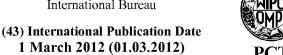
(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization

International Bureau





(10) International Publication Number WO 2012/025765 A1

(51) International Patent Classification: A61B 5/0476 (2006.01) A61N 1/00 (2006.01) G06F 19/00 (2011.01)

(21) International Application Number:

PCT/GB2011/051616

(22) International Filing Date:

26 August 2011 (26.08.2011)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

1014333.7

27 August 2010 (27.08.2010)

GB

(71) Applicant (for TT only): HOARTON, Lloyd [GB/GB]; Sherborne House, 119 - 121 Cannon Street, London, Greater London EC4N 5AT (GB).

(72) Inventors; and

- (71) Applicants: JUFFALI, Walid [--/CH]; Fraumünsterstrasse 16, CH-8001 Zürich (CH). EL-IMAD, Jamil [-CH]; Fraumünsterstrasse 16, CH-8001 Zürich (CH).
- (74) Agent: HOARTON, Lloyd; Sherborne House, 119-121 Cannon Street, London, Greater London EC4N 5AT (GB).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

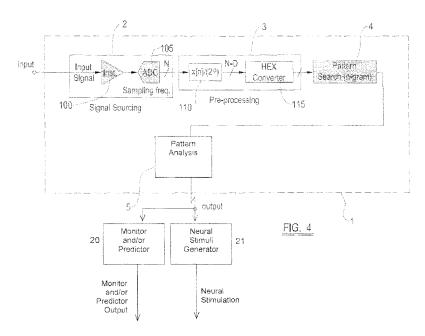
AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(54) Title: A MONITORING OR PREDICTING SYSTEM AND METHOD OF MONITORING OR PREDICTING



(57) Abstract: A monitoring or predicting system to detect the onset of a neurological episode, the system comprising :a neurological electrical input, the input being a digital representation of a neurologically derived signal; a converter to convert the digital signal into a digital data string; a pattern analyser to identify recurring patterns in the digital data string; and a monitor to measure a pattern-derived parameter, wherein an output from the monitor gives an indication of the onset or occasion of a neuronal activity in dependence on the pattern-derived parameter.



Title: A MONITORING OR PREDICTING SYSTEM AND METHOD OF MONITORING OR PREDICTING

5

15

20

25

Description of Invention

Field of the invention

This invention relates to a monitoring or predicting system and to a method of monitoring or predicting neurological electrical signals.

Background

Major attempts are constantly being made to monitor and predict epileptic seizures. Most predictive methods analyse electrical signals representing neuronal activity in the brain using electrode pickups located at the level of the scalp, externally, under the scalp or deep within the brain.

An electroencephalogram (EEG) is a system for recording electrical activity in the brain produced by the firing of neurons within the brain. Multiple electrodes are placed around the scalp but electrodes can also be placed in direct contact with the brain or within the brain. The EEG signal is composed of different wave patterns operating in a spectrum going from below 4Hz to over 100Hz. There are other mechanisms for detecting and recording neuronal activity such as an electrocorticogram (ECoG) where the signal is derived directly from the cerebral cortex or functional magnetic resonance imaging (FMRI).

Epilepsy is just one example of a potential neurological episode.

In order that the present invention may be more readily understood, embodiments thereof will now be described, by way of example, with reference to the accompanying drawings, in which:

25

Figure 1 shows a first set of potential electro positions for use with a device or system embodying the present invention;

Figure 2 shows another potential set of electro positions for use with a device or system embodying the present invention;

Figure 3 is a graph showing a relationship between seizure risk and neuronal activity signal anomalies;

10 Figure 4 is a block diagram of a monitoring or predicting device embodying the present invention;

Figure 5 is a schematic block diagram showing a system embodying the present invention for gather and analysing neuronal activity signals embodying the present invention;

Figure 6 is a table of anomaly results achieved using an embodiment of the system of figure 5;

Figure 7 shows an example of the pattern count during pre-itcal and ictal periods, the ictal period being shaded;

Figure 8 is a graph showing an example of the pattern count varying over time;

Figure 9 shows a graphical user interface designed to analyse neuronal activity data signals in accordance with an embodiment of the invention;

Figure 10 is another block diagram representation of a monitoring or predicting device embodying the present invention.

Table I shows a 10 nibble pattern matrix;

Table II shows an example of a first part of a 9 nibble pattern matrix;

5 Table III shows an example of a first part of an 8 nibble pattern matrix;

Table IV shows an example of a first part of a 7 nibble pattern matrix;

Table V shows an example of a first part of a 6 nibble pattern matrix;

10

Table VI shows some initial results distinguishing pre-ictal from ictal periods;

Table VII shows historical results related to pattern count changes when analysing full data sets;

15

Figure 11 is a snap-shot of over 12000 electronic readings taken from a single patient, the bold trace reflecting normal state and the fainter trace representing readings taken from the same patient during seizure;

Figure 12 is a detail of the electronic readings from figure 11 running from electronic readings 4000 to 5200;

Figure 13 is a detail of the electronic readings from figure 11 running from electronic readings 4800 to 5040;

25

Figure 14 shows a case list of available data for different patients;

Figure 15 shows raw data and process data for case 7;

Figure 16 gives a pattern count for 10 nibble patterns identified during seizure conditions – run 13 and a summary of the anomaly percentage; and

4

Figure 17 gives the same information as the pattern count shown in figure 16 but for run 14 taken from the same patient during a normal state.

5 Figure 18 shows a second graphical user interface designed to analyse neuronal activity data signals in accordance with an embodiment of the invention.

One embodiment of the present invention is a neurological signal monitoring or predicting device. The device receives input from one or more sensors which are suitable for receiving signals indicative of neuronal activity from the brain.

Electrodes or electrical contacts are the preferable form of sensors to detect neuronal activity from the brain, i.e. neuronal activity sensors. For the sake of convenience, this specification refers to neuronal activity sensors as electrodes or electrical contacts but non-electrical sensors to detect or derive neuronal activity are possible alternatives or equivalents to electrical sensors. As well as being used as inputs, the electrical contacts may also be configured as outputs to provide neuronal stimulation to a part or parts of the brain.

There are conventions for positioning and fixing of EEG electrodes (see figures 1 and 2) so that aspect will not be discussed further here.

25

30

The electrical signals from the brain comprise rhythmic patterns and anomalies. By anomalies, we are referring to electrical signals which are random in nature and do not conform to rhythmic signal patterns. It is one premise of the invention that as the proportion of anomalies to rhythmic patterns in the electrical signal increases, then the likelihood of a neurological

10

5

PCT/GB2011/051616

episode such as an epileptic fit also increases. This relationship is shown graphically at figure 3.

Specific identification of individual anomalies, such as signatures, is not necessary to provide useful information to predict or monitor the likelihood of a neurological event such as an epileptic seizure. Some specific anomalies are, however, indicators of the onset of a neurological event.

As well as detecting patterns using signal processing techniques and creating pattern ratios to identify threshold between patterns indicating a normal state and using those patterns to distinguish from a seizure state, one can also use more observational techniques to distinguish between the different classes of signal pattern.

15 The electrical signals received from EEGs are received as floating point data. The floating point data is then digitised and weighted in accordance with predetermined characteristics which can be pre-set or controlled by a user. Figure 11 shows such a weighted graph derived from the floating point data. In figure 11 the electronic readings are taken at a rate of 256 per second. The 20 bolder line in figure 11 represents a floating point data which has been digitised and weighted, taken from the patient when in a normal state. The fainter trace represents electronic readings taken from the same patient preseizure and during seizure. Exactly the same scaling and weighting has been applied to the processed floating point data. It is clear from figure 11 that 25 there is an almost rhythmic nature to the electronic reading when in the normal state. When in the seizure state, the electronic reading is clearly more erratic. An observation can be made looking at this data that the rhythmic electronic readings are characteristic of a normal state and the almost pseudorandom electronic readings are characteristic of a seizure state. 30 These characterisations can be used through electronic processing/signal processing to determine a likelihood of the patient being in the normal state or in the seizure state. Usefully, when the electronic reading characteristics decay from the almost rhythmic pattern, observance of this decay can be used as a trigger to provide an alert that the patient is moving from a normal state towards a seizure state.

5

10

15

20

25

30

Embodiments of the invention use a number of different measures to make threshold decisions and some of those measures are discussed below. The invention bases decisions on pattern-derived parameters which may involve thresholding or reacting to a profile of a particular pattern-derived parameter. Thus, if a pattern derived parameter exceeds or falls below a predetermined or learned threshold, then a decision can be taken in response to that and an indicator given. Similarly, pattern-derived parameters can be profiled so when a parameter follows a particular trend such as decaying, then a decision can be taken in response to that and an indicator given. A pattern-derived parameter is a parameter derived from an observation of or operation on a digital data string which gives information about one or more patterns that recur in the digital data string. Examples of pattern-derived parameters are: the number of patterns identified in a data run; the proportion of patterns of a certain length compared to the total data payload; and combinations of these and including profiles or signatures of pattern-derived parameters such as monitoring the rate of change of a particular pattern-derived parameter.

The thresholds or profiles of pattern-derived parameters can be learnt by the monitoring or predicting system and varied according to individual characteristics of the user being monitored. Monitor learning uses known heuristics, neural network and artificial intelligence techniques.

A basic embodiment of a signal gathering and analysing system takes a neuronal activity signal either in digital form or converts it from analog to digital and then presents the signal as a character string. The character string may be in binary, hexadecimal or other base. The character string is

preferably of the characters 0...9; A...F making up the hexadecimal character set. What is important is that the characters can provide a pattern of characters.

5 A sliding window of predetermined bit length or nibble length is placed over the data string and the data characters sitting within the window are considered to be a pattern. The pattern and the number of further occurrences of that pattern are logged as the window is slid over the entire data string. The window may be stepped incrementally through the data 10 string bit by bit, in steps of multiple bits or potentially even pseudo-randomly. In basic terms, the system counts the number of occurrences of each pattern and creates various parameters or characterisations of the data based on pattern count. Variations in pattern count have been shown to provide an indication of whether or not the brain is in a pre-ictal or ictal period. The 15 system also includes an output giving an indication of the onset of an ictal state based on the parameters derived from or characterisation of the pattern count.

The most basic embodiment of a monitoring or predicting system makes use of this relationship between pattern count and changes in neuronal activity to provide a monitoring or predicting system to provide a warning to a user based on an analysis which determines whether there has been a change in pattern count indicative of a change in neuronal activity indicative of onset of a seizure or the like. The analysis is based on internally stored historical ratios of pattern counts or can be processed by the monitoring or predicting device on the fly and compared with predetermined thresholds given the different parameters for the incoming data and the user.

20

25

30

The output of the monitoring or predicting system can be a wired output, a wireless output, a Bluetooth[™] output, an optical output, an audio output or any other mechanism of alerting a user or reporting to a user. A particularly

preferred method is the use of a traffic light indicator giving an alert status continually. The status of the indicator goes from green where there is no indication of onset of an ictal period, through amber where there is a potential risk of onset of an ictal period; to red where an ictal period is indicated as being imminent or ongoing.

The monitoring or predicting device is configured as a piece of electronic hardware with input connections to one or more neuronal activity sensors such as EEG electrodes which form part of a skull cap or an array of electrodes positioned on and attached to the skull. The device is preferably located on headgear or attached to the skull so that the path or distance from the or each sensor to the monitoring or predicting device is as short as possible. The device preferably has an internal power source but can be connected to an external power source.

15

20

25

10

5

The monitoring or predicting device 1 in one embodiment of the invention shown in figure 4 comprises a number of modules defined by their functionality. In various embodiments, the modules are: either all held in a common housing of the monitoring or predicting device; or some modules are remote from the skull or body-located monitoring or predicting device and connected thereto by a wired or wireless connection.

There are four basic modules making up the monitoring or predicting device 1: a signal sourcing module 2 which receives input signals representing neuronal activity from sensors; a pre-processing module 3 which takes a sampled signal and creates a data string; a pattern search module 4 which analyses the data string and shows repeated patterns; and a pattern monitor module 5 which analyses the patterns and generates a monitor and/or predictor output in dependence on the analysed patterns.

WO 2012/025765

Figure 14 shows a case list of available historical EEG data taken from patients in various conditions, usually either normal or abnormal, abnormal indicating pre-ictal or ictal state.

- In a further embodiment of the device, as shown in figure 4, a neural stimulator is provided to furnish electrical or other stimuli to a part or parts of the brain. The stimuli are preferably furnished in response to the monitor and/or predictor output of the device.
- 10 Figure 15 shows the raw data and the process data for case 7. The raw data comprises the original floating point data from the EEG before it has been digitised and weighted. The process data shows the hexadecimal characters representing the digitised and weighted data from which patterns can be derived.

15

Figure 16 shows the patterns identified in case 7 in run 13 for which the data was captured during seizure. The size of the file is 40732 bits and for a 10 nibble pattern 4156 patterns were identified leaving 36576 anomalies giving an anomaly density or ratio of 89.8%.

20

25

30

Figure 17 shows the results for run 14 of case 7 which is data captured when the same patient in case 7 was in a normal state. Again, the file size is 40732 bits but the number of patterns identified is 39090 leaving only 1642 anomalies, giving an anomaly density or ratio of 4.03%. This conveys an immediate distinction between the pattern/anomaly density or ratio allowing immediate characterisation of the data signals as being either captured during a normal state or during a seizure state. The percentage of anomalies present during a seizure state is vastly greater than the percentage of anomalies present during a normal state. A threshold can be determined or even learned by the monitoring or predicting device which can constantly monitor, for example 10 second readings in real time and make a judgement on

whether the pattern ratio or pattern threshold has been decayed or passed and provide an alert or prediction in response to monitoring of this pattern—derived parameter. Conventional pattern analysis and pattern derivation mechanisms can be used to derive, identify, count and monitor patterns.

5

20

25

Figure 5 shows the modules 2,3,4 and 5 of a monitoring or predicting device 1 as part of a larger and more detailed network which includes the facility to stream live data or run stored data through the modules.

10 Referring to figure 4, the signal sourcing module 2 has an amplifier 100 or pre-amplifier to receive neuronal activity input signals (an analog signal) preferably from EEG electrodes. Downstream of the amplifier there are one or more analog to digital converters 105 (or a multiplexed analog to digital converter) operating at a sampling frequency fs and having as their input the respective amplified EEG signals from the electrodes 10.

The sampled output of the analog to digital converters 110 is a binary string which is preferably converted to hexadecimal by HEX converter 115. The use of hexadecimal is particularly helpful to gain a visible and direct appreciation of the presence of patterns in the signal being monitored.

An analog-to-digital converter is used with typical sampling frequencies (fs) of 128-512Hz for EEG and ECoG to 10-30KHz for single neuron and local field potential (LFP) signals. The conversion, depending upon the application can result in 8-16bit data. When stored for software (and microcontroller hardware) this information is represented at its lowest level in binary, but in a higher level of abstraction in hexadecimal (HEX). Hence, the data is already available in an alphanumeric format.

30 The hexagonal output is fed to the pattern search module 4 which is configured in this example as an n-gram model.

10

15

20

30

Additionally, we can adjust the level of lossiness of the data representation by dividing the data (an N bit number) by 2^D where D is an integer, to result in a reduced data format - i.e. reducing a 16bit number to an 8bit one by dividing down with D = 8.

The n-gram process in the pattern search module 4 extracts any patterns in the signals. Once patterns are extracted the number of significant patterns are counted. A significant pattern is a pattern that has occurred more than 2 times but other threshold limits can be selected and may be usefully varied for different pattern sizes. The greater the pattern size, i.e. string length, the less repeating patterns there will be.

The pattern count is monitored and when the pattern count drops below a historically derived threshold stored in the pattern monitor, the pattern monitor outputs a change of status. A significant pattern count is quantified in two ways: (1) to count out of the number of significant patterns the total number of occurrences of all these patterns and (2) out of the patterns found what percentage were significant. The former is shown in the below results, the latter method quantified similar results so is not shown here. These pattern counts can then be quantified as a ratio between a current window of analysis and a previous window during an inter-ictal state (ictal refers to the state during a seizure).

25 The hexadecimal output is sampled and patterns identified and counted.

In figure 6, there are four sets of results 6A,6B,6C and 6D. The "NC" columns are data taken in the time prior to a neurological event (pre-ictal). The "ANC2" columns are data taken during a seizure onset and during the event (ictal) – see also the timing diagram at the foot of the table in figure 6.

10

15

30

PCT/GB2011/051616

6A gives the raw results. 6B recognises that certain patterns occur very frequently particularly those patterns representing a saturated signal for a null signal which in hexadecimal terms would equate to "00" or "FF". These patterns are therefore excluded from the list of patterns. 6C removes all repeat patterns from the list of patterns. A repeat pattern is a sub-set of a pattern which occurred in a larger pattern size pattern list.

The other figures give similar pattern matrices for 9, 8, 7 and 6 nibbles taken for the same data string. Tables I to V show the first page of patterns and frequency of occurrence for the five pattern sizes of 10 to 6 nibbles.

Preferably the data is sampled as 6, 7, 8, 9 or 10 nibbles from a sliding window applied to the hexadecimal data output string and the occurrence of each individual distinct nibble pattern is logged. In the 10 nibble pattern matrix shown in Table I, the two most popular occurring 10 nibble patterns in the "NC" data acquisition period are 020100FFFE and 20100FFFEF which patterns both occur 5 times in the "NC" data acquisition period. Many other 10 nibble patterns occur during the "NC" period.

The signal sourcing module receives input signals S1-S7 representing neuronal activity from one or more EEG sensors 10 (see figures 1 and 2) attached to the skull in a conventional manner (of both attachment and/or array). The input signals in this example are electrical signals S1-S7 direct from EEG sensors 10. In other embodiments, the input signals may be remotely streamed from a live feed or a recorded data set.

In the preferred embodiment, the number of repeated patterns in NC is compared to the number of repeated patterns in ANC2. There are usually more repeated patterns in NC rather than ANC2 during the actual seizure. As a consequence, there are less patterns identifiable during a seizure, meaning that there are also more anomalies occurring during seizure hence the

WO 2012/025765

13

PCT/GB2011/051616

premise of the invention that an increase in the proportion of anomalies to repeated patterns is an indicator or predictor of the onset of a neurological event such as an epileptic seizure.

A relative increase in the number of repeated patterns is a direct indicator of the onset of a neurological episode and is useful information to allow the device to perform an episode prediction function. The likelihood of the onset of a neurological episode increases as the number of repeated patterns increases.

10

Aspects of the invention deal with one of the bottlenecks of analysis of epileptic seizure activity. An aspect of the invention allows the ability to work with consistent data which is well annotated and databased to establish a framework for future work and storage of results into the same framework.

15 The system shown at figure 5 provides this framework.

Figure 5 shows data acquisition, user interface and processing blocks. In theory each of these components could be placed in a different technological implementation, such as the acquisition being an implantable neural monitoring or predicting device, the user interface being on a mobile phone or PC and the processing units being a web-accessed cloud (such as the Amazon Elastic Compute Cloud). The distribution of these elements will vary depending upon the signal processing requirements (computational complexity) and application space.

25

30

20

Pattern analysis of historical data yields sets of parameters concerning the patterns. Predictions or decisions on whether a neural event is upcoming can be taken by comparing in either relative or absolute terms real-time patterns with stored parameters, pre-determined patterns and thresholds. The monitoring or predicting device provides an output indicative of whether a

WO 2012/025765

5

30

neural event is unlikely, likely or imminent, much like a traffic light output: red, amber and green.

The electrodes or electrical contacts that are used to detect neuronal activity from the brain are the inputs to the monitoring or predicting device. These inputs may be reversed to provide a stimulus output. The present invention also includes the provision of neuronal stimulation to a part or parts of the brain.

The stimulus may be provided in response to any of the parameters measured or monitored by the monitoring or predicting device, such as a change in pattern count indicative of a change in neuronal activity, an onset, a seizure or the like. Thus, the traffic light output from the device can be used to trigger a neural stimulation, perhaps targeted stimulation, in an attempt to ameliorate, offset, delay or avoid entirely a neurological episode such as an epileptic seizure. The neural stimulation is provided by a neural stimuli generator 21 which can be a part of the device or connectable to a device output, potentially wirelessly, or wired.

20 Referring to figure 6, this data was obtained from the University Hospital of Freiburg Epilepsy Centre, Germany. The data used were pre-sampled at 256Hz and quantised using a 128 channel 16-bit data acquisition. All 21 patients' first seizure was used from this data set. There is a pre-ictal period of up to 1 hour in most cases with seizure durations varying from 15-170 seconds. There were multiple types of seizures present including: simple partial, complex and general tonic-clonic.

Conventional pattern analysis techniques were used. The invention does not relate to the analysis technique but in the identification that patterns and pattern ratios of the digitised and sampled data are characteristic of a patient being in normal, pre-ictal and seizures states.

10

25

30

Two sets of tests were conducted with this data. The first set aimed to quantify whether there were pattern differences between seizure/ictal areas when compared against inter and pre-ictal periods. To do this, sample pre-ictal periods equal in size to the seizure period were extracted. The average pattern count between each of 10 sections of pre-ictal data is computed in order to compare against the seizure pattern count. For this analysis we used D = 8 and analysed the data for n-gram sizes of 12 and 14, where one token was one electrical reading in 1byte or 2HEX characters. These results (shown in Table VI) show that in most cases the pattern count (P) compared to the seizure count (S) was considerably different; 18 out of 21 cases showed a ratio that indicated a greater than 25% change in pattern count. These results aim to distinguish pre-ictal from ictal periods.

The second set of tests analysis used the full pre-ictal period, segmented into 5 and 10 second windows. We analysed the data using D = 8 and with n-gram sizes 10 and 14. A typical pattern count found in these data sets is shown in figure 7. The results for all 21 patients are shown in Table VII. Table VII shows heuristic results (related to pattern count changes) when analysing the full data sets. The descriptions refer to the changes that occur that are visible changes compared to the pre-ictal period.

It is clear patterns exist and interestingly some patterns change or exist for certain n-gram sizes but not for others. An interesting pattern was an increase followed by a slow decrease over several minutes – see sharp increase at 60 minutes in figure 8. These findings conclude that out of the 21 patients, 18 can be detected using the features outlined in figure 6. Table VII shows patterns at different n-gram sizes. Patterns are identical using different n-gram sizes while making sure that patterns in an n-gram of 12 are not replicated in an n-gram size of 10, i.e. making sure that patterns are unique and not a subset of a larger pattern in the data. Also, one needs to

identify data parameters (e.g. types of seizure) to identify if certain patterns correlate with patient-specific information.

To gather further historical data and develop pattern parameters and thresholds there is disclosed a modular analysis framework as shown in figure 5.

The system of figure 5 is an open online and/or real-time analysis tool (www.winam.net) with an SQL database that is used to examine multiple cases and runs of data sets and presents in a webpage form as shown I figure 9. As in figure 5 the structure is such that the data sourcing can be through an RSS feed, or offline data source. The processing (n-gram) is implemented through a separate processing cluster allowing multiple parallel processing efficiently. This is an open system that allows users to freely access and carry out the algorithmic techniques described in this paper. The database structure itself is designed to allow users to input multiple patient cases, and for each case run particular data sets (EEG, ECoG, ECG etc...) or parts of these data sets.

10

15

- 20 Figure 18 shows a second graphical user interface designed to analyse neuronal activity data signals in accordance with an embodiment of the invention. This interface is used to set the parameters, in real-time or offline, of the logics module 4 and/or the downstream analysis module.
- In Figure 18, a number of parameters may be monitored and/or adjusted and applied to the data in real time (and not just post-analysis). The listed parameters are not exclusive and other parameters or sub-parameters can also be modified.
- 30 The "weighting" parameter refers to the rounding of the EEG signal. For example, the EEG signal may be sampled at 5Hz, and then the number of

samples may be divided by 128 to remove noise - effectively "zooming in" on the results. The signal then needs to be rounded as a 5Hz sample frequency divided by 128 will not give an integer number of samples. In a preferred embodiment, the signal is rounded up.

5

15

20

25

The "interval" parameter is the window length the user wishes to process cycles in. In one embodiment, the interval length may be 1 minute.

The "frequency" parameter is a frame frequency and relates to the number of frames to be processed. If, for example, the user has 1 hour of data and the 11th to 20th minutes are of interest, the user can skip to the 11th minute and select how many frames will be read – e.g. 20 frames at a 30s interval length.

The "optimiser" parameter determines the optimum pattern length to determine a suitable anomaly ratio. For example, with a pattern length of 2 bits it is likely there will be very few or no anomalies, but with a pattern length of 20 bits, it is likely there will be several anomalies. The optimiser effectively sets a benchmark for the anomaly ratio. In a preferred embodiment, the optimiser parameter determines the pattern length of each pattern type A, B, C, D, (see, for example, Figure 17, where the length of pattern A is 10 nibbles, and patterns B,C and D are 0) such that anomaly ratio is less than 10%. The optimiser can automatically determine the ideal settings for each of the pattern groups (shown as GNBP(A-D) on the user interface). The pattern group settings may be overridden manually by adjusting, respectively, GNBP(A-D) individually or jointly.

The "SD" parameter control relates to the threshold standard deviation of the results.

30 Other importing functionality is readily implemented as is reporting documentation to further visualise, analyse the results and further develop

18

pattern-based parameters on which to base neuronal event monitoring or predicting decisions.

When used in this specification and claims, the terms "comprises" and "comprising" and variations thereof mean that the specified features, steps or integers are included. The terms are not to be interpreted to exclude the presence of other features, steps or components.

The features disclosed in the foregoing description, or the following claims, or the accompanying drawings, expressed in their specific forms or in terms of a means for performing the disclosed function, or a method or process for attaining the disclosed result, as appropriate, may, separately, or in any combination of such features, be utilised for realising the invention in diverse forms thereof.

19

Annex:
WiNam
Core Logic
Jamil El-Imad
May 2010

5

Neural Binary Pattern Storage Table

(NBPST)

Each pattern group from(A, B, C or D) has a length defined by Pattern_n_length (where n = a, b, c or d) will have a storage table where'unique' patterns are stored. Each pattern stored has an associated count and the last offset (from the start of frame).

15 Pattern A - (validation A>B>C>D)

Pattern_a_name: xxxxxxxx (Key)
Pattern_a_count: 32,768 (16bit / 2byte)
Pattern_a_last_offset: 32,768 (16bit / 2byte)

20 Sample:

Pattern_A_name	A1 10 7F 33	3F 51 A2 9F		75 00 D1 01
Pattern_A_count	1	3	••••	1
Pattern_A_last_offset	1	11		23

25

30

35

Pattern B

Pattern_b_name: xxxxxxxx (Key)
Pattern_b_count: 32,768 (16bit / 2byte)
Pattern_b_last_offset: 32,768 (16bit / 2byte)

Pattern C

Pattern_c_name: XXXXXX (Key)
Pattern_C_count: 32,768 (16bit / 2byte)
Pattern c last offset: 32,768 (16bit / 2byte)

Pattern D

Pattern_d_name: XXXXXX (Key)
Pattern_d_count: 32,768 (16bit / 2byte)
40 Pattern_d last_offset: 32,768 (16bit / 2byte)

NBP Working Storage

(NBPWS)

5

Pattern_a_length: As per user input: 2-24 byte patterns
Pattern_b_length: 2-24 byte patterns
Pattern_c_length: 2-24 byte patterns
Pattern_D_length: 2-12 byte patterns

10

Each data value is 1 byte in length (8bits). Pattern_N_length determines the number of 1 byte patterns that constitute a pattern – example: Pattern_A_length = 3 refers to 'XX XX XX', such as '10 7F 33'.

15 Offset: 32,768 (16bit / 2byte), initial value -1 LLA: 32,768 (16bit / 2byte), initial value 0

NBP Process

20

- 1. Open Input File -> Apply weight factor (user input: Pattern Weight, Weight Range,) to 1 or 2 byte (2 Character Hex)-
- Read Input File -> Using user inputs: Skip to, Frame Length, Frame Frequency, Frame
 Gap
 - 3. Write unformatted data to input storage table
 - **4. Open Exclude List File (**Using user input: Exclude List**):**

Write to Exclude List Storage Table (ELST)

1. Start_logic

Offest = Offset+1

35

If LLA = 0 skip to **Update Pattern Table Routine**

Compare LLA with Offset range A-D

40 Overlap? Y: Start Logic

N: Continue

2. Update Pattern Table Routine

IF Pattern d Length > o then

21

Compare offset + Pattern d Length of input storage table to Pattern d name table in NBPST. Duplicate key? Yes: Set duplicate flag to d, continue 5 No: Continue IF Pattern c Length > o then Compare offset + Pattern c Length of input storage table to Pattern c name table in NBPST. 10 Duplicate key? Yes: Set duplicate flag to c, continue No: Continue IF Pattern b Length > o then 15 Compare offset + Pattern b Length of input storage table to Pattern b name table in NBPST. Duplicate key? Yes: Set duplicate flag to b, continue 20 No: Continue IF Pattern a Length > o then Compare offset + Pattern a Length of input storage table to Pattern a name table in NBPST. 25 Duplicate key? Yes: Set duplicate flag to a, continue No: Continue Duplicate flag = ON? (will equal a, b, c or d) 30 a. NO Move offset to pattern a last offest Move 1 to pattern a count 35 Move offset + Pattern a length of input storgae table to Pattern a name If Pattern name in ELST Return to Start_logic Else Write table entry into NBPST 40 Move offset to pattern b last offest Move 1 to pattern b count Move offset + Pattern b length of input storgae table to Pattern b name

45

22

		If Pattern_name in ELST Return to Start_logic Else Write table entry into NBPST
5		Move offset to pattern_c_last_offest Move 1 to pattern_c_count Move offset + Pattern_c_length of input_storgae_table to Pattern_c_name
10		If Pattern_name in ELST Return to Start_logic Else Write table entry into NBPST
15		Move offset to pattern_d_last_offest Move 1 to pattern_d_count Move offset + Pattern_d_length of input_storgae_table to Pattern_d_name
20		If Pattern_name in ELST Return to Start_logic Else Write table entry into NBPST
20		Return to Start Logic Loop Till EOF
25	b.	YES Move offset to pattern_n_last_offest (n = a, b, c or d – found from Duplicate_flag) Move offset to LLA Add 1 to pattern_count
30		Re-Write table entry
		If Pattern_count not > ELST count Return to Start_logic Else Update correlation bit map table
35		Return to Start Logic Loop Till EOF

Claims

- 1. A monitoring or predicting system to detect the onset of a neurological episode, the system comprising:
- a neurological electrical input, the input being a digital representation of a neurologically derived signal;
 - a converter to convert the digital signal into a digital data string;
 - a pattern analyser to identify recurring patterns in the digital data string; and
- a monitor to measure a pattern-derived parameter, wherein an output from the monitor gives an indication of the onset or occasion of a neuronal activity in dependence on the pattern-derived parameter.
- A system according to claim 1, wherein the pattern-derived parameter
 is related to a count or a proportion of recurring patterns in the digital data string.
 - 3. A data acquisition and analysis system comprising:
- a neurological electrical input comprising a digital representation of a neurologically derived signal;
 - a converter to convert the digital signal into a digital data string;
 - a pattern analyser to identify recurring patterns in the digital data string; and
- a monitor to measure a pattern-derived parameter related to a count or a proportion of recurring patterns in the digital data string, wherein an output from the monitor gives an indication of the onset or occasion of a neuronal activity in dependence on the pattern-derived parameter.

4. A system according to any preceding claim, wherein the digital data string is a character data string, a binary data string or a hexadecimal data string.

24

5 S. A system according to any preceding claim, wherein the system further comprises a neural stimuli generator for stimulating a part of a brain.6. A method of detecting the onset of a neurological episode comprising:

receiving a neurological electrical input comprising a digital representation of a neurologically derived signal;

10 converting the digital signal into a digital data string; identifying recurring patterns in the digital data string;

monitoring a pattern-derived parameter related to a count or a proportion of recurring patterns in the digital data string; and

providing an output giving an indication of the onset or occasion of a neuronal activity in dependence on the pattern-derived parameter.

7. The method of claim 6, further comprising:

weighting the digital signal when converting the digital signal into a digital data string.

20

- 8. The method of claim 6 or 7, further comprising: sampling the digital data string with a bit length of 6, 7, 8, 9 or 10 bits.
- 9. The method of any of claims 6 to 8, further comprising:25 monitoring the rate of change of the pattern-derived parameter.
 - 10. The method of any of claims 6 to 9, further comprising: counting significant recurring patterns.
- 30 11. The method of any of claims 6 to 10, further comprising:

WO 2012/025765

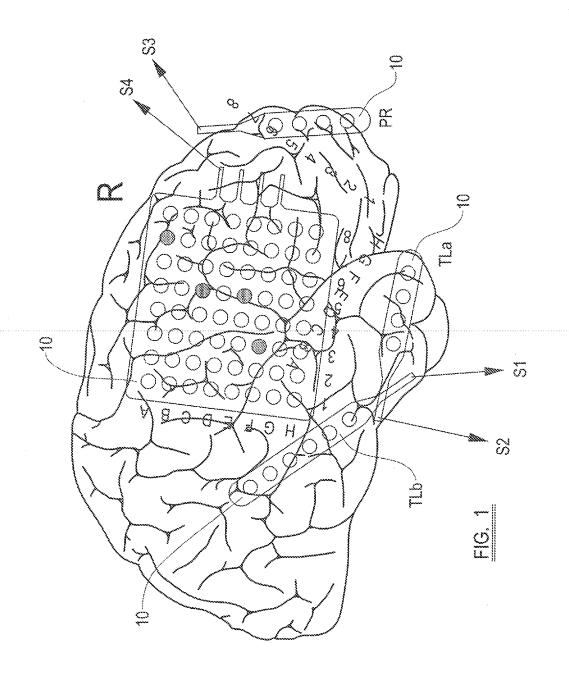
5

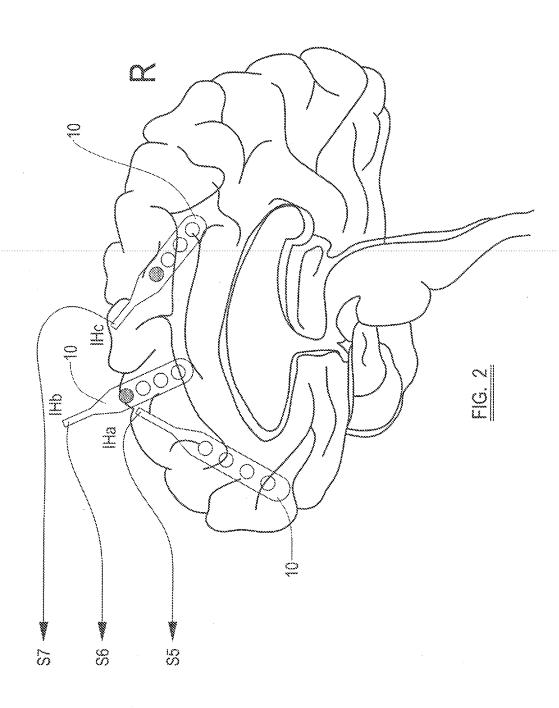
25

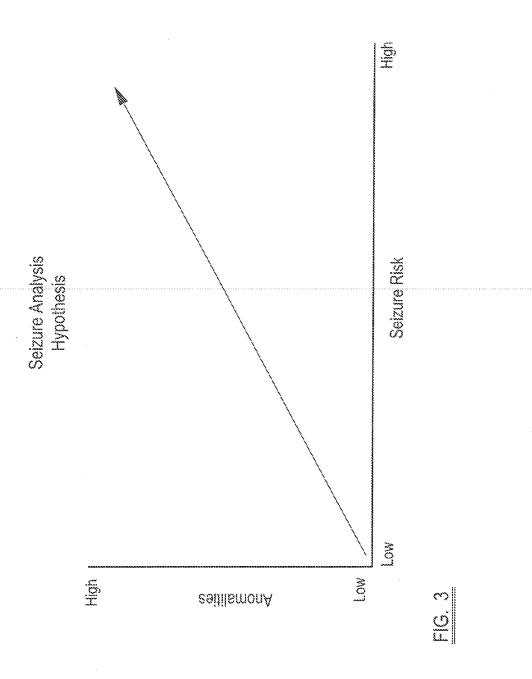
PCT/GB2011/051616

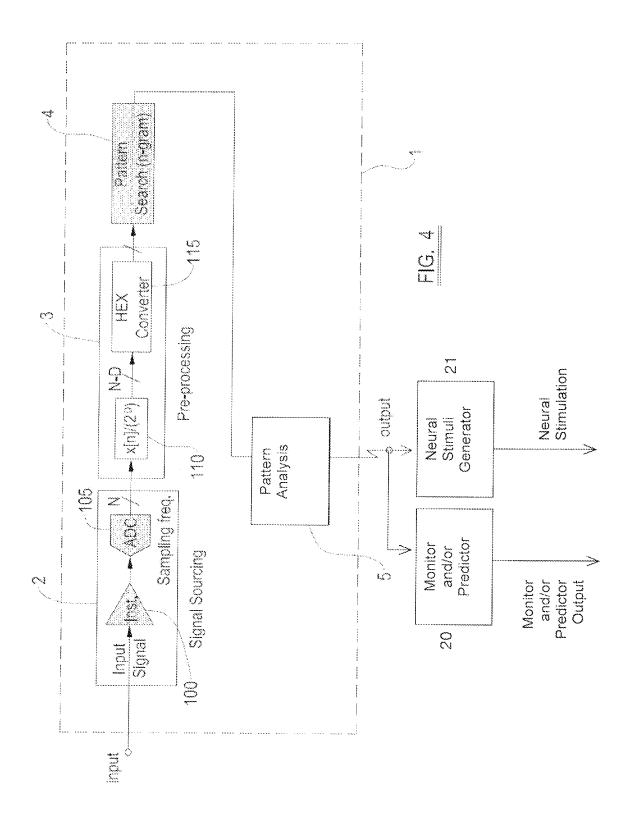
excluding patterns in the data string that are identified as null signals from the significant recurring pattern count.

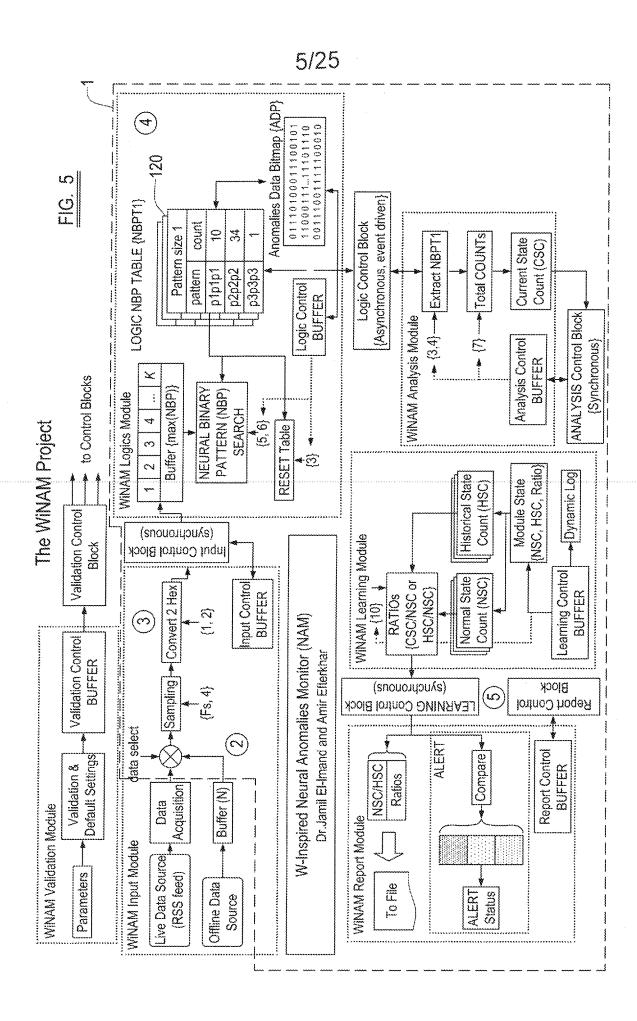
- 12. The method of any of claims 6 to 11, further comprising: detecting or identifying the type of neurological episode.
 - 13. The method of any of claims 6 to 12, wherein the output giving an indication of the onset or occasion of a neuronal activity is determined based on either:
- analysing internally stored historical ratios of pattern counts; or processing by a monitoring device and comparing with a predetermined threshold.
- 14. The method of claim 13, wherein the predetermined threshold is learned from the user profile using known heuristics, neural network and/or artificial intelligence techniques, or determined by the total number of significant patterns and/or a percentage of significant patterns found.
- 15. The method of any of claims 5 to 14, further comprising:20 stimulating a part of a brain using a neural stimuli generator.

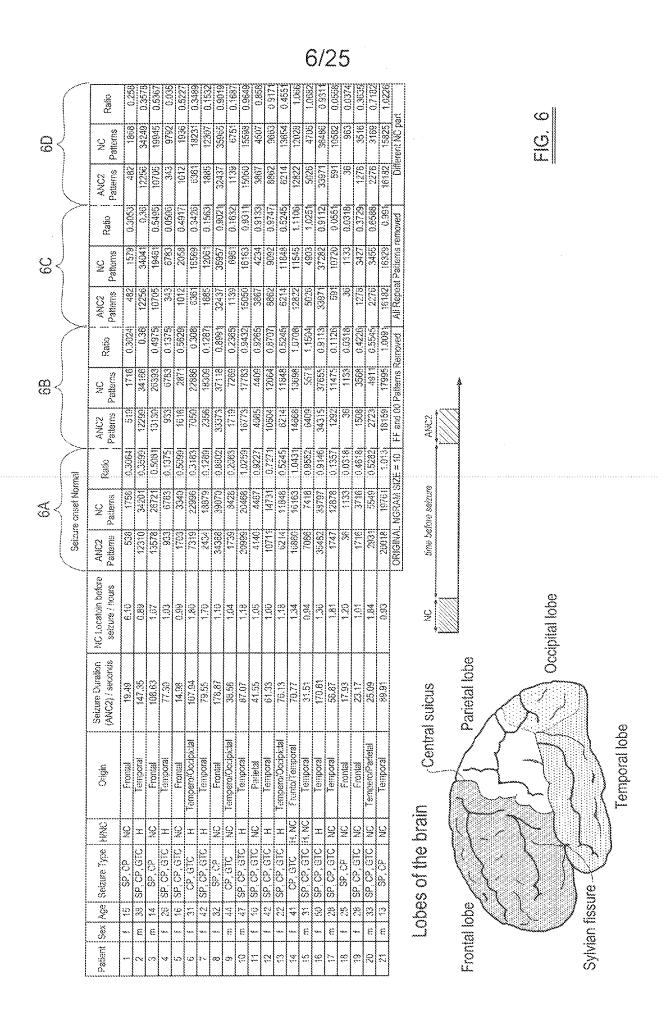














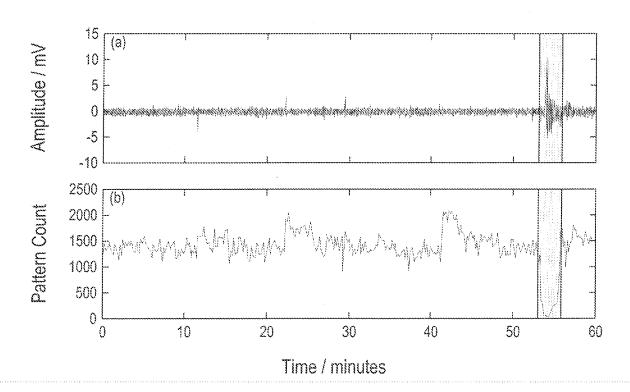


FIG. 7

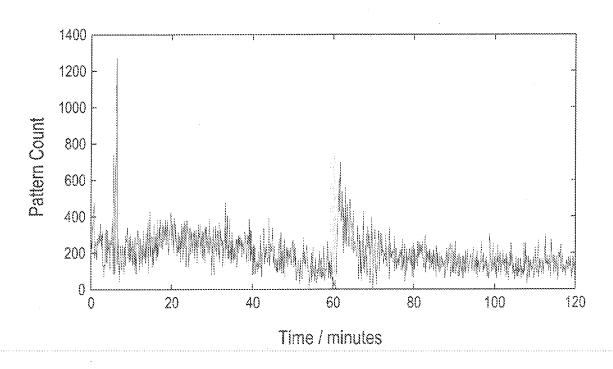
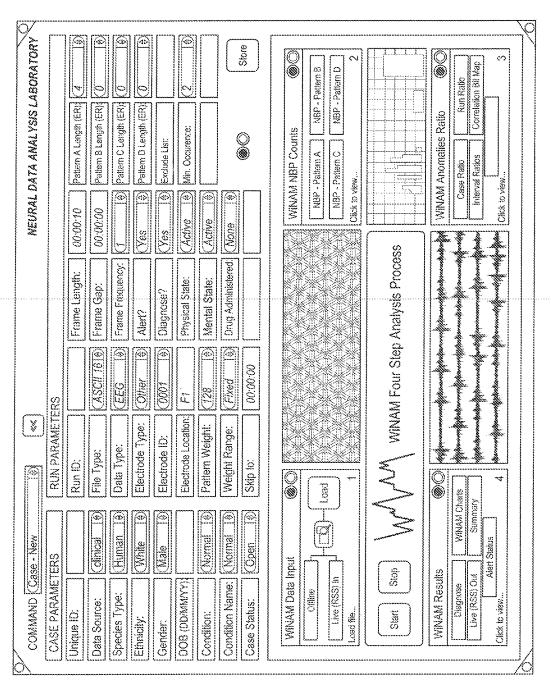
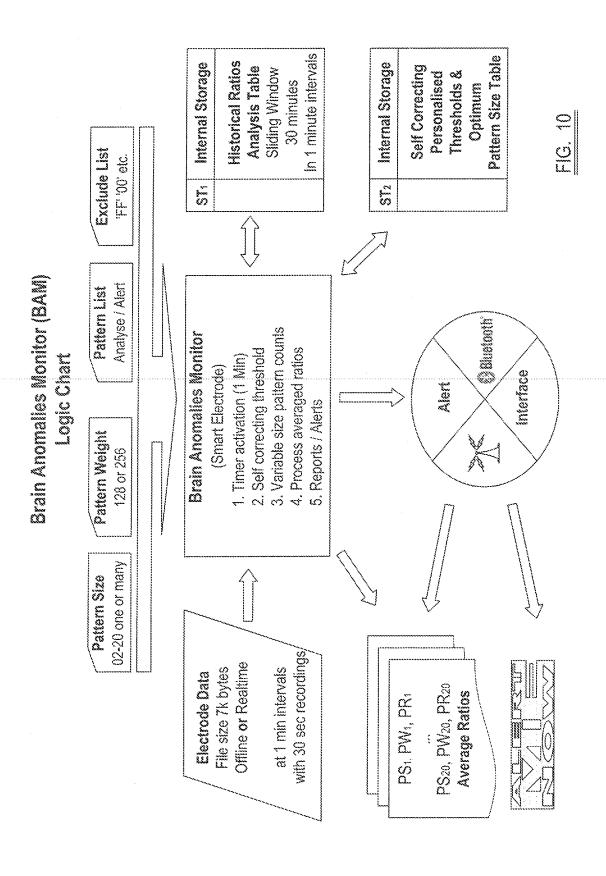


FIG. 8



10/25



					10 Mibble (half byte) pattern Waters	byte) pa	ttern Kaltrix			مدستند		
			Data One						Data Two			
9255 555	¥		AMC		ANC2		Ş		ANC		AMC2	***************************************
	DECTOOPFEE	(C)	7050555050	-ST		~~~	0303030303	605	FE0E1E2E2E	<u> </u>	[E2E2E2E2	ã
CV	20103FFFEF	S	0705050505	ব	10101010101			2	DFE0E16262	Į.	2E2E2E2E	18
м	FEFTFAFAF9	Ą	B0E0F 10103	Ω.		- T			DEDDOODBDA	12		
e;	GETEAFAFSF	43	50%0402020	c ₂			The same of	4	ZE (E (EZEZE	2		-
س	4040404040	77	2040463016	2		3:	1	m	E1E2E2E3E4	3		
<i>ن</i>	0404040404	吹	(002030200F	23		103		~	CROSOCOODE	3	****	
	FFEFOFBFAF	ಣ	F4F4F4F4F5	n		######################################		9	ESESETEODF	<u></u>		-
0X	OC.0A090R06	en	FSFSFSFSFS	in.		(F)	1		DFDEDEDFOF	(2)	***************************************	
G)	EFEFF01030	Ø,	(SFGFGFGFGF	೮		30		,,,,	DCCOOP E2E2	22		
	5	en	SFAFAFAFAF	m		<u>E</u>	E1E0E0E0E0		EAE9E9E9E8	2		
	BECECECECE	60	4F4F4F4F5F	973	-	18:31		~	E2E1E1E2E2	0		
2	OTOOFFFEFF	ಣ	00020202000	ಬ			13.1	3	9E8E4E3E3E	E.		
т.	7080508070	Ó	0606040202	(T)		(E.S.)		0	DRODEOE 1E1	23		
		œ.	FSF4F4F4F4	e.					EDDOCDBDAD	62	********************************	
 స	DFEFOROPOR	83	9506050303	ಣ		8	DSDSDSDADE	l vi	EZEZEZEZ	<u>53</u>	***************************************	-
	(6060808060	2	aEDE0E0E	62		8	1_		ESEREAE3E3	e	-	
<u></u>	2020305060	m	(0102020202	63				8	TEODEDCOCO	<u> </u>	-	
<u></u>		<u>12</u>	18F7F6F7F8F	23		á	OF OF OF OF OF		ZEZEZEZEZE	Įe.	-	
<u>(3)</u>	FBFCFCFCFC	ಪ	(0204040301	က		8	Dependence	543	E DODDOFEZE	52	***	
8	0505080808	22.	080E0F1010	C.I.		8	COCCOCOCO	10%	E1E0DFE0E0	23		
<u></u>	FEFEFF0403	63	0F0E0C0907	77		S	0602070906	67	DEUCEDDEE	m		
8	100FFFEFF	<u>12</u>	(1020202020)	65					AESEBESE	6		
23		3	(60605/43030	<u>65</u>		*******		-	ETEOCEDODC	n		
Ž	FOREFOROFO	m	F0E0039070	<u>e</u>					1.E2E2E3E4E	20	***************************************	*
25.		25.	F8F7F6F7F8	e2.					***************************************		*****	
92 2	C0A0808060	25.3				****						-
S	0606060606	22				***						
% %	FGF6F6F6F7	es.										
(Z)	5050808080	6					***************************************		***************************************			-
30	6F6F5F0F7F	(*)				***************************************			**************************************	-	***************************************	
~ ~)	FFFEFOFBFA	55.5						and the state of t				
 (2)	FSFSF4F2F0	£2.							**************************************		***************************************	
(N)	1020203050	Ω.					€ 6000000000000000000000000000000000000		در الدور الد	ļ	***************************************	
Ř	1F1F1F2F3F	m				-			-	-		
98	3040707060	67	••••									

<u>ab</u>

			•		o renkova priskr	200	s model that bying between modelly					
			Data One			,			Data Two			
373	¥		ANC		ANCO		¥		ANC1		AMC2	
•••	JOYOUFFFEFF	<i>}~</i> _	デキデタドタドルド	£.	101010101	Ð.	E0E0E0E0E	<u>ca</u>	[DCDCDCDCD	(0	ETERERERE	32
c4	040404040	!~	020202020	æ.	010101010	(<u>v</u>)	090303030	80	EZEZEZE	100	2626262	12
ere;		12	060508060	œ.	141414141	0	E7E7E7E7E	22	EODEDCOCO	53	ESEAEBECE	100
ব	FAFBFBFAF	Ç	070505050	တ	080000080	n	DROZOZOZO	23	ESETEODFE	a,	FCEBEAESE	100
ശ	FOFDFOFDF	හ	F8F8F7F6F	4	191A181C1	m	EFEEEOEBE	150	ESEGESESE	ur)	ESESESE	12
Ø	090909090	in.	705050505	4	0201FFFDF	60	E1E1E1E2E	82	E7E6E6E6E	55	Decededadad	122
۲۰.	20100FFFE	183	FSFSFAF	ব্য	181819181	52	ESESESE	<u>(4)</u>	060000000	15	EEEFEFEFE	m
ယ	FAFAFAFAF	9	下級でいる。 である。 で。 でる。 でる。 でる。 でる。 でる。 でる。 でる	200	01010100	0	CECLOROSO!	ļ m	EODFOFDED	S	ECEBESESE	k
ගා	0201005FF	ဖွာ	050506070	4	010404030	<u>673</u>	DEDFORDED	100	E1E0E0DFD	10		-
3Q	PFFEFDFGF	4	070605050	v.	181818181	60	000000000	ल	E364E5E5E	8	-	ļ
\$. \$.	F6F5F6F7F	vy.	0.0500030	*7	FF002030	62	000000000	12	ESESESE	NO.	***************************************	ļ
يم دخ	FBFBFAF7F	থ	000204040	N.	040303030	13	E0E8E7E7E	4	E4E3E2E1E	4	***************************************	ļ.,
5	FAFAFBFOF	4	FEFEFEFEF	*	134006000	<u>m</u>	EFEEEBEAE	2	aggaggagg	4	***	ļ.,
14	FFFEFCFSF	マ	020200FDF	7	020808040	65	COCCERDAD	47	ETEREAECE	4		ļ
<u>۾</u>	1090A0C0CC	κ).	000000000	41.	383838383	(e)	E85757575	24	DFDFDFDED	4	***************************************	ļ
3,8	FEFDFOFBF	4	0505050	Œ.	18181A191	er	E3E2E1E1E	4	EAESESE	**	***************************************	
<u> </u>	000000000	4	030406080	7	OECCOROBO	103	ENERGENORD	a	DOCCOBOAD	4		
స్తు		4	FAF9F9F	4			(E0E0E0E0E	4	FIFTER	4		ļ
<u>ښ</u>	FOFCFUFOF	Ż	080708050	Z.			73/3/3/3/	92	DEDEDDODD	4		1.
33	FOFOFOF	SI.	060606080	**			E 1E 1 E 0 E 0 E	2	DEDFEGE1E	ST.		
1.4 2.4	FSF7FAFAF	ঝ	060605030	*\$*			000000000	3	COBCBOO	×	***************************************	ļ
2	FAFBFBF9F	4	060402020	4			150505050	02	FE0E1E2E2	Z	***************************************	ţ
23	FCFCFE000	4	030305060	7			E (E0E0E0E	<u> </u>	ESESETEAE	4	***************************************	<u>.</u>
24	F8F8F8F8F	Z.	040406076	73			E 55:45:45:65	67	# # # # # # # # # # # # # # # # # # #	4		}
532	****	M.	040403010	ष			E25.10F0F0	3	CAFEDE (ESE	*		ļ
92	0.60506070	শু.	060503030	න			DCDRDAD8D	က	ESESESE	7		-
S		ā	000003030	က			FOEFEEFCE	<u>e</u>	E9EAE9E7E	¥		ļ
78	FOFOFARSE	W.	FSFSFSF3F	œ.			E2E3E2E1E	277	ESESESE	4	********************************	ļ
<u>ස</u>	(030407070	3	F4F4F5F6F	N)			DECISION	62	E2E3E4E5E	4	-	
စ္တ	BF7FAFAF9	শ	0302FFFEF	87 <u>)</u>			8080/0808	3	EAESEGESE	শ	***************************************	ļ
6.5 	404040404	4	F8F7F6F7F	න			DECADADED	2	ESESE3E0D	4	-	
32	FFFFFFFEF	42	1010100F0	ers.			E3E3E2E2E	63	E0E7E7E5E	4		
8	(0.40908080	Ħ.	0202020F	8		-	FZEFEBENE	<u></u>	TODOM STORES	4	***************************************	
*	FEFURORUE	শ	020404030	හ			SE3E7E7E7	2	(EODFOFO	V		ļ
300	FTFAFAF8F	4	000000000	හ		ļ	EGEGESESE	c	(E2E2E3E3E	-1		<u> </u>
88	020504020	4	OZONFOFBF	m	***************************************		DEETEZEZE	3	TEAE SESE	A		ļ

<u>20</u>

					8 Mibbie (hall	essa,	8 Mibbio (naid byte) pattern Matrix		***************************************	NO COLUMNIA DE LA COL	enicense proposed and a second	-
			Data One			6			Data Two	0.00000000		
8	3		ARCI		ANCO S		2		ANC		NO.	
~~	40404040	;	FAFTAFA	<u>.</u>	01010101	<u> </u>	EOFFOEOEO	3	coocococ	}. 	252525	<u></u>
~	102040404	<u>r</u>	4F4F4F4F	<u> </u>	110101010	100	OEOEOEOE	65	CDCDCDC	1	EZEZEZEZ	19
က	OYOOFFFE	<u> </u>	28050508	စ္	01010100		DFOFUFOF	132	E3E1E00F	2	EEEFEFEF	12
4	JEGNEFFEF	7	50505050	œ.	0909090A	8	7.E7.E7.E	8	E 1E0E0DF	8	RCEBEAE8	60
មា	FAFBFBFA	(C)	20202020	9.	83838383	8	ETETETET	9	E2E2E2E	9	CEBEAE9E	60
ဖ	8F9F9F8F	w	00000000	œ.	ZOTEFEDE	m	EFEECEB	တ	DFOEDEOF	19	EEFEFFF	2
۶.,		60	102/02/02/02	æ.	191A181C	200	EGEGEGE	2	2E2E2E2E	<u>se</u>	ECEBESES	c
æ		ග	07050505	S)	81819181	52	E1E1E1E2	lan.	doddddddd	8	CEBESESE	2
os.	1020100FF	ဖာ	70502350	S.	C000000000	8	FEECEBE	10	EDODODBD	60	ESESES	3
3	FCFOFOFO	ಣ	42424344	w.	FOFOFCFE	8	807070708	92	ODEDCOCD	3	43433303	875
£	FAFAFAFA	នា	64536363	4	04030303	67	DSDSDZDS	9	EODFOFOE	le le	SEAFBECE	3
2	AFAFAFAF	জ	104040301	¥	40303030	65	08070707	Le.	30303030	143	SESESE	13
Ç	90909000	K)	08070805	4	8:613181	₩?.	6E6E6E6E	ļu.	EOCHEDED	g)	DROBURDE	575
Œ	FEFEFEFF	S	61010161	4	FFFFFF	(C)	FOTOTOTO	1	EDDE DODC	2	EZDCDADB	(e.)
భ	20100FFF	īΰ	(05050607	4	FF000203	67	ESESE 1DF	92	38383636	2	BD308080	
స్ట	Crororor	ю.	40403010	4	00000010	65	08077080s	9	E3£4£5£5	3	ESEAEBEC	n
2	09090909	80	FOFOFOEO	ai	DECCOSOS	2	11E1E1E2E	12	1005 05:00:00	10	-	*****
<u></u>	4344444	nţ.	80402020	Х.	41434141	43	F2F4F4F1	4	36363636	n's		***************************************
Ω.	FFFEFCF3	7"	90508000)	<u>'ā</u> .	FOCO0000	e3.	00000000	Z.	E7E6E6E6	vo.		
្ត	REDECHBE	4	(80706050	4	01040403	ന	ERERETE 1	4	ESESES	3	-	
<u>~</u>	OFORDEDE	2	FOFEFOFA	33.	10404030	67)	3E2E1E1E	A.	83636363	9		_
22	FAFAFBFC	¥.	E00239070	7	38383838	45	COCCOCCO	4	3E (EQDFE	100		
22	FAFSFSFS	ā.	OF CIF-OF CE	<u>4</u>	(18181918	ক্য	SESETETE.	Ç.	90000000	wo.		
Š	FFEFDFOF	Ŋ	0600030	2	STONERCO	375	DDCDBDAD	-31_	E0£0E0E0	50		
93	3	77	20200FDF	W.	81814191	~ 0	EFEEBBEA	Z	1E0E0DFD	10	***************************************	
8	AF8F8F9	I.	100204040	24	CZOTFFFD	40)	ESEBETET	4	3646566	ın.		
27		4	FBFCFCFC	7.	08090AD	e9:	0000000	Ā.	30303937	2		
SS.	FOFOFOF	Ą	70805050	4.	20101812	e5.	8E7E7E7E	3.	DFDFDFDE	85		-
<u>@</u>	FFEFOFB	ধ	(020200FD	\$	118181439	27	NO CO COS CA	4	COSCISCO	4		
8		* 3	FFFF0000	6 7	1414:414	n.	COCCCCCC	4	TESEAECE	4	e de la destación de la companya por porte de la companya de la co	
 	(05050607	4	10101010	ক্	F0002030	65	DEDDDDDDC	4	COCCOCCO	×		
S	04050402	Ą	30408080	4	16181818	9	E25.0F0F	4	DFDFDFDF	3		
g	00040908	4	for or ar sr	Ž.,	03020400	63	SEZETOFO	4	OE 1E2E2E	X		
<u>~~</u>	\$6F5F8F7F	4	(8F8F7F6F	<u>z</u> .	10401005	67	E0E0E1E1	7	E4E3E2E1	4		ļ.,
32	FIFAFAFS	ST	0E0F1010	×i.	00000000	63	E0E1E1E1	4	2E2E3E3E	Z.		-
8	FEFORCES	<u></u>	30305040	Œ.	13100ECC	62	E8E7E7E7	4	COBOBOCO	4		-

<u>0</u>

E6E4E3E EFEFEFE 000000 ESE7E8E F2F2F2F ESESESE EAESEBE EEECEBE ECECECE EDECEBE DBDSDBD ECEBEAE EDEDECE EBEBECE DSDADED EBEAE9E ESESEAE ECEAERE ESEAEBE 0808090 EFEEEDE EEFEFEF ESESESE ESESEAE E5E5E5E **E8E8E9E** EAESESE E9E9E8E E6E7E9E E8E7E5E F6F7F8F ర్ల లై 2 2 N O 2222222 G) 9 Q) Data Two ANCI DEDUDCO E2E2E3E E1E2E2E EAEAE9E CDCDCDC E0E0E1E 0000000 0800000 DEDEDED OF DFDED guadaaa 0000030 EGEGESE E3E3E4E E1E2E3E E9E9E E7E7E7E E4E3E3E E2E3E3E 0000000 OFC/FDDD DFDFDFD EODFDFD 000000 DADAD9D ESESESE ETETEZE DFE UE 1E E3E4E5E E3E2E1E E0E1E2E ESESEZE ESESE4E E4E5E5E 991223 7 Mibble (half byte) pattern Matrix $\frac{\mathcal{Q}}{\mathcal{Z}}$ 0606060 ETETETE ETETETE DEDEDED DEDEDED DEUDDDD ESESSESSE DECEDED EDECE DE DADADBO DCDCDCD ECEGE1E DADADAD DEDFE1E E3E3E2E EGESESE EAESESE EPEEECE EBEZETE DADSDSD EGENESE ESENESE SBE7E7E CKCED20 1E1E2E EGEGESE E3E3E2E Capacita EZETETE E2E2E3E FOFOFOF E8E8E8E E 2E 3E 2E so us 4 XXX 0302010 100E0D0 0706060 0909090 CAOBCCC OBOBOAG FORDED OBOACAC OACACAC 0800000 0404030 OFFFEF 0000000 0904080 CECDODO 3838383 0101010 1414141 311111 100E0C0 0E0F101 ODFFOZO 1818181 1914181 0704040 1818191 1010111 0909090 0103040 0101040 0805040 2405040 0406080 1010101 2 2225 = 6 6 6 6 (3) Data One AMC.1 FSFSFSF FOFCFCF FOFCFOF FBFBFBF 0404030 F7F8F6F FFFFFFF SF 7FBF 0606080 0408080 OFUFUED 0403020 0909090 FCFDFDF FOTOTOR FRESFER 0202020 0000000 F7F787F FEFSFSF 0605040 306080 0206070 F4F4F4F 0404040 FEFSFSF 0304040 3002040 3203040 0303030 0402080 0504040 0705050 0807080 0608060 స్ చ = 9 9 9 5 5 5 5 5 Ü ¥ Fafafaf Fbfbfaf FEFEFEF FDFOFOF FSFSFSF 0A0C0C0 FSF9F8F FAF8F8F 0202020 FOFOFOF FOFOFOF FEFOFOF FAFBFBF 0807060 F8F8F9F 0403020 FFFEFOF FBFAF9F POPOPOP FFEFF0 FOFBFAF EFEFFO 3344500 FAFBFOF EFCF8F Faraps 0404030 CADOFFF 07080AD 03090A0 FEFOF7F 3808060 0102020 3607080 0808080 0909080 8 1 2 2 2 2 2 2 2 2 3 3 3 3 3 3 3 888888 10 00 m ත න 60 4

Table IV

	***************************************	************			5 Mibbis fratt	27/0	6 Nibble (nelf byte) pattern Matrix		***************************************			
			Data One		6 000 000 000 000 000 000 000 000 000 0				Data Two			
2000	2		ANC		XX.03		2		ANC		ANCZ	
~ ~	***************************************	<u>ئ</u>	35 35 35 35 35 35 35 35 35 35 35 35 35 3	ñ	010101		EDEGEO	53	000000	32	m m m cr	23
CV.	FOFOFO	15	202020	14	101010	<u>2</u>	303030	17	FOFOFO	155	2E2E2E	23
Ġ	DEDFUS	î.	020202	य ्र	000000	ಹು	E 15. 15. 15. 15. 15. 15. 15. 15. 15. 15.	13	EZEZEZ	35	DECEBE	-
10	404040	ŝ	000000	13	111111	œ	DFDFDF	12	515050	120	EFEFEF	7
m	040404	<u>ئ</u>	605050	<u></u>	ACACAC	1~	FDFDFD	2.	DEDEDE	13	EDECEB	7
S	333370	33	050505	<u>و</u>	040403	۲.	CEDEDE	4.5	ZEZEZE	125	DFEDEZ	8
ķ . •,	000000	<u></u>	9F9F9F	2,	080804		E7E7E7	-	ETEODE	15	E TEOE 6	60
99	OOFFFE	<u>60</u>	656563	23	00000	1	121818	F. F.	393939	14	CEBEAE	8
(2)	FEFOFC	<u></u>	F4F4F4	Ç	808040		7E7E7E	7	6.56.56.5	ž	080808	3
9	TOTOTO O'CO	Ğ.	4F4F4F	2	FFFFFF	<u>.</u>	(D8080)	10	DEDEDE	E	FE052E	82
7	EFDFOF	22	lor or or	2	818181	Ç	190307D	9).	COCCO	Œ	[5E5E5E	8
2	5000	2	FDFCFC	11	OEOEOE	ώ.	SESESE SESESE	63	202020	12	ESESES	8
೮	FFFEFF	***	404040	13	336303	<u>.</u>	SESESE SESESE	8	4E5E5E	ā	DBDRDB	8
 	೯೪೯೪೯೦	~~ ~~	111111	;_	14:434	123	GGGGGE	6	031323	*	goggaga	æ
18	FRFBFA	~~	DECECE	,	1020201	ಲ	COCOCO	8	EAESES	E.	ECEBEA	8
<u>3</u> 2	BFBFAF	13	040404	~	800000	ώ.	E9E9E9	6	(EDEUED	Z.	DEDEDE	3
::	FEFEFE		303030	<u>5</u>	12:8:8	φ.	E5E3E1	8	DFE0E1	5	200000	io.
2	EFERT THE	~	OFOFOE	5	05/1010	es.	707070	රා	EGOFOF	£		u)
13	AFAFAF		F3F7F6	<u>0</u>	080080	ço.	3E2E2E	Œ1	EFFERE	12	638383	2
R	FAFBFC	**	040463	<u>.</u>	404030	ω	ESEZEI	Çħ	DFUFUE	53	8E8E9E	S.
23	EFEFFO	7	8F7F6F	ت. ت	030408	<u>დ</u>	E3E2E2	es.	OE1E2E	5	DEDECE	2
S	FAFAFA		630303	20	414141	φ.	ERERES	න	DECOSO	27	202020	E.
g	8505 35		505030	9	TOTO C	¥3	070707	က	FE0E1E	22	CECECE	ਘੜ
8	000000	30	050506	0	303030	S)	000030	CPA	EOE1E2	2	BEBECE	νΩ
8	FEFEF	2	101013	10	191A18	ഗ	ECEDED	ආ	90000	=	343434	2
8	040403	2	FCFCFC	<u>5</u>	040504	ഗ	0£0FE0	ಣ	(E5E5E3	Ξ	8E4E3E	rc.
27	016262	3	FFFF00	<u>~</u>	466.85	<u>:0</u>	404040	æ	3E4E5E	<u></u>	E3E1E0	ıo.
8	08080E	\$	705050	0	005000	us.	ESESES	හ	ESCHEO	Ξ	EBE4E3	w.
83	FDFCFC	2	070508	0	403030	127	SE 6E 6E	αú	DEOFDF	-	EBEREC	M2
8	000000	9	CROPOR	Ç	1818191	<u>\$2</u>	DADADE	හ	E3E2E1	7.	230303	9
6	000000	2	080706	Ç0	C08080	ಜ	939393	හ	636160	-	030303	2
S	102020	2	304040	G)	040303	<u>10</u>	AESESE	ඟ	DEDEDF	-	E060E0	9
8	046302	30	FOFOEO	0)	104040	យ	20000	ĸΌ	EAEAE3	***	EFEEED	\$
ž	404030	Ģ.	FBFBFB	8	302040	<u> </u>	636363	œ	E3E4E5	Σ.	857656	¥
8	608060	8	040608	Ç5	706060	S)	808080	83	FOFDED		2F2F2F	4
g	808080	30	04040E	ÇT:	A08000	tΩ	EOE OE 1	හා	SESESE	÷	eCecso)	4
33	5556	30	6F8F5F	G)	181819	20	30 de 20 de	æ	000030	,	(CEC8EBE	8

able V

Table VI

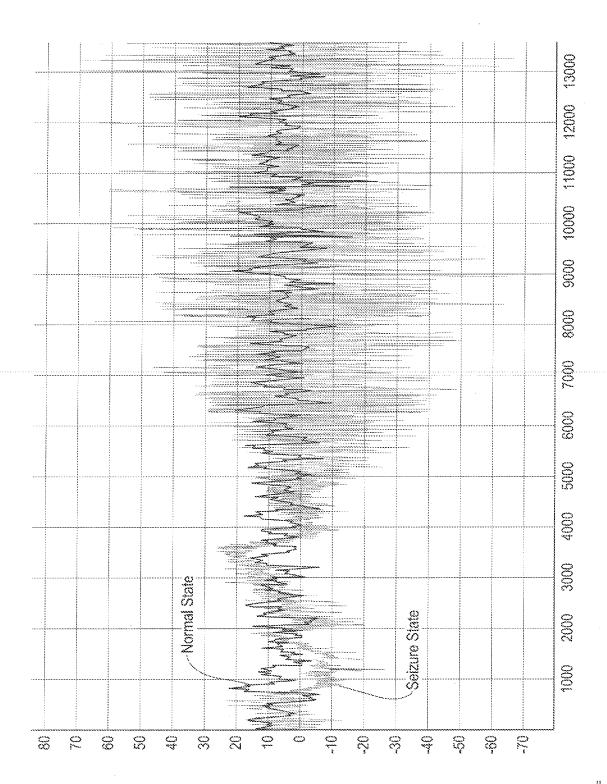
*************************	***************************************	***************************************	1	VGRAM = 1	2		VGRAM = 1	4
Patient	Sdur/s	Pdur/hrs	S	Р	Ratio	S	P	Ratio
1	19.49	6.10	514	778.9	0.66	269	393.3	0.684
2	147.35	0.89	6000	28727.5	0.209	2805	21811.3	0.129
3	108.63	1.67	11029	25517.8	0.432	8150	23742.1	0.343
4	77.30	1.03	743	324.6	2.289	577	83.2	6.935
5	14,98	0.99	1455	3246.8	0.448	1138	2991.8	0.38
6	107.94	1.80	2974	13409.7	0.222	1606	9053.5	0.177
7	79.55	1.70	938	16917.8	0.055	719	14890.9	0.048
8	178.87	1.10	27969	34800.6	0.804	19923	27931.6	0.713
9	38.56	1.04	990	6939.9	0.143	702	5465.6	0.128
10	87.07	1.18	14280	19114.6	0.747	10639	17416.9	0.611
11	41.55	1.05	2241	2216.3	1.011	981	861.8	1.14
12	61.33	1.00	2032	12806.2	0.159	1091	11541.4	0,095
13	76.13	1.18	4214	4809.5	0.876	1791	2451.3	0.731
14	70.77	1.34	14268	13165.1	1.084	12212	11027.6	1.11
15	31.51	0.94	5326	5523.1	0.964	4305	4452.6	0.97
16	170,61	1.36	29278	37282.8	0.785	21912	33935.4	0.646
17	58.87	1.81	1256	11120.3	0.113	988	9095,3	0.109
18	17.93	1.20	Ö	401.6	0	0	154.9	0
19	23.17	1.01	850	2688.7	0.316	469	1679.1	0.279
20	25.09	1.84	1323	4629	0.286	946	4098.1	0.231
21	89.91	0.93	17693	20965.5	0.844	15120	19932.2	0.759

Table VII

***************************************	NGRA	M = 10	NGRAM = 14
Patient	10s	5s	5s
10	increase/decrease	increase/decrease	increase/decrease
11	none	none	none
12	decrease	decrease	increase/decrease
13	none	none	none
14	none	none	none
15	none	none	none
16	decrease/increase	decrease/increase	decrease/increase
17	decrease	decrease	increase
18	reduce variance	reduce variance	reduce variance
19	decrease/increase	decrease/increase	increase
1	decrease	none	none
20	decrease	decrease	decrease
21	none	decrease	decrease
2	decrease	decrease	decrease
3	decrease	decrease	decrease
4	none	increase	increase
5	decrease	decrease	decrease
6	decrease	decrease/increase	increase
7	decrease	decrease	increase/decrease
8	decrease	decrease	none
9	decrease	decrease	increase

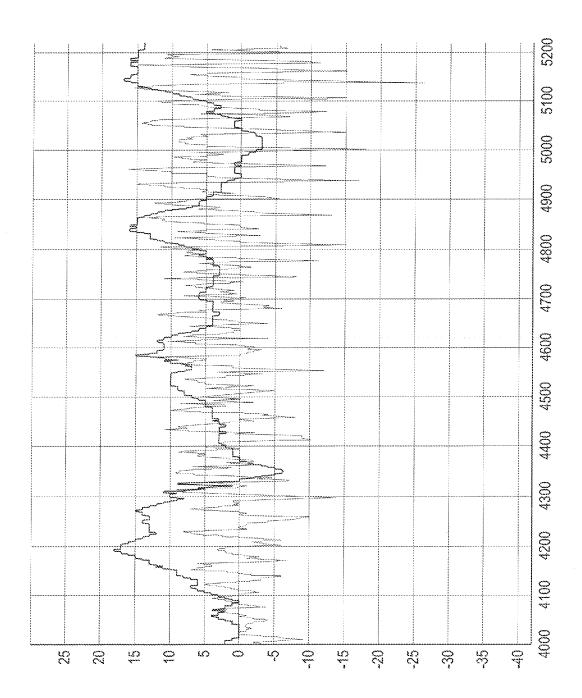
WO 2012/025765 PCT/GB2011/051616

18/25



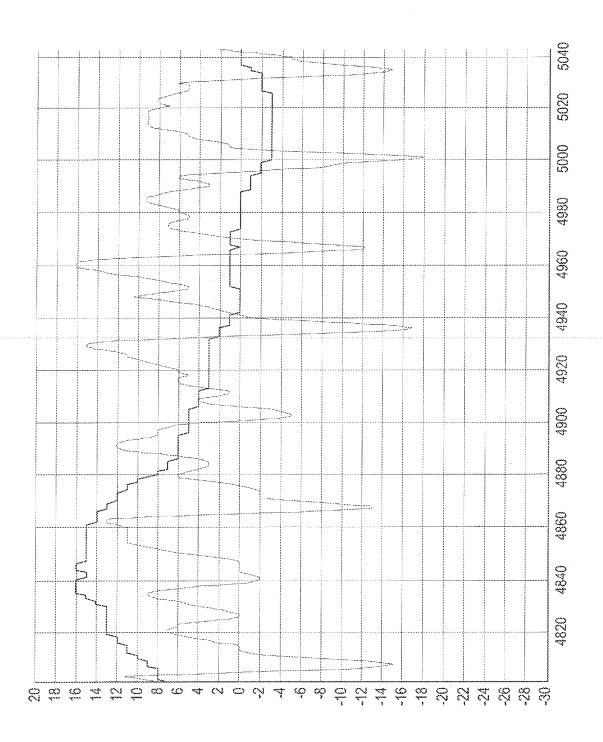
₩ ₩

19/25



WO 2012/025765 PCT/GB2011/051616

20/25



	~~~~	~~~~		~				~~~~~		
<b>4</b>	Select Command									
	Open	Abnormal Inconclusive								
	Abnormal	i								
	05/1/1995	11/1/1972	05/1/1996	08/1/1984	05/1/1994	09/1/1979	12/1/1968	09/1/1978	12/1/1966	13/1/1963
	Female	Male	Male	Female	Female	Female	Female	Female	Male	Male
	Unknown									
	Human									
	Clinical									
	0001	0002	0003	0004	0005	9000	0007	8000	6000	0010

FIG. 14

Cass CO	7000		Data Source:		Cimca	-	************	and desired and address
Species;	Human	integrisamentigeneen septemberial seat a bisha bara da bara bara bara bara bara bara	Gender	A THE STREET OF THE STREET OF THE STREET, STRE	Female	وماواو والوهود والجواولية	***************************************	
DOB:	12/01/196	12/01/1988	Condition:	errorrer e en e	Abnoma		معدند مدنده مدادات مودود	*************
***************************************		***************************************						***************************************
mun Parameters		EL A BER A BURBARITATION CONTROLOGICO CONTRO						
Run ID:	0013		Filename:		sample data txt	ata txt	and the second s	-
File Type:	ASC	18	Data Type:		Deep Brain	ć.		
Pattern Weight:	255		Wolght Range	m	Fixed			
Pattern A Length (ER	i (ER)   10		Pattern B Length	198	0			marketakakakaka masa maya p
Pattern O Length (ER	ı (ER)  0	***************************************	Pattern D Length	(38)	0			***************************************
Raw Data	and a superior and a	***************************************	***************************************	Serveres establishes establishes establishes establishes establishes establishes establishes establishes estab	Processed Data	ed Data	***************************************	
-3.51000006+002	2.3800000e+002	-1 0500000e+002	-3.20000008+001	1-1.2000000e+001	31 3333	301 3333	00001 0000	a now
	7. 1000000e+001	1,6100000e+002	[3.2200000e+002	5.14000006+002	.,		1	7
	7,18000000e+002	7.1000000e+002	(6.6400000e+002	5,97000000+002	-	0000	3	7
	4.7000000e+002	4,47000000+002	4.4700000e+002	4.4700000e+002	7		*****	7
	6.1500000e+002	6.88000000e+002	7.42000003=+002	7.22000000+002	-	30 2300	0003 10000	<del>~~~</del>
	6,07000006+002	8.3300000e+002	6.83000000+002	7,69000006+002	}	00.002	02 0003	3 8008
	6.5600000e+002	9.21000006+002	1.0830000e+003	1,30300000+003	1	<u> </u>	0004 10004	4 0005
	1,80000000+003	[1.9300000e+003	1.97300000+003	1,9540000e+003	9000	9007 PE		5
1.9360000e+003	1.8650000e+003	1.85 (00B0e+003	1.7920000e+003	1.578(1000e+003	8000	2000	0007 0007	7 0006
	-2.1130000e+003	-1,70900000+903	-1.4010000e+003	-1.2160300e+003	99	### ##################################	17 20 17 17	9 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
	£00++00000006916/	-9 0800000e+002	-8.2800000e+002	-7.68000000e+002	FFFC F	FFFC FF	FFFC FFFD FFFD	ddd G
	-4.13000000+002	-2.9600000e+002	-1.8500000k+002	-1 25000000e+002	3444	FFFE F	FFFF FF	FFFF   0000
·	-6.7000000c+001	-5.8000000e+001	-2.8000000e+001	3,1000000be+001	1	1	į	0000
	1.8700000e+002	2,3300000e+002	[2,33000000+002	2.3300000e+002				5
	2.2708600e+662	1.2860000e+002	-1.6000000e+001	~1.6800000e+002	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		1	0000
	-1.8700000e+002	-1.8709000e+002	-1.7500000e+002	-1.2100000e+002	त्री जनन्त्र	14 5444	3434 3433	90000
3.0000000e+000	1.4500000e+002	3.3800000e+002	15, 13000000e+002	6.8600000b+002	0000		0001 0002	2 0003

		(3057	Data Source	arce:		Clinical	ب معدد المعادلة المعا
Species:		Histian	30000		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	Female	المتكثيث ومالية والمتارية والمتاركة
DOB:		12/01/1988	Condition	(2)		Abnormal	
Run List	***************************************		***************************************	***************************************	***************************************	***************************************	***************************************
Andrews of the second of the s	C)vo.g	A STATE OF S	,	200 ento	Size	\$238	20
1004	0013	Sample data txt		46, 732	4, 158	36, 576	89 80%
2002	0014	sample data bit		40, 732	39, 090	1,642	4.03%
Run Parameters		***************************************		***************************************	***************************************	***************************************	
Run ID:	***************************************	00013	Filename	8	***************************************	sample data tx	X.
File Type:		ASC# 16	Data Type:	28;	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	Deep Brain	
Pattern Weight	ight	288	\$ 450 e 33	Weight Range	بيونست دودود زده دود د دود دود دود	Fixed	
`attern Å L	ength (EA)	Ş.	Pattern E	B Length	~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~		***************************************
Pattern C Leng	ength (ER)	0	Pattern (	Pattern D Length		0	er en
sequence	•	Pattern					Count
0000	***************************************	0005 0005 0005	0005 0005 0005 0005 0005 0005 0005 0004 0004 0004	0004 0004	2002	***************************************	-
6003	4,000,000,000,000,000,000,000,000,000,0	0005 0005 0005	0005 0005 0005 0005 0005 0005 0004 0004	0004 0004	0000	***************************************	9
2002	· 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6	9000 9000 9000	0006 0005 0006 0005 0005 0005 0005 0005	0000 0000	0005	***************************************	3
0003		0005 0005 0005	0005 0005 0005 0005 0008 0006 0008 0006 0006	9000 9000	9000	***************************************	2
X002	444444444444444444444444444444444444444	9000 9000 9000	0005 0005 0006 0006 0008 0005 000 0008 0008	9000 9000	9000	***************************************	c
0000	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0002 0002 0002	0002 0002 0002 0002 0002 0002 0002 0003 0003 0003	5000 5000	0003		5
0008	***************************************	0003 0003 0003	0003 0003 0003 0003 0003 0003 0003 000	0003 0003	0003	وا و دار این ما در دارد و این ما در دارد و دارد	
90036		0006 0006 0008	OXOG TIYES OTOS GOIDS OFOS FOOT GRO7 GRO7 OTT7 GOOT	0007 0007	2000	*******************************	
20037		1000 C1000 C1000	8000 2000 2000 0000 0000 0000 0000 0000	00000	2C 000B		3
0038		5000 5000 5000	0603 0003 0003 0003 0002 0002 0002 0002	0002 0002	2000	***************************************	3
9639		7000 70007 0007	00.07 0.007 0.007 0.007 0.007 0.007 0.007 0.005 0.005	0007 0006	900	***************************************	C.3
0040		0000 0000 1000	0001 0000 0000 0000 0000 0000 0000 0000 0000	0000 0000	0000		5. 5. 5. 5. 5. 5. 5. 5. 5. 5. 5. 5. 5. 5

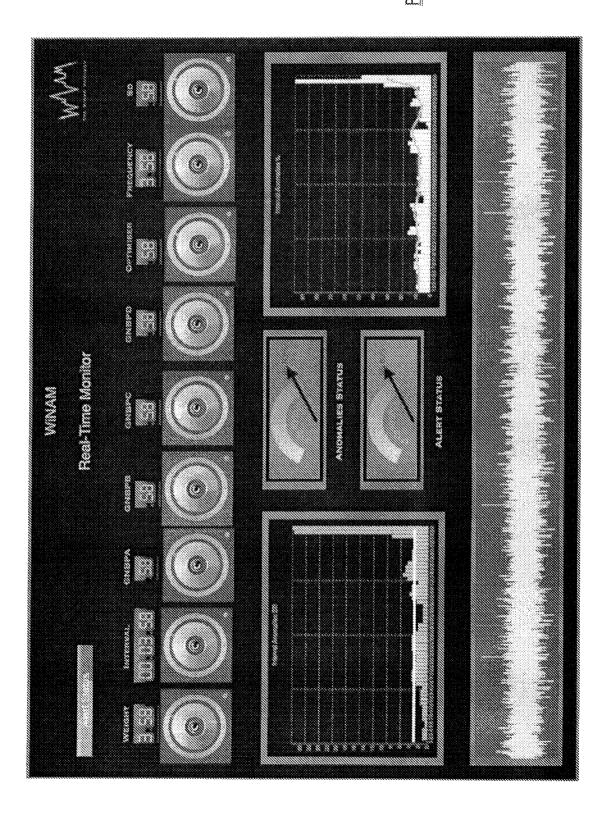
Rue (D.	200. 200.	Flerance	sample data.txt	***************************************
File Type:	ASC:: '6	Dan Type:	Deep Brain	
Pattern Weight	258	Weight Range	Fixed	***********
Pattern A Length (ER)	20	Paken Blengh	9	
Pattern C.Length (ER)	()	Pattern D Length		
Sequence	Pattern	***************************************	COUNT	***************************************
CCCC	3000 6000 6000 6000	8000 6000 6000 6000 6000 6000 6000 6000	£9}	and the same of th
3001	0008 0008 0008 0006	0008 0003 0008 0008 0008 0008 0008 0008	48	***************************************
3002	0005 0005 0005 0006	0.005 0.005 0.005 0.005 0.005 0.005 0.005 0.005 0.005	47	***************************************
2003	0007 0007 0007 0007	0007 0007 0007 0007 0007 0007 0007 0007 0007 0007	4.7	***************************************
2004	0005 0005 0005 0005	0005 0005 0005 0005 0005 0006 0006 0005 0006 0006	42	*****
900	0008 0008 0008 0006	0008 0008 0008 0009 0009 0009 0009 0009	4.3	************
9000	000 0000 0000 0000	2000 000C 000C 000C 000C 000C 000C 000C		
				***************************************
270	000 2000 2000 2000	MM7 MM7 OWN OWN OWN OWN BOOK OWNS OWNS OWNS	C. S. Jonanna na n	
0.528	200 3000 3000 3000	7 7000 0000 0000 0000 0000	A CALL	-
040	מאאר מסטר טמאר מסנ	HAY, BOOK WAY, WALL BACK BOOK BOOK BOOK	7	
0049	1000C 000C 000C 000	HAYC BONC OLOC GROC BOOC GROC BONS OLOS GROS GROS	33	
0060	0008 0008 0008 0008	0008 0009 0008 0008 0007 0007 0007 0007	50	The second secon
(1054	0007 0007 0007 0007	0007 0007 0007 0007 0007 0007 0008 0008	are a service and a service an	
2542	***************************************			The second secon

(C)

WO 2012/025765 PCT/GB2011/051616

## 25/25

:1G. 18



#### INTERNATIONAL SEARCH REPORT

International application No PCT/GB2011/051616

A. CLASSIFICATION OF SUBJECT MATTER INV. A61B5/0476 G06F19/00

ADD. A61N1/00

According to International Patent Classification (IPC) or to both national classification and IPC

#### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61B G06F A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUM	ENTS CONSIDERED TO BE RELEVANT	
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Х,Р	WALID JUFFALI ET AL: "The WiNAM project: Neural data analysis with applications to epilespy", BIOMEDICAL CIRCUITS AND SYSTEMS CONFERENCE (BIOCAS), 2010 IEEE, IEEE, 3 November 2010 (2010-11-03), pages 45-48, XP031899695, DOI: 10.1109/BIOCAS.2010.5709567 ISBN: 978-1-4244-7269-7 the whole document	1-14
А	US 6 658 287 B1 (LITT BRIAN [US] ET AL) 2 December 2003 (2003-12-02) abstract; claims 1,21; figures 1-4 column 1, line 50 - column 2, line 11 column 5, lines 29-60 column 5, line 62 - column 7, line 10	1-14

X Further documents are listed in the continuation of Box C.	X See patent family annex.			
"A" document defining the general state of the art which is not considered to be of particular relevance  "E" earlier document but published on or after the international filing date  "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  "O" document referring to an oral disclosure, use, exhibition or other means  "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone  "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.  "&" document member of the same patent family			
Date of the actual completion of the international search	Date of mailing of the international search report			
19 January 2012	25/01/2012			
Name and mailing address of the ISA/  European Patent Office, P.B. 5818 Patentlaan 2  NL - 2280 HV Rijswijk  Tel. (+31-70) 340-2040,  Fax: (+31-70) 340-3016	Authorized officer  Medeiros Gaspar, Ana			

3

International application No. PCT/GB2011/051616

### **INTERNATIONAL SEARCH REPORT**

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. X Claims Nos.: 15 because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  See FURTHER INFORMATION sheet PCT/ISA/210
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest  The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.  The additional search fees were accompanied by the applicant's protest but the applicable protest
fee was not paid within the time limit specified in the invitation.
No protest accompanied the payment of additional search fees.

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 15

The method claim 15 contains the step of "stimulating a part of a brain using a neural stimuli generator", said method step being described in the description of the application as being carried out, subsequent to the monitoring and predicting steps, "in an attempt to ameliorate, offset, delay or avoid entirely a neurological episode such as an epileptic seizure" (page 14 lines 10-15). The presence of such a step renders the methods of claim 15 methods of therapy practised on the human body, with the aim of maintaining or restoring the health. It is furthermore pointed out that the above mentioned additional step of the dependent claim 15 also appears to encompass methods involving different kinds of physical interventions practised on the human body considered to be of surgical nature, by means of which the claimed methods are also seen as methods for treatment of the human body by surgery, thereby also for that reason falling within the provisions of Rule 39.1(iv)/67.1(iv)PCT. Consequently, no search has been carried out and no opinion will be formulated by this Authority with respect to novelty, inventive step or the industrial applicability on the subject-matter of claim 15 (Article 34(4)(a)(i) PCT).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.2), should the problems which led to the Article 17(2) declaration be overcome.

### INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2011/051616

C(Continua	ation). DOCUMENTS CONSIDERED TO BE RELEVANT	
ategory*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2006/111644 A1 (GUTTAG JOHN V [US] ET AL) 25 May 2006 (2006-05-25) abstract; claims 58,63,64,99; figures 22,23 paragraphs [0006] - [0010]	1-14
Α	US 5 995 868 A (OSORIO IVAN [US] ET AL) 30 November 1999 (1999-11-30) abstract; figures 1,5 column 4, line 41 - column 6, line 63 column 10, line 57 - column 12, line 64	1-14
A,P	WO 2010/115939 A2 (NAT UNIVERSITY OF IRELAND CORK [IE]; FAUL STEPHEN DANIEL [IE]; TEMKO A) 14 October 2010 (2010-10-14) abstract; figure 4 page 10, line 5 - page 11, line 16	1-14

3

### INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/GB2011/051616

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6658287 B	1 02-12-2003	NONE	
US 2006111644 A	1 25-05-2006	US 2006111644 A1 US 2011257517 A1 WO 2005117693 A1	25-05-2006 20-10-2011 15-12-2005
US 5995868 A	30-11-1999	AU 1752897 A DE 69736592 T2 EP 0898460 A1 JP 3769023 B2 JP 2002502270 A US 5995868 A US 6549804 B1 WO 9726823 A1	20-08-1997 14-12-2006 03-03-1999 19-04-2006 22-01-2002 30-11-1999 15-04-2003 31-07-1997
WO 2010115939 A	2 14-10-2010	EP 2416703 A2 WO 2010115939 A2	15-02-2012 14-10-2010