determining changes in arterial volume based on measured blood pressure using a pressure cuff. The pressure cuff is held near diastolic pressure for about ten minutes after an artery occlusion until the artery returns to its normal state. The measured pressure during this time is used to determine the endothelial function of the patient. The extended period of applying cuff pressure to the limb affects circulation, which in turn impacts the measurements.

[0009] U.S. Pat. No. 7,390,303 (to Dafni), which is incorporated herein by reference in its entirety, describes a method of assessing arterial dilation and endothelial function, in which the relative changes in the cross sectional area of a limb artery are assessed using a bio-impedance technique to monitor cross-sectional area of a conduit artery. Measurements of bio-impedance are difficult to perform. Since bio-impedance measurements involve applying electrical to the skin of the patient, such measurements are poorly tolerated by patients due to skin irritation. Further, the measured signals vary greatly.

[0010] U.S. Patent Nos. 7,074,193 (to Satoh et al.) and 7,291,113 (to Satoh et al.) ,which are incorporated herein by reference in their entirety, describe a method and apparatus for extracting components from a measured pulse wave of blood pressure using a fourth order derivative and an n-th order derivative, respectively.

[0011] A clinical need exists for a system and method that are inexpensive, easy to perform, non-invasive, well tolerated by patients, and provide an indication of the ability arteries to respond to an increase in blood flow.

SUMMARY

[0012] A method and diagnostic system provide for assessing changes in arterial volume of a limb segment of a mammal. In one aspect, the present invention refers to a method for assessing change in arterial volume of a limb segment of a mammal, said method comprising:

determining amplitudes of component pulse waves of detected volume pulse waves of a limb segment detected during a baseline period to determine a baseline arterial volume of the limb segment;

applying a stimulus to the mammal to induce a period of change in the arterial volume of the limb segment;

determining amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after the stimulus has been applied to the mammal to induce a period of change in the arterial volume of the limb segment; and

determining relative change in arterial volume of the limb segment during the time period after the stimulus relative to the arterial volume of the limb segment during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves during the baseline and after the stimulus;

wherein determining relative change in arterial volume of the limb comprises:

calculating an average component pulse wave amplitude during the baseline period;

generating a curve fit of component pulse wave amplitudes during the after-stimulus period;

calculating a maximum of the fitted curve;

determining a time between beginning of the after-stimulus period and the time of the maximum of the fitted curve;

determining a relative amplitude change from the baseline to the maximum of the fitted curve; and

determining a relative change in arterial volume from the relative amplitude change from the baseline to the maximum of the fitted curve and the average component pulse wave amplitude during the baseline period.

[0012a] In another aspect, the present invention refers to a method for assessing change in arterial volume of a limb segment of a mammal, said method comprising:

monitoring a limb segment to record detected volume pulse waves of the limb segment during a baseline period;

determining amplitudes of component pulse waves of the detected volume pulse waves of the limb segment detected during the baseline period to determine a baseline arterial volume of the limb segment;

applying a stimulus to the mammal to induce a period of change in the arterial volume of the limb segment;

monitoring the limb segment to record detected volume pulse waves of the limb segment during an after-stimulus period after the stimulus has been applied;

determining amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during the after-stimulus period; and

determining relative change in arterial volume of the limb segment during the after-stimulus period relative to the arterial volume of the limb segment during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves during the baseline and after-stimulus periods;

wherein monitoring the limb segment during the baseline and after-stimulus periods each comprise:

applying, in a series, an external pressure to the limb segment at a mean arterial pressure of the limb; and

detecting volume pulse waves of the limb segment.

[0012b] In yet another aspect, the present invention refers to a method for assessing change in arterial volume of a limb segment of a mammal, said method comprising:

monitoring a limb segment to record detected volume pulse waves of the limb segment during a baseline period;

determining amplitudes of component pulse waves of the detected volume pulse waves of the limb segment detected during the baseline period to determine a baseline arterial volume of the limb segment;

applying a stimulus to the mammal to induce a period of change in the arterial volume of the limb segment;

monitoring the limb segment to record detected volume pulse waves of the limb segment during an after-stimulus period after the stimulus has been applied;

determining amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during the after-stimulus period; and

determining relative change in arterial volume of the limb segment during the after-stimulus period relative to the arterial volume of the limb segment during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves during the baseline and after-stimulus periods;

wherein monitoring the limb segment during the baseline and after-stimulus periods each comprise:

applying an external pressure to the limb segment at a pressure level which allows blood flow through the artery to produce said volume pulse waves in response to the applied external pressure.

[0012c] In yet another aspect, the present invention refers to a method for assessing change in arterial volume of a limb segment of a mammal, said method comprising:

determining amplitudes of component pulse waves of detected volume pulse waves of a limb segment detected during a baseline period to determine a baseline arterial volume of the limb segment;

applying a stimulus to the mammal to induce a period of change in the arterial volume of the limb segment;

determining amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after a stimulus has been applied; and

determining relative change in arterial volume of the limb segment during the time period after the stimulus relative to the arterial volume of the limb segment during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves during the baseline and after the stimulus;

wherein the component pulse wave is an early systolic component; and

wherein determining amplitude of early systolic component of a volume pulse wave comprises:

computing a fourth derivative of the detected volume pulse wave;

determining a time at which the fourth derivative reaches a third zero crossing;

determining a pressure value on the detected volume pulse wave at said time;

determining a pressure value at the beginning of the volume pulse wave; and

assessing the amplitude of the early systolic component of the volume pulse wave as the difference between said pressures values.

[0012d] In yet another aspect, the present invention refers to a diagnostic system for assessing change in arterial volume of a limb segment of a mammal comprising:

a sensor for detecting volume pulse waves of a limb segment during a baseline period and for detecting volume pulse waves of the limb segment during a period of an after-stimulus change in arterial volume;

a processor coupled to the sensor to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during the baseline period to determine a baseline arterial volume of the limb segment, to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after a stimulus has been applied to the mammal to induce a period of change in the arterial volume of the limb segment, and to determine relative change in arterial volume of the limb segment during the time period after the stimulus relative to the arterial volume of the limb during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves at baseline and after the stimulus;

wherein the processor calculates an average pulse wave amplitude during the baseline period, generates a curve fit of pulse wave amplitudes during the after-stimulus period, calculates a maximum of the fitted curve, determines a time between beginning of the after-stimulus period and the time of the maximum of the fitted curve, determines a relative amplitude change from the baseline to the maximum of the fitted curve, and determines a relative change in arterial volume from the relative amplitude change from the baseline to the maximum of the fitted curve and the average pulse wave amplitude during the baseline period to determine relative change in arterial volume of the limb.

[0012e] In yet another aspect, the present invention refers to a diagnostic system for assessing change in arterial volume of a limb segment of a mammal comprising:

a sensor for detecting volume pulse waves of a limb segment during a baseline period and for detecting volume pulse waves of the limb segment during a period of an after-stimulus change in arterial volume;

a processor coupled to the sensor to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during the baseline period to determine a baseline arterial volume of the limb segment, to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after a stimulus has been applied to the mammal to induce a period of change in the arterial volume of the limb segment, and to determine relative change in arterial volume of the limb segment during the time period after the stimulus relative to the arterial volume of the limb

during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves at baseline and after the stimulus; and

a pressure cuff coupled to the sensor and the processor to apply a stimulus to the mammal by inflating to a pressure above systolic for application to the limb segment for a period of time sufficient to induce change in arterial volume of the limb segment after releasing the inflation pressure of the cuff;

wherein the processor controls the cuff to apply, in a series, an external pressure to the limb segment at a mean arterial pressure of the limb, and controls the sensor to detect volume pulse waves of the limb segment during the baseline and after the stimulus.

[0012f] In yet another aspect, the present invention refers to a diagnostic system for assessing change in arterial volume of a limb segment of a mammal comprising:

a sensor for detecting volume pulse waves of a limb segment during a baseline period and for detecting volume pulse waves of the limb segment during a period of an after-stimulus change in arterial volume;

a processor coupled to the sensor to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during the baseline period to determine a baseline arterial volume of the limb segment, to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after a stimulus has been applied to the mammal to induce a period of change in the arterial volume of the limb segment, and to determine relative change in arterial volume of the limb segment during the time period after the stimulus relative to the arterial volume of the limb during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves at baseline and after the stimulus; and

a pressure cuff coupled to the sensor and the processor to apply a stimulus to the mammal by inflating to a pressure above systolic for application to the limb segment for a period of time sufficient to induce change in arterial volume of the limb segment after releasing the inflation pressure of the cuff;

wherein the processor controls the cuff to apply an external pressure to the limb segment at a pressure level which allows blood flow through the artery to produce said volume pulse waves in response to the applied external pressure during the baseline and after the stimulus.

[0012g] In yet another aspect, the present invention refers to a diagnostic system for assessing change in arterial volume of a limb segment of a mammal comprising:

a sensor for detecting volume pulse waves of a limb segment during a baseline period and for detecting volume pulse waves of the limb segment during a period of an after-stimulus change in arterial volume; and

a processor coupled to the sensor to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during the baseline period to determine a baseline arterial volume of the limb segment, to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after a stimulus has been applied to the mammal to induce a period of change in the arterial volume of the limb segment, and to determine relative change in arterial volume of the limb segment during the time period after stimulus relative to the arterial volume of the limb during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves at baseline and after the stimulus;

wherein the component pulse wave is an early systolic component; and

wherein the processor computes a fourth derivative of the detected volume pulse wave, determines a time at which the fourth derivative reaches a third zero crossing, determines a pressure value on the detected volume pulse wave at said time, determines a pressure value at the beginning of the volume pulse wave, and assesses the amplitude of the early systolic component of the volume pulse wave as the difference between said pressures values to determine the amplitude of early systolic component of a volume pulse wave.

[0012h] In yet another aspect, the present invention refers to a non-transitory machine-readable medium encoded with instructions, that when executed by one or more processors, cause the processor to carry out a process for assessing change in arterial volume of a limb segment of a mammal, the process comprising:

determining amplitudes of component pulse waves of detected volume pulse waves of a limb segment detected during a baseline period to determine a baseline arterial volume of the limb segment;

determining amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after a stimulus has been applied to the mammal to induce a period of change in the arterial volume of the limb segment; and

determining relative change in arterial volume of the limb segment during the time period of the stimulus relative to the arterial volume of the limb during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves at baseline and after the stimulus;

wherein determining relative change in arterial volume of the limb comprises:

calculating an average component pulse wave amplitude during the baseline period;

generating a curve fit of component pulse wave amplitudes during the after-stimulus period;

calculating a maximum of the fitted curve;

determining a time between beginning of the after-stimulus period and the time of the maximum of the fitted curve;

determining a relative amplitude change from the baseline to the maximum of the fitted curve; and

determining a relative change in arterial volume from the relative amplitude change from the baseline to the maximum of the fitted curve and the average component pulse wave amplitude during the baseline period.

[0012i] In one example, the diagnostic system determines amplitudes of component pulse waves of detected volume pulse waves of a limb segment detected during a baseline period to determine a baseline arterial volume of the limb segment. The diagnostic system determines amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after a stimulus has been applied to the mammal to induce a period of change in the arterial volume of the limb segment. The diagnostic system determines relative change in arterial volume of the limb segment during the time period after the stimulus relative to the arterial volume of the limb during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves at baseline and after the stimulus.

[0013] In another example, the diagnostic system determines relative change in arterial volume by comparing the amplitudes of the component pulse waves of volume pulse waves at baseline and after the stimulus.

[0014] In another example, the component pulse wave is an early systolic component. In another example, the diagnostic system determines relative change in arterial volume by comparing maximum amplitudes of the early systolic components of the volume pulse waves during the baseline period and maximum amplitudes of the early systolic components of the volume pulse waves after the stimulus.

[0015] In another example, the diagnostic system monitors the limb segment to detect the detected volume pulse waves of the limb segment during the baseline period, and monitors the limb segment to detect the detected volume pulse waves of the limb segment during an after-stimulus period.

[0016] The features and advantages described in the specification are not all inclusive and, in particular, many additional features and advantages will be apparent to one of ordinary skill in the art in view of the drawings, specification, and claims. Moreover, it should be noted that the language used in the specification has been principally selected for readability and instructional purposes, and may not have been selected to delineate or circumscribe the inventive subject matter.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] Figure 1 is a pictorial diagram illustrating a diagnostic system in accordance with the present invention.

[0018] Figure 2 is a block diagram illustrating the diagnostic system of Figure 1.

[0019] Figure 3 is a flow chart illustrating an operation of arterial volume change assessment of the diagnostic system of Figure 1.

[0020] Figure 4 is a timing diagram illustrating pressure applied to a limb during baseline testing and analysis and after-stimulus testing and analysis of Figure 3 with an occlusion providing a stimulus.

[0021] Figure 5 is a timing diagram illustrating amplitudes of early systolic components of pulse waves measured during a baseline period and an after-stimulus period of Figure 4.

What is claimed is:

1. A method for assessing change in arterial volume of a limb segment of a mammal, said method comprising:

determining amplitudes of component pulse waves of detected volume pulse waves of a limb segment detected during a baseline period to determine a baseline arterial volume of the limb segment;

applying a stimulus to the mammal to induce a period of change in the arterial volume of the limb segment;

determining amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after the stimulus has been applied to the mammal to induce a period of change in the arterial volume of the limb segment; and

determining relative change in arterial volume of the limb segment during the time period after the stimulus relative to the arterial volume of the limb segment during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves during the baseline and after the stimulus;

wherein determining relative change in arterial volume of the limb comprises:

calculating an average component pulse wave amplitude during the baseline period;

generating a curve fit of component pulse wave amplitudes during the after-stimulus period;

calculating a maximum of the fitted curve;

determining a time between beginning of the after-stimulus period and the time of the maximum of the fitted curve;

determining a relative amplitude change from the baseline to the maximum of the fitted curve; and

determining a relative change in arterial volume from the relative amplitude change from the baseline to the maximum of the fitted curve and the average component pulse wave amplitude during the baseline period.

2. The method of claim 1, wherein the component pulse wave is an early systolic component.

3. The method of claim 2 wherein the determining relative change in arterial volume includes comparing maximum amplitudes of the early systolic components of the volume pulse waves during the baseline period and maximum amplitudes of the early systolic components of the volume pulse waves after the stimulus.

4. The method of claim 2 or claim 3, wherein determining amplitude of early systolic component of a volume pulse wave comprises:

determining an occurrence of an inflection point in the volume pulse wave;

determining a time of the occurrence of the inflection point;

determining a pressure value on the detected volume pulse wave at said time;

determining a pressure value at the beginning of the volume pulse wave; and

assessing the amplitude of the early systolic component of the volume pulse wave as the difference between said pressure values.

5. The method of any preceding claim, further comprising:

monitoring the limb segment to record the detected volume pulse waves of the limb segment during the baseline period;

monitoring the limb segment to record the detected volume pulse waves of the limb segment during a period of an after-stimulus period.

6. The method of claim 5, wherein the component pulse wave is an early systolic component.

7. The method of any preceding claim, wherein the stimulus comprises a mechanical stimulation, a thermal stimulation, a chemical stimulation, an electrical stimulation, a

neurological stimulation, a mental stimulation or a physical exercise stimulation, or any combination thereof, to include a change in arterial volume of the limb segment.

8. The method of any preceding claim, wherein applying the stimulus comprises inflating a cuff that is disposed on the limb segment to a pressure above systolic for a period of time sufficient to induce change in arterial volume of the limb segment after releasing the inflation pressure of the cuff.

9. The method of any preceding claim, wherein calculating an average pulse wave amplitude during the baseline comprises:

determining an average pulse wave amplitude for each inflation/deflation cycle of a plurality of inflation/deflation cycles over the baseline period; and

calculating an average pulse wave amplitude during the baseline from the average pulse wave amplitudes of the plurality of inflation/ deflation cycles.

10. The method of any preceding claim, wherein generating a curve fit of pulse wave amplitudes comprises generating a fourth-order polynomial function to fit the after-stimulus pulse wave amplitudes.

11. The method of any preceding claim, wherein determining relative change in arterial volume of the limb further comprises integrating an area under the fitted curve from a time period of the end of the stimulus to a time when the measured amplitude returns to a baseline amplitude.

12. A method for assessing change in arterial volume of a limb segment of a mammal, said method comprising:

monitoring a limb segment to record detected volume pulse waves of the limb segment during a baseline period;

determining amplitudes of component pulse waves of the detected volume pulse waves of the limb segment detected during the baseline period to determine a baseline arterial volume of the limb segment;

applying a stimulus to the mammal to induce a period of change in the arterial volume of the limb segment;

monitoring the limb segment to record detected volume pulse waves of the limb segment during an after-stimulus period after the stimulus has been applied;

determining amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during the after-stimulus period; and

determining relative change in arterial volume of the limb segment during the after-stimulus period relative to the arterial volume of the limb segment during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves during the baseline and after-stimulus periods;

wherein monitoring the limb segment during the baseline and after-stimulus periods each comprise:

applying, in a series, an external pressure to the limb segment at a mean arterial pressure of the limb; and

detecting volume pulse waves of the limb segment.

13. A method for assessing change in arterial volume of a limb segment of a mammal, said method comprising:

monitoring a limb segment to record detected volume pulse waves of the limb segment during a baseline period;

determining amplitudes of component pulse waves of the detected volume pulse waves of the limb segment detected during the baseline period to determine a baseline arterial volume of the limb segment;

applying a stimulus to the mammal to induce a period of change in the arterial volume of the limb segment;

monitoring the limb segment to record detected volume pulse waves of the limb segment during an after-stimulus period after the stimulus has been applied;

determining amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during the after-stimulus period; and

determining relative change in arterial volume of the limb segment during the after-stimulus period relative to the arterial volume of the limb segment during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves during the baseline and after-stimulus periods;

wherein monitoring the limb segment during the baseline and after-stimulus periods each comprise:

applying an external pressure to the limb segment at a pressure level which

allows blood flow through the artery to produce said volume pulse waves in response to the applied external pressure.

14. The method of claim 13, wherein applying the external pressure comprises:

varying gradually the external pressure between near-systolic and near diastolic, and

detecting the volume pulse waves while the external pressure is between systolic and diastolic.

15. The method of claim 13, wherein applying the external pressure comprises: initially applying the external pressure at a pressure near systolic; and gradually reducing the external pressure to a pressure near diastolic.

16. The method of claim 13, wherein applying the external pressure comprises: initially applying the external pressure at a pressure near diastolic; and gradually increasing to a pressure near systolic.

17. The method of claim 13, wherein applying the external pressure comprises cycling the external pressure between a high level and a low level, wherein determining the amplitudes of component pulse waves of the volume pulse waves includes said determining while the external pressure is at the high level.

18. The method of claim 17, wherein the high level is near mean arterial pressure and the low level is below venous pressure.

19. A method for assessing change in arterial volume of a limb segment of a mammal, said method comprising:

determining amplitudes of component pulse waves of detected volume pulse waves of a limb segment detected during a baseline period to determine a baseline arterial volume of the limb segment;

applying a stimulus to the mammal to induce a period of change in the arterial volume of the limb segment;

determining amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after a stimulus has been applied; and

determining relative change in arterial volume of the limb segment during the time period after the stimulus relative to the arterial volume of the limb segment during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves during the baseline and after the stimulus;

wherein the component pulse wave is an early systolic component; and

wherein determining amplitude of early systolic component of a volume pulse wave comprises:

computing a fourth derivative of the detected volume pulse wave;

determining a time at which the fourth derivative reaches a third zero crossing;

determining a pressure value on the detected volume pulse wave at said time;

determining a pressure value at the beginning of the volume pulse wave; and

assessing the amplitude of the early systolic component of the volume pulse wave as the difference between said pressures values.

20. The method of claim 19, wherein the determining the pressure value at the beginning of the volume pulse wave includes determining a minimum of the pulse wave corresponding to a diastole of a heart.

21. A diagnostic system for assessing change in arterial volume of a limb segment of a mammal comprising:

a sensor for detecting volume pulse waves of a limb segment during a baseline period and for detecting volume pulse waves of the limb segment during a period of an after-stimulus change in arterial volume;

a processor coupled to the sensor to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during the baseline period to determine a baseline arterial volume of the limb segment, to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after a stimulus has been applied to the mammal to induce a period of change in the arterial volume of the limb segment, and to determine relative change in arterial volume of the limb segment during the time period after the stimulus relative to the arterial volume of the limb during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves at baseline and after the stimulus;

wherein the processor calculates an average pulse wave amplitude during the baseline period, generates a curve fit of pulse wave amplitudes during the after-stimulus period, calculates a maximum of the fitted curve, determines a time between beginning of the after-stimulus period and the time of the maximum of the fitted curve, determines a relative amplitude change from the baseline to the maximum of the fitted curve, and determines a relative change in arterial volume from the relative amplitude change from the baseline to the maximum of the fitted curve and the average pulse wave amplitude during the baseline period to determine relative change in arterial volume of the limb.

22. The diagnostic system of claim 21, wherein the processor determines the relative change in arterial volume by comparing the amplitudes of the component pulse waves of volume pulse waves at baseline and after the stimulus.

23. The diagnostic system of claim 21 or claim 22, wherein the component pulse wave is an early systolic component.

24. The diagnostic system of claim 23, wherein the processor determines the relative change in arterial volume by comparing maximum amplitudes of the early systolic components of the volume pulse waves during the baseline period and maximum amplitudes of the early systolic components of the volume pulse waves after the stimulus.

25. The diagnostic system of claim 23, wherein the processor determines an occurrence of an inflection point in the volume pulse wave, determines a time of the occurrence of the inflection point, determines a pressure value on the detected volume pulse wave at said time, determines a pressure value at the beginning of the volume pulse wave, and assesses the amplitude of the early systolic component of the volume pulse wave as the difference between said pressures values to determine the amplitude of early systolic component of a volume pulse wave.

26. The diagnostic system of any one of claims 21 to 25, further comprising a pressure cuff coupled to the sensor and the processor for applying a pressure to the limb segment to occlude an artery in the limb segment and for releasing said pressure to the limb segment to allow blood flow in the artery to induce the period of change in arterial volume of the limb segment in response to a control signal from the processor.

27. The diagnostic system of any one of claims 23 to 25, further comprising a pressure cuff coupled to the sensor and the processor to apply a stimulus to the mammal to induce a period of change in arterial volume of the limb segment.

28. The diagnostic system of any one of claims 23 to 25, further comprising a pressure cuff coupled to the sensor and the processor to apply a stimulus to the mammal by

inflating to a pressure above systolic for application of the limb segment for a period of time sufficient to induce change in arterial volume of the limb segment after releasing the inflation pressure of the cuff.

29. The diagnostic system of any one of claims 21 to 28, wherein the processor determines an average pulse wave amplitude for each inflation/deflation cycle of a plurality of inflation/deflation cycles over the baseline period, and calculates an average pulse wave amplitude during the baseline from the average pulse wave amplitudes of the plurality of inflation/deflation cycles to calculate an average pulse wave amplitude during the baseline.

30. The diagnostic system of any one of claims 21 to 29, wherein the processor generates a fourth-order polynomial function to fit the after-stimulus pulse wave amplitudes to generate a curve fit of pulse wave amplitudes.

31. The diagnostic system of any one of claims 21 to 30, wherein the processor integrates an area under the fitted curve from a time period of the end of the stimulus to a time when the measured amplitude returns to a baseline amplitude to determine relative change in arterial volume of the limb.

32. A diagnostic system for assessing change in arterial volume of a limb segment of a mammal comprising:

a sensor for detecting volume pulse waves of a limb segment during a baseline period and for detecting volume pulse waves of the limb segment during a period of an after-stimulus change in arterial volume;

a processor coupled to the sensor to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during the baseline period to determine a baseline arterial volume of the limb segment, to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after a stimulus has been applied to the mammal to induce a period of change in the arterial volume of the limb segment, and to determine relative change in arterial volume of the limb

segment during the time period after the stimulus relative to the arterial volume of the limb during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves at baseline and after the stimulus; and

a pressure cuff coupled to the sensor and the processor to apply a stimulus to the mammal by inflating to a pressure above systolic for application to the limb segment for a period of time sufficient to induce change in arterial volume of the limb segment after releasing the inflation pressure of the cuff;

wherein the processor controls the cuff to apply, in a series, an external pressure to the limb segment at a mean arterial pressure of the limb, and controls the sensor to detect volume pulse waves of the limb segment during the baseline and after the stimulus.

33. A diagnostic system for assessing change in arterial volume of a limb segment of a mammal comprising:

a sensor for detecting volume pulse waves of a limb segment during a baseline period and for detecting volume pulse waves of the limb segment during a period of an after-stimulus change in arterial volume;

a processor coupled to the sensor to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during the baseline period to determine a baseline arterial volume of the limb segment, to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after a stimulus has been applied to the mammal to induce a period of change in the arterial volume of the limb segment, and to determine relative change in arterial volume of the limb segment during the time period after the stimulus relative to the arterial volume of the limb during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves at baseline and after the stimulus; and

a pressure cuff coupled to the sensor and the processor to apply a stimulus to the mammal by inflating to a pressure above systolic for application to the limb segment for a period of time

sufficient to induce change in arterial volume of the limb segment after releasing the inflation pressure of the cuff;

wherein the processor controls the cuff to apply an external pressure to the limb segment at a pressure level which allows blood flow through the artery to produce said volume pulse waves in response to the applied external pressure during the baseline and after the stimulus.

34. The diagnostic system of claim 33, wherein the processor controls the cuff to apply the external pressure to the limb segment as a gradually varying pressure between near-systolic and near-diastolic, and wherein the processor controls the sensor to detect the volume pulse waves while the external pressure is between systolic and diastolic.

35. The diagnostic system of claim 33, wherein the processor controls the cuff to apply the external pressure to the limb segment at a pressure near systolic, and gradually reducing the pressure to near diastolic.

36. The diagnostic system of claim 33, wherein the processor controls the cuff to apply the external pressure to the limb segment at a pressure near diastolic, and gradually increasing to the pressure to near systolic.

37. The diagnostic system of claim 33, wherein the processor controls the cuff to cycle the external pressure applied to the limb segment between a high level and a low level, wherein the processor determines the amplitudes of component pulse waves of the volume pulse waves detected while the external pressure is at the high level.

38. The diagnostic system of any one of claims 33 to 37, wherein the high level is near mean arterial pressure and the los level is below venous pressure.

39. A diagnostic system for assessing change in arterial volume of a limb segment of a mammal comprising:

a sensor for detecting volume pulse waves of a limb segment during a baseline period and for detecting volume pulse waves of the limb segment during a period of an after-stimulus change in arterial volume; and

a processor coupled to the sensor to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during the baseline period to determine a baseline arterial volume of the limb segment, to determine amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after a stimulus has been applied to the mammal to induce a period of change in the arterial volume of the limb segment, and to determine relative change in arterial volume of the limb segment during the time period after stimulus relative to the arterial volume of the limb during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves at baseline and after the stimulus;

wherein the component pulse wave is an early systolic component; and

wherein the processor computes a fourth derivative of the detected volume pulse wave, determines a time at which the fourth derivative reaches a third zero crossing, determines a pressure value on the detected volume pulse wave at said time, determines a pressure value at the beginning of the volume pulse wave, and assesses the amplitude of the early systolic component of the volume pulse wave as the difference between said pressures values to determine the amplitude of early systolic component of a volume pulse wave.

40. The diagnostic system of claim 39, wherein the processor determines a minimum of the pulse wave corresponding to a diastole of a heart of the mammal to determine the pressure value at the beginning of the volume pulse wave.

41. A non-transitory machine-readable medium encoded with instructions, that when executed by one or more processors, cause the processor to carry out a process for assessing change in arterial volume of a limb segment of a mammal, the process comprising:

determining amplitudes of component pulse waves of detected volume pulse waves of a limb segment detected during a baseline period to determine a baseline arterial volume of the limb segment;

determining amplitudes of component pulse waves of detected volume pulse waves of the limb segment detected during a time period after a stimulus has been applied to the mammal to induce a period of change in the arterial volume of the limb segment; and

determining relative change in arterial volume of the limb segment during the time period of the stimulus relative to the arterial volume of the limb during the baseline period from the amplitudes of the component pulse waves of the detected volume pulse waves at baseline and after the stimulus;

wherein determining relative change in arterial volume of the limb comprises:

calculating an average component pulse wave amplitude during the baseline period;

generating a curve fit of component pulse wave amplitudes during the after-stimulus period;

calculating a maximum of the fitted curve;

determining a time between beginning of the after-stimulus period and the time of the maximum of the fitted curve;

determining a relative amplitude change from the baseline to the maximum of the fitted curve; and

determining a relative change in arterial volume from the relative amplitude change from the baseline to the maximum of the fitted curve and the average component pulse wave amplitude during the baseline period.

42. The non-transitory machine-readable medium encoded with instructions of claim 41, wherein the component pulse wave is an early systolic component.

43. The non-transitory machine-readable medium encoded with instructions of claim 41 or claim 42, wherein the instructions for determining relative change in arterial volume

includes instructions for comparing maximum amplitudes of the early systolic components of the volume pulse waves during the baseline period and maximum amplitudes of the early systolic components of the volume pulse waves after the stimulus.

44. The non-transitory machine-readable medium encoded with instructions of any one of claims 41 to 43, further comprising instructions for monitoring the limb segment to record the detected volume pulse waves of the limb segment during the baseline period, and instructions for monitoring the limb segment to record the detected volume pulse waves of the limb segment during the after-stimulus period.

45. The non-transitory machine-readable medium encoded with instructions of claim 44, wherein the component pulse wave is an early systolic component.