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(54) **SYSTEMS AND METHODS FOR MONITORING PATIENT MEDICATION ADHERENCE**

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See application file for complete search history.

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Primary Examiner — Gary Jackson

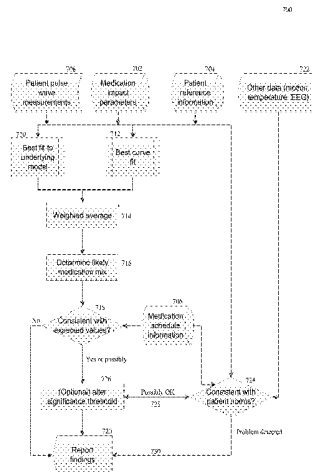
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(57) **ABSTRACT**

Invention for determining a patient's adherence to various prescribed medications. Here a variety of different types of patient pulse wave measurements (blood pressure, pulse oximeter, ECG) and other physiological measurements are obtained. This actual data is compared to calculated measurements that would be expected based on the various patient baseline measurements in the absence of medication, schedule of medications, and impact of medications the various patient baseline measurements. If the actual data meets expectations, then the patient is likely adhering to the regime. Depending on which types of data do not meet expectations, non-adherence to various previously described medications may be reported. Other types of patient physiological readings, such as temperature, motion, lung function, brain wave function (EEG) and the like may also be obtained, and these additional types of readings can be used

(Continued)



to extend the range of different types of drugs/medications that the invention can successfully monitor.

9 Claims, 6 Drawing Sheets

Related U.S. Application Data

(60) Provisional application No. 61/767,839, filed on Feb. 22, 2013, provisional application No. 62/138,377, filed on Mar. 25, 2015.

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Figure 1

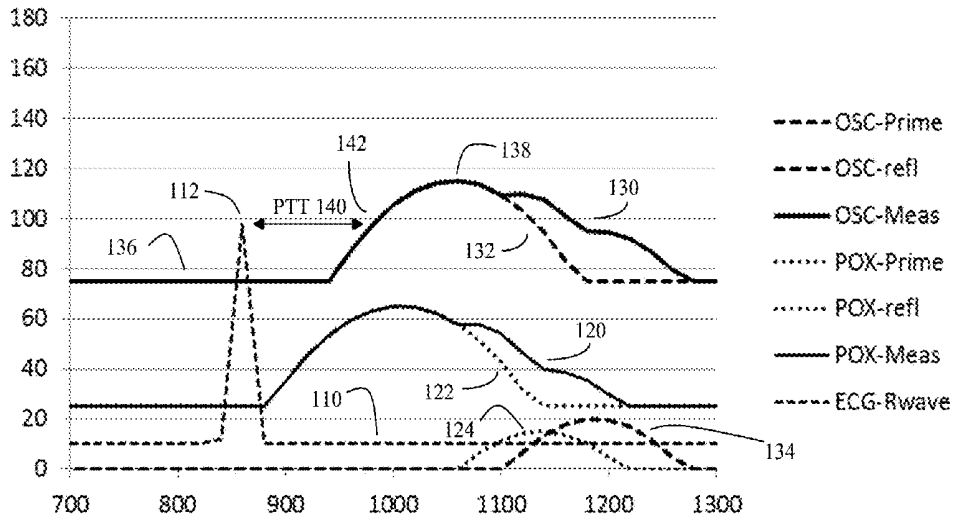


Figure 2

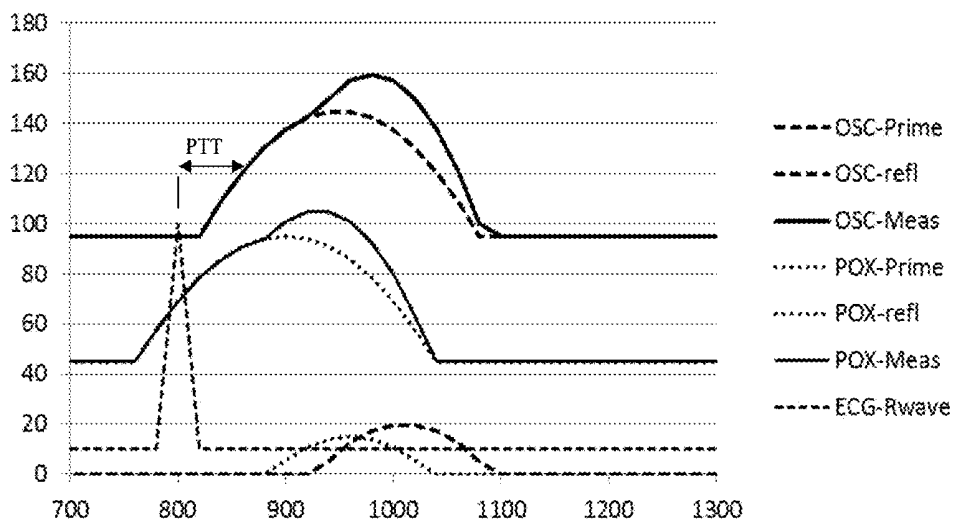


Figure 3

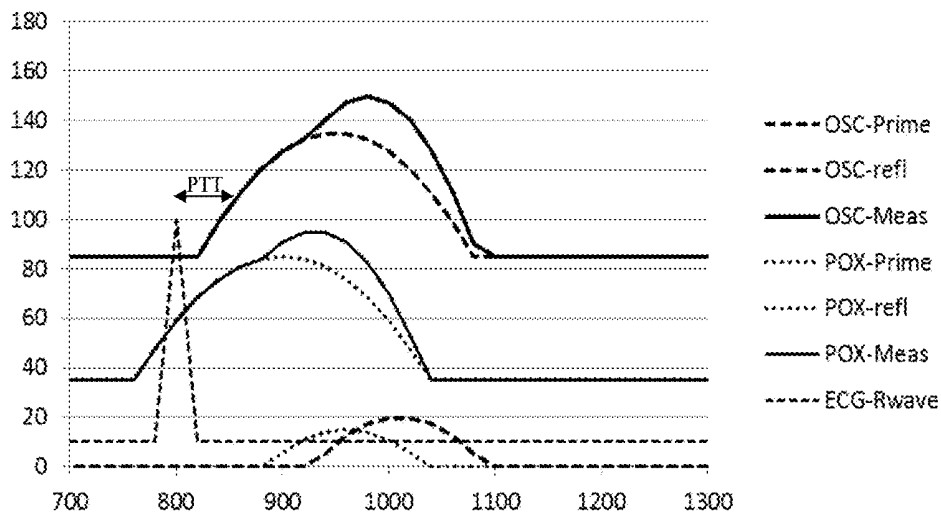


Figure 4

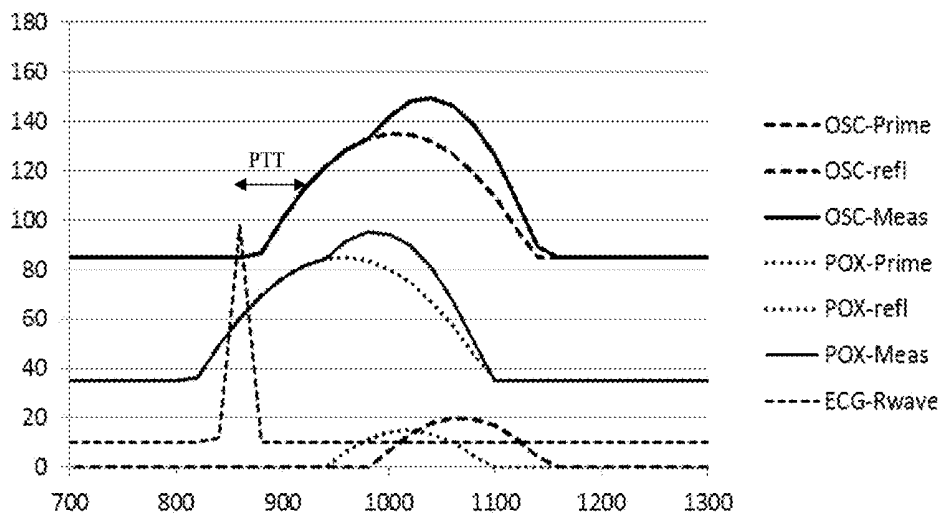


Figure 5

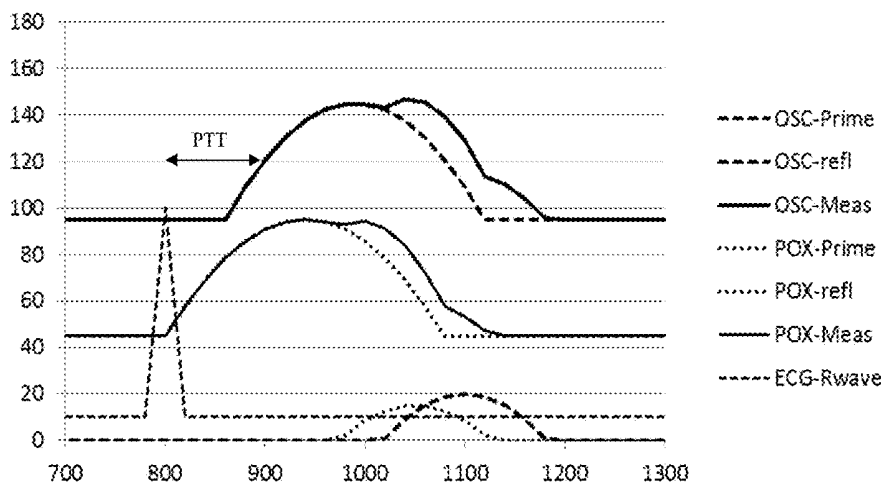
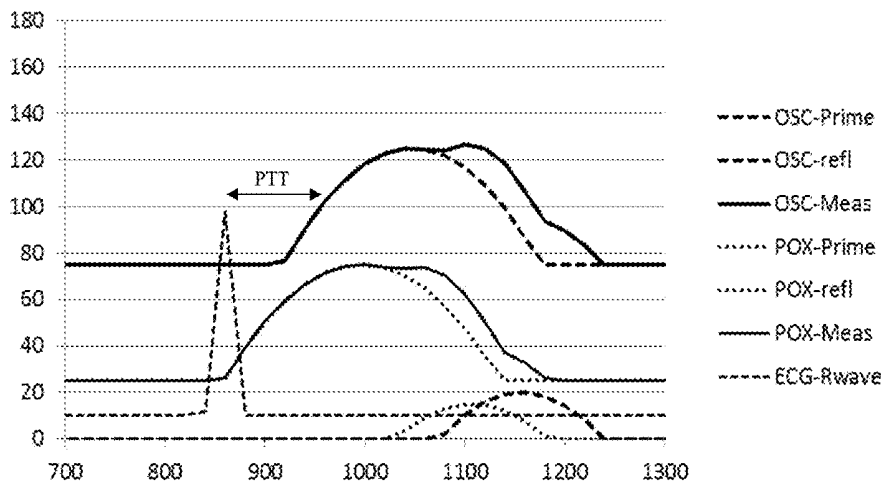


Figure 6



700

Figure 7

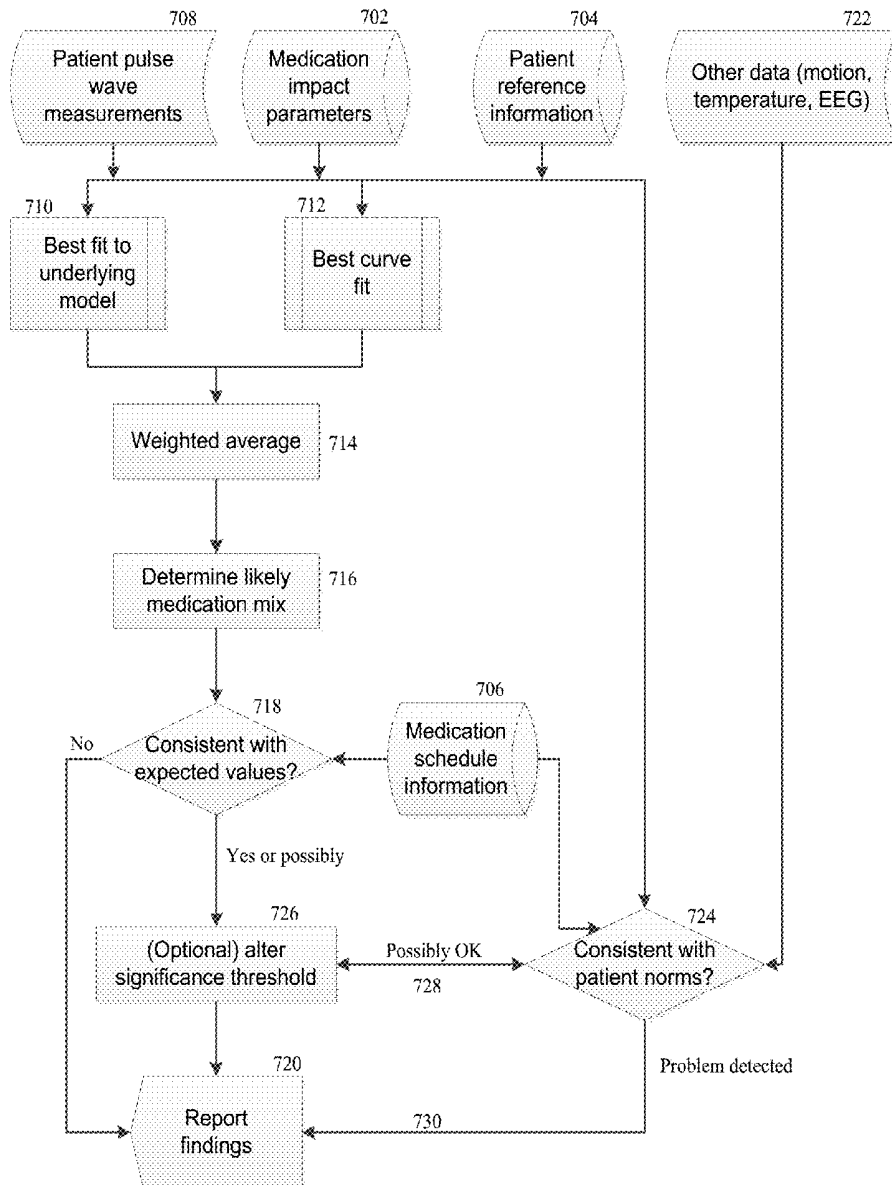


Figure 8

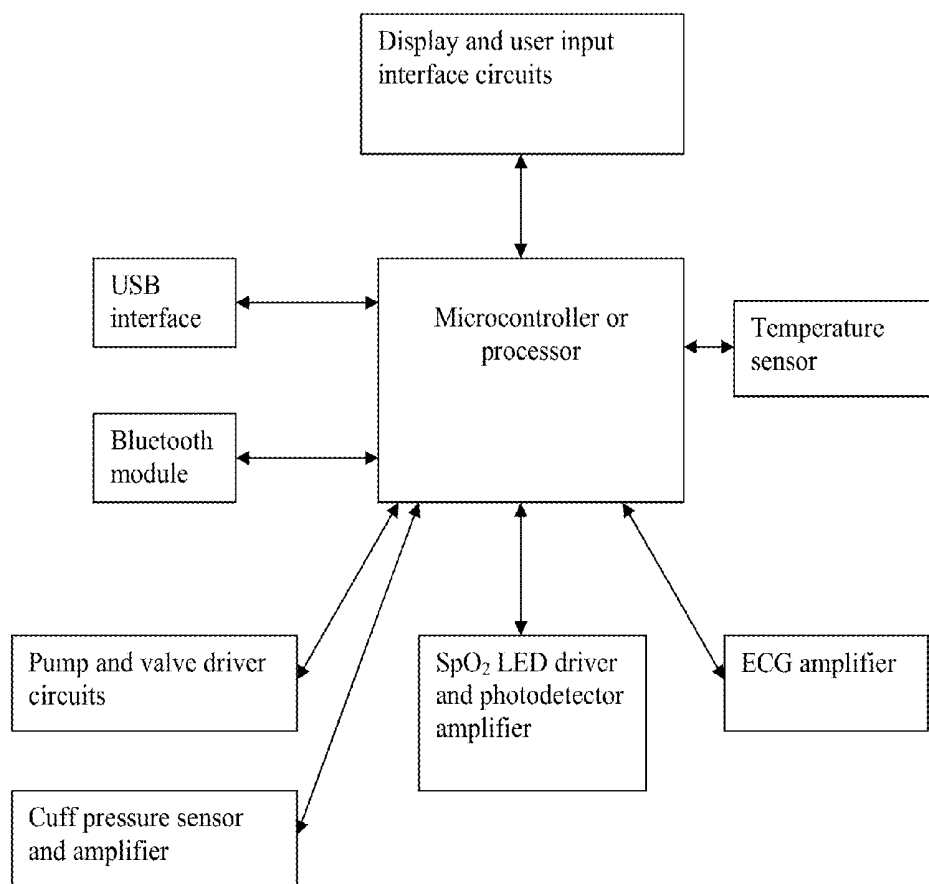
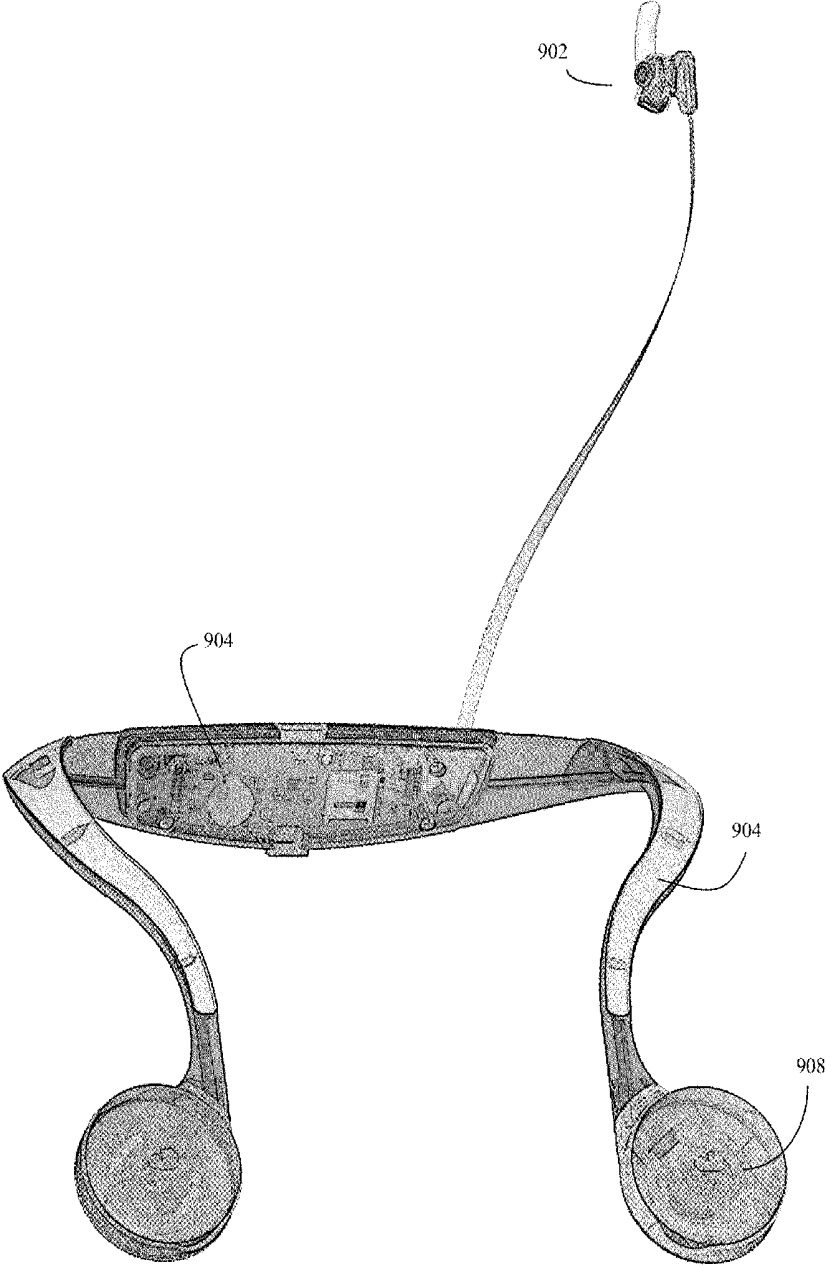


Figure 9



SYSTEMS AND METHODS FOR MONITORING PATIENT MEDICATION ADHERENCE

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the priority benefit of U.S. provisional application 62/138,377, "COMPREHENSIVE BODY VITAL SIGN MONITORING SYSTEM WITH NECK AND EAR MOUNTED DEVICE, filed Mar. 25, 2015; this application is also a continuation in part of U.S. patent application Ser. No. 14/186,151 "SIMULTANEOUS MULTI-PARAMETER PHYSIOLOGICAL MONITORING DEVICE WITH LOCAL AND REMOTE ANALYTICAL CAPABILITY", filed Feb. 21, 2014; application Ser. No. 14/186,151 in turn claimed the priority benefit of U.S. provisional application 61/767,839 "SIMULTANEOUS MULTI-PARAMETER PHYSIOLOGICAL MONITORING DEVICE WITH DUAL LOCAL AND REMOTE ANALYTICAL CAPABILITY", filed Feb. 22, 2013; the entire contents of all of these applications are incorporated herein by reference in their entirety.

BACKGROUND OF THE INVENTION

Field of the Invention

This invention is in the field of patient operated medical diagnostic devices that can be used to determine if a patient is following health care provider medication recommendations.

Description of the Related Art

Patient non-adherence to health care provider medication recommendations is a major medical problem. Center for Disease Control (CDC) materials suggest that between 20-30% of medication prescriptions are never filled, and medication is not taken as prescribed in up to 50% of all cases.

For example, studies have shown that only about 51% of patients being treated for hypertension are adherent to their medication therapy on a long term basis. In this context, "long term" should be viewed as being about six months, since other studies have shown that medication adherence rates drop off after the first six months of treatment. This is a large scale problem. At present over 133 million Americans have a long term chronic condition requiring medication.

It has also been estimated that medication non-adherence can result in up to 125,000 excess deaths annually; also incurring economic costs (due to higher subsequent patient expenses) estimated at \$100 billion to \$300 billion dollars per year.

Thus methods to monitor and encourage patient adherence to prescribed medications are of high interest in the art. Patient adherence to hypertension medication is particularly critical.

Patients, in particular elderly patients, are often put on multiple different medications at the same time. For example, to control hypertension, patients may be put on various combinations of diuretics, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), beta-blockers, vasodilators, calcium channel blockers, aldosterone antagonists, renin inhibitors, alpha blockers, and the like. No one drug alone may be totally effective, but in combination, several drugs may produce the desired results.

Patients with other types of disorders, such as lung disease, chronic obstructive pulmonary disease, epilepsy, diabetes, and the like are of course not immune to hypertension. Many of these patients, sometimes in addition to anti-hypertension drugs, also take additional types of drugs for these disorders. It is not uncommon for these other drugs to also have an impact on cardiovascular system function as well.

In order to improve patient medication adherence, the patient should ideally receive frequent feedback that would promptly warn the patient whenever the patient is not adhering to their prescribed medication properly, or when this medication has otherwise become less than fully effective.

A few such patient operated medical diagnostic tests are presently on the market, such as home blood glucose tests, home blood pressure tests, home pulse oximeters, and even home ECG tests.

With the exception of home tests for blood glucose, there are presently few home diagnostic tests that can warn a patient when he or she is out of compliance for a particular medication. Here prior art home blood pressure tests illustrate the problem—if a patient's blood pressure is non-ideal, is this because the patient skipped one of several anti-hypertensive medications that the patient has been taking, or is it simply because the patient is having a bad day? If the patient skipped a drug, which one was skipped?

Thus further improvements in the art of using patient operated medical diagnostics to monitor patient adherence to medication would be desirable.

BRIEF SUMMARY OF THE INVENTION

The invention is based, in part, on the insight that various types of patient operated instrumentation, such as blood pressure monitors, pulse oximeters, ECG readers and the like discard a huge amount of data in the course of obtaining their various different types of pulse wave measurements. This invention is also based, in part, on the insight that with proper analysis, this massive amount of blood pressure data, pulse oximeter data, ECG reading data, and other types of data could be usefully employed to help solve the major problem of monitoring patient medication adherence.

In some embodiments, the invention may be a method, device or system for determining a patient's adherence to a prescribed medication regime. The invention relies on a plurality of different types of measured (actual) patient pulse wave measurements, such as some combination of oscillometric blood pressure data, oscillometric pulse oximeter data, and ECG data, as well as other types of patient physiological measurements as available.

The invention further relies on additional information, such as patient reference (baseline) information that reports on the various patient pulse wave measurements in the absence of various types of medication, medication schedule information (which informs the invention as to what types of drugs/medications that patient should be taking, and when), and medication impact parameters, which informs the invention as to how the various individual medications would be expected to impact (alter) various specific types of patient pulse wave measurements.

The invention will typically use at least one processor to obtain a various different types of actual patient pulse wave measurements. It will then use its various types of additional information to determine if the actual data is as expected based on the patient baseline pulse wave information, expected medication schedule, and expected impact of these

medications on the patient baseline pulse wave information. If the results are inconsistent, then the invention will typically conclude that the patient is not properly adhering to his medication schedule, and will report this lack of medication adherence accordingly.

Other types of patient physiological readings, such as temperature, motion, lung function (e.g. stethoscope-like microphone pickups and automated sound analysis, spirometers), brain wave function (EEG) and the like may also be obtained, and these additional types of readings can be used to extend the range of different types of drugs/medications that the system can successfully monitor.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows a simplified drawing of patient reference pulse wave measurements for a normal (healthy patient) in the absence of medication. Three different types of patient pulse wave measurements (oscillometric blood pressure measurements, pulse oximeter type measurements, and ECG measurements) are being shown simultaneously, along with some of the underlying patient physiological mechanisms that create some of these various patient pulse waves. Here the time elapsed from the last previous ECG "R" pulse (in milliseconds) is shown on the "X" (horizontal) axis. The "Y" vertical axis shows (for the blood pressure measurements) the blood pressure in millimeters of mercury (mm Hg), or arbitrary units for the other pulse wave measurements.

FIG. 2 shows a simplified version the reference pulse wave measurements for a different (older patient suffering from hypertension) patient in the absence of medication. This is this patient's "baseline" pulse wave information. Note the overall higher blood pressure, and different timing of various components of the various pulse waves, relative to FIG. 1.

FIG. 3 shows a how a specific type medication (here type "A" medication) can impact the pulse wave measurements for the hypertension patient from FIG. 2 (above). The changes in the various and shapes of the curves can be considered to be the "impact parameter" for this type of medication. The impact parameters can be expressed either analytically in terms of the impact of the drug on the underlying patient physiology, and/or empirically in terms of the changes in the shapes of the curves (without needing to understand the mechanism by which the medication impacts the patient's physiology). Here drug "A" lowers the patient's blood pressure overall without otherwise causing much of a change in the timing of the various components of the various pulse waves.

FIG. 4 shows how a different specific type of medication (here type "B" medication) impacts the pulse wave measurements for the hypertension patient from FIG. 2 above. Here drug "B" has altered the timing of the ECG "R" pulse, and has also lowered the blood pressure overall.

FIG. 5 shows how yet another different specific type of medication (here type "C" medication) impacts the pulse wave measurements for the hypertension patient from FIG. 2 above. Here drug "C" has done several things. It has somewhat altered the timing between the ECG "R" pulse, and the onset in the rise in blood pressure. This drug has also altered the timing of some of the various underlying pulse waves (here direct wave and reflected waves) so that they don't superimpose (augment) with each other in an unfavorable manner. This helps reduce the peak (systolic) blood pressure.

FIG. 6 shows the effect of all three mediations (type "A" and type "B" and type "C") on the pulse wave measurements for the hypertension patient from FIG. 2 above. In this case, the effect of all three drugs is additive, and the hypertension patient's blood pressure is brought back to almost "normal" or acceptable values.

FIG. 7 shows a flow chart showing of some of the various steps that may be carried out by the medication adherence device's processor in order to determine if the various physiological measurements taken by the device's various sensors are showing that the patient is likely following his or her assigned medication schedule, or not.

FIG. 8 shows an example of one type of patient operable instrumentation that, with upgrades as described herein, may be used according to the present invention.

FIG. 9 shows an example of a different type of patient operable instrumentation that, with upgrades as described herein, may be used according to the present invention. In this embodiment, the patient operable instrumentation is intended to be worn by the patient over a period of time.

DETAILED DESCRIPTION OF THE INVENTION

Hypertension is a very common and very serious disease that is frequently treated by multiple anti-hypertensive drugs simultaneously. Often these different types of anti-hypertensive drugs (medications) have different, and sometimes even well understood, mechanisms of action on the user's cardiovascular system.

In this discussion, we will first examine some of the various types of cardiovascular system related pulse wave data that may be obtained by patient operable instrumentation, such as the easy to use multiple sensor instrumentation discussed in more detail in U.S. patent application Ser. No. 14/186,151 and 62/138,377, and shown in FIGS. 8 and 9. In these examples, we will examine some hypothetical automated oscillometric cuff type blood pressure pulse wave profiles, automated oscillometric pulse oximeter type pulse wave profiles, and automated electrocardiogram (ECG) pulse wave profiles, as well as some of the underlying physiological changes brought about by hypertension and various drugs on these pulse wave profiles. These examples are intended to make the general principles behind the invention easier to understand, but are otherwise not intended to be limiting.

In this discussion, automated oscillometric cuff type blood pressure sensors will be commonly abbreviated as "oscillometric" or "OSC" sensors. The automated oscillometric pulse oximeter type sensors will be commonly abbreviated as "pulse oximeter" or "PDX" type sensors, and automated electrocardiogram sensors will be commonly abbreviated as "ECG" sensors. See applications 14/186,151 and 62/138,377 for further discussion.

FIGS. 1-6 are based on a simplified model of the cardiovascular system. These figures show both the actual measurements that may be obtained by the various pulse wave sensors, as well as a few details of some of the underlying physiological mechanisms that produce these actual measurements.

In these simplified examples, assume that the major components of the patient's systolic blood pressure caused by a combination of the patient's primary pulse pressure (caused by contraction of the patient's left ventricle), augmented by a reflected wave produced when the primary pulse pressure wave effectively "bounces" off of the patient's major arteries. In younger or healthier patients,

these arteries are more elastic, and this tends to delay the timing of the return “bounce” or “reflected” pressure wave so that it does not significantly augment the pressure of the primary pulse pressure wave. However in older or less healthier patients, the arteries are less elastic, and this tends to speed up the timing of the return “bounce” reflected pressure wave so that the reflected wave pressure and the primary wave pressure additively superimpose and augment each other, thus producing a higher (and typically unhealthy) diastolic pressure.

FIG. 1 shows a simplified drawing of patient reference pulse wave measurements for a normal (healthy patient) in the absence of medication. Here the instrumentation is providing three types of “actual” patient “baseline” pulse wave measurements. These types include pulse waves from an electrocardiograph (ECG) type sensor (110), pulse waves obtained from an oscillometric pulse oximeter type sensor (PDX) (120), and pulse waves obtained from an oscillometric cuff type blood pressure monitor type sensor (OSC) (130).

The actually measured oscillometric type blood pressure waveforms are shown by the solid “OSC-Meas” line (130). These actually measured waveforms are produced by the combination of a primary pulse pressure wave “OSC-Prime” shown in dashed lines (132), and a reflected pulse pressure wave “OSC-refl” shown by the dashed line (134). For these “OSC” waveforms, the vertical “Y” axis should be assumed to read in millimeters of mercury (mm Hg).

The actually measured pulse oximeter blood pressure waveforms are shown by the solid “PDX-Meas” line (120). These actually measured waveforms are also produced by the combination of a primary pressure wave “PDX-Prime” shown in dotted lines (122) and a reflected pulse pressure wave “PDX-refl” (124). Although these measurements could also be expressed in mm Hg, for better readability, the Y axis pulse oximeter readings are shown as being offset from the oscillometric blood pressure readings. Note that the timing and the shape of the pulse oximeter waveforms is not quite the same as the oscillometric type waveforms. This is because the pulse oximeter sensor will typically be located in a different part of the patient’s body (e.g. ear lobe, fingertip) than the oscillometric blood pressure sensor (arm, wrist), and the pulse wave will thus take differing amounts of time to reach the two sensors, with the time being controlled by the pulse wave velocity (PWV). Here assume that in this case, the patient’s pulse oximeter is mounted on an ear lobe, while the oscillometric blood pressure sensor is mounted on a wrist, and the signal pulse wave reaches the ear lobe first.

In this simplified model, assume that the horizontal “X” axis represents the time (in milliseconds) since the peak of the last ECG “R” wave, which occurs at the same frequency as the patient’s pulse. Assume also that the pulse transit time “PTT” (140) is the time delay between the peak of the ECG “R” wave (112) and the rise in the measured pulse (142).

Here also, assume that the baseline of the measured oscillometric waveform (OSC-Meas) (136) represents the patient’s diastolic blood pressure, while the peak of the measured oscillometric waveform (138) represents the patient’s systolic blood pressure. These same conventions and numbering scheme are used throughout FIGS. 1-6.

In FIG. 1, this ideal normal patient has ideal cardiac parameters, such as a pulse rate of 70 beats per minute, and a blood pressure of 115/75 mm/Hg. When the patient’s heart beats (here shown triggered by the ECG “R” wave 112), the contraction of the patient’s ventricle produces both a primary wave (OSC-Prime 132) and (due to rebound from the

patient’s arteries), a time-delayed reflected wave (OSC-refl 134) that, depending on the timing of the reflected wave, can augment or not augment the systolic blood pressure (138) caused by the primary wave.

In this example, assume that the patient has young and flexible arteries. As a result, the reflected wave (134) bounces more slowly, and is thus sufficiently delayed so that the peak pressure of the reflected wave (134) does not add to the peak pressure of the primary wave (132), thus helping to keep the peak systolic pressure (138) at a desired level. Additionally, due to the patient’s more flexible arteries, the speed of the pulse transit time (140) (e.g. time between the peak ECG “R” wave (112) and the raising part of the pulse wave 142) also tends to be somewhat longer, and the patient’s diastolic blood pressure (136) is also at a lower level.

In this example, the processed pulse oximeter readings (120), (122), (124) are generally similar to the oscillometric cuff type blood pressure readings, but due to differences in the location of the two types of sensing device, differ somewhat in timing and pulse shape. Thus to summarize, in FIG. 1, the patient has a normal pulse rate of 70 beats per minute (this can be seen by the fact that the ECG “R” wave (112) has a peak at 857 milliseconds), the patient has a systolic blood pressure reading (138) of 115 mm Hg, a diastolic blood pressure reading (136) of 70 mm Hg, the reflected wave (134) arrives 130 milliseconds after the primary wave (138), and the patient has a pulse transition time (PPT, 140) of 200 milliseconds.

FIG. 2 shows a simplified version of the same type of patient reference information, but in this case obtained from an older patient suffering from hypertension. In the absence of any drugs, this older hypertension patient has a somewhat higher pulse rate (75 beats per minute) (note that the ECG “R” wave now is at 800 milliseconds), a higher diastolic blood pressure (136) of about 95 mm Hg because this patient has generally stiffer arteries. Additionally, this patient’s coronary arteries are also stiffer, thus unfortunately producing a faster acting reflected wave (134) arriving only 60 milliseconds after the primary wave (138). Due to this faster arrival time, the peak of the reflected wave (134) acts to augment the systolic blood pressure produced by the peak of the patient’s primary wave (132), producing a high peak systolic blood pressure of 160 over 95 (138). Additionally, the pulse transit time (140) (e.g. time between the peak ECG “R” wave (112) and the raising part of the pulse wave (142)) tends to be somewhat shorter, and is here 150 milliseconds.

Drugs (medications) alter patient physiology. Sometimes the underlying mechanisms are known, and sometimes the underlying mechanisms are not known. When the underlying mechanisms are known (or at least well characterized from an analytical perspective), then the effects of the drugs can be analyzed by decomposing the various measured signals into the underlying physiological mechanisms or known analytical coefficients. When the underlying mechanisms are less well-known, or analytical methods less adequate, alternative and more empirical methods, such as curve fitting, can instead be used to analyze patient data. Here, these hypertension examples are useful, because both analytical and empirical methods may be used.

FIG. 3 shows a simplified diagram showing, with respect to FIG. 2, the medication impact parameter for older hypertension patient 2 for a “type A” specific type of medicine. Assume in this example that this medication lowers both the patient’s systolic and diastolic pressure by a certain amount (here assume 10 mm Hg for both values), but otherwise does not alter other cardiovascular parameters. Thus FIG. 3

generally resembles FIG. 2, except that the systolic (138) and diastolic values (136) are both 10 mm Hg lower.

FIG. 4 shows a simplified diagram showing, with respect to FIG. 2, the medication impact parameter for patent 2 for a type "B" specific type of medicine. Assume that this medication reduces the patient pulse rate from 75 beats per minute to 70 beats per minute, and the beneficial effects of this medication also reduce the systolic and diastolic values by about 10 mm Hg each (down to 150/85), but otherwise do not impact the other cardiovascular parameters. Here, drug "B" has not only lowered the systolic (138) and diastolic (136) blood pressure readings by about 10 mm Hg each, but it has also changed the timing of the ECG "R" pulse (112) from 800 milliseconds to 857 milliseconds. The timing of the other pulse waveforms has also been altered accordingly.

FIG. 5 shows a simplified diagram showing, with respect to FIG. 2, the medication impact parameter for patent 2 for a type "C" specific type of medicine. Assume that this medication makes the patient's arteries more flexible, and thus changes (delays) the timing for the reflected wave (s) so that the peak of the reflected wave (134, 124) does not augment the pressure effects of the peak of the primary wave (132, 122) in such an unfavorable manner. This change in reflected wave timing (say from an unhealthy 60 milliseconds to a better 110 milliseconds, or a plus 50 millisecond increase) decreases the magnitude of the systolic portion of the blood pressure (138) from 160 mm Hg to 145 mm Hg. Additionally assume that this drug also makes the patient's other major arteries more flexible, such that the more flexible arteries have a longer pulse transit time (140) from 150 milliseconds to 190 milliseconds, for a net gain of 40 milliseconds (ms) over that patient's original baseline values (shown in FIG. 2). Thus the time between the peak ECG "R" wave (112) and the raising part of the pulse wave (142) tends to be somewhat longer as well.

FIG. 6 shows a simplified diagram showing, with respect to FIG. 2, the combined medication impact parameters for patient 2 when the patient is taking all three drugs at once (e.g. drug "A", drug "B" and drug "C"). Here the three drugs all act synergistically to bring the patient's blood pressure from a formerly unacceptable level of 160/95 (systolic/diastolic) to an acceptable target level of about 126/75 mm Hg.

Here, the fact that the different types of drugs have both different underlying mechanisms of actions (on an analytical level), as well as different effects on the shapes of the patient's pulse wave data (on an empirical level) can be used by the invention to help assess if the patient is, or is not, in compliance with his or her medication schedule for these three types of drugs.

For example we know, (and this information can be encoded into the machine's plurality of medication impact parameters) that drug "B", if taken properly (e.g. according to that patient's medication schedule information) should both slow the pulse rate (see the change in the timing of the ECG "R" wave), and also lower both systolic and diastolic blood pressure by a certain expected amount (e.g. 10 mm Hg for each). Thus differences in pulse rate timing (e.g. the ECG "R" pulse 112) can be used to infer the presence of drug "B" using either analytical or empirical methods.

We also know that drug "C" changes the timing of the reflected wave(s) (124, 134) relative to the primary waves (122, 132). This reduces the magnitude to which the peak of the reflected wave augments the peak of the primary wave during the systolic portion of the pulse. This drug also slows down the pulse transit time (here the distance from the "R"

wave to the rise of the pulse) to a more normal level, and this shows up in other waveform changes as well.

Thus differences in the timing of the reflected waves relative to the primary waves can be used to infer the presence or absence of drug "C".

Here the analytical or empirical methods differ however. Using an analytical approach, the shape of the measured waveform(s) such as OCS-Meas (130) and/or PDX-Meas (120) could be analyzed and decomposed (e.g. using Fourier analysis) into the underlying OSC-prime (132), OSC-refl (134) and/or PDX-prime (122), PDX-refl (124) waveforms, and inferences as to the drug effects on the timing of the primary and reflected waves can be drawn directly.

In the analytical method, then with respect to the drug impact parameters for drug "C", the drug impact parameters could report that at this dosage, drug "C" changes the timing differences between the primary wave (132) and the reflected wave (134) by a time value such as from 60 milliseconds to 110 milliseconds, (e.g. +50 milliseconds). Thus this particular medication impact parameter, for an analytical approach, might be a simple number such as +50 milliseconds. It might also be a different number, such as an artery elasticity parameter, that might in turn be converted to a different time delay parameter. But in either event, we are decomposing the observed or "actual" waveforms into some underlying equations, and the medication impact parameters can report on the effects that the various drugs each have on the coefficients of the underlying equations.

By contrast, in an empirical approach, which can be more useful when the underlying mechanisms are not so well known, the medication impact parameters might instead store an average pulse waveform shape for this patient when on the drug. The empirical method might instead look at the patient 2 reference waveform (e.g. FIG. 2 OSC-Meas 130) and the pulse waveform shape assumed to occur when this patient is taking drug C (e.g. FIG. 5) and determine by curve fitting (e.g. model fitting, different types of statistical regression analysis) if the observed patient 2 data fit the drug C pulse waveform shapes above a certain significance threshold. In essence we attempt to see how much of the actual or observed data fits a drug "C" like pulse wave profile, and how much it resembles a baseline profile without drug, and attempt to infer the presence of drug "C" without otherwise decomposing the waveform profiles into underlying equation coefficients.

In terms of analyzing combinations of drugs, note that drug "A" acts to further decrease both the systolic and diastolic blood pressure to a greater extent than would be expected by the combination of drugs "B" and "C" alone. Thus the system can also assume (or infer or deduce) that any further unexpected drop in systolic and diastolic blood pressure, not already assigned to drugs "B" and "C", can likely be attributed to drug "A".

Here, more channels of information (e.g. different types of actual patient pulse wave measurements, obtained from different sensors) are highly useful. This is because combining pulse wave measurements from at least two different types of sensors (e.g. a plurality of different types of actual patient pulse wave measurements) reduces noise, helps confirm positive signals, and can provide more insight than can any single type of measurement by itself.

It should be evident that in the examples above, any two of the various types of pulse waves will give better results than one type of pulse wave information. Thus here, combinations such as at least ECG and Oscillometric measurements, ECG and pulse oximeter measurements, or oscillometric and pulse oximeter measurements may be used.

Combinations of three or more types of pulse wave data can be still more useful and accurate.

Thus in some embodiments, the invention may be a method, device, or system for determining a patient's adherence to a medication regime. The invention will typically comprise, or use, multi-sensor patient operable instrumentation such as that previously described in U.S. patent application Ser. No. 14/186,151 and 62/138,377, the entire contents of which are incorporated herein by reference. See FIGS. 9 and 10 for some examples.

This patient operable instrumentation will typically comprise at least one computer processor (microprocessor, microcontroller, etc.), memory (at least one of local or remote memory) and various different types of physiological monitoring devices, each configured to obtain a plurality of different types of actual patient pulse wave measurements. The instrumentation will typically be designed so that it is at least capable of operation by an average patient in the absence of a healthcare practitioner. Of course in some cases, this instrumentation may alternatively be operable by an average caregiver who will typically not need to be a licensed or professional healthcare practitioner. The idea in any event is to make the invention's instrumentation convenient and easy to use so that it is used very frequently.

In a preferred embodiment, this patient operable instrumentation and its various physiological monitoring devices will be configured to provide various different types of actual patient pulse wave measurements. Preferably at least two different types of pulse wave measurements will be

obtained. For example, these various types of patient pulse wave measurements can include oscillometric pulse oximeter data (e.g. pulse waves that report on varying blood oxygen saturation levels), electrocardiograph (ECG) readings, and pulse waves that report on blood pressure measurements (e.g. oscillometric measurements from a cuff type device).

In a preferred embodiment, the patient operable instrumentation will not consist entirely of independent stand-alone monitoring devices. Instead at least some and preferably all of the monitoring devices will form a unitized system where all devices are managed by at least one common processor, preferably at least one common processor local to the patient operable instrumentation. Here again, see the patient operable instrumentation shown in FIGS. 9 and 10 as specific examples. This patient operable instrumentation will typically be referred to as "the device" for these discussions.

In order to determine if a patient is adhering to a particular medication, the device, system, or method will, in addition to patient baseline physiological data (e.g. data in the absence of drugs/medication) also need to know the patient's medication schedule information (e.g. what drugs is the patient supposed to take, and when) and the expected impact of these drugs (or at least the drugs where monitoring is desired) on the various patient physiological parameters.

Thus the invention will typically be configured to store and retrieve a variety of different types of information. This information can include medication schedule information that pertains to at least one medication and medication dosing schedule for at least one given patient. For the patient shown in FIGS. 2-6, for example, this can be a list or simple record stored in computer memory showing that this patient takes drugs "A", "B", and "C" on a daily basis, usually around 9:00 pm. Thus the device, for example, can store medication schedule information pertaining to at least one medication and medication dosing schedule for that patient.

TABLE 1

Medication schedule information example		
Drug	Days	Times
A	Daily	9:00 pm
B	Daily	9:00 pm
C	Daily	9:00 pm

The invention will also typically store a plurality of medication impact parameters. Here each individual medication impact parameter provides information on how a specific medication alters a specific type of pulse wave measurements. Here various types of data can be stored and used depending on if the system processor is going to be using either an analytical approach, an empirical approach, or both approaches. An example of the medication impact parameters for drugs "A", "B", and "C" on a patent similar to that shown in FIGS. 2-6 is shown below:

TABLE 2

Medication impact parameters example						
Drug	Δ ECG-R	Δ PTT	Δ Reflected	Δ systolic	Δ diastolic	Waveform example(s)
A	0	0	0	-10 mm/Hg	-10 mm/Hg	FIG. 3 curves
B	+57 ms	0	0	-10 mm/Hg	-10 mm/Hg	FIG. 4 curves
C	0	+40 ms	+50 ms	computed	computed	FIG. 5 curves

In this case, an "individual medication parameter" corresponds to a single row in the above list or record stored in memory, and the plurality of medication impact parameters corresponds to the above table as a whole.

The invention will also store a plurality of patient reference information, where each individual patient reference information provides information on a specific type of patient baseline pulse wave measurements in an absence of a specific type medication. For the patient in FIG. 2, the patient baseline information in the absence of all medication can include, for example, all of the information shown or discussed in FIG. 2.

According to the invention, at least one processor (preferably at least one local device processor, but alternatively also may be a remote processor) is configured so that when the patient operable instrumentation is used on the patient, this at least one processor will analyze the plurality of different types of actual patient pulse wave measurements. Here the processor will know what time this analysis is done relative to the medication schedule information. This time information can be used to adjust the analysis accordingly. Thus the processor may be configured so that if the readings are taken just before the patient was scheduled to take the medication, then any aberrant readings can be discounted. However if the readings are taken at several hours after the medication was expected, and aberrant readings are still

obtained, then the aberrant results may be given a correspondingly higher weighting and be reported accordingly.

The invention will then use at least one processor to determine which of the various actual patient pulse wave measurements are inconsistent with calculated patient pulse wave measurements that the system would normally expect for that patient. This calculation is based on the medication schedule information, the time (here time means time and the date) the actual data was taken, the various patient reference information, and the various medication impact parameters.

The invention can then do various things with the results, in a preferred embodiment varying depending on what is found. The invention may just store the findings in memory, or inform the patient, or inform caregivers, or inform relevant healthcare professionals, or keep human readable records. At a minimum, however, the invention will least store a record in the invention's memory (either local and/or remote) of at least those medications where inconsistent findings were found (i.e. evidence that the patient was not responding to the medication as would be expected).

In a preferred embodiment, the invention's at least one processor may be further configured to provide patient alarm information. This patient alarm information could report when various patient physiological parameters, such as blood oxygen saturation, blood pressure measurements, or electrocardiograph readings fall outside of previously established boundaries. The invention may also be configured so that the device uses this patient alarm information, as well as those medications where inconsistent findings were obtained, to determine and report that the patient may be out of compliance with taking these expected medications.

Value of Combining Different Types of Pulse Wave Measurements:

In a preferred embodiment, the invention will use its at least one processor to determine if inconsistent findings were obtained over more than one different type of actual patient pulse wave measurements. For example, do the oscillometric cuff blood pressure and pulse oximeter finds agree? Are any of these results consistent with the ECG results? Here the invention can be configured so when at least two different types of actual patient pulse wave measurements both report inconsistent findings (i.e. both report a possible medication adherence problem, so both are consistent with each other), the device can more definitively determine and report that the patient may be out of compliance with taking those particular medications.

Methods of Obtaining Medication Impact Parameters:

In general, any method of obtaining the medication impact parameters may be used. Here, however, although the gold standard would almost certainly be experimenting on the patient by selectively withholding all medications, and then introducing one at a time, and monitoring results, this method will often not be practical. This is because both doctors and patients may (quite properly) object to deliberately withholding important medication. Thus various substitute methods will often be needed in order to obtain the medication impact parameters in a safer and more ethically responsible way.

Often methods that attempt to estimate the medication impact parameters based on the patients data in the known presence of adequate medication, as corrected by the typical known effects of a given medication may be used. Here the probable changes in the various patient waveforms caused by the various drugs can be calculated, and these values used

for the medication impact parameters. Not as good as performing the unethical experiment, but better than nothing.

In some embodiments, these various medication impact parameters can be obtained by taking averages over a plurality of similar type patients in the presence and absence of a given medication (here results from clinical studies may be used), and the differences between the various pulse waveforms in the presence and absence of a given medication can be calculated based on such clinical study data. Again, not as good as performing unethical experiments on the actual patient being monitored, but better than nothing.

Similarly, the various types of patient reference information (e.g. various pulse wave waveforms in the absence of drugs) may be obtained by averaging over a plurality of similar type patients in the absence of the various medications. Here again, data from clinical studies may be used. Alternatively, various mathematical models may be used. Again, not as good as performing unethical experiments on the actual patient being monitored, but better than nothing.

As will be described later on in this disclosure, the invention may also be configured so as to take advantage of "natural experiments" when the patient has forgotten to take one or more medications to ethically obtain more accurate patient reference information.

In some embodiments, the invention may be configured so that the device's at least one processor calculates the expected patient pulse wave measurements from the previously stored medication schedule information (and the time), plurality of patient reference information, and plurality of medication impact parameters. Here the invention can use its least one processor to transform the plurality of patient reference information into the expected patient pulse wave measurements by various mathematical operations. For each individual medication (as expected from the medication schedule information), these operations can include: 1: selecting corresponding individual medication impact parameters from list or record of various medication impact parameters, thereby retrieving the selected individual medication impact parameters.

2: Applying (using either analytical methods based on underlying equations that attempt to reproduce aspects of the patients physiology, or by empirical curve fitting methods), these selected individual medication impact parameters to the various patient reference information, thereby producing intermediate transformed patient reference information. For example, if the patient reference information is as shown in FIG. 2, then applying drug "C" to this patient reference information would produce the results shown in FIG. 5, and so on.

3: Repeating the above steps until all of the individual medication (drugs) in the medication schedule information has been processed, thereby producing the expected patient pulse wave measurements. For example, going down through the list, and applying drug "A", drug "B", and drug "C" to the patient reference data from FIG. 2, thus producing FIG. 6. If the actual patient data resembles FIG. 6, and the timing is appropriate, then the patient is probably taking all three drugs. If the actual patient data does not match, the invention can then alternatively try further by seeing if any partial combination of drugs fits the observed data. The system can then report on its findings (based on which combination of expected drugs best fits the observed data, and which deficiency in the combination of expected drugs best fits the observed data.)

Other Types of Medication and Patient Monitoring Sensors:

Although for simplicity, much of the discussion so far has focused on pulse wave measurements and anti-hypertension drugs, it should be evident that the concepts disclosed herein may be used for a broader range of patient physiological measurements and a broader range of drugs as well,

In some embodiments, the invention may be further configured with additional types of sensors. These sensors could include one or more additional types of sensors such as body temperature sensors, patient motion sensors (e.g. accelerometers), lung function sensors (e.g. microphones, spirometers), ECG electroencephalographic (EEG) sensors, and the like. In these embodiments, the various categories of stored information would be extended to accommodate these additional types of physiological data, drug types, and medication impact data.

Thus, for example, the patient reference information data would be extended to further comprise baseline body information pertaining to these additional types of sensors. This can be, for example, at least one of baseline body temperature information, baseline patient motion data, baseline patient lung status data, or baseline patient EEG data.

Similarly the individual medication impact parameters can be extended to further provide information on how a specific medication alters at least one of these additional types of sensor data, such as baseline body temperature information, baseline patient motion data, baseline patient lung function, and patient baseline EEG data.

In these embodiments, the invention's at least one processor can be further configured to use this (suitably extended) medication schedule information, the known time of data acquisition, the various patient reference information and at least some of the individual medication impact parameters to further determine if at least some of these additional (e.g. non-hypertension) medications are also producing inconsistent findings (e.g. provide evidence that the patient is also not adhering to this additional medication as well).

To better visualize these various steps, processes, and methods, consider FIG. 7. FIG. 7 shows a flow chart of some of the various steps that may be carried out by the device's processor. Here the patient's various medication impact parameters (702), which report on how each individual medication taken by the patient alters a specific type of pulse wave measurements, are stored in memory. Additionally, patient reference information (704), which provides information on an individual patient's pulse wave measurements in the absence of either all medications, (exemplified by FIG. 2), or in the absence of at least some medications, are also stored in memory. The patient's medication schedule information (reporting on which medications the patient is taking, and when (e.g. the dosing schedule) is also stored in memory (706).

When the patient operable instrumentation and its plurality of physiological monitoring devices (here exemplified by patient pulse wave data such as rapidly time varying blood oxygen saturation levels (e.g. using a pulse oximeter type sensor), blood pressure readings (e.g. using an oscillometric type blood pressure sensor), and electrocardiograph readings (e.g. using one or more ECG electrodes) is taken, this data is also stored in memory as well (708) as a series of different types of pulse wave measurements.

Once the patient pulse wave measurements (data) have been obtained, the invention will then use at least one processor to analyze this data. As previously discussed, there are two general approaches that can be used here, and the invention may use either approach or both approaches.

In a first, more analytical approach, the invention's processor(s) will attempt to analyze the various patient pulse wave measurements according to one or more analytical models. Using cardiac pulse waves as an example, examples of such analytical models can include, but are not limited, to models such as Moens-Korteweg equation, the Bramwell-Hill equation, the Waterhammer equation, Windkessel theory, and the like. The invention's processor's may attempt to obtain fundamental values such as the time differences between cardiac forward waves and reflected waves, systolic and diastolic blood pressure, pulse transit times (PTT), pulse wave velocities (PWV) and the like. This is shown in (710).

In a second, more empirical approach, the invention's processor(s) attempt to analyze the various patient pulse wave measurements according to a best fit to underlying basis curves approach (712). Here, the invention will draw upon various underlying pulse wave curves that describe the patient's pulse waves according to the effect of each different type of drug on that patient's baseline (e.g. in the absence of all drugs) profile. When this option is used, the underlying patient pulse waves may be stored in memory as well. Here, for example, the patient baseline curves may be stored as either part of the patient reference information (704), while the empirical impact of various drugs on that patient's various types of pulse waves may be stored along with the medication impact parameters (702). Other data storage schemes can also be used.

Although the invention may use either the model based (710) or the empirical approach (712) on a stand-alone basis, in a preferred embodiment, which may have the advantages of being more noise resistant in some cases, the invention may determine which approach fits the underlying data best, and then combine the results from both approaches to produce a weighted average of the two. Here, the approach that fits the underlying data the best (best fit may be determined by a least squares approach or other best fit determination algorithm) may be given a higher weight. This optional but preferred embodiment is shown as (714).

Using either approach, the invention will then determine which likely medication mix best fits the available pulse wave data (716).

In step (718), the invention's processors will then compare the observed medication mix information (716) with the medication mix expected from the patient's medication schedule information (706). The processor may employ various rules or rubrics to help implement this comparison process. For example, the processor may use rules such as, "the patient is likely to take all medications at once, or skip all medications" in this analysis. The medication impact parameter information (706) may further contain information regarding the half-lives of the various drugs. Thus, for example, if a patient stopped taking all medication, the effects of the drug with the shortest half-life would diminish first, and the effects of the drugs with longer half-lives would diminish later.

If in step (718), the pulse wave results are clearly inconsistent with the medication schedule information (706), then the analysis can clearly determine already that there is a problem, and report it at step (720) (or at least store this in memory, and preferably also notify a person or machine).

In some embodiments, the invention may further double check its apparently OK results, and/or or alternatively report other types of potential medication problems. In these embodiments, the invention may often monitor other types of physiological parameters as well. For example, the patient operable instrumentation may be further configured to

include other types of sensors, such as accelerometers (particularly useful for patient worn instrumentation), patient temperature sensors, electroencephalographic (EEG) reading sensors, breathing status sensors (stethoscope-like microphones and sound analysis algorithms, spirometer sensors), and the like. This other data from the other types of sensors will be stored in memory as (722).

In this “extended other data” embodiment, the patient reference information (704) may further include information pertaining to this “other data”, such as information pertaining to the patient’s typical motion (e.g. does the patient tend to shake or move in an atypical manner), typical body temperatures, typical EEG waveforms (e.g. example baseline waveform for a patient with epilepsy), breathing parameters (e.g. respiratory data pertaining to conditions such as asthma) and the like. This can not only act as a double check to help insure that any cardiovascular drugs are being adequately monitored, but can also be used to extend the variety of different types of drugs and medical conditions that can be successfully monitored by the invention.

Here the medication impact parameters (702) and medication schedule information will also typically be extended to report on the impact of these other types of medications on the patient, as well as report on the schedule by which the patient takes such other types of drugs.

For example, consider a patient with epilepsy or Parkinson’s disease. Here, improper epilepsy or Parkinson’s medication may not show up in the patient’s pulse wave measurements, but may show up as either abnormal motion data (e.g. patient trembling, patient abnormal motion) or as abnormal EEG readings, or even abnormal temperature readings.

At the same time, patients with other ailments, such as epilepsy or Parkinson’s disease, are hardly immune from common high blood pressure and other cardiac difficulties. Thus in some embodiments, it is useful to have the same patient operable instrumentation monitor drugs directed towards completely different types of disease states.

In some other types of disorders, in particular breathing or lung disorders (e.g. asthma, chronic obstructive pulmonary disease, other chronic lung disorders), the underlying medical condition and the various medications used to treat the lung disorder, can interrelate with the patient pulse wave measurements. Thus in these embodiments of the invention, the invention will also simultaneously evaluate these other factors as well.

Consider the case where the patient’s other (non-pulse wave) data (722) is also inconsistent with the patient’s typical reference information (704) for this other type of (non-pulse wave data). This consistency can be checked at step (724). The relationship between findings obtained from this other (non-pulse wave) data at step (724) and the pulse wave data findings (718), and the medication schedule information (706) can help with the analysis of both types of data.

For example, given that on a statistical basis, a patient that has forgotten one type of medication is also more likely to forget to take another type of medication; findings of abnormal pulse wave values tend to make other types of abnormal data more significant. Similarly findings of abnormal non-pulse wave data tend to make findings of abnormal pulse wave data more significant.

Due to measurement noise and general physiological variability, often the invention’s methods may not produce results are entirely clear cut. Instead the invention will typically obtain compliance data that is best expressed in a more probabilistic numeric score, in which the system may

judge, for example, that the probability that a patient is in compliance with a given drug, such as drug “C”, at any time is a probability number, such as 70%.

In some embodiments, data obtained from the non-pulse wave “other” data may be used to change the weighting or significance level that the system uses to interpret its findings and report results. A patient with a borderline pulse and blood pressure data, as obtained from the pulse wave data, may be more likely to be scored as non-compliant with the medication schedule information if the patient is also exhibiting breathing problems, and vice versa. Thus in some embodiments, it may be useful to compare findings between the pulse wave and non-pulse wave wings of the analysis and use this comparison to alter (728) the significance threshold (726) by which the system reports problematic findings. This option (728) may be most useful when the significance of any abnormal findings is somewhat uncertain. If it is very clear that abnormal patient physiological parameters are being detected by the “other data” wing (722, 724), then these clearly abnormal results may be reported immediately (730). Here, the medication schedule information (706) may be used to suggest which medications may be at issue here.

Reporting Findings, and Interfacing with Remote Network Connected Devices:

In some embodiments, the invention may further be configured with means (e.g. touch screens, buttons, voice interface, network interface) to receive compliance information from the patient. Here the patient (or caregiver) can also report on periods when it is known that the patient was out of compliance with at least one known medication. This in essence constitutes an ethical “natural experiment” that can be used to obtain further calibration information for the invention. To take advantage of this ethical “natural experiment”, the invention’s at least one processor can be further configured to use this compliance (or lack of compliance) information to select at least some of the actual patient pulse wave measurements for use in establishing or refining at least some of the patient’s medication impact parameters and/or the patient reference information.

Say that the patient has forgotten all medications for several days. Here the system can at least take advantage of this unfortunate fact and gather more accurate patient reference information.

In some embodiments, the invention may be further configured with network interface means (e.g. WiFi or Bluetooth™) or wired or other type of computer network interface) to allow the invention to connect with at least one remote computerized device over a network (preferably a computer network). Here the invention’s at least one processor can be further configured to report at least some of those medications where inconsistent findings were obtained to a remote computerized device (e.g. a caretaker device, a patient smartphone tablet, or computer device, a healthcare professional computerized device, and so on).

In these embodiments, the invention’s at least one processor can be further configured to enable any of the various medication impact parameters, patient reference information, and medication schedule information to be uploaded or downloaded over a network from a remote computerized device. Here, for example, a healthcare professional, upon prescribing a new medication, might also contact the invention and upload the medication, preferred use schedule, and medication impact information to the invention so that patient compliance can then be monitored.

Examples of Patient Operable Instrumentation:

FIG. 8 shows an example of one type of patient operable instrumentation that may be used according to the present invention. This type of device is discussed in more detail in copending application Ser. No. 14/186,151 and its provisional application 61/767,839; the entire contents of both of which are incorporated by reference in their entirety.

FIG. 9 shows an example of a different type of patient operable instrumentation that may be used according to the present invention. In this embodiment, the patient operable instrumentation is intended to be worn by the patient over a period of time. This type of device is discussed in more detail in provisional patent application 62/138,377, the entire contents of which are incorporated herein by reference. This device (900) can comprise an optional ear attachment device (902) that may have any of a temperature sensor and a pulse oximeter sensor. The device can also comprise a neck mounted device (904) that may contain an ECG sensor, batteries, and a computer processor. This neck mounted device may also comprise other types of sensors such as accelerometers, lung function sensors (e.g. microphones and audio processing circuitry to provide stethoscope like lung function assessment), and the like.

In some embodiments, other types of devices may also be attached to the neck mounted device. These other devices may include arm connectors (906) and armature wires that extend down to patient worn ECG electrodes (908), and the like.

User Medication Adherence Methods, and Machine Learning Methods:

In some embodiments, the invention may be configured to receive input from the user pertaining to which medications the user believes he or she has taken. Here, the invention may query the user regarding these medications (usually via a graphical user interface such as a touch sensitive display, or other methods such as audio queries and machine language recognition of audio responses).

For example, the invention may ask the user questions or surveys such as: "Did you take your medication [here the system may also provide an optional list of medications] on time today?" and give appropriate statistical weight to the user's responses. Here, for example, a "no" answer or a "non-response" answer might make the system give higher weight to the possibility that the user (patient) is not properly adhering to his or her medication schedule.

Similarly, the invention may also be configured to receive input relating to other indicia of user/patient cooperation with healthcare professional recommendations. For example, input pertaining if the patient is adhering to other parts of the user/patient's health care plan, such as taking vital sign readings, adhering to scheduled meetings/consultations, providing on-time answers to questionnaires, and the like can also provide further information as to that user/patient's likely adherence to their medication schedule.

Thus, for example, in situations where the physiological readings as to medication adherence, such as in FIG. 7 steps (724 and 726) are unclear, evidence that the patient has indicia of not cooperating with other healthcare recommendations may be used to alter the significance levels at which medication non-adherence is reported as being a potential problem.

Additionally, user surveys or behavioral data with regards to other aspects of healthcare compliance can also be used to extend the utility of the invention for a broader range of medications. This user survey or behavioral data may, for example, be particularly useful for patents (e.g. psychiatric

patients) that may also be on medication that may not produce obvious changes in pulse wave data, for example.

Additionally, in some embodiments, various types of machine learning methods may also be used to enhance the utility of the invention. Examples of such machine learning methods include supervised learning approaches, such as the k-nearest neighbors algorithm (KNN) (see N. S. Altman, "An Introduction to Kernel and Nearest-Neighbor Nonparametric Regression", *The American Statistician* 46(3), 1992, pages 175-185). Other machine learning methods, such as artificial neural networks (ANNs) methods (Ganesan et. al., "Application of Neural Networks in Diagnosing Cancer Disease Using Demographic Data", *International Journal of Computer Applications* (0975-8887) Volume 1-No. 26, 2010); use of support vector machines or support vector networks (SVMs), (Cortes and Vapnick, "Support-vector networks", *Machine Learning* September 1995, Volume 20, Issue 3, pp 273-297) and the like may also be used.

These machine learning models may be pre-trained using data from investigational studies. Alternatively or additionally, the input for these supervised machine learning techniques can be obtained from various combinations of the patient or user input, including healthcare professional input, and/or from the patient caretaker input as well.

In some embodiments, these machine learning models will also employ features that could include any combination of the inputs gathered within the invention, such as the various physiological signals (or derived metrics), patient alarms, medication scheduling, patient demographic information, and the like.

The machine learning models (or indeed the invention in general) may in turn provide various types of output pertaining to patient medication adherence. In some embodiments, the output may be represented as a binary output (e.g. an automated "yes"/"no" assessment as to medication adherence).

In other embodiments, the learning models (or again, the invention in general) may provide multi-value outputs pertaining to patient medication adherence. For example, the patient may be scored on a non-binary scale (such as very compliant, moderately compliant, and non-compliant). In other embodiments, the learning models (or again, the invention in general) may provide numerical scores as to likely patient compliance (e.g. a 0.0-10.0 score, such as 9.8 out of 10.0). Other compliance output ratings, such as graphical or calendar data that show likely periods of compliance and non-compliance, and the like may also be provided. In general, any graphical, alphanumeric, sound or even tactile output pertaining to patient medication compliance may be provided by the invention.

The invention claimed is:

1. A method for determining a patient's adherence to a mix of medications in a medication regimen, said method comprising:

providing patient operable instrumentation comprising:
 a plurality of physiological monitoring devices configured to obtain a plurality of different types of actual patient pulse wave measurements comprising electrode-based time varying electrocardiograph readings, and time varying blood oxygen saturation levels, and time varying blood pressure measurements; at least one processor configured to control the plurality of physiological monitoring devices and memory; wherein said patient operable instrumentation and said physiological monitoring devices are a unitized, common processor controlled, system including;

wherein said time varying blood pressure measurement types are oscillometric cuff type blood pressure measurements;

obtaining a plurality of medication impact parameters, each individual medication impact parameter providing information on how a specific medication alters a specific type of pulse wave measurements, the plurality of medication impact parameters including medication impact parameters for each medication in the mix;

obtaining a plurality of patient reference information, each individual patient reference information providing information on a specific type of patient baseline pulse wave measurement in an absence of patient medication; wherein said plurality of medication impact parameters and plurality of patient reference information further provide information corresponding to all of said different types of actual patient pulse wave measurements; obtaining dosing schedule information for the mix of medications of the medication regimen;

storing the plurality of medication impact parameters, the plurality of patient reference information, and the dosing schedule information in said memory;

obtaining said plurality of different types of actual patient pulse wave measurements with the patient operable instrumentation;

analyzing, using said at least one processor, said plurality of different types of actual patient pulse wave measurements;

calculating, using said at least one processor, expected patient pulse wave measurements, corresponding to all of the different types of actual patient pulse wave measurements, based on the mix of medications, said dosing schedule information and said plurality of patient reference information and said plurality of medication impact parameters;

identifying which one or more medications from the mix of medications in the regimen was not taken by the patient, based on determining, using said at least one processor, which of said plurality of different types of actual patient pulse wave measurements are inconsistent with said expected patient pulse wave measurements; and

issuing an alarm reporting the one or more medications not taken by the patient.

2. The method of claim 1, further obtaining patient alarm information, said patient alarm information reporting on any of the blood oxygen saturation, blood pressure measurements, or electrocardiograph readings that fall outside of previously established boundaries.

3. The method of claim 1, further determining with said processor when inconsistent findings were obtained over more than one different type of actual patient pulse wave measurements.

4. The method of claim 1, wherein determining said plurality of medication impact parameters by said processor by from at least one of either:

a) averages over a plurality of other patients in a presence and absence of said a medication from the mix of medications, further computing difference parameters between said presence and absence of said a medication from the mix of medications;

b) data obtained from said patient in said presence and absence of said a medication from the mix of medications, further computing difference parameters between said presence and absence of said a medication from the mix of medications.

5. The method of claim 1, wherein said plurality of patient reference information by said processor from at least one of either:

a) averages over a plurality of other patients in an absence of said a medication from the mix of medications;

b) data obtained from said patient in said absence of said a medication from the mix of medications.

6. The method of claim 1, wherein the determining said expected patient pulse wave measurements by said processor, includes:

for each individual medication in said patient medication schedule information;

a) using selected corresponding individual medication impact parameters from said plurality of medication impact parameters to produce selected individual medication impact parameters;

b) applying, either analytically or empirically, said selected individual medication impact parameters to said plurality of patient reference information to produce intermediate transformed patient reference information;

c) producing said expected patient pulse wave measurements by repeating steps a and b until all individual medication in said mix information has been processed.

7. The method of claim 1, wherein said patient operable instrumentation is further configured to receive compliance information from said patient reporting on periods of at least one of patient medication compliance or non-compliance, and to use said compliance information to select at least some actual patient pulse wave measurements for use in establishing or refining at least some of said medication impact parameters or said patient reference information.

8. The method of claim 1, further reporting at least some of those medications where inconsistent findings were determined by said processor to a remote computerized device over a network; and storing least some of those medication where inconsistent findings were obtained in at least one remote network computer memory.

9. The method of claim 1 wherein any of said plurality of medication impact parameters, plurality of patient reference information, and dosing schedule information is either uploaded or downloaded by said processor over a network from a remote computerized device.

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专利名称(译)	用于监测患者药物依从性的系统和方法		
公开(公告)号	US9946844	公开(公告)日	2018-04-17
申请号	US15/060514	申请日	2016-03-03
[标]申请(专利权)人(译)	云DS公司公司		
申请(专利权)人(译)	云DX, INC., 特拉华州的一家公司		
[标]发明人	KAUL ROBERT ROSS HOWE SARA PEDRO JUSTIN		
发明人	KAUL, ROBERT ROSS-HOWE, SARA PEDRO, JUSTIN		
IPC分类号	A61B5/00 A61B5/0205 A61B5/1455 A61B5/0225 A61B5/02 G06F19/00 A61B5/021 A61B5/0404		
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审查员(译)	JACKSON, GARY		
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其他公开文献	US20160188839A1		
外部链接	Espacenet USPTO		

摘要(译)

用于确定患者对各种处方药物的依从性的发明。在此, 获得各种不同类型的患者脉搏波测量 (血压, 脉搏血氧计, ECG) 和其他生理测量。将该实际数据与基于不存在药物时的各种患者基线测量值, 药物计划表和患者基线测量值的药物影响而预期的计算测量值进行比较。如果实际数据符合预期, 那么患者可能会坚持该制度。根据哪种类型的数据不符合预期, 可以报告不遵守各种先前描述的的药物。还可以获得其他类型的患者生理读数, 例如温度, 运动, 肺功能, 脑电波功能 (EEG) 等, 并且这些额外类型的读数可以用于扩展不同类型的药物/药物的范围。本发明可以成功监控。

