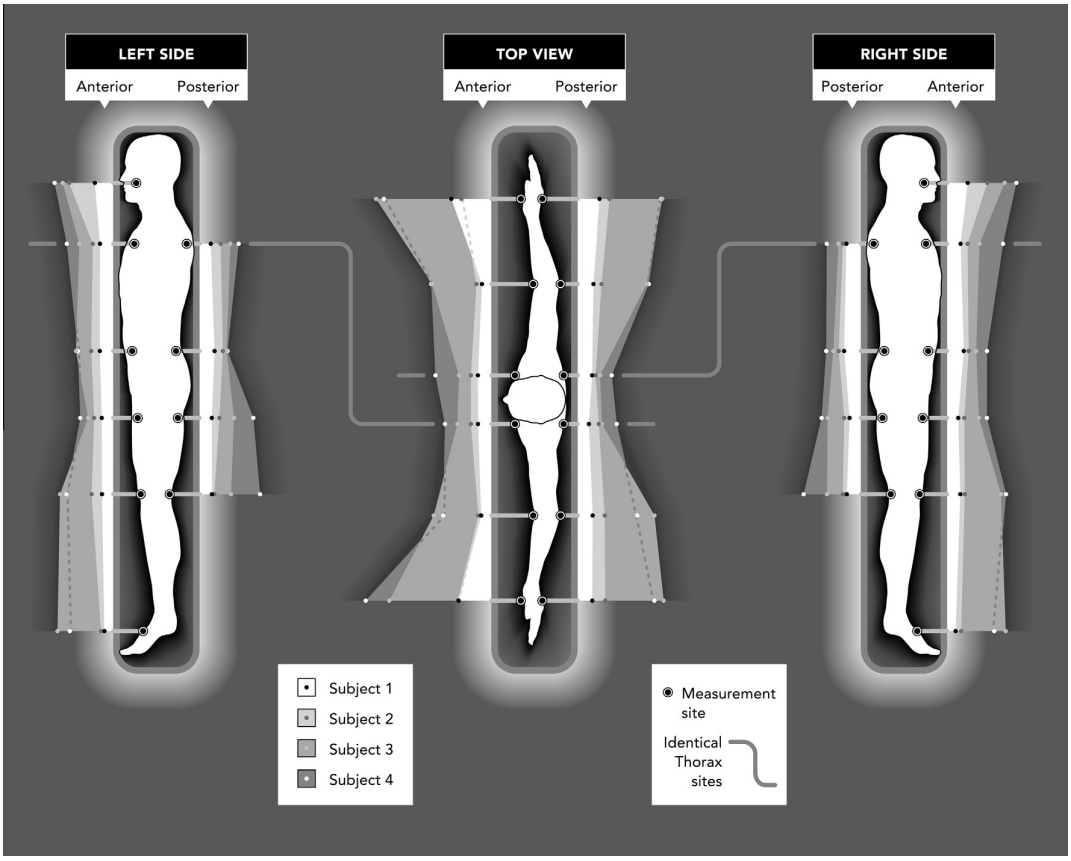

Fig. 2. Topographical variation of UPE utilizing data on multi-site spontaneous photon emission of 4 subjects (data from Refs. [26,27]). The measurement sites on the body give insight on the dorsal–ventral and left–right symmetry. The average overall UPE intensity was different for the 4 subjects. The subject with the lowest overall emission is represented in white; the subject with the highest emission is represented by the darkest gray. Data illustrate the high degree of symmetry within each subject as well as the "common" human emission pattern.

3.3. Confirmation of a UPE anatomical pattern using CCD imaging

At the time that PMT data on an anatomical pattern became available, a breakthrough in imaging technology was made by Kobayashi [32]. He imaged a human's upper torso, head and hand utilizing a cryogenically cooled (at −100 °C) CCD camera system. The anatomical body emission pattern was studied using both the movable PMT and the CCD camera system [33,34]. The CCD data confirmed the high degree of symmetry observed during the PMT measurements. Additionally, the CCD images illustrated the complicated photon emission of the head and the hands.

3.4. Confirmation of superior central torso and hand UPE pattern using a short PMT protocol in group measurements

The concept of a pattern was further studied by focusing on the emission gradient from low emission sites over the abdomen to high emission sites over the forehead and the palms of the hand (Fig. 2). Such protocol included measurements of 12 anatomical locations within 45 min while subjects lay in only one position. The protocol was not experienced as exhausting and could be used in studies with a larger number of human subjects. The purpose was to estimate the contribution of each anatomic location to the total emission. The sum of emissions from 12 anatomic locations could differ by almost a factor of 5 between subjects [33,34]. Each anatomic location's percentage of emission from each subject participated in total emission with a constant percentage. The contribution of each anatomic location corresponded with the frontal-torso gradient as observed in a CCD image as part of a "common" human anatomic percentage distribution emission pattern.

4. Spontaneous temporal changes of UPE

4.1. Types of changes

The observations that UPE can change has influenced researchers to study this question more in detail. Two strategies have been followed. The first strategy focuses on "spontaneous" changes and the second on "induced" changes. In studies of the first type, small numbers of subjects (or even a single subject) participated frequently and/or for a long time. In such studies, the discomfort was limited by measuring only a few anatomical locations which primarily were strong emitting locations such as hands and/or forehead.

4.2. Spontaneous changes during the year

In a long-term daily systematic study by Cohen and Popp [24,25], photon emission from the hands and forehead of one subject was evaluated over a period of 9 months. Recordings demonstrated a clear preference of left and right hand correlation. A long-term biological rhythm of spontaneous emission became evident with Fourier analysis. The long-term phases of the

oscillations for left and right hand were in correspondence. However, a deviating pattern was observed from the forehead. Another long-term study addressed changes of human hand photon emission in three healthy subjects for 1 year with weekly measurements [35]. During the year, average photon emission values depended on the month of the year with seasonal fluctuations on the dorsal sides being twice that of the palms [35]. These features could not be explained simply by external conditions (such as sunlight exposure). The authors speculated about a relationship between the dynamics of diurnal and annual rhythms in photon emission and *yin/yang* dynamics according to TCM and Korean Medicine [36].

4.3. Spontaneous changes during the day

A study on changes in UPE during a 24 h period was performed by recording ventral and dorsal sites of both right and left hands every 2 h in 5 separate experiments using PMT. Data demonstrated that intensity as well as left–right symmetry varied diurnally. Emission intensity was low during the day, rose during the evening and was high at night. Time patterns for left and right hands were different. Fluctuations of UPE were more over dorsal than ventral sites [37,38]. In another study, a CCD system was utilized to investigate the temporal variations of photon emission of the upper torso and face over 24 h. Emission intensity of specific areas as well as the size of areas could fluctuate with equal brightness. The diurnal rhythm of photon emission was not a consequence of a change in temperature [39].

4.4. Spontaneous changes in the course of hours and minutes

A CCD system was used for imaging photon emission changes of hands [40]. The emission pattern of left and right hands were almost similar. Emission intensity was highest at the fingertips. When spontaneous changes occurred, the images demonstrated that emission intensity of specific areas as well as the size of areas with equal brightness continually changed (Fig. 3). The images suggested that shifts in brightness followed a specific anatomical pattern [40]. If changes in both left and right hands are studied utilizing time scales of minutes to evaluate if both hands change at the same time, it is important to know that CCD imaging requires 15 or more min of exposure. For such studies, simultaneous recordings must utilize two PMT's. Although such systems have been recently used in a few studies, data on changes in the min range have not yet been published.

5. Induced changes in photon emission

5.1. Induced changes in photon emission by adaptogens

The influence by the consumption of plant adaptogens (Rhodiola rosea and ADAPT-232) regarding human photon emission have been evaluated in a randomized double-blind placebo-controlled study [41]. Thirty subjects were randomly assigned to three groups: one group ($n = 10$) taking Rhodiola rosea (SHR-5) pills, one group ($n = 10$) taking ADAPT-232 supplements (the latter being a fixed combination of the following three adaptogens: Eleutherococcus senticosus, Rhodiola rosea and Schisandra chinensis), and one group ($n = 10$) taking placebo pills. All subjects underwent measurements to determine ultra-weak photon emission (UPE) of the dorsal side of their hands, both before and after a week of taking the supplements. In addition, the experienced levels of stress and fatigue (tiredness) were evaluated. After 1 week of supplementation, the Rhodiola group revealed a significant decrease in photon emission in comparison with the placebo group. Furthermore, after supplementation, a significant decrease ($p = 0.049$) in the level of fatigue in the Rhodiola group was observed compared with the placebo group. No significant changes were observed in both photon emission and fatigue levels between the ADAPT-232 and the placebo group.

5.2. Induced changes in photon emission by UV exposure

Exposure of skin to ultraviolet (UV) radiation triggers oxidative stress in skin tissue [27,29–31]. The effect of UV was studied using a fractionated exposure protocol. In the study, 25 healthy female subjects participated [29]. Repeat UV exposure resulted in a long-term increase of spontaneous UPE. It was assessed by measuring spontaneous UPE at 80 min after each UV exposure. The authors suggested that it is likely due to depletion of anti-oxidant capacity of skin. In the same study, the effect of oligomeric proanthocyanidins (OPCs, having an anti-oxidant activity on the skin) were studied. OPCs immediately topically applied after UV exposure resulted in a reduced long term increase in spontaneous UPE.

6. Relaxation/meditation: Application of the protocol in life style research

6.1. Psychological aspects of measurement

In long term human measurements, particularly in a dark room, psychological factors need to be considered. Subjects relaxed in different manners and the question was asked whether a subject's

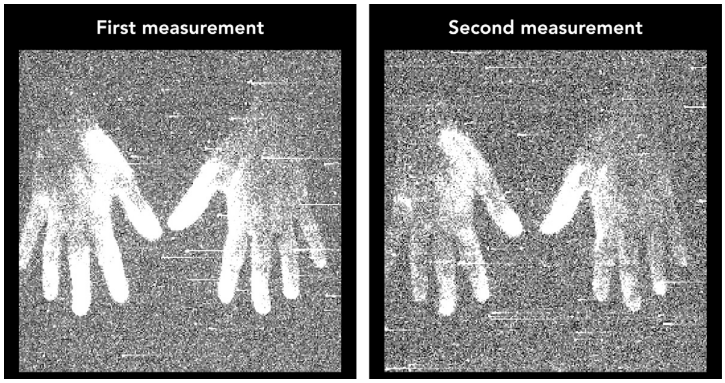

Fig. 3. Illustrative example of CCD images on a change in ultra-weak photon emission of the dorsal sides of the right and left hand of a long-term dark-adapted subject. The time between the images was 140 min illustrating a change in brightness following a specific anatomical pattern. Other data are in Ref. [40].

personal history of using special relaxation (i.e., meditation) techniques had an influence on UPE levels in a relaxed state (during recording). The question is not only interesting because meditation has become a prominent mind–body therapy [42–44] but also because a link between meditation and lower lipid peroxide levels in plasma of practitioners of Transcendental meditation, Zen meditation, and yoga have been detected [45–47]. Meta-analyses of clinical studies have also suggested that Transcendental meditation has been associated with larger effect sizes than the other techniques [48]. Meditation utilizes a variety of different techniques influencing physiological and psychological processes [49].

6.2. UPE and meditation

A comparative study utilized a short protocol (paragraph 3.4) to measure photon signals from twelve anatomical sites in sixty male subjects [50,51]. The subjects were in three groups each of twenty members differing primarily in the type of meditation practiced over the last ten years. The study included 20 practitioners of Transcendental meditation (TM), 20 practitioners of other meditation types (OM) and 20 control subjects without any experience in meditation. The subjects were healthy and free of medications. The groups were not different with respect to age or BMI. The average overall photon emissions in the TM and OM groups were 27% and 17% lower, respectively, compared to the group. Both TM and OM demonstrated lower emissions than control subjects for each anatomic location, whereas the TM practitioners demonstrated lower emissions than OM practitioners in 11 of 12 locations, indicating systematic group differences. The percent emission contribution of each anatomic location to total emission for each group of subjects was very similar for the three groups. Taken together, the data suggest that the type of relaxation practiced in daily life has influence on UPE in a subject's relaxed state, but the anatomic emission pattern was highly idiosyncratic [51].

6.3. Sleep studies

In long-term studies, the advise to relax and to remain in the relaxed state is difficult to keep continuously. A subject may even fall asleep. For this reason it is important to recognize the change in UPE emission, if any, when a subject in a dark room falls asleep. Such studies have not been published yet.

7. Towards novel variables of photon count distributions

7.1. Necessity to extend signal analysis

In most studies, the mean intensity or strength of the signal was utilized to quantify the signal. This is only one of many variables of the signal. Its value is limited. This is easy to understand because a shift in the emission spectrum results in a change in measured intensity due to the shape of the wavelength dependency of quantum efficiency of the counting tube. The estimation of the human emission spectrum is too time consuming to be included in a protocol for human emission measurements. Therefore, another strategy has focused on the distribution of counts in a photon signal and the discovery of novel photon count distribution parameters. It is evident that such additional signal variables need physiological and physical substantiation in the future. A few of the possible novel variables have been studied.

7.2. Squeezed state model approach

In one study, the photon count distribution was described as "Best fitting" according to a squeezed state model with its specific variables [52,53]. A first calculation of these squeezed state model parameters was based on photon count distributions of three human body sites [54]. The squeezed state parameters of different body locations were not different for a single subject. This line of research has been continued using large groups of subjects [55,56]. A recent study has extensively described the attributes (parameters) of the photon count distribution of time series of counts according to the squeezed state model: the squeezed state parameters $|\alpha|$, r, θ and ϕ, the squeezed state index, and sum of the squares of residue [57].

7.3. Fano factor approach

Fano factor is another property of the photon count distribution in time series. The ratio of variance to the mean of a time series is called Fano Factor [58]. Fano Factor of a UPE signal changes with the bin size of the time series. The fluctuations were around a line specified by its slope and intercept. Fano factor properties have been estimated in a few human studies [57,59,60].

7.4. Relationship between parameters and systemic organization

The set of parameters requires testing for their value to characterize subjects in different types of systemic organization. In a recent publication [57] cluster analysis was used to determine the discriminating power of the parameters using data on meditation discussed in paragraph 6.2. The data set contained UPE signals measured at twelve sites in sixty human subjects, in three groups of twenty members differing in type of meditation. The data specifying the subjects belonging to different clusters were compared with the type of meditation of the same subjects. The agreement between members in clusters and subjects in meditation groups was correct or nearly correct for several (combinations of) parameters. In particular the combination of intercept and slope of Fano Factor curve correctly identified the group association of every subject. It was concluded that all parameters contain biological, but different amounts of information.

8. Towards a correlation analysis of UPE and metabolomics

8.1. Summarizing the content of this review

This review has summarized the human photon research that has led to the presently used procedure for reliable data collection. The knowledge includes the constant anatomical pattern of photon emission in healthy male subjects, the duration of measurement, the influence of relaxation during measurement, and the search for additional variables based on photon count distribution. Moreover, the complementary measurements using a photomultiplier tube (for temporal information) and CCD imaging equipment (for spatial information) have been discussed. With such a package of knowledge, it was possible to design the most simple device for characterizing human photon emission. It consists of a two-hand device that allows the simultaneous measurement of left and right hand and can be used to estimate left–right symmetry, dorsal–ventral symmetry with data sets that facilitate the analysis of many variables of the photon signal (e.g., mean, Fano factor, squeezed state model parameters). The device consists of a box that does not need a complete dark room, but rather only dim-light. Another advantage of this construction is psychological. Subjects prefer this open situation making communication possible and it easily avoids falling

asleep. Therefore, it can be utilized in experiments requiring sampling photon data in large groups of subjects.

8.2. Technology to detect changes in metabolomics

The photon emission sampling system offers good perspectives regarding two other experimental setups. It offers the possibility to introduce specific new and immediate challenges during recording. It is also easy to simultaneously sample small quantities of blood for the estimation of metabolites utilizing metabolomics studies. Ongoing technological developments in the area of metabolomics currently allows for the processing of large numbers of samples which can be employed to measure metabolic rhythms. It now becomes possible to simultaneously measure rhythmicity in large numbers of metabolites. Various classes of metabolites with oscillatory behavior have been discovered such as amino acids, carbohydrates, nucleotides, lipids and vitamins [61]. It has also been applied in plasma metabolomics internal body time with time shifts from jet-lag that can be accurately estimated as well as other circadian rhythm disorders [62,63]. It now becomes possible to compare endogenous and exogenous metabolic rhythmicity with the fluctuations of UPE. Such data will make it possible to stimulate UPE research in biomedicine opening up a systems based orientation in which the focus is placed on the type of metabolic interplay that is reflected in the UPE.

8.3. Towards a combination of UPE and metabolomics in health and disease

The broader aim of the presented combined UPE/metabolomics research is to proceed towards today's clinical practice. The link between human photon emission and disease has been studied revealing several interesting observations based on the intensity of the signal. A study imaging of the two-dimensional pattern from the index and middle fingers was used to differentiate hypothyroidism, a lower state of metabolic activity than normal [64–66]. Photon emission in those patients with hypothyroidism was always less intense than normal. This lower emission was also found in patients whose thyroid glands had been removed. These results may connect the intensity of UPE with type of metabolism and may be interesting for future combined UPE/metabolomics studies. A second parameter for disease (e.g., the percentage of difference in emission between left and right hand) was introduced in another study. The left–right symmetry of photon emission from the palm and the dorsum of the hands of hemiparesis patients were compared with similar data from the hands of healthy controls. They suggested that in certain diseases, left–right symmetry of UPE from hands was broken [67].

8.4. Perspective

In forward-looking medical systems science, connectivity and network biology are becoming a focal point of research efforts [15]. In network biology, important steps are made to better understand the structure and function of networks. However, the concept of these networks in disease and intervention is still the subjects of debate [68,69]. Moreover, an understanding that new properties emerge within a system at different levels of complexity clearly underlines the need to study the behavior of an entire system rather than focus on studying its components in isolation. It is hoped that the unification of the UPE and metabolomics research can enrich the system dynamic disease concept.

9. Abbreviations

UPE	Ultra-weak photon emission
ROS	Reactive oxygen species
PMT	Photomultiplier tube
CCD	Charge coupled device
NMR	Nuclear magnetic resonance
GC-MS	Gas chromatography mass spectroscopy
LC-MS	Liquid chromatography mass spectroscopy
UV	Ultra-violet
OPC	Oligomeric proanthocyanidins.

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