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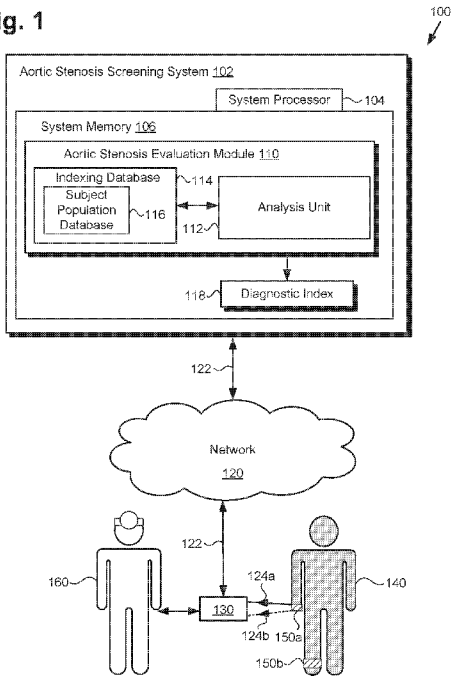
(54) Title: AORTIC STENOSIS SCREENING

Fig. 1



(57) Abstract: There are provided systems and methods for performing aortic stenosis screening. An aortic stenosis screening system includes a hardware processor, a system memory, and an aortic stenosis evaluation module stored in the system memory. The hardware processor is configured to execute the aortic stenosis evaluation module to receive a first signal corresponding to an arterial pressure of a living subject, and to apply a transfer function to transform the first signal to a second signal corresponding to a central arterial pressure of the living subject. The hardware processor is further configured to execute the aortic stenosis evaluation module to derive parameters from the second signal, and to determine a degree of aortic stenosis of the living subject based on those parameters.

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AORTIC STENOSIS SCREENING

BACKGROUND

Aortic stenosis (AS) can be a progressive, debilitating, and life threatening condition if left untreated. Subjects with AS are typically free from cardiovascular symptoms, such as angina, syncope, or heart failure, for example, until late in the course of disease progression. However, once symptoms manifest, the prognosis for the subject is often poor. As a result, early detection and diagnosis of AS prior to the manifestation of symptoms is important.

AS has traditionally been screened for through cardiac auscultation, typically using a stethoscope to listen to a subject's heart. Although the detection of heart sounds can enable early identification of a subject suffering from AS, there are disadvantages to relying on this approach for AS screening. One disadvantage flows from changes in the way clinicians are trained. As high technology diagnostic techniques are increasingly taught, the importance of traditional and relatively low technology diagnostic techniques may receive less emphasis, resulting in fewer diagnosticians being skilled in the use of cardiac auscultation. Another disadvantage results from the general aging of the subject population. Especially in older subjects, heart sounds indicative of AS may be present, but may not reliably indicate significant aortic valvular obstruction requiring medical intervention.

SUMMARY

There are provided systems and methods for performing aortic stenosis screening, substantially as shown in and/or described in connection with at least one of the figures, and as set forth more completely in the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a diagram of an exemplary aortic stenosis (AS) screening system, according to one implementation;

Figure 2 shows another exemplary implementation of an AS screening system;

Figure 3 shows an exemplary system and a computer-readable non-transitory medium including instructions enabling performance of AS screening;

Figure 4 is a flowchart presenting an exemplary method for use by a system to perform AS screening;

Figure 5A shows a diagram of an exemplary implementation for detecting arterial pressure non-invasively at an extremity of a living subject;

Figure 5B shows a diagram depicting transformation of an arterial pressure detected at an extremity of a living subject to a central arterial pressure of the subject, according to one implementation;

Figure 6A shows a trace of an exemplary central arterial pressure waveform; and

Figure 6B shows an exemplary region of diagnostic interest on the central arterial waveform trace of Figure 6A.

DETAILED DESCRIPTION

The following description contains specific information pertaining to implementations in the present disclosure. One skilled in the art will recognize that the present disclosure may be implemented in a manner different from that specifically discussed herein. The drawings in the present application and their accompanying detailed description are directed to merely exemplary implementations. Unless noted otherwise, like or corresponding elements among the figures may be indicated by like or

corresponding reference numerals. Moreover, the drawings and illustrations in the present application are generally not to scale, and are not intended to correspond to actual relative dimensions.

The present application discloses systems and methods for performing aortic stenosis (AS) screening. By enabling performance of AS screening based on an arterial pressure measurement obtained non-invasively from a living subject, the AS screening methods and systems disclosed in the present application advantageously avoid arterial cannulation of the subject during the screening process, thereby enhancing subject comfort and safety. In addition, by enabling substantially continuous beat-to-beat monitoring of arterial pressure at an extremity of the living subject, such as at the subject's finger, the present application discloses a compact, portable AS screening solution suitable for deployment to cardiology offices or primary care sites. Moreover, by substantially automating the AS screening process, the solution disclosed by the present application advantageously enables early detection of AS by clinicians having little or no expertise in cardiac auscultation.

The present solution for performing AS screening includes receiving a first signal corresponding to an arterial pressure of a living subject. Such a signal may be obtained as a result of a non-invasive arterial pressure measurement taken at an extremity of the subject, for example, at a finger or wrist of the subject. The present solution also includes applying a transfer function to transform the first signal to a second signal corresponding to a central arterial pressure of the living subject. The present solution further includes deriving parameters that may be indicative of AS from the second

signal, and determining the degree of AS present in the subject based on those parameters.

Figure 1 shows a diagram of an exemplary AS screening system, according to one implementation. As shown in Figure 1, AS screening system 102 is situated within AS diagnostic environment 100 including communication network 120, client system 130, living subject 140 (hereinafter "subject 140"), and healthcare worker 160 trained to utilize client system 130 (hereinafter "user 160"). AS screening system 102 includes system processor 104, implemented as a hardware processor, and system memory 106 storing AS evaluation module 110 including analysis unit 112 and indexing database 114 having AS subject population database 116 stored therein.

In addition, Figure 1 illustrates arterial pressure sensors shown in the alternative as non-invasive finger or wrist arterial pressure sensor 150a and non-invasive toe or ankle arterial pressure sensor 150b. Figure 1 further shows signals received by client system 130 and corresponding to an arterial pressure of subject 140 in the alternative as wired signal 124a and wireless signal 124b. It is noted that although Figure 1 depicts signal 124a/124b being received from non-invasive finger or wrist arterial pressure sensor 150a, in other implementations, signal 124a/124b may be received from non-invasive toe or ankle arterial pressure sensor 150. Also shown in Figure 1 are network communication links 122 interactively connecting client system 130 and AS screening system 102 via communication network 120, and diagnostic index 118 generated by AS evaluation module 110.

According to the implementation shown in Figure 1, user 160 may utilize client system 130 to interact with AS screening system 102 over communication network 120,

for example to transmit signal 124a/124b to AS evaluation module 110 or to download AS evaluation module 110 to client system 130. In one such implementation, AS screening system 102 may correspond to one or more web servers, accessible over a packet network such as the Internet, for example. Alternatively, AS screening system 102 may correspond to one or more servers supporting a local area network (LAN), or included in another type of limited distribution network.

System processor 104 is configured to execute AS evaluation module 110 to receive signal 124a/124b corresponding to an arterial pressure of subject 140 via client system 130 and communication network 120. System processor 104 is further configured to execute AS evaluation module 110 to use analysis unit 112 to apply a transfer function for transforming signal 124a/124b to a signal corresponding to a central arterial pressure of subject 140. For example, where signal 124a/124b is provided by non-invasive finger or wrist arterial pressure sensor 150a, analysis unit 112 may be used by AS evaluation module 110 to apply a transfer function for transforming signal 124a/124b to an aortic pressure or a brachial pressure of subject 140.

System processor 104 is also configured to execute AS evaluation module 110 to derive parameters that may be indicative of the presence of AS in subject 140 from the signal corresponding to the central arterial pressure of subject 140. Examples of those parameters include the rate of change of the central arterial pressure with respect to time, the second derivative of the central arterial pressure with respect to time, and/or the time duration of the systolic rise or systolic decay of the central arterial pressure, to name a few. In addition, system processor 104 is configured to execute AS evaluation module

110 to use indexing database 114 to determine the degree of AS of subject 140 based on the derived parameters.

In some implementations, for example, system processor 104 is configured to execute AS evaluation module 110 to utilize indexing database to identify, from AS subject population database 116, known parameters corresponding to the parameters derived by analysis unit 112. For instance, known parameters may be identified as corresponding to the derived parameters when one or more of the known parameters are identified as being within a predetermined range of respective one or more of the derived parameters. System processor 104 may be further configured to execute AS evaluation module 110 to generate diagnostic index 118 based on a comparison between the derived parameters and corresponding known parameters.

It is noted that although Figure 1 depicts diagnostic index 118 as residing in system memory 106, in some implementations, diagnostic index 118, when generated, may be copied to non-volatile storage (not shown in Figure 1), or may be transmitted to client system 130 via communication network 120, for display to user 160. It is further noted that client system 130 may be implemented as a computer workstation or personal computer (PC), a dedicated handheld or otherwise portable diagnostic system, or any type of mobile computing device, such as a smartphone or tablet computer, among others.

Referring to Figure 2, Figure 2 shows a more detailed exemplary implementation of client system 230, which may be configured to perform AS screening. AS diagnostic environment 200 in Figure 2 includes client system 230 interactively connected to AS screening system 202 over network communication link 222. As shown in Figure 2, AS

screening system 202 includes system processor 204, and system memory 206 storing AS evaluation module 210a including analysis unit 212a and indexing database 214a having AS subject population database 216a stored therein. As further shown in Figure 2, client system 230 includes client processor 234, and client memory 236 storing AS evaluation module 210b including analysis unit 212b and indexing database 214b having AS subject population database 216b stored therein. Also shown in Figure 2 is diagnostic index 218 generated by AS evaluation module 210b on client system 230.

Network communication link 222, and AS screening system 202 including system processor 204 and system memory 206 correspond in general to network communication link 122, and AS screening system 102 including system processor 104 and system memory 106, in Figure 1. In addition, AS evaluation module 210a including analysis unit 212a, indexing database 214a, and AS subject population database 216a, in Figure 2, corresponds to AS evaluation module 110 including analysis unit 112, indexing database 114, and AS subject population database 116, in Figure 1. In other words, AS evaluation module 210a, analysis unit 212a, indexing database 214a, and AS subject population database 216a may share any of the characteristics attributed to corresponding AS evaluation module 110, analysis unit 112, indexing database 114, and AS subject population database 116 shown in Figure 1 and described above.

Client system 230 corresponds in general to client system 130, in Figure 1. Moreover, AS evaluation module 210b including analysis unit 212b, indexing database 214b, and AS subject population database 216b corresponds to AS evaluation module 110/210b including analysis unit 112/212b, indexing database 114/214b, and AS subject population database 116/216a. As a result, AS evaluation module 210b, analysis unit

212b, indexing database 214b, and AS subject population database 216b may share any of the characteristics attributed to corresponding AS evaluation module 110, analysis unit 112, indexing database 114, and AS subject population database 116 shown in Figure 1 and described above.

According to the exemplary implementation shown in Figure 2, AS evaluation module 210b including analysis unit 212b and indexing database 214b having AS subject population database 216b stored therein is located in client memory 236, having been received from AS screening system 202 via network communication link 222. In one implementation, network communication link 222 corresponds to transfer of AS evaluation module 210b including analysis unit 212b, indexing database 214b, and AS subject population database 216b over a packet network, for example. Once transferred, for instance by being downloaded over network communication link 222, AS evaluation module 210b including analysis unit 212b, indexing database 214b, and AS subject population database 216b may be persistently stored in client memory 236 and may be executed locally on client system 230 by client processor 234.

Client processor 234 may be the hardware central processing unit (CPU) for client system 230, for example, in which role client processor 234 runs the operating system and/or firmware for client system 230 and executes AS evaluation module 210b. In the exemplary implementation of Figure 2, a user, such as user 160, in Figure 1, can utilize AS evaluation module 210b on client system 230 to generate diagnostic index 218, which corresponds in general to diagnostic index 118.

Moving now to Figure 3, Figure 3 shows an exemplary system and a computer-readable non-transitory medium including instructions enabling performance of AS

screening, according to one implementation. System 330, in Figure 3, includes computing unit 338 including processor 334 and memory 336, interactively linked to display 332. Display 332 may take the form of a liquid crystal display (LCD), a light-emitting diode (LED) display, an organic light-emitting diode (OLED) display, or another suitable display screen that performs a physical transformation of signals to light. System 330 including processor 334 and memory 336 corresponds in general to any or all of AS screening system 102 and client system 130, in Figure 1, and AS screening system 202 and client system 230, in Figure 2.

Also shown in Figure 3 is computer-readable non-transitory medium 319 having AS evaluation module 310 stored thereon. The expression "computer-readable non-transitory medium," as used in the present application, refers to any medium, excluding a carrier wave or other transitory signal, that provides instructions to processor 334 of computing unit 338. Thus, a computer-readable non-transitory medium may correspond to various types of media, such as volatile media and non-volatile media, for example. Volatile media may include dynamic memory, such as dynamic random access memory (dynamic RAM), while non-volatile memory may include optical, magnetic, or electrostatic storage devices. Common forms of computer-readable non-transitory media include, for example, optical discs, RAM, programmable read-only memory (PROM), erasable PROM (EPROM), and FLASH memory.

According to the implementation shown in Figure 3, computer-readable non-transitory medium 319 provides AS evaluation module 310 for execution by processor 334 of computing unit 338. AS evaluation module 310, when executed by processor 334, instantiates an AS evaluation module corresponding to AS evaluation module

110/210a/210b, in Figure 1/2, and capable of performing all of the operations attributed to those corresponding features by the present disclosure.

Example implementations of the present disclosure will be further described below with reference to Figure 4 and Figures 5A, 5B, 6A, and 6C. Referring first to Figure 4, Figure 4 presents flowchart 400 outlining an exemplary method for use by a system to perform AS screening. The method outlined in flowchart 400 can be performed using AS evaluation module 110/210a/210b/310 described above.

Flowchart 400 begins with receiving, by AS evaluation module 110/210a/210b/310 executed by respective processor 104/204/234/334, signal 124a/124b corresponding to an arterial pressure of subject 140 (action 472). As noted above, signal 124a/124b may correspond to an arterial pressure of subject 140 measured non-invasively at an extremity of subject 140. It is noted that although subject 140 is depicted as a living human subject, such as a patient receiving diagnostic care from healthcare worker 160, for example, in other implementations, subject 140 may be a living non-human animal subject.

Referring to Figure 5A, Figure 5A shows a diagram of an exemplary implementation for detecting arterial pressure non-invasively at an extremity of a living subject, once again depicted as a human subject. Diagram 572, in Figure 5A, shows system 502/530 including AS evaluation module 510 receiving signal 524 corresponding to an arterial pressure of subject 540. As further shown by Figure 5A, the arterial pressure of subject 540 is detected non-invasively at finger 542 of subject 540 using finger arterial pressure sensing cuff 550. Subject 540, signal 524, and finger arterial pressure sensing cuff 550 correspond respectively to subject 140, signal 124a/124b, and

either of finger or wrist arterial pressure sensor 150a or toe or ankle arterial pressure sensor 150b, in Figure 1, and may share any of the characteristics attributed to those corresponding features, above. Moreover, system 502/530 including AS evaluation module 510, in Figure 5A, may correspond to AS screening system 102/202 including AS evaluation module 110/210a, in respective Figures 1 and 2, and/or to client system 130/230/330 including an AS evaluation module corresponding to AS evaluation module 210b/310, in Figures 1, 2, and 3, and may share any of the characteristics attributed to those corresponding features, above.

According to the implementation shown in Figure 5A, finger arterial pressure sensing cuff 550 is designed to detect an arterial pressure of subject 540 non-invasively. Moreover, as shown in Figure 5A, finger arterial pressure sensing cuff 550 may take the form of a small, lightweight, and comfortable arterial pressure sensor suitable for extended wear by subject 540. It is noted that such extended wear capability may also be attributed to finger or wrist arterial pressure sensor 150a and toe or ankle arterial pressure sensor 150b, in Figure 1. As a result, finger arterial pressure sensing cuff 550 and arterial pressure sensors 150a/150b may be configured to provide substantially continuous beat-to-beat monitoring of the arterial pressure of subject 140/540 over an extended period of time, such as minutes or hours, for example.

Flowchart 400 continues with applying a transfer function to transform signal 124a/124b/524 to a signal corresponding to a central arterial pressure of subject 140/540 (action 474). Referring to Figure 5B, Figure 5B shows diagram 574 depicting transformation of signal 524 corresponding to an arterial pressure of subject 540 detected using finger arterial pressure sensing cuff 550, to signal 544 corresponding to a central

arterial pressure of subject 540, according to one implementation. For example, as shown in Figure 5B, signal 524 provided by finger arterial pressure sensing cuff 550 is transformed to signal 544 corresponding to an aortic pressure or a brachial pressure of subject 540. As further shown by Figure 5B, such a transformation is performed by analysis unit 512 of system 502/530 through application of a transfer function to signal 524. That is to say, application of such a transfer function may be performed by AS evaluation module 110/210a/210b/310/510 executed by a processor corresponding to processor 104/204/234/334, and using an analysis unit corresponding to analysis unit 112/212a/212b/512.

The body of subject 540 acts to filter a central arterial pressure signal corresponding to signal 544, so as to cause a modified signal (i.e., an attenuated or otherwise filtered signal) corresponding to signal 524 to be detectable at an extremity of subject 540. As a result, a transfer function for substantially reproducing the central arterial pressure from the arterial pressure measured at the extremity of subject 540 can be identified. Such a transfer function will typically vary depending upon the location on the body of subject 540 at which the arterial pressure corresponding to signal 524 is detected, e.g., at finger 542, as well as upon the specific central arterial pressure being reproduced, e.g., aortic or brachial. Moreover, and as also shown in Figure 5B, in one implementation, signals 524 and 544 may be provided as waveforms corresponding respectively to a finger arterial pressure and a central arterial pressure of subject 540.

Flowchart 400 continues with deriving parameters from signal 544 (action 476). As noted above, the parameters derived from signal 544 may be indicative of the presence of AS in subject 540. As further noted above, examples of those parameters

include the rate of change of the central arterial pressure with respect to time, the second derivative of the central arterial pressure with respect to time, and/or the time duration of the systolic rise or systolic decay of the central arterial pressure, to name a few. An exemplary but non-exhaustive table of suitable parameters, as well as exemplary sampling times associated with their derivation, is provided in Appendix A of the present application.

Derivation of such parameters from signal 544 can be performed by AS evaluation module 110/210a/210b/310/510 executed by a processor corresponding to processor 104/204/234/334. Referring to Figure 6A, Figure 6A shows trace 676 of exemplary central arterial pressure waveform 644. As shown in Figure 6A, central arterial pressure waveform 644 is expressed as a function of time, and includes heartbeat parameters 682, 684, 686, and 688. Heartbeat parameters 682, 684, 686, and 688 correspond respectively to the start of a heartbeat, the maximum systolic pressure marking the end of systolic rise, the presence of the dicrotic notch marking the end of systolic decay, and the beginning of the next heartbeat of subject 140/540. It is noted that central arterial pressure waveform 644 corresponds to signal 544 in Figure 5B, while heartbeat parameters 682, 684, 686, and 688 may be included among the parameters derived by AS evaluation module 110/210a/210b/310/510 from signal 544 during action 476 of flowchart 400.

Flowchart 400 can conclude with determining a degree of AS of subject 140/540 based on the parameters derived from signal 544 and corresponding to central arterial pressure waveform 644, e.g., based on some or all of heartbeat parameters 682, 684, 686, and 688 (action 478). Referring to Figure 6B, it is noted that in some implementations, it

may be advantageous or desirable to place greater emphasis on parameters derived from region 680 of central arterial pressure waveform 644 when determining the degree of AS of subject 140/540. In other words, in some implementations, it may be advantageous or desirable to focus primarily on parameters derived from the interval shortly after the beginning of the heartbeat and extending to heartbeat parameter 684 corresponding to the maximum systolic pressure and marking the end of systolic rise.

In some implementations, AS evaluation module 110/210a/210b/310/510 may be configured to determine the degree of AS of subject 140/540 using an indexing database corresponding to indexing database 114/214a/214b. For example, indexing database 114/214a/214b may include reference ranges for the parameters derived from signal 544, and determination of the degree of AS of subject 140/540 may include comparison between the derived parameters and those reference ranges.

In other implementations, AS evaluation module 110/210a/210b/310/510 may be configured to determine the degree of AS of subject 140/540 using subject population database 116/216a/216b. Determination of the degree of AS of subject 140/540 may then include identifying, from subject population database 116/216a/216b, parameters corresponding to the parameters derived from signal 544. Such a determination may also include generating diagnostic index 118/218b based on comparison between the parameters identified in subject population database 116/216a/216b and those derived from signal 544. In some implementations, for example, subject population database 116/216a/216b may take the form of a multi-dimensional subject population space having coordinate axes defined by parameters corresponding respectively to the parameters derived from signal 544. AS evaluation module 110/210a/310b/310/510 may

be configured to project the parameters derived from signal 544 onto the subject population space, and apply a nearest neighbor algorithm to identify a nearest neighbor subject of the subject population database as indicative of the degree of AS of subject 140/540.

Thus, by enabling performance of AS screening based on an arterial pressure measurement obtained non-invasively from a living subject, the AS screening methods and systems disclosed in the present application advantageously avoid arterial cannulation of the subject during the screening process, thereby enhancing subject comfort and safety. In addition, by enabling substantially continuous beat-to-beat monitoring of arterial pressure at an extremity of the living subject, such as at the subject's finger, the present application discloses a compact, portable AS screening solution suitable for deployment to cardiology offices or primary care sites. Moreover, by substantially automating the AS screening process, the solution disclosed by the present application advantageously enables early detection of AS by clinicians having little or no expertise in cardiac auscultation.

From the above description it is manifest that various techniques can be used for implementing the concepts described in the present application without departing from the scope of those concepts. Moreover, while the concepts have been described with specific reference to certain implementations, a person of ordinary skill in the art would recognize that changes can be made in form and detail without departing from the scope of those concepts. As such, the described implementations are to be considered in all respects as illustrative and not restrictive. It should also be understood that the present application is not limited to the particular implementations described herein, but many

rearrangements, modifications, and substitutions are possible without departing from the scope of the present disclosure.

APPENDIX A

Parameter Description	Sampling Time
1. Flag showing that the current 20 sec segment signal is bad	20 sec
2. Flag showing that the current 20 sec and the past 40 sec segment signals are bad	20 sec
3. Flag: the signal has been bad in most of the 20 sec iterations in the last 5 min	20 sec
4. Flag: signal drift detected in CO: no drift 0, drift 1	20 sec
5. Flag: the standard deviation of the blood pressure signal is too high	20 sec
6. Flag: the standard deviation of the blood pressure signal is too low	20 sec
7. Flag: the artifacts detected in the respiratory envelope of the signal	20 sec
8. The Windkessel Compliance (Based on the Langewooters paper)	20 sec average
9. Cardiac Output	20 sec average
10. Cardiac Output (CO) - 5 min average	5 min average
11. Heart Rate (HR): 5 min average	5 min average
12. Mean Arterial Pressure (MAP): 5 min average	5 min average
13. Stroke Volume Variation (SVV): 5 min average	5 min average
14. CO: estimated with a multivariate model on normal patients	20 sec average
15. HR	20 sec average
16. Arterial tone estimate: 1 min average	1 min average
17. Arterial tone estimate: 20 sec	20 sec average
18. The kurtosis of the pressure waveform within a beat - (fourth statistical moment)	20 sec median

19. The kurtosis of the 20 sec reconstructed waveform	20 sec
20. MAP	20 sec median
21. The mean value of the 20 sec reconstructed waveform	20 sec
22. The standard deviation of the 20 sec reconstructed waveform	20 sec
23. The skewness of the pressure waveform within a beat – (third statistical moment	20 sec median
24. The skewness of the 20 sec reconstructed waveform	20 sec
25. The standard deviation of the pressure waveform within a beat	20 sec median
26. The standard deviation of the pressure waveform within a beat adjusted with the kurtosis	20 sec median
27. SVV computed with the detection of the respiratory cycles in the signal	20 sec median
28. FloTrac SVV	20 sec median
29. Systolic Pressure	20 sec median
30. Diastolic Pressure	20 sec median
31. Flag showing variability in HR	20 sec
32. Flag showing impact of HR variability on SVV	20 sec
33. Count rejected PVCs	20 sec
34. Data Quality Index	20 sec
35. Systolic pressure minus the pressure at the dicrotic notch	20 sec median
36. The pressure at the dicrotic notch minus the diastolic pressure	20 sec median
37. The duration of the systolic phase: the time from the start of the beat to the dicrotic notch	20 sec median
38. The duration of the diastolic phase: the time from the dicrotic notch to the start of the next beat	20 sec median

39. The bias of the diastolic slope	20 sec median
40. Diastolic slope	20 sec median
41. CO computed with a heavy weighted multivariate model derived from patients in hyperdynamic conditions	20 sec average
42. Vascular tone computed with a heavy weighted multivariate model derived from patients in hyperdynamic conditions	1 min average
43. Vascular tone computed with a heavy weighted multivariate model derived from patients in hyperdynamic conditions	20 sec average
44. Flag indicating hyperdynamic conditions	20 sec
45. Multivariate classification model to detect peripheral decoupling during hyperdynamic conditions	1 min average
46. Multivariate classification model to detect low flow conditions	1 min average
47. Vascular tone computed with a balanced multivariate model derived from patients with mild hyperdynamic conditions	1 min average
48. Vascular tone computed with a weighted multivariate model derived from patients with severe hyperdynamic conditions	1 min average
49. Multivariate classification model to detect peripheral decoupling during hyperdynamic conditions	20 sec average
50. CO computed for patients in normal cardiovascular conditions	20 sec average
51. CO computed for patients in hyperdynamic cardiovascular conditions	20 sec average
52. CO computed for patients in mild hyperdynamic cardiovascular conditions	20 sec average
53. CO computed for patients in severe hyperdynamic cardiovascular conditions	20 sec average
54. Flag for model switching when peripheral decoupling is detected	20 sec
55. Flag indicating peripheral decoupling conditions	20 sec
56. Peripheral decoupling indicator showing the amount of peripheral decoupling	20 sec

57. Peripheral decoupling indicator showing the amount of peripheral decoupling, calculated slightly differently than the one above	20 sec
58. Area under the pressure waveform greater than the beat mean	20 sec median
59. Time from the first beat sample exceeding the beat mean to the dicrotic notch	20 sec median
60. The time from the start of the beat to the systolic max	20 sec median
61. The time from the systolic max to the dicrotic notch	20 sec median
62. The time from the systolic max to the start of the next beat	20 sec median
63. The area under the whole beat	20 sec median
64. The area under the whole beat normalized by the number of samples	20 sec median
65. The area under the systolic phase of the beat: from start to the dicrotic notch	20 sec median
66. The area under the systolic phase normalized by the number of samples	20 sec median
67. The area from the start of the beat to the systolic max	20 sec median
68. The area from the start of the beat to the systolic max normalized by the number of samples	20 sec median
69. The area from the systolic max to the dicrotic notch	20 sec median
70. The area from the systolic max to the dicrotic notch normalized by the number of samples	20 sec median
71. The area from the systolic max to the start of the next beat	20 sec median
72. The area from the systolic max to the start of the next beat normalized by the number of samples	20 sec median
73. The area under the diastolic portion of the waveform: from the dicrotic notch to the start of the next beat	20 sec median

74. The area under the diastolic portion of the waveform normalized by the number of samples	20 sec median
75. The area under the whole beat with subtracted diastolic pressure	20 sec median
76. The area under the whole beat with subtracted diastolic pressure and normalized by the number of samples	20 sec median
77. The area under the systolic portion of the waveform with subtracted diastolic pressure	20 sec median
78. The area under the systolic portion of the waveform with subtracted diastolic pressure and normalized by the number of samples	20 sec median
79. The area from the start of the beat to the systolic max with subtracted diastolic pressure	20 sec median
80. The area from the start of the beat to the systolic max with subtracted diastolic pressure and normalized by the number of samples	20 sec median
81. The area from the systolic max to the start of the next beat with subtracted diastolic pressure	20 sec median
82. The area from the systolic max to the start of the next beat with subtracted diastolic pressure and normalized by the number of samples	20 sec median
83. The area under the diastolic portion of the waveform: from the dicrotic notch to the start of the next beat with subtracted diastolic pressure	20 sec median
84. The area under the diastolic portion of the waveform: from the dicrotic notch to the start of the next beat with subtracted diastolic pressure and normalized by the number of samples	20 sec median
85. The standard deviation (representing pulsatility) of the systolic portion of the waveform	20 sec median
86. The standard deviation (representing pulsatility) of the diastolic portion of the waveform	20 sec median
87. The standard deviation (representing pulsatility) of the portion of the waveform extending from the start of the beat to the sys max	20 sec median
88. The standard deviation (representing pulsatility) of the portion of the waveform extending from the sys max to the dicrotic notch	20 sec median

89. The standard deviation (representing pulsatility) of the of the portion of the waveform extending from the sys max to the start of the next beat	20 sec median
90. The mean of the systolic portion of the waveform	20 sec median
91. The mean of the of the diastolic portion of the waveform	20 sec median
92. The mean of the portion of the waveform extending from the start of the beat to the sys max	20 sec median
93. The mean of the portion of the waveform extending from the sys max to the dicrotic notch	20 sec median
94. The mean of the portion of the waveform extending from the sys max to the start of the next beat	20 sec median
95. The mean of the systolic portion of the waveform with subtracted diastolic pressure	20 sec median
96. The mean of the of the diastolic portion of the waveform with subtracted diastolic pressure	20 sec median
97. The mean of the portion of the waveform extending from the start of the beat to the sys max with subtracted diastolic pressure	20 sec median
98. The mean of the portion of the waveform extending from the sys max to the dicrotic notch with subtracted diastolic pressure	20 sec median
99. The mean of the portion of the waveform extending from the sys max to the start of the next beat with subtracted diastolic pressure	20 sec median
100. Standard deviation of the entire waveform, using diastolic pressure instead of the average in the standard deviation equation	20 sec median
101. The standard deviation of the systolic portion of the waveform, using diastolic pressure instead of the average in the standard deviation equation	20 sec median
102. The standard deviation of the diastolic portion of the waveform, using diastolic pressure instead of the average in the standard deviation equation	20 sec median
103. The standard deviation of the portion of the waveform extending from the start of the beat to the sys max, using diastolic pressure instead of the average in the standard deviation equation	20 sec median

104. The standard deviation of the portion of the waveform extending from the sys max to the dicrotic notch, using diastolic pressure instead of the average in the standard deviation equation	20 sec median
105. The standard deviation of the portion of the waveform extending from the sys max to the start of the next beat, using diastolic pressure instead of the average in the standard deviation equation	20 sec median
106. The slope of the systolic rise	20 sec median
107. The max of the first derivative	20 sec median
108. The max of the second derivative	20 sec median

CLAIMS

What is claimed is:

1. An aortic stenosis screening system comprising:

a hardware processor;

a system memory; and

an aortic stenosis evaluation module stored in the system memory;

wherein the hardware processor is configured to execute the aortic stenosis evaluation module to:

receive a first signal corresponding to an arterial pressure of a living subject;

apply a transfer function to transform the first signal to a second signal corresponding to a central arterial pressure of the living subject;

derive a plurality of parameters from the second signal; and

determine a degree of aortic stenosis of the living subject based on the plurality of parameters.

2. The aortic stenosis screening system of claim 1, wherein the first signal corresponds to an arterial pressure of the living subject detected non-invasively at one of a finger and a toe of the living subject.

3. The aortic stenosis screening system of claim 1, wherein the first signal corresponds to an arterial pressure of the living subject detected non-invasively at one of a wrist and an ankle of the living subject.

4. The aortic stenosis screening system of claim 1, wherein the central arterial pressure of the living subject is one of an aortic pressure and a brachial pressure.

5. The aortic stenosis screening system of claim 1, wherein the plurality of parameters includes at least one of a rate of change of the central arterial pressure with respect to time, and a second derivative of the central arterial pressure with respect to time.

6. The aortic stenosis screening system of claim 1, wherein the plurality of parameters includes at least one of a time duration of a systolic rise of the central arterial pressure, and a time duration of a systolic decay of the central arterial pressure.

7. The aortic stenosis screening system of claim 1, wherein to determine the degree of aortic stenosis of the living subject, the hardware processor is further configured to:

identify, from an aortic stenosis subject population database, a second plurality of parameters corresponding to the plurality of parameters; and

generate a diagnostic index based on comparison between the plurality of parameters and the second plurality of parameters.

8. A method for use by an aortic stenosis screening system including a hardware processor and an aortic stenosis evaluation module stored in a system memory, the method comprising:

receiving, by the aortic stenosis evaluation module executed by the hardware processor, a first signal corresponding to an arterial pressure of a living subject;

applying a transfer function to transform the first signal to a second signal corresponding to a central arterial pressure of the living subject;

deriving a plurality of parameters from the second signal; and

determining a degree of aortic stenosis of the living subject based on the plurality of parameters.

9. The method of claim 8, wherein the first signal corresponds to an arterial pressure of the living subject detected non-invasively at one of a finger and a toe of the living subject.

10. The method of claim 8, wherein the first signal corresponds to an arterial pressure of the living subject detected non-invasively at one of a wrist and an ankle of the living subject.

11. The method of claim 8, wherein the central arterial pressure of the living subject is one of an aortic pressure and a brachial pressure.

12. The method of claim 8, wherein deriving the plurality of parameters from the second signal includes deriving at least one of a rate of change of the central arterial pressure with respect to time, and a second derivative of the central arterial pressure with respect to time.

13. The method of claim 8, wherein deriving the plurality of parameters from the second signal includes deriving at least one of a time duration of a systolic rise of the central arterial pressure, and a time duration of a systolic decay of the central arterial pressure.

14. The method of claim 8, wherein determining the degree of aortic stenosis of the living subject based on the plurality of parameters comprises:

identifying, from an aortic stenosis subject population database, a second plurality of parameters corresponding to the plurality of parameters; and

generating a diagnostic index based on comparison between the plurality of parameters and the second plurality of parameters.

15. A computer-readable non-transitory medium having stored thereon instructions, which when executed by a hardware processor, instantiate a method comprising:

receiving a first signal corresponding to an arterial pressure of a living subject;

applying a transfer function to transform the first signal to a second signal corresponding to a central arterial pressure of the living subject;

deriving a plurality of parameters from the second signal; and

determining a degree of aortic stenosis of the living subject based on the plurality of parameters.

16. The computer-readable non-transitory medium of claim 15, wherein the first signal corresponds to an arterial pressure of the living subject detected non-invasively at one of a finger and a wrist of the living subject.

17. The computer-readable non-transitory medium of claim 15, wherein the central arterial pressure of the living subject is one of an aortic pressure and a brachial pressure.

18. The computer-readable non-transitory medium of claim 15, wherein deriving the plurality of parameters from the second signal includes deriving at least one of a rate of change of the central arterial pressure with respect to time, and a second derivative of the central arterial pressure with respect to time.

19. The computer-readable non-transitory medium of claim 15, wherein deriving the plurality of parameters from the second signal includes deriving at least one of a time duration of a systolic rise of the central arterial pressure, and a time duration of a systolic decay of the central arterial pressure.

20. The computer-readable non-transitory medium of claim 15, wherein determining the degree of aortic stenosis of the living subject based on the plurality of parameters comprises:

identifying, from an aortic stenosis subject population database, a second plurality of parameters corresponding to the plurality of parameters; and

generating a diagnostic index based on comparison between the plurality of parameters and the second plurality of parameters.

Fig. 1

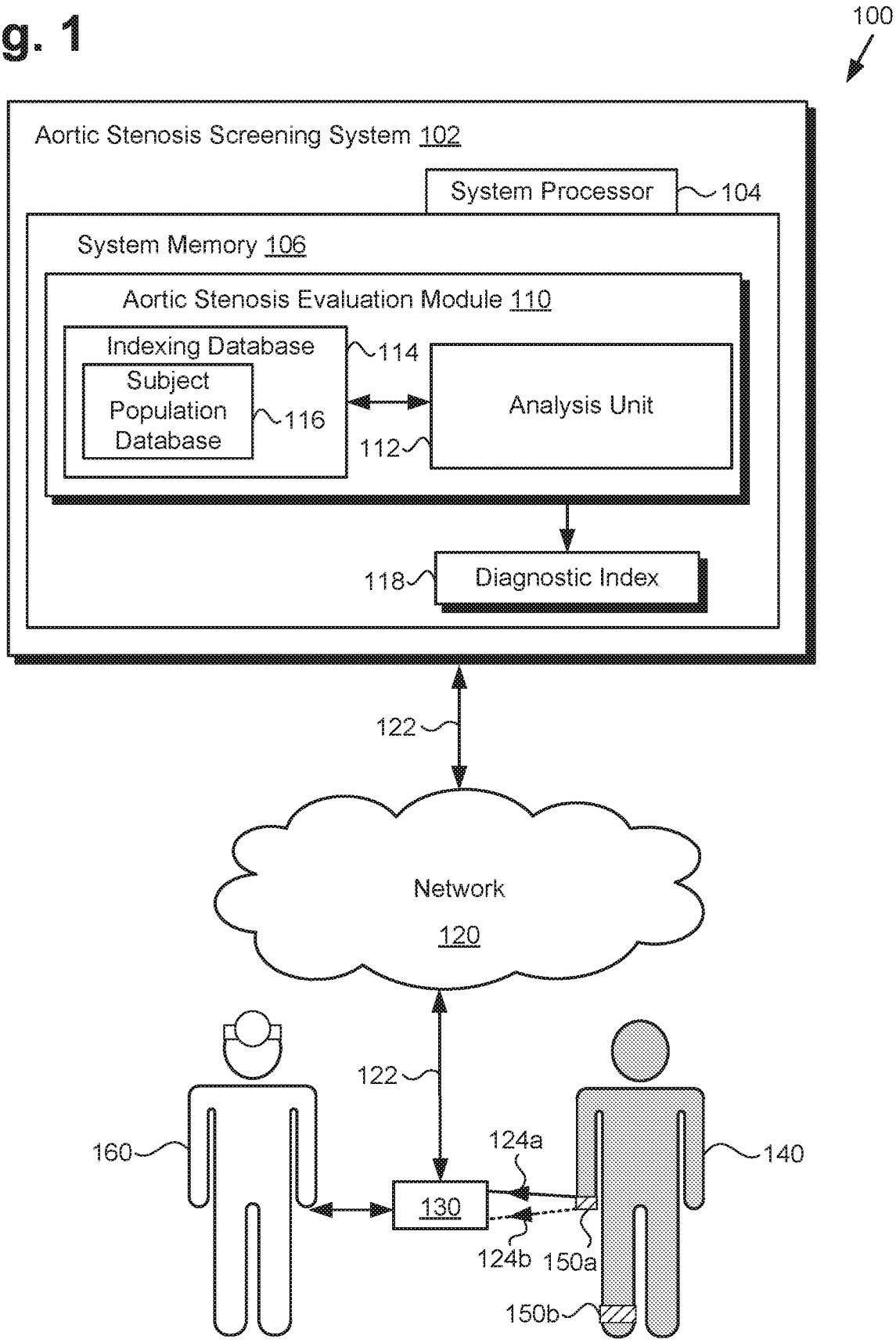

100
Aortic Stenosis Screening System 102
System Processor
104
System Memory 106
Aortic Stenosis Evaluation Module 110
Indexing Database
114
Subject Population Database
116
Analysis Unit
112
118
Diagnostic Index
122
Network
120
122
160
124a
140
130
124b
150a
150b

Fig. 2

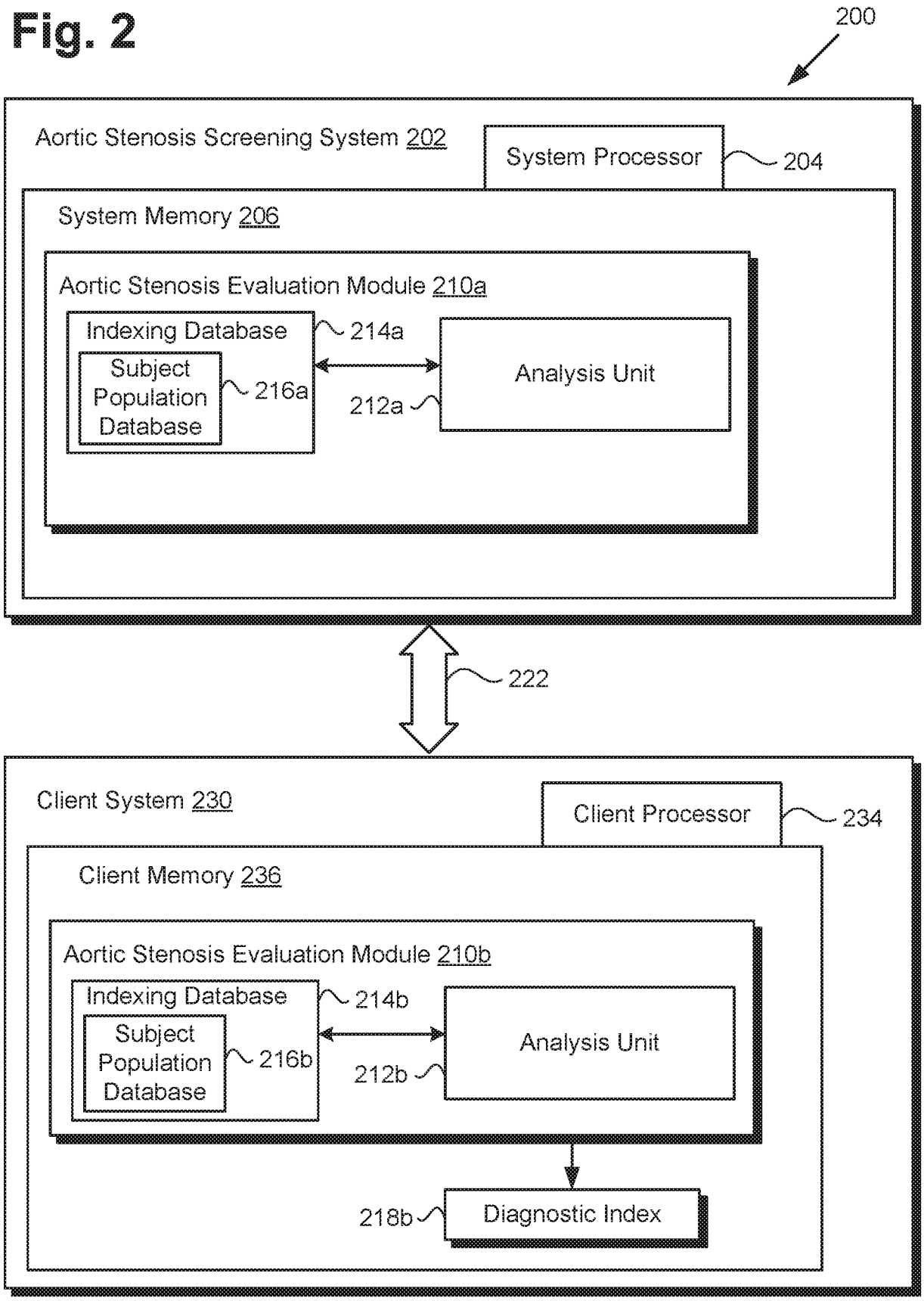

200
Aortic Stenosis Screening System 202
System Processor
204
System Memory 206
Aortic Stenosis Evaluation Module 210a
Indexing Database
214a
Subject Population Database
216a
Analysis Unit
212a
222
Client System 230
Client Processor
234
Client Memory 236
Aortic Stenosis Evaluation Module 210b
Indexing Database
214b
Subject Population Database
216b
Analysis Unit
212b
218b
Diagnostic Index

Fig. 3

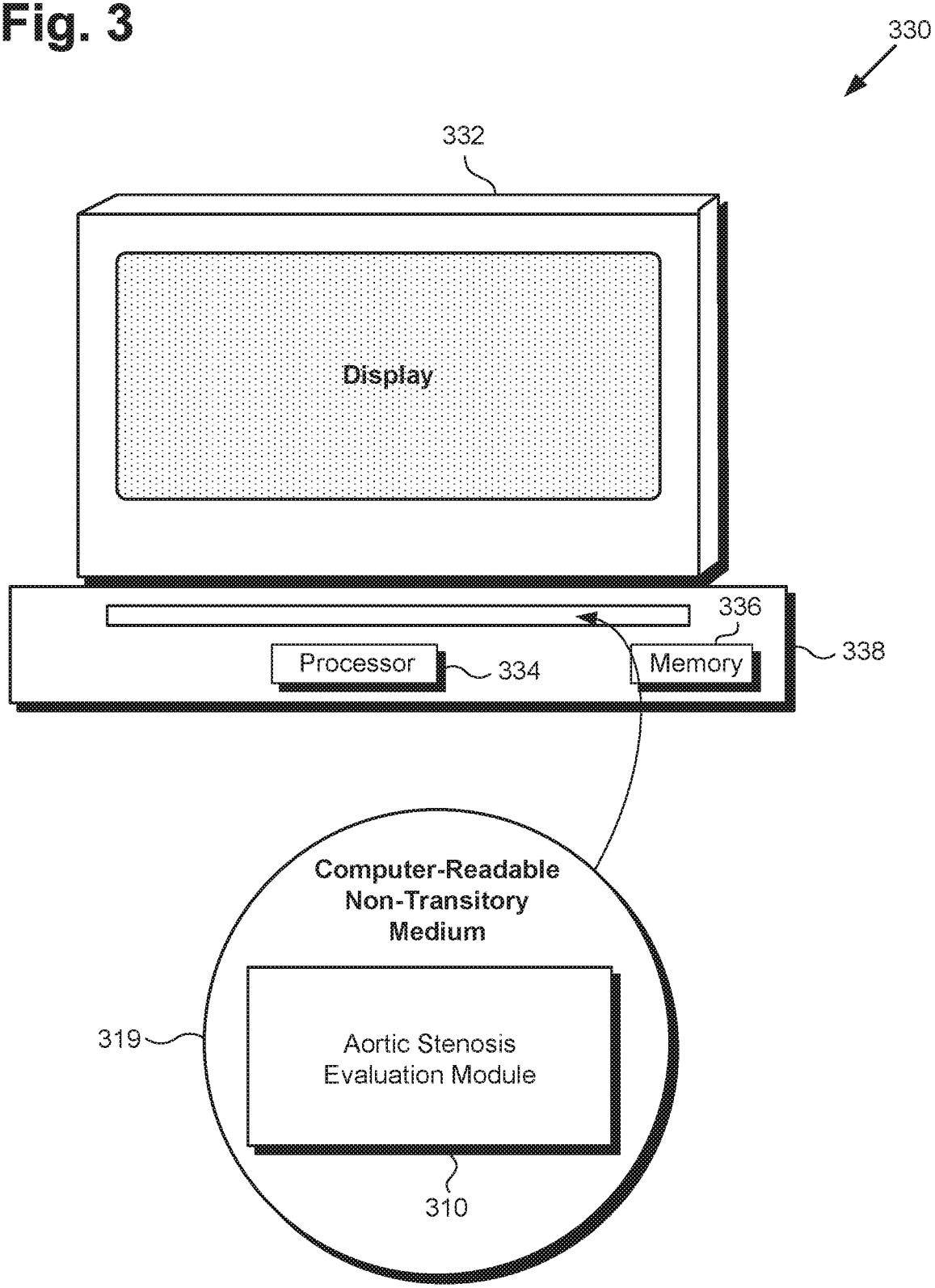
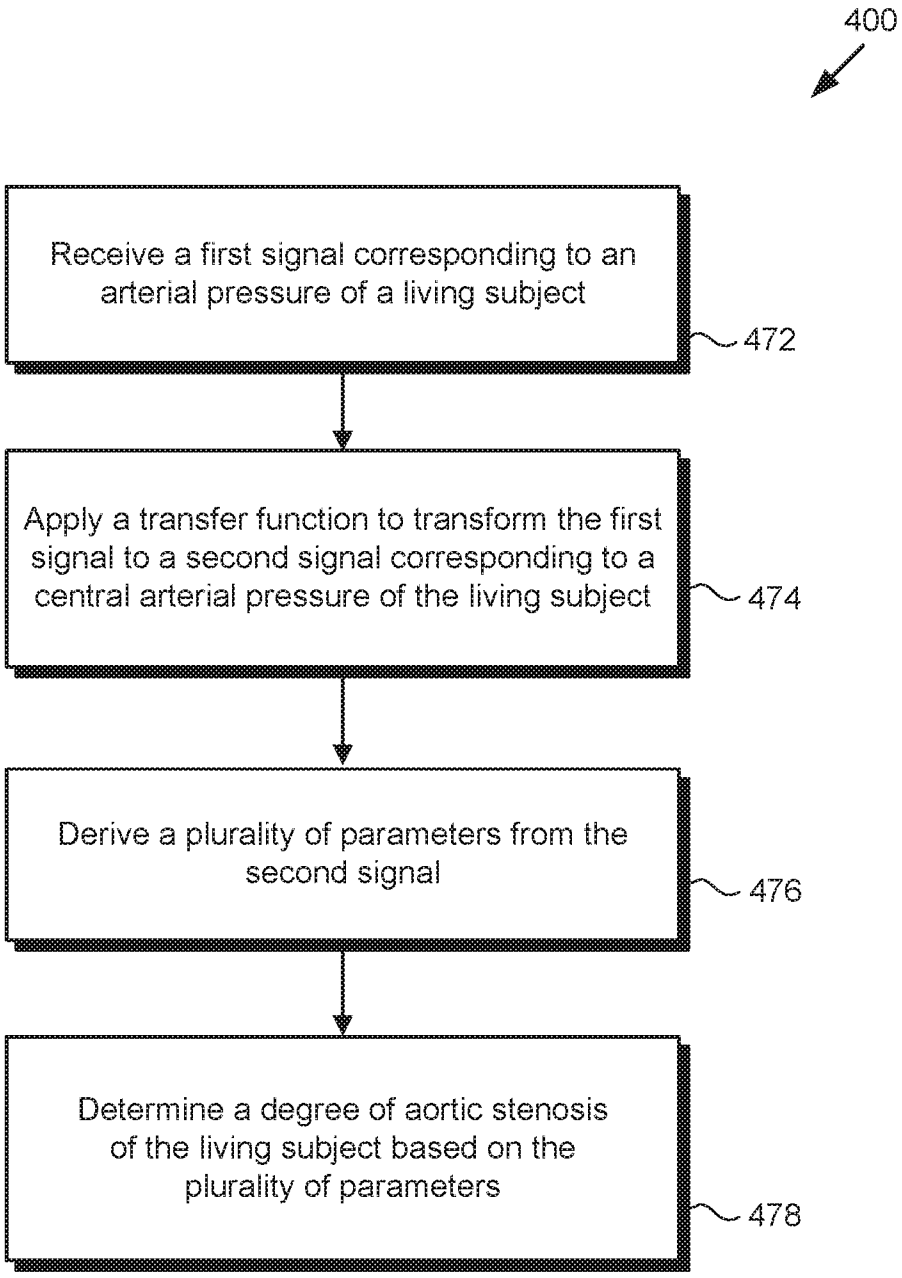

330
332
Display
336
338
Processor
334
Memory
Computer-Readable
Non-Transitory
Medium
319
Aortic Stenosis
Evaluation Module
310

Fig. 4


400
Receive a first signal corresponding to an arterial pressure of a living subject
472
Apply a transfer function to transform the first signal to a second signal corresponding to a central arterial pressure of the living subject
474
Derive a plurality of parameters from the second signal
476
Determine a degree of aortic stenosis of the living subject based on the plurality of parameters
478

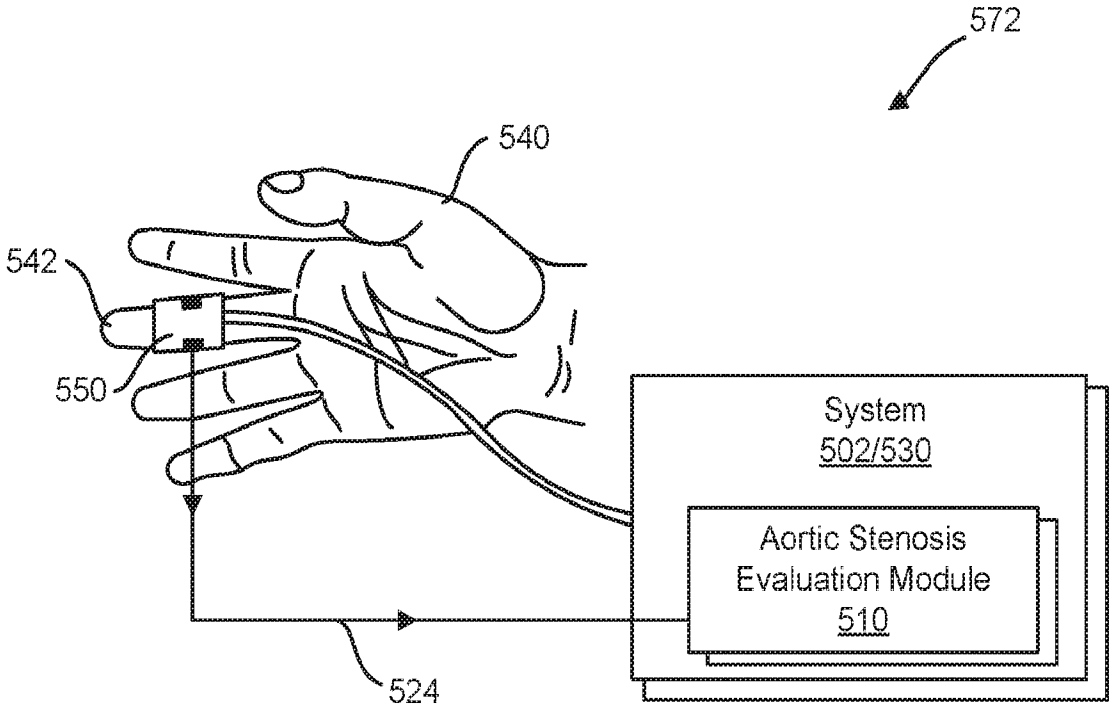

572
540
542
550
System
502/530
Aortic Stenosis
Evaluation Module
510
524

FIG. 5A

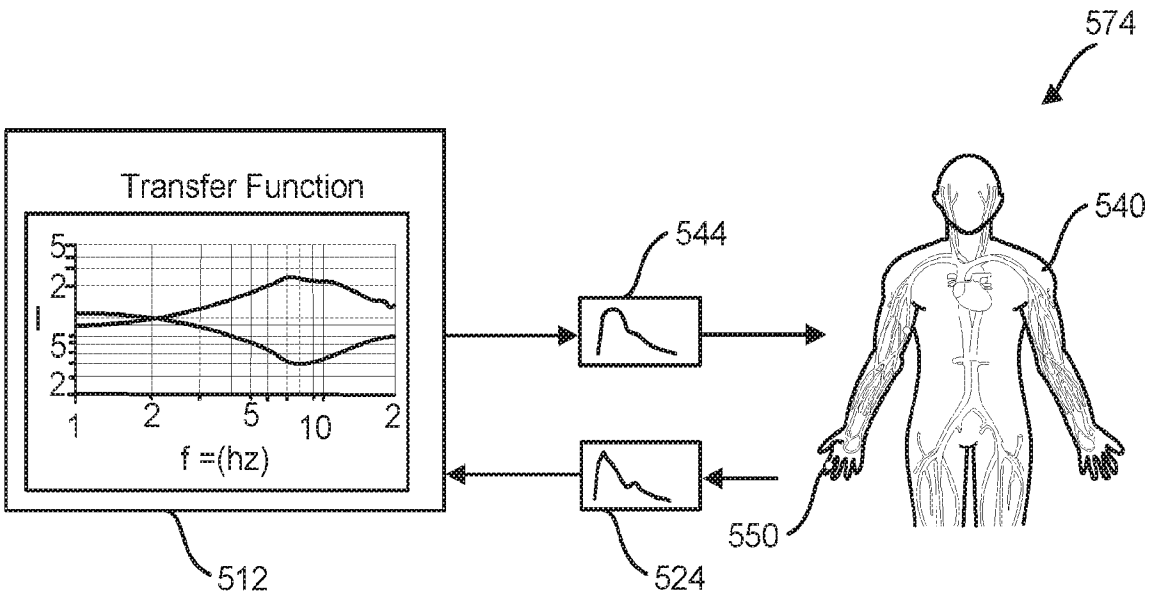

574
Transfer Function
5
2
1
5
2
1
2
5
10
2
f =(hz)
544
540
550
512
524

FIG. 5B

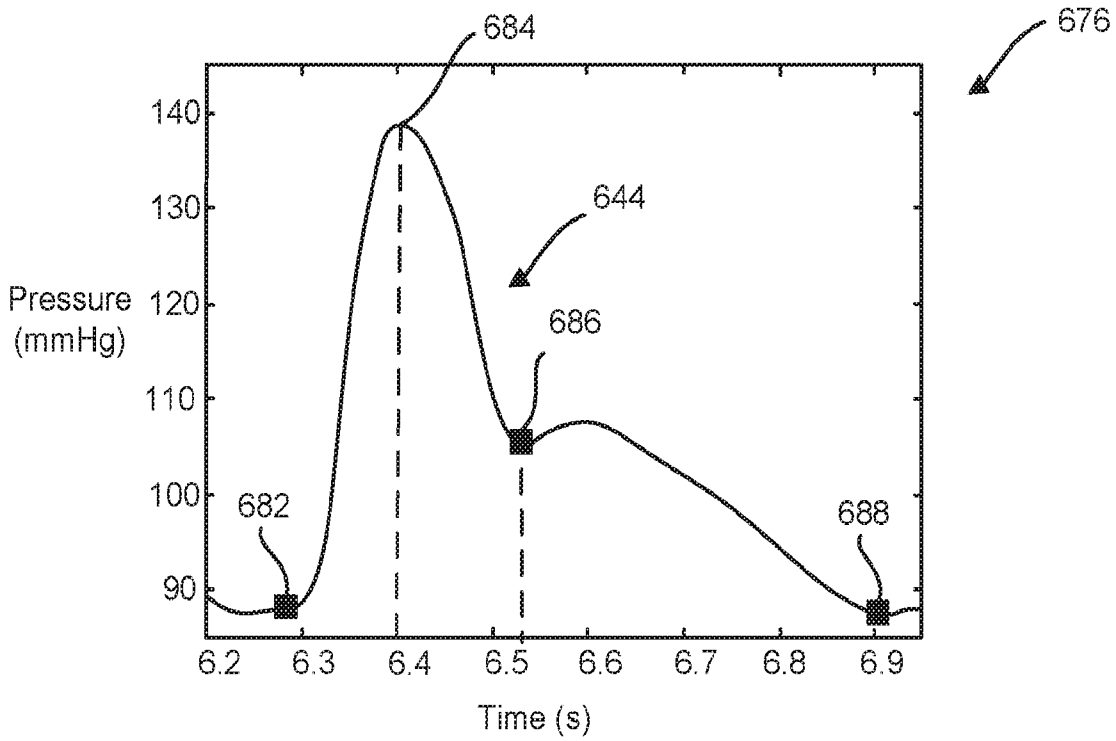

676
684
644
686
682
688
140
130
120
110
100
90
Pressure (mmHg)
6.2
6.3
6.4
6.5
6.6
6.7
6.8
6.9
Time (s)

FIG. 6A

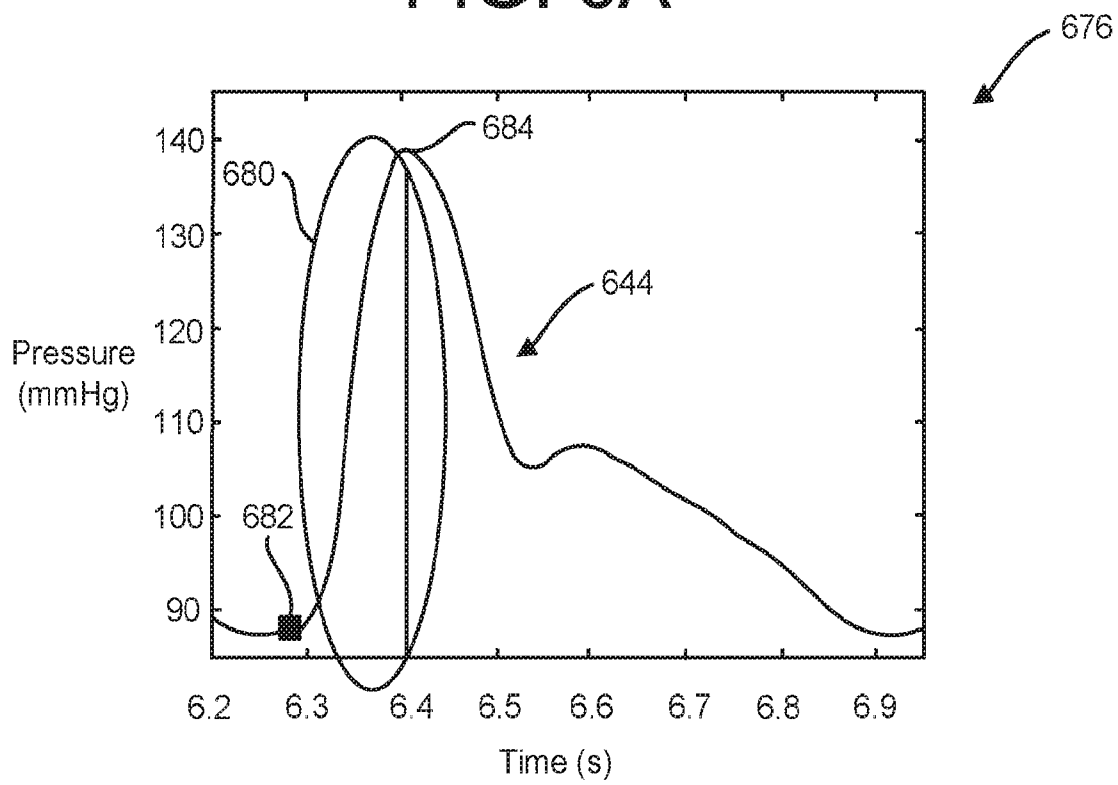

676
684
680
644
682
140
130
120
110
100
90
Pressure (mmHg)
6.2
6.3
6.4
6.5
6.6
6.7
6.8
6.9
Time (s)

FIG. 6B

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2016/025322

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:

1. ☒ Claims Nos.: 8-14
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 8-14 pertain to diagnostic methods, and thus relate to a subject matter which this International Searching Authority is not required to search under PCT Article 17(2)(a)(i) and PCT Rule 39.1(iv).

2. ☐ Claims Nos.:
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:

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:

1. ☐ As all required addtional 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 any 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.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2016/025322

A. CLASSIFICATION OF SUBJECT MATTER

A61B 5/02(2006.01)i

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 5/02; G06F 19/12; A61B 5/021; A61B 5/0285; A61B 5/055

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: stenosis, pressure, arterial, aortic

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2011-0137183 A1 (STOK) 09 June 2011 See abstract, paragraph [56] and claims 10-13.	1-7,15-20
Y	US 2012-0123246 A1 (KING et al.) 17 May 2012 See abstract, paragraphs [55]-[61] and claim 5.	1-7,15-20
A	US 2012-0095353 A1 (MORI et al.) 19 April 2012 See abstract and paragraphs [125],[126].	1-7,15-20
A	US 2013-0246034 A1 (SHARMA et al.) 19 September 2013 See abstract and claims 1-14.	1-7,15-20
A	US 2015-0230714 A1 (IMPERIAL COLLEGE OF SCIENCE, TECHNOLOGY AND MEDICINE et al.) 20 August 2015 See abstract and claims 1-10.	1-7,15-20

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent 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
29 December 2016 (29.12.2016)	**29 December 2016 (29.12.2016)**

Name and mailing address of the ISA/KR
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Telephone No. +82-42-481-3325

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2016/025322

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		EP 2334229 A1	22/06/2011
		EP 2334229 B1	14/08/2013
		EP 2334229 B8	02/10/2013
		WO 2010-002250 A1	07/01/2010
US 2012-0123246 A1	17/05/2012	DK 2437654 T3	19/01/2015
		EP 2437654 A1	11/04/2012
		EP 2437654 B1	22/10/2014
		ES 2528168 T3	04/02/2015
		JP 2012-520102 A	06/09/2012
		JP 5665776 B2	04/02/2015
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		CN 102469942 B	25/11/2015
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		CR 20130379 A	16/05/2014
		EP 2661216 A1	13/11/2013
		IL 227351 D0	30/09/2013
		JP 2014-504923 A	27/02/2014
		KR 10-1572337 B1	26/11/2015
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		NZ 613147 A	26/06/2015
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		US 9026384 B2	05/05/2015
		WO 2012-093266 A1	12/07/2012