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(56) Documents Cited:
WO 2016/097708 A1 **WO 2015/150096 A1**
WO 2015/003938 A1 **CN 106491117 A**
US 20160310084 A1 **US 20140275852 A1**

(58) Field of Search:
Other: **EPODOC, WPI**

(54) Title of the Invention: **Adaptive media for measurement of blood glucose concentration and insulin resistance**
Abstract Title: **Measurement of insulin resistance, glucose or bio-markers using adaptive media**

(57) A device (e.g. a mobile phone, smart watch, or wearable device such as glasses) monitors a subject e.g. by video Super-Pulse information is extracted, possibly using a decision tree, representing the best possible pulse wave excluding noise aberrations. The Super-Pulses are stable and repeatable digital volume pulses, characteristic of an individual and similar to a finger print. The Super-Pulse may be characterised by Gaussian coefficients, using minimisation of the difference between it and a suitable Gaussian, giving a unique vector value related for example to variable heart rate or vascular stiffness. A neural network may be trained to determine data from the Super-Pulse. Other bio-markers may be determined such as blood glucose, insulin resistance or blood pressure and the system is non-invasive. The effect of medications, functional foods, vitamins or exercise on baseline glucose or insulin resistance, or the efficacy of a prescribed routine, may be monitored.

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ADAPTIVE MEDIA FOR MEASUREMENT OF BLOOD GLUCOSE CONCENTRATION AND INSULIN RESISTANCE

Diabetes mellitus (DM), of which type 2 diabetes mellitus (T2DM) represents 85–95% of cases of diabetes in adults, has increased dramatically to pandemic proportions.T2DM affected 450 million adults in 2014, approximately 8.5% of the world population and is predicted to rise 11.6% by 2025.

Increased insulin resistance is a biomarker of T2DM subjects. Impaired glucose tolerance marks the progression between normal glucose tolerance and diabetes (Lillioja et al., 1993; Reaven, 1988).

Surprisingly, the inventors have found that the onset of impaired insulin resistance can be detected by an adaptive media, described herein which employs aspects of reflective pulse wave analysis. Furthermore, the inventors have determined that the characteristic varies throughout the day/night and month of year in concert with circadian rhythms.

The present invention relates to a user health and wellbeing system utilising a combination of technologies and software to establish a health assessment. More particularly the system comprises a measure of human homeostasis (human body regulatory mechanisms). Homeostasis is supported by 2 main functions: autonomic nervous and endothelial functions. The autonomic nervous system (ANS) is an extensive neural network whose main role is to regulate the internal environment and body functions by controlling homeostasis which includes haemodynamics, blood pressure, heart rate, blood glucose level, sweating and visceral functions. The ANS acts through a balance of stimulation or inhibition of its own two components—the sympathetic and parasympathetic nervous systems. Sympathetic and parasympathetic branches act via neurotransmitters and receptors activation. The endothelial function is related to the ability of the blood vessels to dilate or constrict when necessary. Endothelial dysfunction can be defined as reduced bio-availability of Nitric Oxide (NO), which plays many roles in

maintaining vascular health. Hence, endothelial dysfunction is defined as an impairment of endothelium dependent vasodilation.

One method for monitoring cardiovascular events and peripheral circulation is through reflective video photoplethysmography (RVPPG) analysis. RVPPG uses reflected red light to measure relative blood volume in peripheral mammalian tissue such as the fingertip toe or ear lobe. RVPPG waveforms are characteristics of blood movement in cutaneous vessels and can be used to identify synchronous depolarization of cardiovascular tissue. The fundamental frequency of the RVPPG waveform, typically around 1 Hz reflects the heart rate. Lower frequency components such as respiratory, thermoregulatory and sympathetic nervous system effects are also contained within the RVPPG signal. Arterial stiffness, indicative of endothelial dysfunction, may also be measurable from calculations made using the RVPPG waveforms analysis.

The present invention relates to the identification of the on-set of or near onset of Type II Diabetes Myelitis, which is a means of providing simple tests to identify problems which would not normally result in the need for clinical diagnosis. Since it is inappropriate to undertake ambulatory time-of-day blood measurements to determine blood glucose levels, on people who have not been diagnosed with symptoms of Type II diabetes, the use of non-invasive adaptive media as a cost-effective imaging cytometry platform installed on a cell-phone or other such device to perform rapid analysis measuring the systemic changes which correspond to impaired insulin resistance is considered of great value. The data so recorded can also be remotely accessed by the user or a competent person such as a physician to review the effectiveness of an intervention medication or to confirm that the patient is taking their medication.

In one embodiment of the invention, the user of the mobile adaptive device, which can be mobile phone, a so called smart watch, a wearable device such as glasses or contact lens or any device including a fixed computer system capable of recoding videos, tracks and records biological and physiological parameters. The user consumes medications or functional foods, vitamins, or foods in a changed diet

regime as prescribed permits the user's data to be returned to a central registry such that a population-related benefit of the particular medication or functional foods, vitamins, or foods in a changed diet can be demonstrated in a pseudo parallel use environment such that many thousands of participants' data can be combined. This type of analysis allows the recording of the change in the health of a typical or average user classified by a number of selected parameters such as age, gender, BMI, country, ethnicity, exercise routine and medication consumed, such that the benefit of the medication or functional foods, vitamins, or foods in a changed diet can be unequivocally demonstrated. This embodiment is particularly valuable for assessing the change in or improvement in type II diabetes.

In yet another embodiment of the invention, the user is an employee of a corporation or organisation in need of medical or occupational health management for example as may be the case with sedentary workers, or workers in locations where dust or solvents are prevalent or particularly for night shift workers be they in general industry or service industries or hospital workers, or military personnel including submariners and astronauts. In such a case the user of the mobile adaptive device is an employee, who is advised to undertake a preferred routine such as exercise or to change their diet to include supplements, vitamins functional of healthy foods. The analysis of the data allows the recording of the change in the health of the user classified by and linked to their medical records including data for a number of selected parameters such as age, gender, BMI, country, ethnicity, exercise routine, medication or functional foods, vitamins, or foods in a changed diet, sleep period, heart rate and its variability (by way of example, not limited here) such that the benefit of the regiment can be unequivocally demonstrated and actions advised to improve and demonstrate the improvements in health of the subject. This embodiment is particularly useful in cohorts where the user is pre-disposed to weight gain or lack of exercise.

In yet another aspect of the invention, the user of a mobile adaptive device consumes a product which reduces their increase in insulin resistance, as is the case with people experiencing mild cognitive impairment. In this aspect a connected device measures appropriate physiological parameters, and the mobile

device system provides an on-screen cognitive test series, specifically related to executive function and memory associated with increase brain glucose or ketone bodies. The user of the mobile adaptive device permits their data to be returned to a central registry such that the population-related benefits of the product which can be medication or a medical food or a food for special medical purpose or functional foods, vitamins, or foods in a changed diet can be demonstrated in a pseudo parallel clinical trial. In this way the costs of acquiring the long-term efficacy data is reduced by many orders of magnitude. In this context, cognitive confusion or delirium is often associated with urinary tract infections and this invention is particularly useful at eliminating those individuals suffering in this way from cohort cognitive tests.

In yet another aspect of the invention, the mobile device system is dedicated to the Bluetooth of similar finger-tip device and the product which it is connected to. For example, a blood pressure reducing medication which provides a daily dose of the required medication is combined with a mobile phone or smartphone application which are access enabled with a prescribed medication such that the effectiveness can be monitored remotely by a clinician. In this way the effectiveness of the medication can be determined by both the patient, the clinician and the manufacturer of the medication. In addition, the manufacturer gains valuable access to the users' characteristics, irrespective of the point of prescription.

Methods of Demonstration

For example, a proof of concept trial was undertaken to demonstrate that a finger and facial reflective video using the red, green and blue colour scale was used to measure the pulse wave which characterises the systolic and diastolic or reflective peak. The video signal was converted into a frame brightness value as a simple average of the pixel colour values. The variation over time provides physiological information such as the systolic peak, representing the action of the heart as blood is ejected from the left ventricle and diastolic peak which represents the reflective wave. The heart rate can be determined by undertaking a fast Fourier transform of the input signal and selecting the highest peak frequency associated with the heart

beat window. Similarly, the breathing rate can be identified and recorded. It is desirable to minimise the length of time of the video stream to minimise continual variability resulting from artefacts embedded in the signal, such as those arising from movement and the micro-changes on positioning of the camera. It can be shown that there are many difficulties experienced by all such methodologies which are confounded by the presence of noise artefacts. Such noise arises out of subject movement, source light flicker and video light loss. It is desirable to operate the video frame rate greater than 30 fps and that the video sequence used for heart and respiration rate should be no greater than 30 seconds excluding an amount of the signal at the start of the sequence which is discarded. The measurement of the variability of the heart rate, in contrast much be undertaken with greater than 60 seconds of signal in order to capture the desired variability. Therefore in a further embodiment of the invention is a procedure which ensures that the heart and respiration rate sequence is preferably half the heart rate variability sequence with the heart and respiration rate signal analysis being performed at least twice every time the heart rate variability is analysed.

In order to eliminate the noise (motion artefacts) it is necessary to apply signal filtering such that the raw signal can produce a “Super-Pulses” which represent the best possible pulse wave containing all required characteristics but excluding noise aberrations. Noise elimination can also be achieved by reconstructing the “noise base signal” by removing the heart rate and respiration rate frequency peaks from the fast Fourier transform and then reconstructing the “noise” signal by performing an inverse Fourier transform. The noise signal can then be removed from the raw input signal to provide an improved de-noised pulse wave signal.

Unfortunately, it is often found that physiological changes during a test period can create variations in the pulse wave signal which do not have their origins in noise derived from motion artefacts or harmonics. A pulse trace of this type cannot be analysed simply to provide the necessary high quality pulse wave for physiological parameters to be quantified.

Surprisingly, we have discovered that by applying a decision tree we are able to synthesise a pulse wave which is similar in characteristic to an individual's "fingerprint". This is unique to an individual and further its shape and characteristics can be modified by the action of a medication or functional foods, vitamins, or foods in a changed diet and exercise and furthermore can be used to identify the result of consuming food on blood glucose levels. We are able, as a result to synthesise the Gaussian structures of the pulse wave using up to 9 Gaussian curves for which the non-linear constants are each determined by using a non-linear optimisation method whereby the objective "cost" function represented by the minimisation of the sum of the squares of the difference between the Super Pulse and the Gaussian solution. When the constants are determined such that the objective function has a value of <0.0001 the constant vector is converted into an absolute index which is a numeric value which uniquely characterises the individual and changes with medication intake.

In a further embodiment of the invention the start time of the reflective pulse is determined from the Super Pulse and the time dilation between the start of the systole and the onset of the reflective wave together with the distance of travel to the point of measurement provides the pulse wave velocity, a gold standard measure of arterial stiffness index, by the use of a single measurement site.

The Gaussian constants (3 for each curve, so 3 Gaussian curves are covered by 9 constants, 5 by 15 etc.) can be used as part of a test protocol to predict a starting or chronic pulse wave of an individual. It is desirable for the protocol to be aligned with the data analysis being performed. For example, the Variable Heart Rate protocol can be established as the first test conducted soon after waking. This gives access to the chronic baseline, from which further acute tests can be undertaken to demonstrate the effectiveness of medications or functional foods, vitamins, or foods in a changed diet or exercise. In a similar way this protocol can be used to represent the fasting blood glucose level of a user.

The process of optimisation is computationally complex and time consuming, therefore, once a vector characterising the Gaussian constants has been

determined, the starting pulse wave can be calculated with little computing power. The starting chronic baseline can be represented by the absolute value of the "fingerprint" Super-Pulse vector, and the change or improvement in the absolute value of the "fingerprint" represents the improvement resulting from consuming a medication. In yet another embodiment of the invention the Super Pulse "fingerprint" can be analysed in such a way as to highlight the change in alertness of the subject, typically be computing the areas under the curve for that part of the Super Pulse representing the systole and the diastole. The ratio of these factors changing as a direct result of a subject undertaking a task where the use of a medication, or functional foods, vitamins, or foods in a changed diet, or exercise can be demonstrated to directly affect the ratio. In this way the subject's response the intervention can be measured and presented as an index. In a further embodiment of the invention, the adaptive device can be used to record the medications, functional foods, vitamins, or foods consumed on a daily basis by scanning a barcode. In this way a clear record of consumption can be made without recourse to "after the event" food consumption questionnaires.

The Super-Pulse reconstructed from the Gaussian functions defining the shape of the pulse wave, contains valuable information about the orthogonal orientation of red and white blood cells with respect to time. The orthogonal orientation of the blood cells defines the velocity of the cells. The object of this invention is to obtain a region of interest where it is known that the forward motion of the blood cell is stationary. Herewith we disclose that that point can be identified when the red blood cells have an average orthogonal alignment with the lumen wall. This is the point of the systole. The time stamped systole point is thereafter used as the source of the data for measuring the point of correlation with blood glucose concentration across an effective frozen plane of view.

In yet a further aspect of the invention, is provided a simple low cost method of demonstrating pharmaceutical proof of concept, specifically but not exclusively related to cardiovascular medication or functional foods or vitamins used to reduce blood pressure either acutely or chronically.

The computations and memory required to complete the video pulse wave Super-Pulse system is not compatible with current generations of smartphones. As a result the inventors have disclose a system specifically for use with a medication or functional foods, vitamins, or foods in a changed diet or exercise aimed at reducing the onset of type II diabetes. The system involves recording a video either using the front or back camera of a smartphone or similar adaptive device including a fixed video camera. The videos can be converted from RGB to HVC format. The video stream of interest is selected by identifying a region of interest (ROI) which is defined as a zone within the frame window where the change in brightness is the greatest as measured by the first derivative of the average brightness over a defined quadrant during a pre-assessment or calibration period. The ROI is hereby defined as a region without colour saturation in either the RGB or HVC spectra. This is part of a pre-conditioning or initialising section of the protocol which can also include a controlled relaxation stage in order to minimise motion artefacts and noise. The system also includes access to accelerometer data to restart the sequence if the motion artefacts exceed a certain threshold. All subsequent tests are undertaken using the quadrant of interest as the measurement location. The system ensures that the quadrant of interest is used in the measurement of the video but that the quadrant of interest is re-assessed each time a video is recorded.

The data recorded form the quadrant of interest is recorded at a frame rate commensurate with the adaptive mobile device but never less than 24 Hz, preferably in the range of 30 Hz to 60 Hz or more. Those experienced in the art will understand that the memory and time for computation is proportional to the frame rate but that higher frame rates contain more information but also contain more noise and motion artefacts including micro motion artefacts. Typically, modern smartphones are able to record videos at frame rates higher than 60 Hz but the quality reduces and therefore manufacturers constrain the frame rate to 60 Hz maximum. Furthermore, when a higher frame rate is adopted, the frame data transfer rate cause the video pixel information to be incorrectly recorded. It is therefore vital to maximise the information contained in the video without exceeding the adaptive device's RAM.

To ensure that this doesn't occur, the system utilises a short term buffer memory to hold the signal data to allow follow-on video frames to be accessed without overflow. The mobile colour detection system utilises static system functionality to analyse the signal for parameters such as the signal to noise ratio and computes the systolic pulse frequency and the underlying respiration rate, both by fast Fourier transform methods. The signal in the form of a transformed one dimensional vector is sent via an interface to a server system containing the functionality and capability to decompose the video colour signal into the systolic and diastolic signal spectra. The signal is de-noised by the removal of the noise spectra and the resultant signal analysed for Super-Pulses which are characterised as stable and repeatable digital volume pulses. The digital volume pulse of the Super-Pulse is shown to be characteristic of an individual similar to a finger print. The system then characterises the Super-Pulse using non-linear Gaussian curve fitting during which time the signal frequency of the Super-Pulse is amplified to greater than 1000 Hz. The amplification of the Gaussian optimised Super-Pulse allows the identification of the phase angle between the systolic and diastolic pulse waves from which it is easy to determine the time delay which is correlated with the subject's age and vascular health. The amplified Gaussian optimised Super-Pulse also allows the identification of the depth of the dicrotic notch which is a variable more readily changed by the action of certain medications, functional foods, vitamins, or foods in a changed diet and exercise.

The Gaussian coefficients which characterise the Super-Pulse are recorded as a subject vector the absolute value of which provides a convenient and reproducible single numeric Super-Pulse value. The Super-Pulse value allows the acute and chronic changes on vascular health to be recorded and related to other factors such as pulse wave velocity, variable heart rate, stiffness index and flow mediated dilatation and stress and metal fatigue indexes.

Surprisingly, the inventors discovered that when it is required to issue the system to corporate or medically determined users, say those associated with a particular General Practitioner practice, it is necessary to make the system available with a

named look, but until now this was required to be downloaded by an individual who is part of the user cohort. Typically all applications published via the main internet sources such as the App Store automatically become available to the general public and therefore any individual is free to download the system onto a mobile adaptive device. This is not appropriate for bespoke systems designed and developed for specific clients who wish to use within a specified cohort. Furthermore, the value of a known cohort of individuals becomes eroded as users who are not part of the cohort install the system on their mobile device. In order to overcome these limitations, the inventors have implemented a system whereby there is a primary system which is made available from a public download host. The system is a core application which has no branches and no specific configurations for any individual organisation or user. In addition to the core application system there is provided a core development system. When a user of the organisation which is in need of a specific configuration registers to use the system, with a specific code provided to them, the system in the public download host, poles the inventors system and the user receives a custom set of details for that code. These can be logo, accent, style and colours via RGB values for example. In this was the system becomes tailored to the needs of the user organisations and restricted to those who are not authorised to be part of the cohort. This system can be maintained with just two files without having to test and debug potentially hundreds of different versions of the system. In a further embodiment of the invention is the use of the system in pre-clinical proof of concept trials and clinical trials in general. In such trials the cohort of individuals which have access to the system must be controlled and managed. The system devised provides the necessary level of control without allowing full public access but is freely available through public download sites.

When all the aforementioned aspects are combined it is possible to identify the correlation of the power spectral density of the recorded information and utilise that information to correlate with measure insulin resistance. The inventors have developed a system which relates the all the aforementioned aspects of non-invasive video reflective pulse wave analysis using an adaptive device to invasively measured bio-markers. Examples of which are insulin resistance, blood

glucose concentration, systolic and diastolic blood pressure and core temperature. In order to achieve the relationship between the non-invasively measured and invasively measured bio-markers, it is necessary to establish, dimensionally normalise and train a neural network using real invasively measure data containing a number of hidden nodes or deep nodes that allows a large number of parameters contained within the "super pulse" or analysis of the "super pulse" as herein described to be directly related to the bio-marker. In this way the inventors have shown that it is possible to accurately determine blood glucose, insulin resistance and blood pressure values for a user from non-invasive reflective video Photoplethysmograms. Furthermore, the inventors have shown that the effect of medications, functional foods, vitamins, or foods consumed on a daily basis or exercise can be reflected in the baseline blood glucose levels and a general improvement in (reduction of) insulin resistance.

It will be appreciated that the term "treatment" and "treating" as used herein means the management and care of a patient or subject for the purpose of combating a condition, such as a disease or a disorder or health issue related to over work, stress or burnout. The terms treatment of treating are intended to include the full spectrum of treatments for a given condition from which the patient is suffering, such as administration of the active compound to alleviate the symptoms or complications, to delay the progression of the disease, disorder or condition, to alleviate or relief the symptoms and complications, and/or to cure or eliminate the disease, disorder or condition as well as to prevent the condition, wherein prevention is to be understood as the management and care of a patient or subject for the purpose of combating the disease, condition, or disorder and includes the administration of the active compounds or functional foods, vitamins, or foods in a changed diet or exercise to prevent the onset of the symptoms or complications. The patient to be treated is preferably a mammal, in particular a human being, but it may also include animals, such as dogs, cats, cows, sheep, horses and pigs.

CLAIMS

1. An adaptive media such as a mobile phone, wearable device, tablet computer or computer which contains a system to read, record, analyse and display the glucose and insulin resistance of a user and the health related benefits of any medications, functional foods, vitamins, or foods consumed on a daily basis or exercise routine by way of the synthesis of a Super-Pulse as defined herein, and to the use of the information thereof to guide the users' improvement in health.

2. A system, according to Claim 1, which is capable of monitoring and displaying information embodied in the Super-Pulse recorded by the adaptive media device, mobile phone, wearable device or tablet computer or computer which provides a way of verifying the efficacy of a prescribed routine to reduce the user's insulin resistance and/or blood glucose levels over time.

3. A system according to Claim 2 whereby the information embodied in the user's Super-Pulse is related directly through a neural network and trained using time synchronised invasively measured bio-markers.

4. A system according to Claim 2 and Claim 3 where a particular bio-marker is Insulin Resistance.

5. A system according to Claim 2 and Claim 3 where a particular bio-marker is Blood Glucose Level.

6. A system according to Claim 4 and Claim 5 whereby the Super-Pulse contains a particular artefact which represents the quasi-stationary point of blood flow.

7. A system according to Claim 2, which can be downloaded and installed onto adaptive media, mobile phone, wearable device, tablet computer or computer which is capable of being made available to the public via a

public download site, which is capable of being accessed only by users residing within an approved cohort of individuals, such cohort being members of a class, such as a disease grouping, a group of employees or any other cohort as may be considered of interest. The system when installed is capable of receiving information containing specific instructions for use, logo's style, user test protocol information or other such information, such that the results associated with the cohort may be identified and processed as a cohort or as individuals to determine the benefits as described in Claims 1 and 2.

8. A system according to claim 3, which can be downloaded and installed onto adaptive media, mobile phone, wearable device, tablet computer or computer by scanning a barcode present on the packaging of a medication, functional foods, vitamin, or foods such that the scanned item is related to the system only from which the provider of the medication, functional foods, vitamin, or food or exercise regime as well as or in addition to a prescribing clinician, monitoring organisation or individual is able to gain specific information relating to the product user cohort and the efficacy of the product resulting from its regular use.

9. A system according to claims 1 to 5 that is capable of interpreting the data into a Super-Pulse and to analyse the Super-Pulse to provide a unique numerical value of the Super-Pulse which can be used to present acute and chronic changes in health and further to analyse the data to give heart rate (BPM), respiration rate, variable heart rate, blood gas saturation, stiffness index, peak-to-peak time, vascular age, left ventricle eject time and other parameters such as augmentation index and pulse wave velocity, stress index and any other non-invasive measurement.

10. A system according to claim 9 which is capable of recording successive data such that they form a series which can be displayed to provide the user with a history of results following the consumption of a medication, functional foods, vitamin, or foods in a changed diet or exercise regime

whereby the readings taken before the change provide the chronic baseline data and readings taken after consumption of a medication provides the acute changes.

11. A system according to claim 10 whereby the successive data records are returned to a central depository of data which can subsequently be used to demonstrate the benefit to the subject, of the medication, functional foods, vitamin, or foods in a changed diet or exercise.

12. A system according to claims 3, 10 and 11 which is capable of recording data such that the proof of efficacy of a pharmaceutical medication, functional foods, vitamin, or foods in a changed diet can be determined at low cost amongst selected users or cohorts to prove early stage concept efficacy.

13. A system according to the preceding claims whereby a machine learning decision tree is used to synthesise the Super-Pulse.

14. A system according the preceding claims whereby the Super-Pulse is characteristic of an individual and may be used to confirm the identity of the individual using the mobile adaptive device. In this way the user identity becomes integral to the system described in the preceding claims to ensure the integrity of cohort data.

15. A system according to the preceding claims whereby changes to the derived Super-Pulse are related through machine learning techniques to the health characteristics within the general population.

Application No:	GB1708591.1	**Examiner:**	Peter Burns
Claims searched:	1-15	**Date of search:**	23 November 2018

Patents Act 1977: Search Report under Section 17

Documents considered to be relevant:

Category	Relevant to claims	Identity of document and passage or figure of particular relevance
X	1-15	WO 2016/097708 A1 (TARASSENKO & DALY) refer to all figures and to pages 4 (line 24) - 5 (line 14), 8 (line 7) - 9 (line 12), and page 12 in particular
X	1-15	WO 2015/003938 A1 (KAESTLE) see figures 1-4 & 7 along with page 9 (line 10) - page 10 (line 18) and page 15 in particular
X	1-15	US 2014/0275852 A1 (HONG et al.) whole document is relevant, see in particular paragraphs 0120, 0178-0179, 0223-0224, 0301 & 400
X	1-15	CN 106491117 A (DAI) refer to EPODOC abstract, WPI abstract accession number 2017-205945 and paragraphs 0013-0014, 0052-0054 & 0103
X	1-15	US 2016/0310084 A1 (BANERJEE et al.) refer to figures 1-4 and 6A-6B, associated description and paragraphs 0002-0004 in particular
X	1-15	WO 2015/150096 A1 (VERKRUIJSSE et al.) refer to figure 1 and page 5 (from line 10) & page 11 (from line 9) in particular

Categories:

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.

Field of Search:

Search of GB, EP, WO & US patent documents classified in the following areas of the UKC^{X} :

Worldwide search of patent documents classified in the following areas of the IPC

The following online and other databases have been used in the preparation of this search report

EPODOC, WPI

International Classification:

Subclass	Subgroup	Valid From
A61B	0005/024	01/01/2006
A61B	0005/00	01/01/2006
A61B	0005/021	01/01/2006