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(54) **METHOD FOR ESTIMATING FLOW RATES AND PRESSURE GRADIENTS IN ARTERIAL NETWORKS FROM PATIENT SPECIFIC COMPUTED TOMOGRAPHY ANGIOGRAM-BASED CONTRAST DISTRIBUTION DATA**

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USPC **600/425**

(57) **ABSTRACT**

An embodiment in accordance with the present invention provides a method for non-invasively determining the functional severity of arterial stenosis in a selected portion of an arterial network. The method includes gathering patient-specific data related to concentration of a contrast agent within an arterial network using a coronary computed tomography angiography scan (CCTA). The data can be gathered under rest or stress conditions. Estimation of a loss coefficient (K) can be used to eliminate the need for data gathered under stress. The data is used to calculate a transluminal attenuation gradient (TAG). The data may be corrected for imaging artifacts at any stage of the analysis. TAFE is used to determine an estimate of flow velocity. Once velocity is determined, pressure gradient, coronary flow reserve, and/or fractional flow reserve can be determined through a variety of methods. These estimates can be used to estimate functional severity of stenosis.

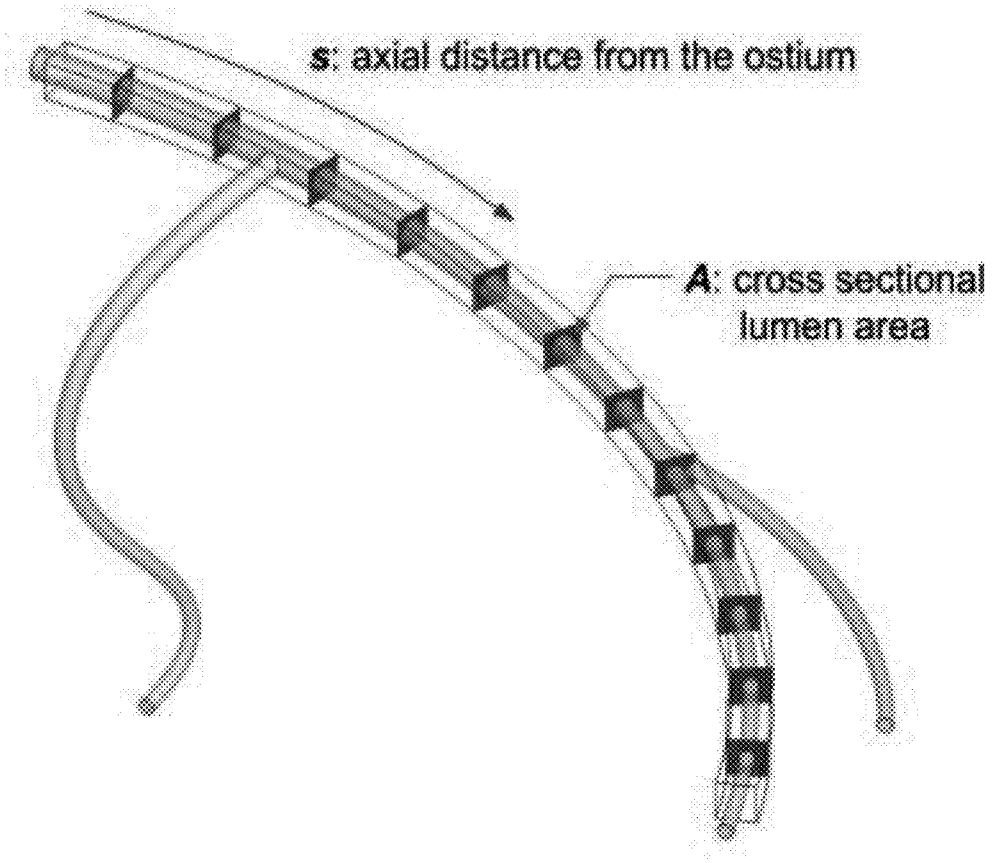


FIG. 1A

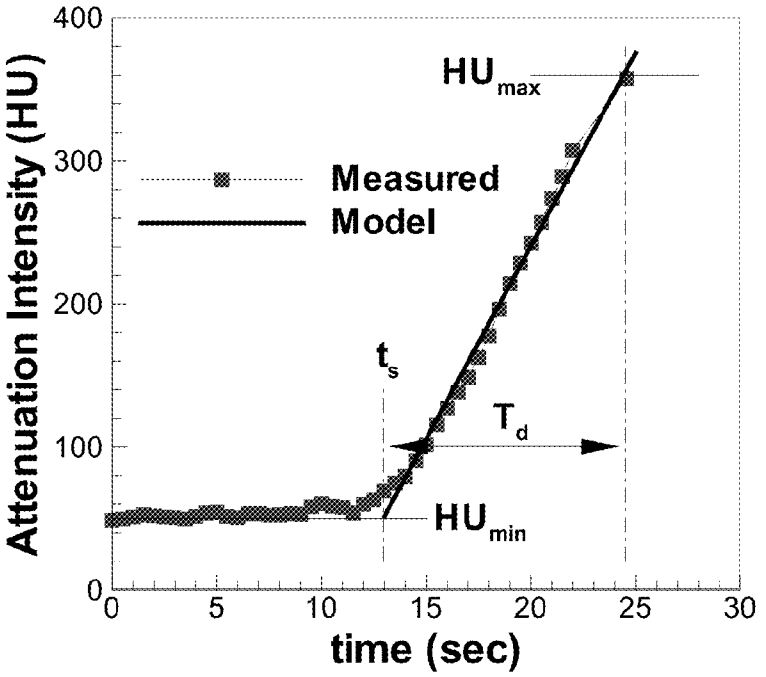

400
300
200
100
0
Attenuation Intensity (HU)
HU max
Measured
Model
t s
T d
HU min
0
5
10
15
20
25
30
time (sec)

FIG. 1B

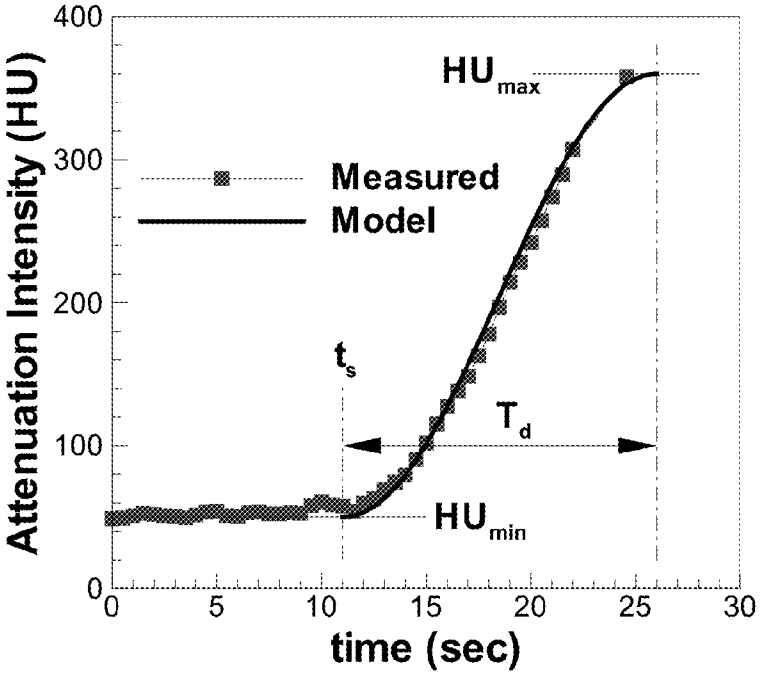

400
300
200
100
0
Attenuation Intensity (HU)
HU max
Measured
Model
t s
T d
HU min
0
5
10
15
20
25
30
time (sec)

FIG. 2

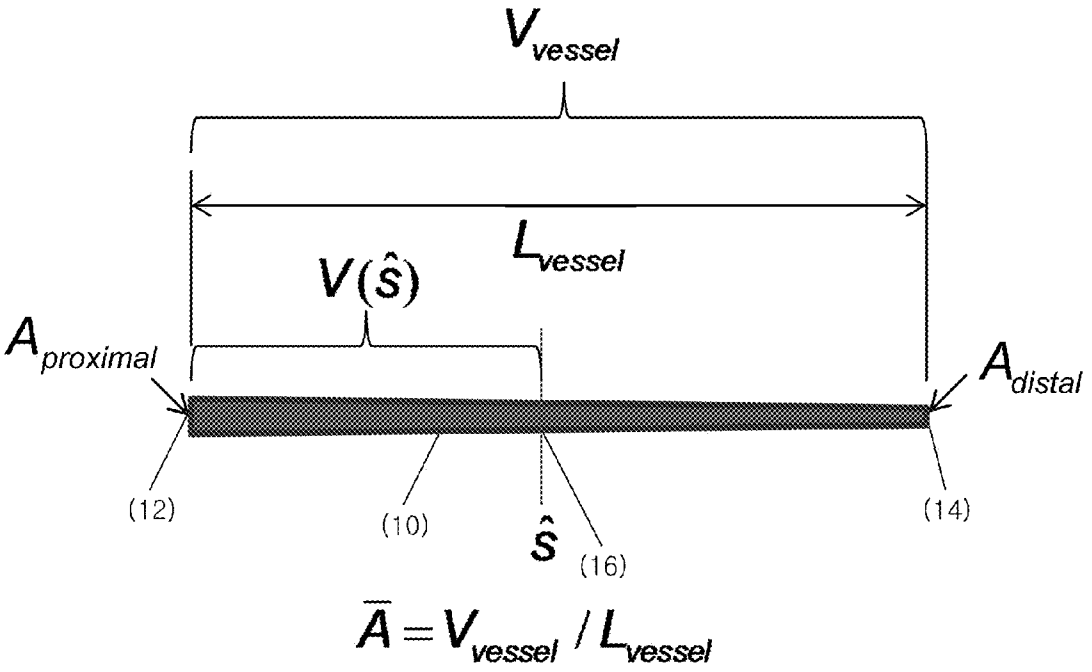

V_{vessel}
L_{vessel}
$V(\hat{s})$
$A_{proximal}$
A_{distal}
(12)
(10)
$\hat{s}$
(16)
(14)
$\bar{A} = V_{vessel} / L_{vessel}$

FIG. 3A

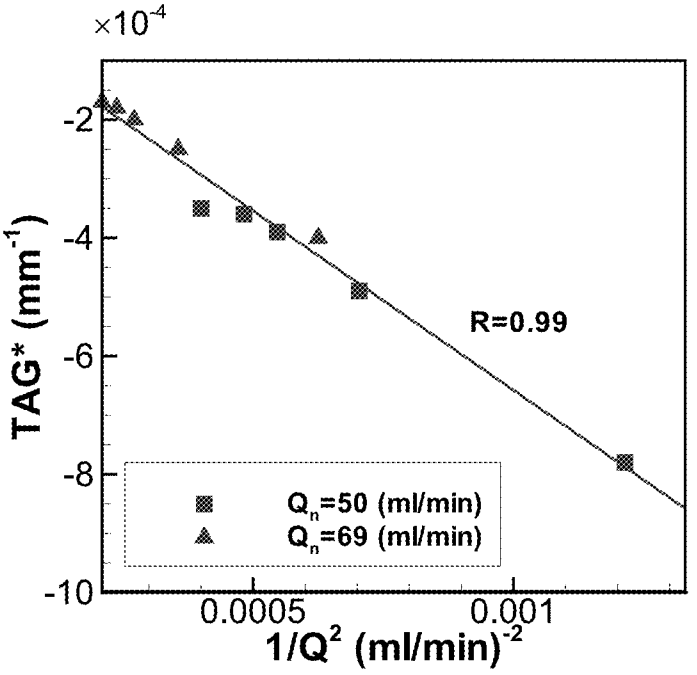

×10^-4
-2
-4
-6
-8
-10
TAG* (mm^-1)
R=0.99
Q_n=50 (ml/min)
Q_n=69 (ml/min)
0.0005
0.001
1/Q^2 (ml/min)^-2

FIG. 3B

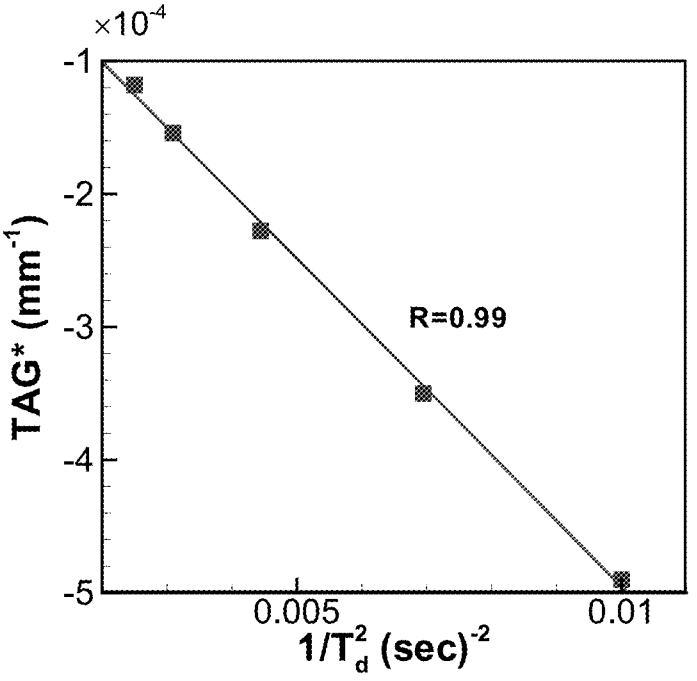

×10^-4
-1
-2
-3
-4
-5
TAG* (mm^-1)
R=0.99
0.005
0.01
1/T_d^2 (sec)^-2

FIG. 4

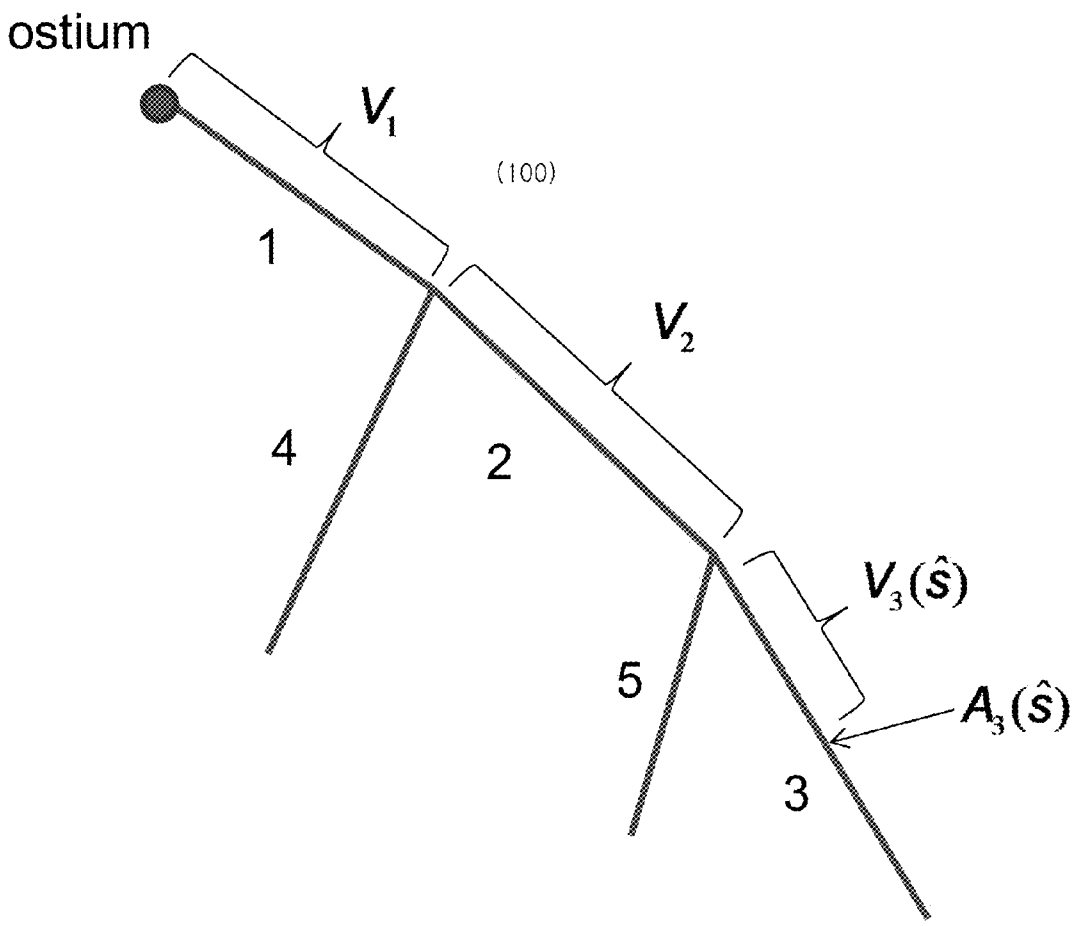


FIG. 5A

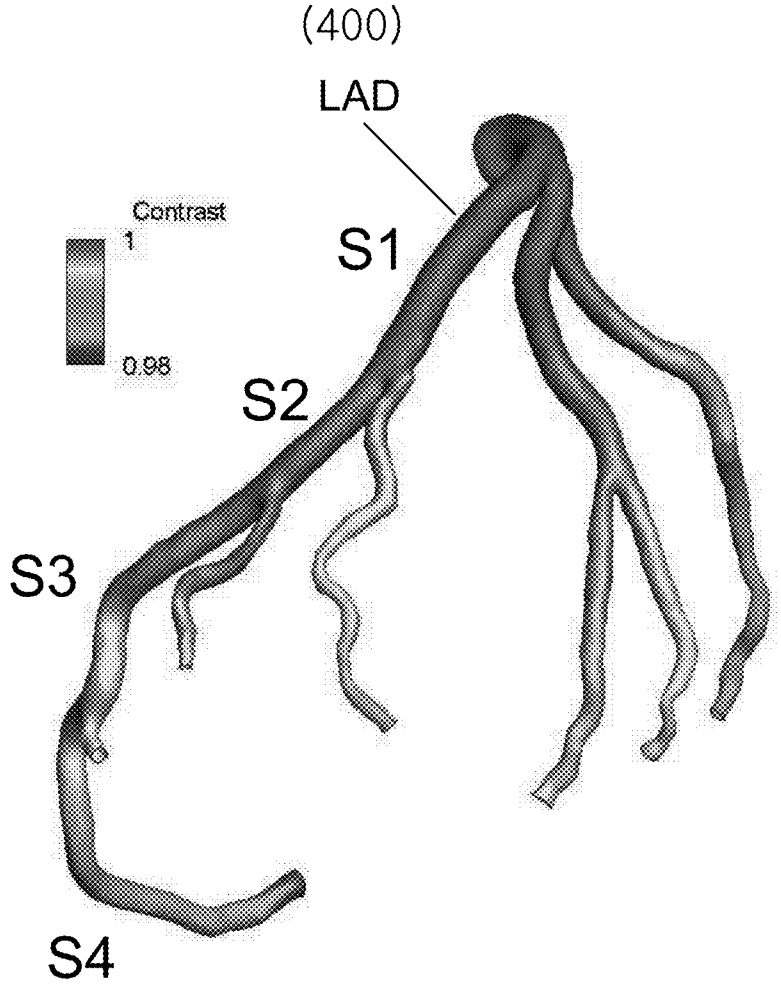


FIG. 5B

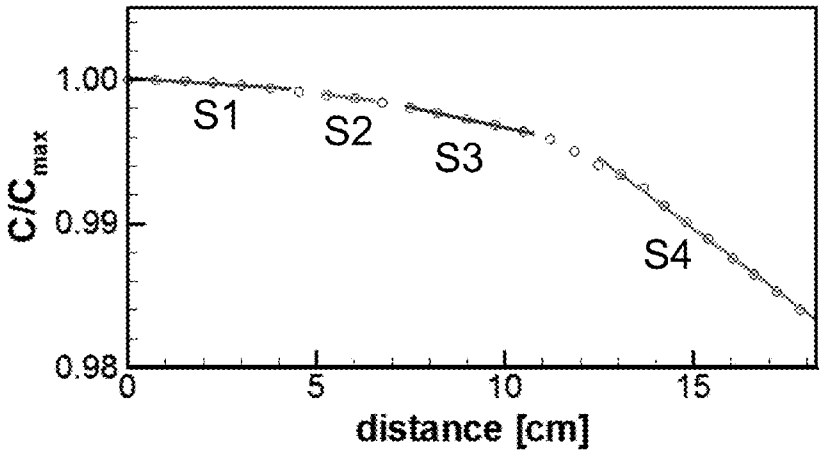


FIG. 5C

	V(s) (mL)	V_{inner} (mL)	$\bar{A}$ (cm^2)	T_d (sec)	TAG* (/cm)	TAG'' (sec^2/mL)	τ (sec)	Q_{TAFE} (mL/sec)	Q_{CFD} (mL/sec)
S1	0.5643	1.13E+00	2.40E-01	10	-1.69E-04	0.0142615	0	**6.29**	6.59
S2	1.31476	3.85E-01	1.74E-01	10	-3.40E-04	0.0394841	0.18038	**5.41**	5.78
S3	1.86992	6.91E-01	1.48E-01	10	-5.60E-04	0.0768063	0.25145	**4.33**	4.49
S4	2.63869	7.75E-01	1.18E-01	10	-1.95E-03	0.3360072	0.41119	**1.90**	2.12

FIG. 6

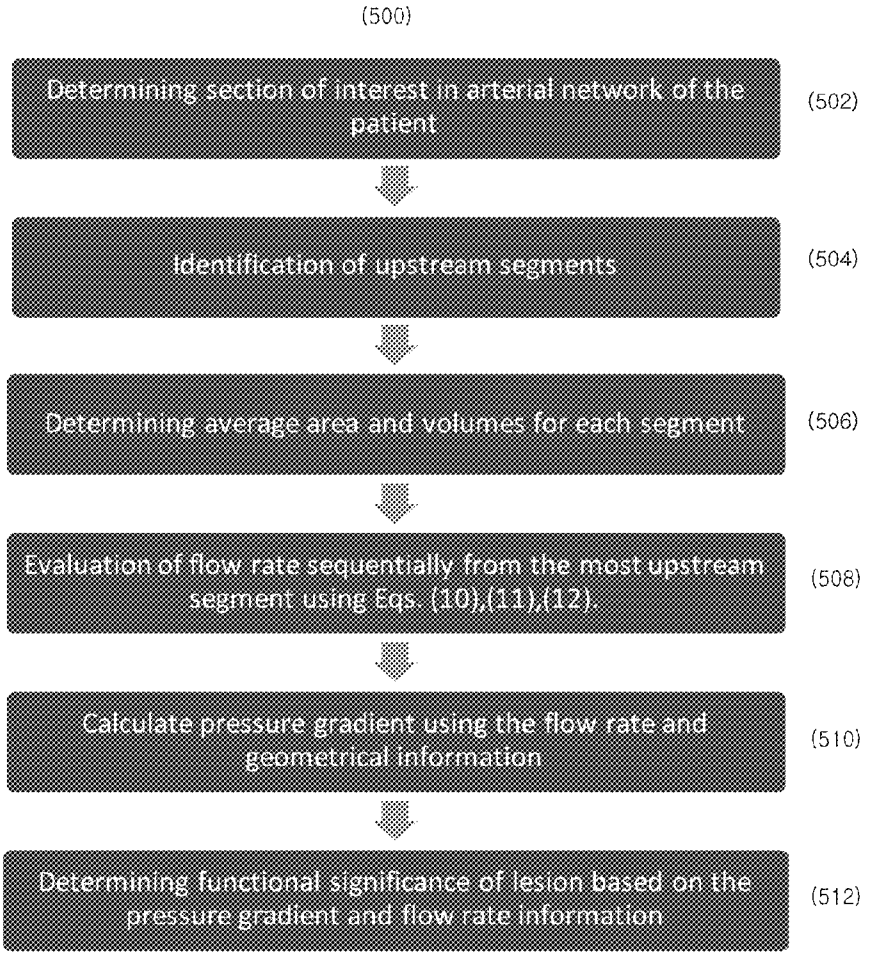

(500)
Determining section of interest in arterial network of the patient
(502)
Identification of upstream segments
(504)
Determining average area and volumes for each segment
(506)
Evaluation of flow rate sequentially from the most upstream segment using Eqs. (10),(11),(12).
(508)
Calculate pressure gradient using the flow rate and geometrical information
(510)
Determining functional significance of lesion based on the pressure gradient and flow rate information
(512)

FIG. 7A

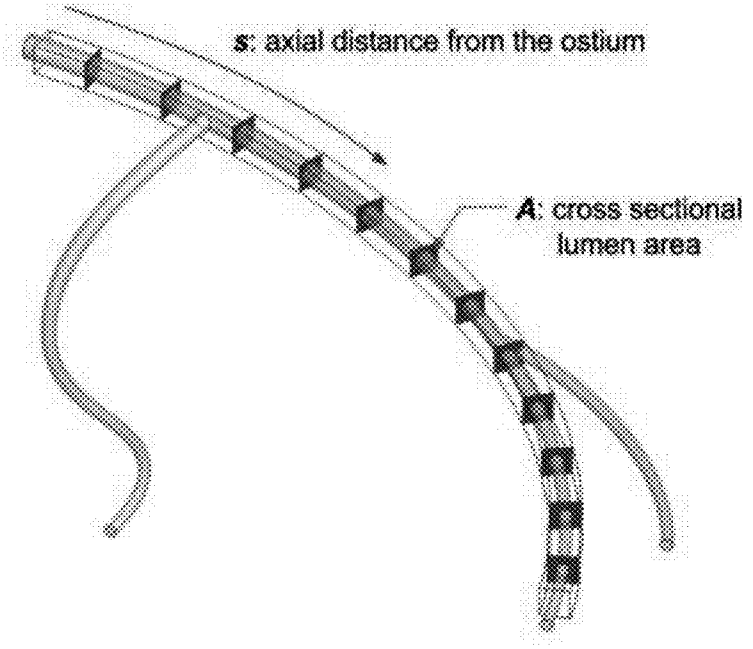

s: axial distance from the ostium
A: cross sectional lumen area

FIG. 7B

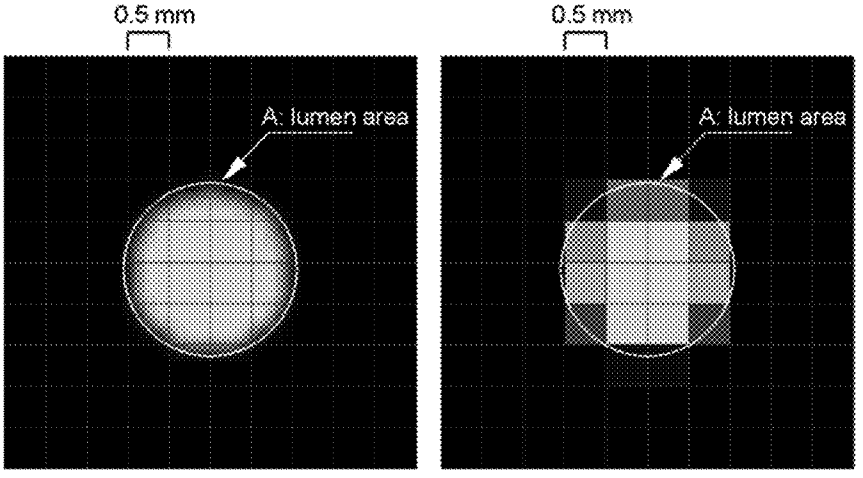

0.5 mm
A: lumen area
0.5 mm
A: lumen area

FIG. 8

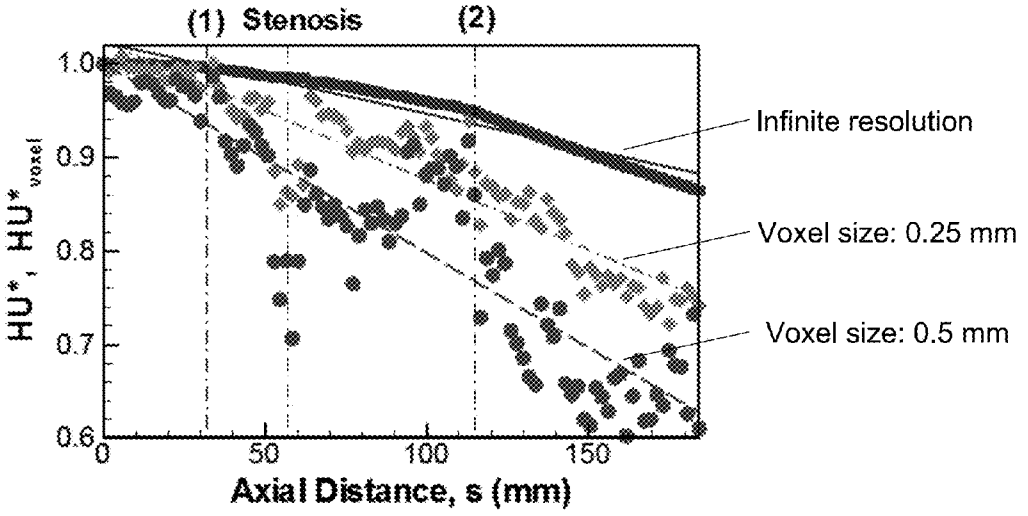

(1) Stenosis
(2)
1.0
0.9
0.8
0.7
0.6
0
50
100
150
HU*, HU*voxel
Axial Distance, s (mm)
Infinite resolution
Voxel size: 0.25 mm
Voxel size: 0.5 mm

FIG. 9

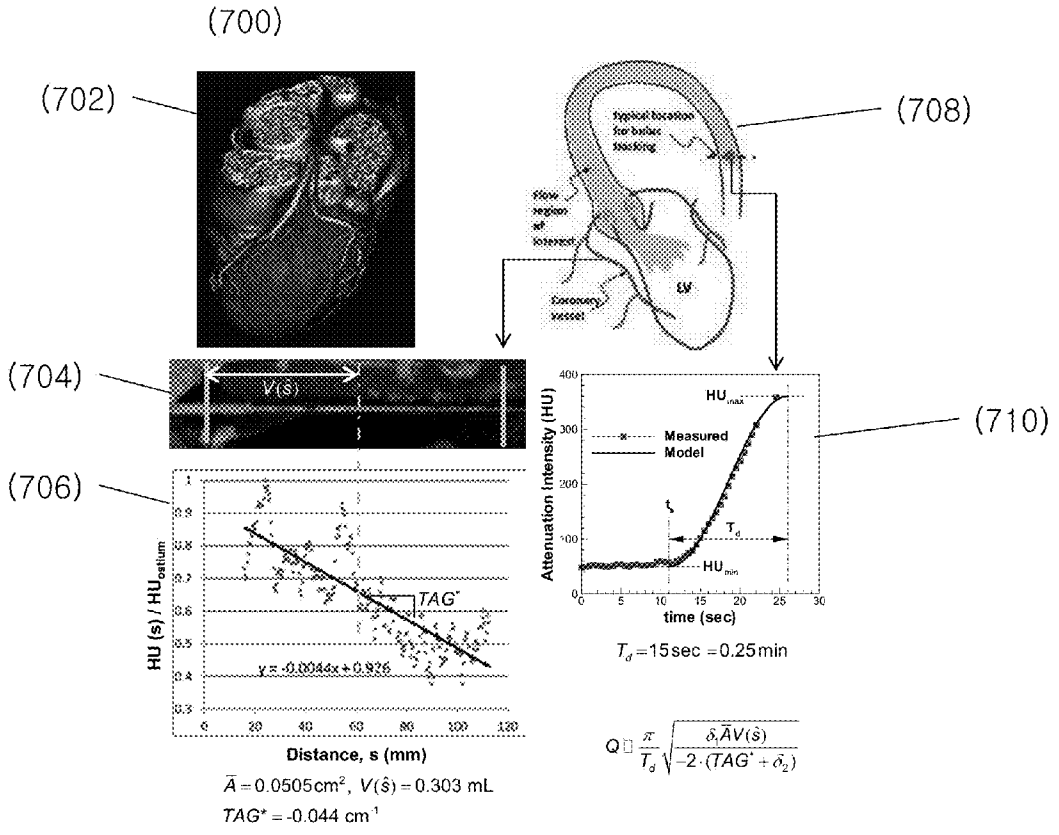

(700)
(702)
(708)
(704)
(706)
(710)
V(ŝ)
HU (s) / HU_ostium
TAG*
y = -0.0044x + 0.976
Distance, s (mm)
Ā = 0.0505cm², V(ŝ) = 0.303 mL
TAG* = -0.044 cm⁻¹
Attenuation Intensity (HU)
HU_max
HU_min
Measured
Model
t_s
T_d
time (sec)
T_d = 15sec = 0.25min
Q □ π/T_d √(δ₁ĀV(ŝ) / (-2·(TAG* + δ₂)))

FIG. 10

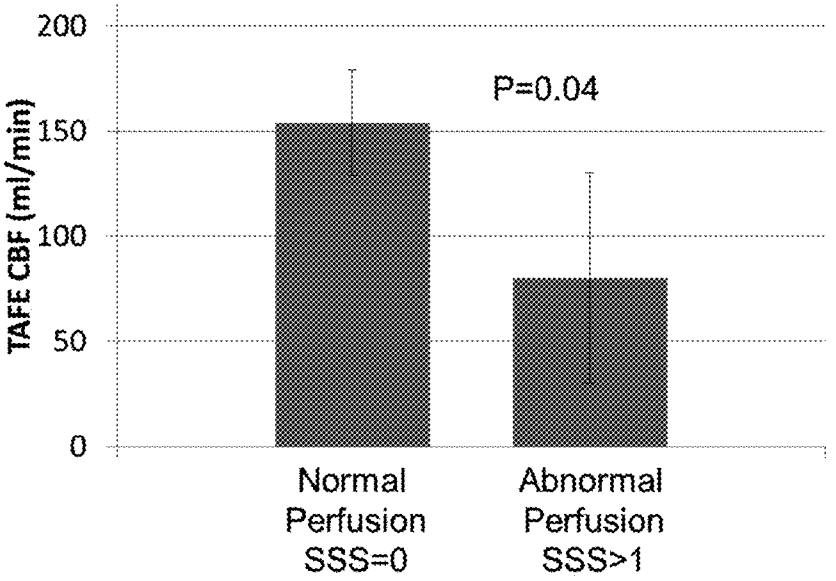

200
150
100
50
0
TAFE CBF (ml/min)
P=0.04
Normal Perfusion SSS=0
Abnormal Perfusion SSS>1

FIG. 11

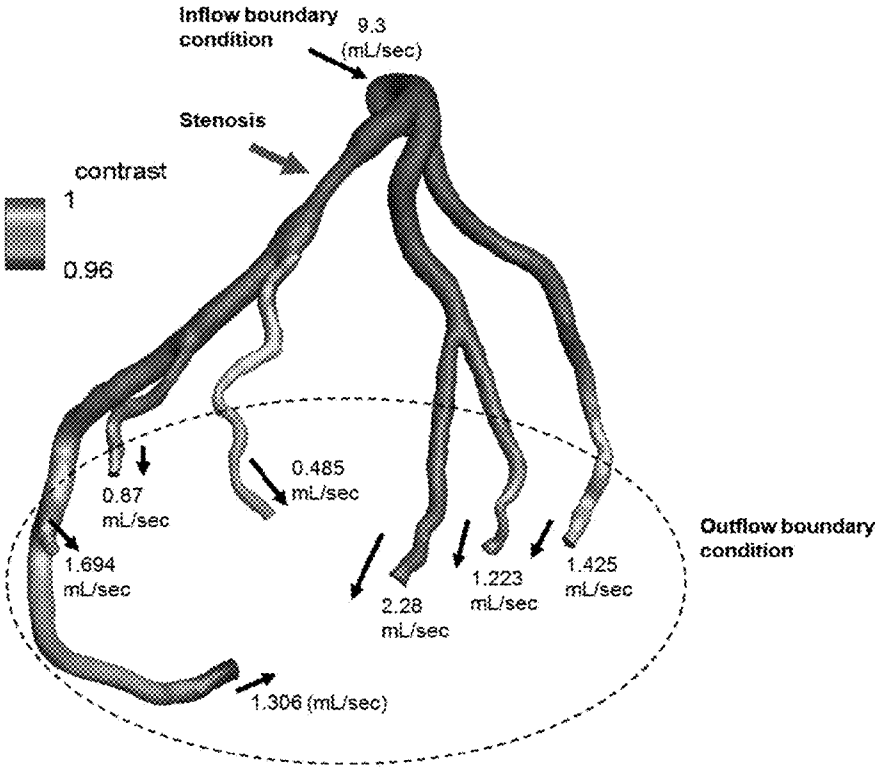
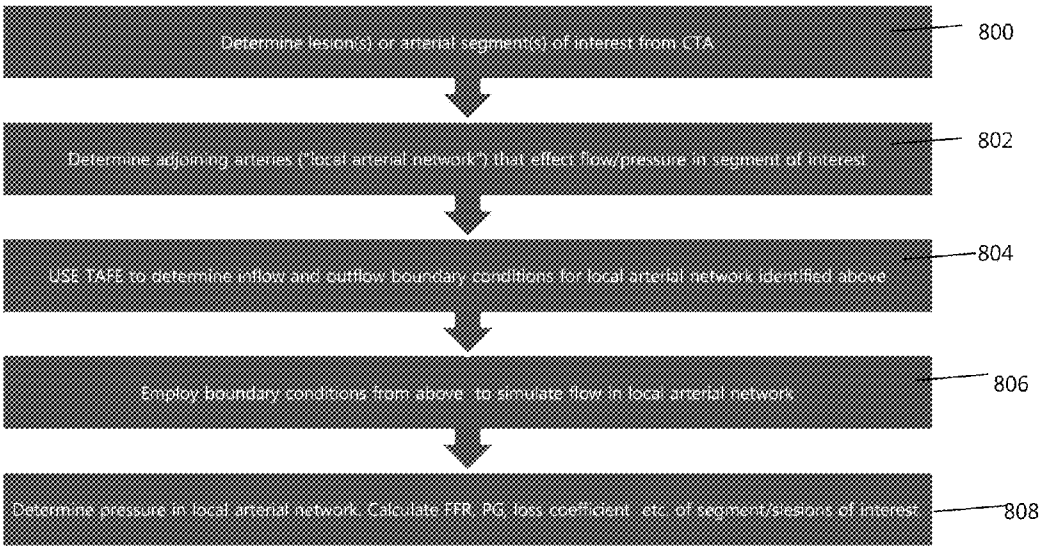

Inflow boundary condition
9.3 (mL/sec)
Stenosis
contrast
1
0.96
0.87 mL/sec
0.485 mL/sec
1.694 mL/sec
2.28 mL/sec
1.223 mL/sec
1.425 mL/sec
Outflow boundary condition
1.306 (mL/sec)

FIG. 12


Determine lesion(s) or arterial segment(s) of interest from CTA
800
Determine adjoining arteries ("local arterial network") that effect flow/pressure in segment of interest
802
Use TAFE to determine inflow and outflow boundary conditions for local arterial network identified above
804
Employ boundary conditions from above to simulate flow in local arterial network
806
Determine pressure in local arterial network. Calculate FFR, PG loss coefficient, etc. of segment/sections of interest
808

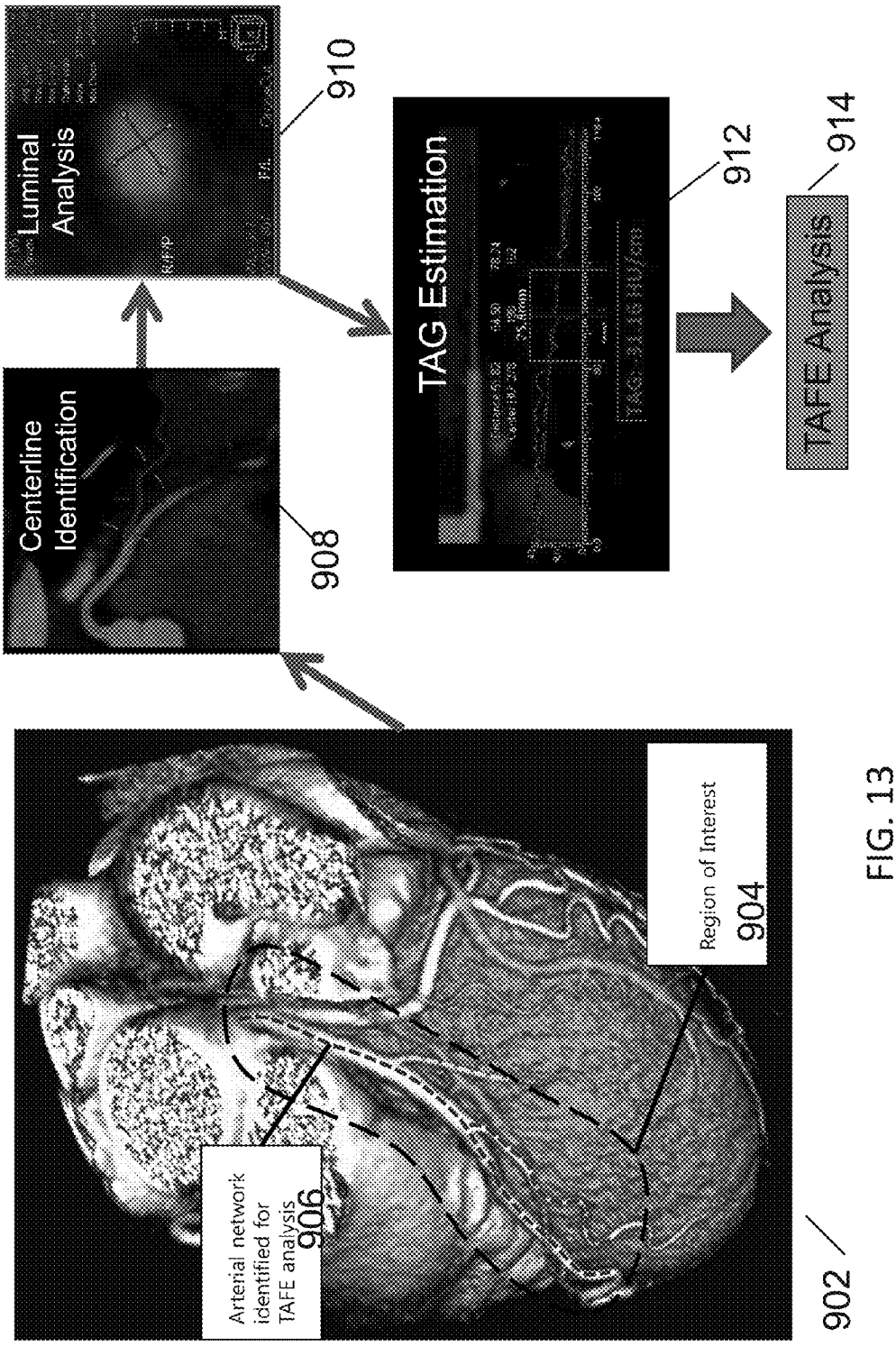

Luminal Analysis
910
Centerline Identification
908
TAG Estimation
912
TAFE Analysis
914
Arterial network identified for TAFE analysis
906
Region of Interest
904
902

FIG. 13

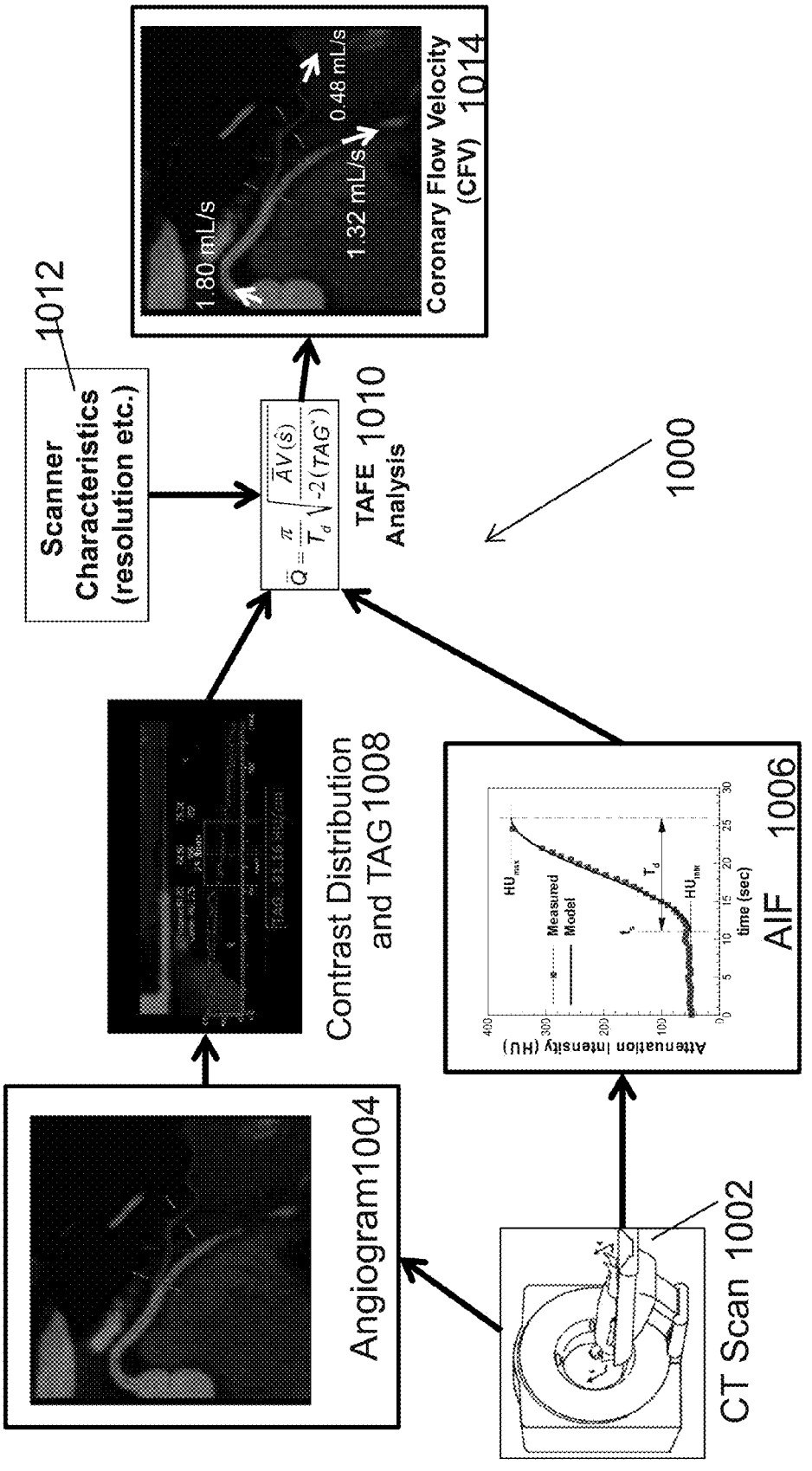

CT Scan 1002
Angiogram1004
Contrast Distribution and TAG1008
AIF 1006
Attenuation Intensity (HU)
time (sec)
Measured
Model
TAFE 1010
Analysis
Scanner Characteristics (resolution etc.)
1012
1000
Coronary Flow Velocity (CFV) 1014
1.80 mL/s
1.32 mL/s
0.48 mL/s

FIG. 14

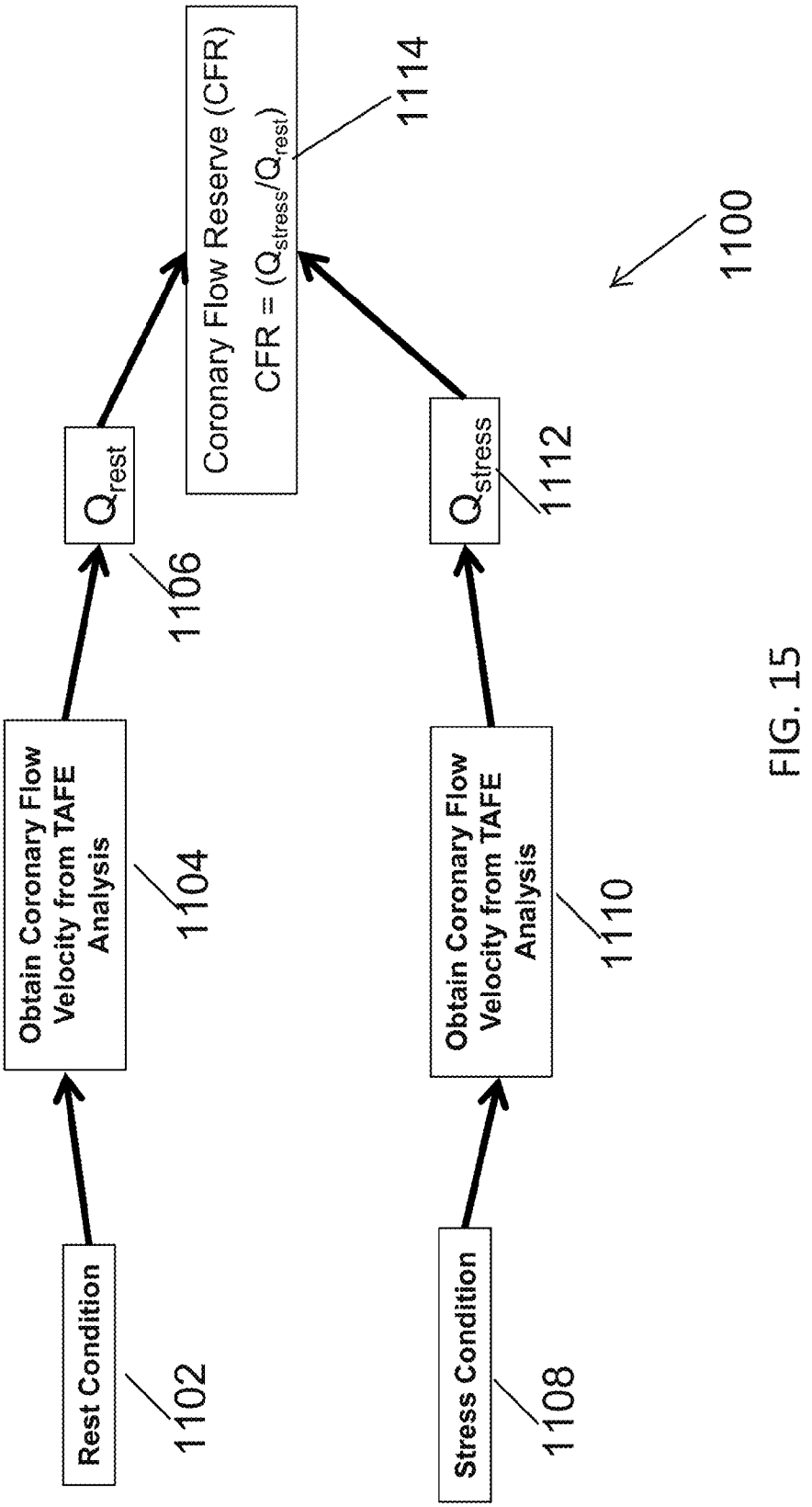

Rest Condition
1102
Obtain Coronary Flow Velocity from TAFE Analysis
1104
Q_{rest}
1106
Coronary Flow Reserve (CFR)
$CFR = (Q_{stress}/Q_{rest})$
1114
1100
Q_{stress}
1112
Obtain Coronary Flow Velocity from TAFE Analysis
1110
Stress Condition
1108

FIG. 15

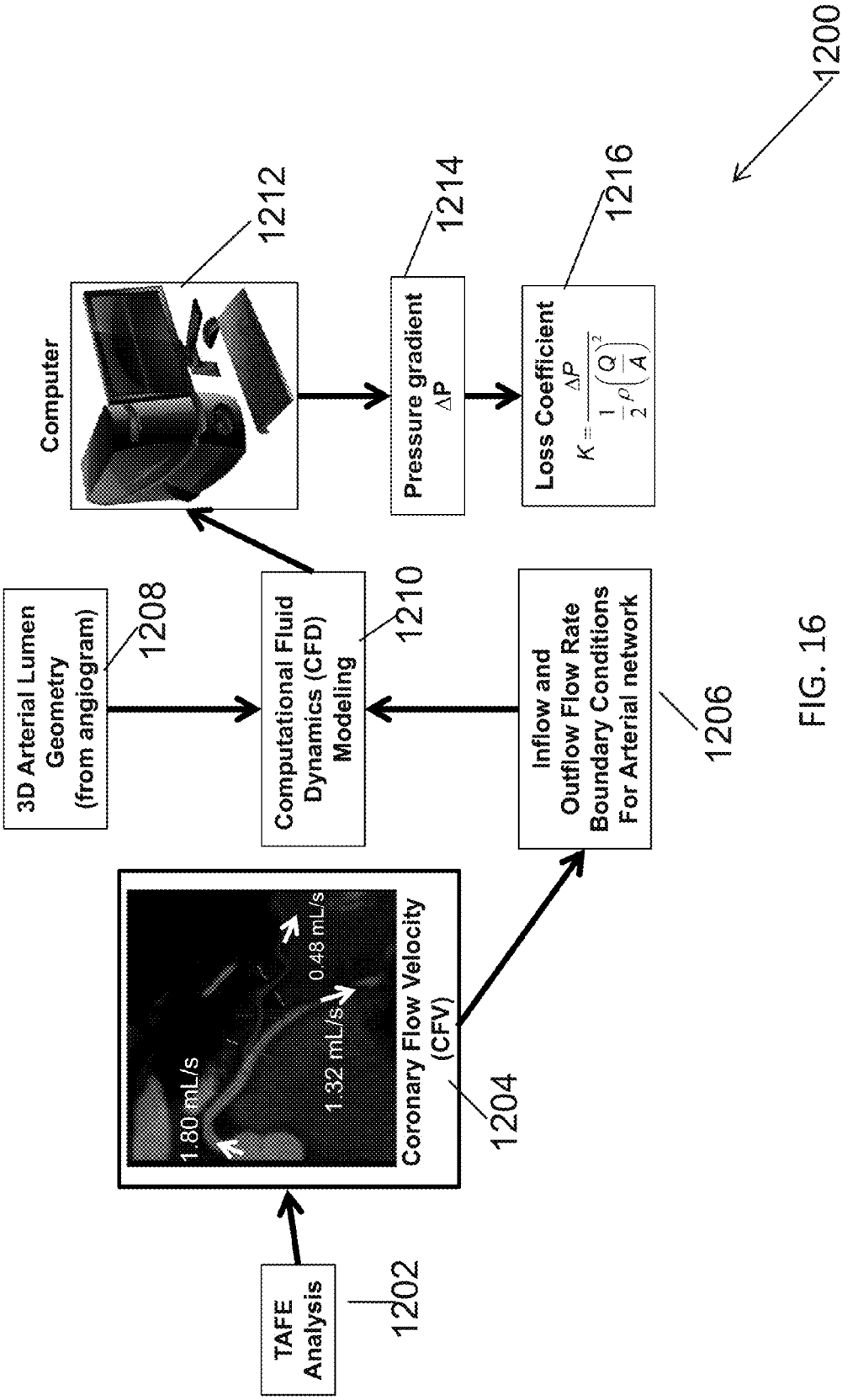

1200
TAFE Analysis
1202
Coronary Flow Velocity (CFV)
1.80 mL/s
1.32 mL/s
0.48 mL/s
1204
3D Arterial Lumen Geometry (from angiogram)
1208
Inflow and Outflow Flow Rate Boundary Conditions For Arterial network
1206
Computational Fluid Dynamics (CFD) Modeling
1210
Computer
1212
Pressure gradient ΔP
1214
Loss Coefficient
$K = \frac{\Delta P}{\frac{1}{2}\rho\left(\frac{Q}{A}\right)^2}$
1216

FIG. 16

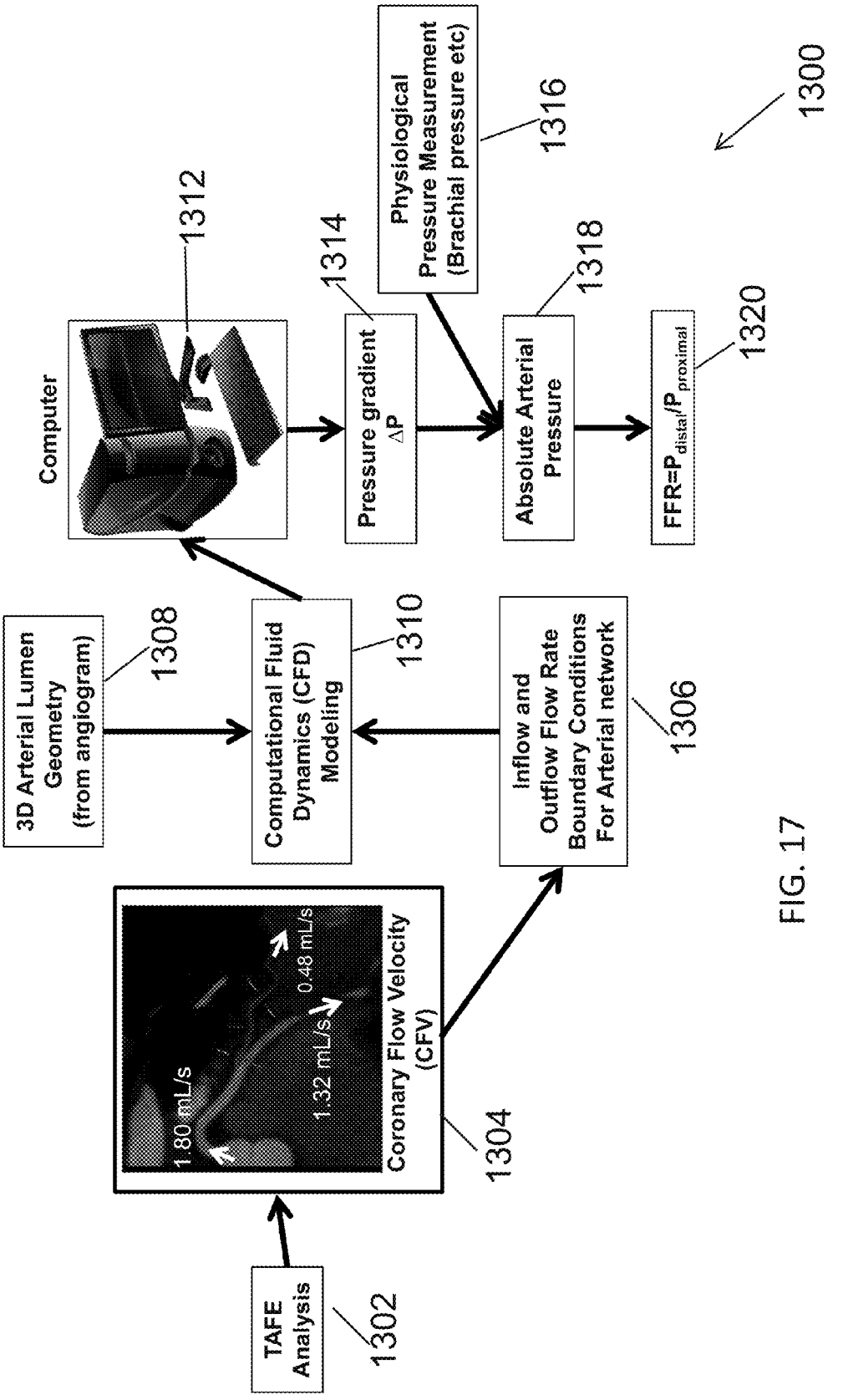

TAFE Analysis
1302
Coronary Flow Velocity (CFV)
1.80 mL/s
0.48 mL/s
1.32 mL/s
1304
3D Arterial Lumen Geometry (from angiogram)
1308
Inflow and Outflow Flow Rate Boundary Conditions For Arterial network
1306
Computational Fluid Dynamics (CFD) Modeling
1310
Computer
1312
Pressure gradient ΔP
1314
Physiological Pressure Measurement (Brachial pressure etc)
1316
Absolute Arterial Pressure
1318
FFR=P distal/P proximal
1320
1300

FIG. 17

METHOD FOR ESTIMATING FLOW RATES AND PRESSURE GRADIENTS IN ARTERIAL NETWORKS FROM PATIENT SPECIFIC COMPUTED TOMOGRAPHY ANGIOGRAM-BASED CONTRAST DISTRIBUTION DATA

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation-in-part of U.S. patent application Ser. No. 13/868,697 filed on Apr. 23, 2013, which claims the benefit of U.S. Provisional Patent Application No. 61/705,422 filed on Sep. 25, 2012, and International Application No. PCT/US2013/037804, all of which are incorporated by reference, herein, in their entirety.

FIELD OF THE INVENTION

[0002] The present invention relates generally to cardiology. More particularly, the present invention relates to a computed tomography cardiac imaging based method for determining flow rates, pressure gradients and fractional flow reserve in an arterial network.

BACKGROUND OF THE INVENTION

[0003] The coronary arteries supply the myocardium, or muscle of the heart with oxygen and nutrients. Over time the coronary arteries can become blocked with cholesterol and other material known as plaque. Coronary artery disease results from this buildup of plaque within the walls of the coronary arteries. Excessive plaque build-up can lead to diminished blood flow through the coronary arteries and low blood flow to the myocardium leading to chest pain, ischemia, and heart attack. Coronary artery disease (CAD) can also weaken the heart muscle and contribute to heart failure, a condition where the heart's efficiency as a pump is compromised. This state can lead to electrical disorders of the heart that increase the possibility for sudden cardiac death. Coronary artery disease is the leading cause of death for both men and women in the United States. CAD affects 17.6 million Americans and results in nearly half a million deaths per year. Despite access to sophisticated diagnostic imaging tests at a cost of $6.3 billion per year, over 1,000,000 US patients are referred to unnecessary invasive catheterization procedures exposing patients to inherent risks and a staggering $8 B financial burden to the US healthcare system.

[0004] There are several different diagnostics that are currently used to assess coronary artery disease and its severity. Non-invasive tests can include electrocardiograms, biomarker evaluations from blood tests, treadmill tests, echocardiography, single positron emission computed tomography (SPECT), and positron emission tomography (PET). Unfortunately, these non-invasive tests do not provide data related to the size of a coronary lesion or its specific effect on coronary blood flow, pressure gradients and fractional flow reserve.

[0005] Quantitative coronary angiography (QCA) is a well-established invasive method for visualizing and quantifying the size of an arterial lesion such as those associated with coronary artery disease. In this method, a radiopaque contrast agent is injected into the blood and an x-ray scan movie is acquired when the contrast agent has traveled into the coronary arteries. Clinicians can use this information to visually examine and to quantify the degree of obstruction. An area obstruction of greater than 70% has traditionally been considered flow-limiting and a candidate for percutaneous coronary intervention (PCI) (also known as coronary angioplasty).

[0006] While the above procedure can be used to visualize and quantify the size of the lesion or the degree of obstruction, it does not necessarily correlate to the functional significance of the lesion, i.e. the degree to which the lesion affect the rate of flow of blood through the artery. Therefore, additional assessments have been developed to determine functional significance of coronary artery lesions. In this regard catheter measured coronary flow velocity (CFV), pressure gradient (PG) i.e. the pressure difference across various arterial segments, coronary flow reserve (CFR), and fractional flow reserve (FFR) are the gold standards for assessment of the functional significance of coronary artery stenosis. These metrics are currently determined using diagnostic cardiac catheterization, an invasive procedure in which a catheter is inserted into a peripheral artery (for instance in a patient's leg) and threaded through the vasculature to the relevant areas of the coronary arteries. FFR is determined by calculating the ratio of the mean blood pressure downstream from a lesion divided by the mean blood pressure upstream from the same lesion. These pressures are measured by inserting a pressure wire into the patient during the diagnostic cardiac catheterization procedure. While this procedure provides an accurate measure of FFR for determining the functional severity of the coronary stenosis, it incurs the risk and cost of an invasive procedure.

[0007] Advances in multi-detector computed tomography (CT) technology now allows noninvasive access to several important factors in regards to coronary event risk: the overall coronary arterial plaque burden, the severity of coronary arterial stenoses, the location and consistency of plaque, and plaque configuration. While anatomic information on CAD by CT is important and has been shown to correlate with patient outcomes, there are other important determinants of patient outcome with CHD including the degree of epicardial blood flow reduction and the extent and severity of provocable myocardial ischemia. CT allows the assessment of coronary anatomy, coronary blood flow, and myocardial perfusion and thus, is uniquely positioned to acquire comprehensive information to guide the evaluation and management of patients with suspected CHD.

[0008] While coronary CTA has been shown to be an accurate test to diagnose the presence of coronary atherosclerosis and percent stenosis it has been shown to poorly predict myocardial ischemia compared to invasive and non-invasive standards. Compared to positron emission tomography, a 50% stenosis by CTA has a positive predictive value for myocardial ischemia of 26% a finding that has been reproduced in a number of studies. Compared to FFR, the invasive gold standard for determining the physiologic significance of a stenosis, percent stenosis by CTA shows only a moderate overall correlation ($r=0.55$) and no significant correlation with lesions ≤ 10 mm in length ($r=0.16$).

[0009] FFR can also be estimated based on a highly complex computational fluid dynamics (CFD) modeling in CT derived, patient-specific coronary artery models. This approach by HeartFlow Inc. and called FFR_{CT}™ requires a high level of sophistication, is computationally intensive, and generally requires that patient-specific data be transmitted out of the hospital environment to a third party vendor. It is also expensive and can take several days to obtain results. Addi-

tionally, recent data testing this approach to predict actual FFR in a multicenter trial have been disappointing. For instance, the study did not meet its pre-specified primary endpoint, which was diagnostic accuracy of >70% of the lower bound of the one-sided 95% CI. One factor contributing to the computational complexity as well as the reduced accuracy of this approach is the lack of precise boundary and input conditions for velocity/flow rate for the artery of interest. An attempts to overcome this is made in FFR_{CT}™ by combining a variety of information including patient-specific ventricular mass, resting coronary flow from population derived relationships and population derived measures of coronary resistances. The above information is combined with physiologic data such as blood pressure, heart rate and computational fluid dynamic (CFD) modeling of the ascending aorta and all the major coronary vessels. This CFD model is also connected with the rest of the circulatory system via lumped-element (or "windkessel") models which contain a number of population derived parameters. However, this approach necessitates the use of ad-hoc parameters and generic (non-patient-specific) factors which can reduce the accuracy of the computed FFR. The quality of the CFD solution is highly sensitive to the computational grid that is employed and the need to generate a grid over the large section of the circulatory system (ascending aorta and coronary arteries) also introduces an additional source of inaccuracy and uncertainty in the results from the CFD calculation.

[0010] It would therefore be advantageous to provide an alternative non-invasive CT based method for assessing hemodynamic parameters such as determining the CFV, PG, CFR, and/or FFR for a given patient's coronary arteries. If such a method is computationally simple and relatively inexpensive, it could be implemented in the scanner or locally on a computer at the scanning facility, and the results made available within a relatively short time (order of minutes) after the completion of the scan. This would also allow the radiologist/clinician to interact in near-real time with the analysis tool. Such an approach would fundamentally change the practice of clinical cardiology and allow clinicians to accurately and rapidly identify specific vessels that are resulting in a reduction in the blood flow to the myocardium.

SUMMARY OF THE INVENTION

[0011] The foregoing needs are met, to a great extent, by the present invention, wherein in one aspect a method for determining functional significance of an arterial stenosis or lesion in a patient including determining an area of interest an arterial network of the patient. The method includes obtaining a CT scan of the patient during an angiogram procedure, resulting in data on the area of interest and using the data obtained from the CT scan to calculate an arterial input function (AIF) for the area of interest. Additionally, the method includes using the data obtained from the CT scan to determine contrast distribution and transluminal attenuation gradient (TAG) for the area of interest and calculating transluminal attenuation flow encoding (TAFE) using contrast distribution, TAG, and AIF. The method also includes modeling flow velocity using TAFE.

[0012] In accordance with an aspect of the present invention, the method includes augmenting the calculation of TAFE with data related to characteristics of the scanner used to obtain the CT scan and programming a non-transitory computer readable medium to execute the method. The method also includes bringing the patient to a rest condition before obtaining the CT scan of the patient during the angiogram and calculating the coronary flow velocity for the area of interest for the patient at the rest condition. The method also includes bringing the patient to a stressed condition before obtaining the CT scan of the patient during the angiogram and calculating the coronary flow velocity for the area of interest for the patient at the stress condition. In addition, the method includes obtaining a CT scan of the patient during an angiogram with the patient at rest and obtaining a CT scan of the patient during an angiogram with the patient under stress and

calculating flow rate for the patient at rest and under stress. The method also includes calculating coronary flow reserve for the area of interest as a ratio of Q_{stress} to Q_{rest}.

[0013] In accordance with another aspect of the present invention, a method for determining functional significance of an arterial stenosis or lesion in a patient includes determining an area of interest an arterial network of the patient and obtaining a CT scan of the patient during an angiogram procedure, resulting in data on the area of interest. The method includes using the data obtained from the CT scan to calculate an arterial input function (AIF) for the area of interest and using the data obtained from the CT scan to determine contrast distribution and transluminal attenuation gradient (TAG) for the area of interest. The method also includes calculating transluminal attenuation flow encoding (TAFE) using contrast distribution, TAG, and AIF. Additionally, the method includes modeling flow velocity using TAFE and using the coronary flow velocity to determine inflow and outflow rate and boundary conditions for the area of interest. The method includes determining 3D arterial lumen geometry, performing CFD modeling for the area of interest using the boundary conditions, inflow and outflow rates, and the 3D arterial lumen geometry, and calculating a pressure gradient for the area of interest using the CFD model. The method also includes using the pressure gradient to determine a loss coefficient for the area of interest.

[0014] In accordance with another aspect of the present invention, the method includes augmenting the calculation of TAFE with data related to characteristics of the scanner used to obtain the CT scan. The method also includes programming a non-transitory computer readable medium to execute the method.

[0015] In accordance with yet another aspect of the present invention, a method for determining functional significance of an arterial stenosis or lesion in a patient including determining an area of interest an arterial network of the patient. The method includes obtaining a CT scan of the patient during an angiogram procedure, resulting in data on the area of interest and using the data obtained from the CT scan to calculate an arterial input function (AIF) for the area of interest. The method also includes using the data obtained from the CT scan to determine contrast distribution and transluminal attenuation gradient (TAG) for the area of interest, calculating transluminal attenuation flow encoding (TAFE) using contrast distribution, TAG, and AIF, and modeling flow velocity using TAFE. Additionally, the method includes using the coronary flow velocity to determine inflow and outflow rate and boundary conditions for the area of interest, determining 3D arterial lumen geometry, performing CFD modeling for the area of interest using the boundary conditions, inflow and outflow rates, and the 3D arterial lumen geometry, calculating a pressure gradient for the area of interest using the CFD model, and using the pressure gradient to determine a loss

coefficient for the area of interest. The method also includes measuring brachial pressure, calculating an absolute arterial pressure, and calculating fractional flow reserve at rest for the patient.

[0016] In accordance with another aspect of the present invention, the method includes augmenting the calculation of TAFE with data related to characteristics of the scanner used to obtain the CT scan. The method also includes programming a non-transitory computer readable medium to execute the method.

[0017] In accordance with still another aspect of the present invention, a system for determining functional significance of an arterial stenosis or lesion in a patient includes a CT scanner configurable to obtain patient specific data related to an area of interest of an arterial network of the patient. The method also includes a non-transitory computer readable medium programmed for determining an area of interest an arterial network of the patient, obtaining the patient specific data on the area of interest, and using the patient specific data obtained from the CT scan to calculate an arterial input function (AIF) for the area of interest. The non-transitory computer readable medium is also programmed for using the patient specific data obtained from the CT scan to determine contrast distribution and transluminal attenuation gradient (TAG) for the area of interest, calculating transluminal attenuation flow encoding (TAFE) using contrast distribution, TAG, and AIF, and modeling flow velocity using TAFE.

[0018] In accordance with yet another aspect of the present invention, the method includes obtaining patient specific data during an angiogram with the patient at rest and obtaining patient specific data during an angiogram with the patient under stress. The method also includes calculating flow rate for the patient at rest and under stress. Additionally, the method includes calculating coronary flow reserve for the area of interest as a ratio of Q_{stress} to Q_{rest}. The method also includes using the coronary flow velocity to determine inflow and outflow rate and boundary conditions for the area of interest, determining 3D arterial lumen geometry, performing CFD modeling for the area of interest using the boundary conditions, inflow and outflow rates, and the 3D arterial lumen geometry, calculating a pressure gradient for the area of interest using the CFD model, and using the pressure gradient to determine a loss coefficient for the area of interest. In addition, the method includes measuring brachial pressure, calculating an absolute arterial pressure, and calculating fractional flow reserve at rest for the patient.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] The accompanying drawings provide visual representations, which will be used to more fully describe the representative embodiments disclosed herein and can be used by those skilled in the art to better understand them and their inherent advantages. In these drawings, like reference numerals identify corresponding elements and:

[0020] FIGS. **1**A and **1**B illustrate two of the many possible arterial input functions that could be considered for the derivation of transluminal attenuation flow encoding (TAFE) formulations.

[0021] FIG. **2** illustrates a schematic diagram of a blood vessel, according to an embodiment of the present invention.

[0022] FIGS. **3**A-**3**B illustrate the relationship between flow and transluminal attenuation gradient (TAG) and TAG and bolus duration, according to an embodiment of the present invention.

[0023] FIG. **4** illustrates an exemplary schematic diagram of a selected portion of an arterial network, segmented, according to an embodiment of the present invention.

[0024] FIGS. **5**A-**5**C illustrate a quantitative example of determining Q from TAFE formulation, according to an embodiment of the present invention.

[0025] FIG. **6** illustrates a flow diagram detailing steps in accordance with a method **500** of the present invention.

[0026] FIGS. **7**A-**7**B illustrate a method for assessing partial volume averaging effect from CFD data, according to an embodiment of the present invention.

[0027] FIG. **8** illustrates a CFD simulated contrast concentration profile for a stenosis with 70% area constriction for different voxel resolutions, according to an embodiment of the present invention.

[0028] FIG. **9** illustrates a summary of the process for implementation of the current method according to an embodiment of the present invention.

[0029] FIG. **10** illustrates graphs modeling results for specific patient data according to an embodiment of the present invention.

[0030] FIG. **11** illustrates a quantitative example of determining Q or TAFE, for the purposes of providing boundary conditions for CFD model according to an embodiment of the present invention

[0031] FIG. **12** illustrates a summary of the process for implementation of the current method for computational modeling (i.e. CFD calculation) according to an embodiment of the present invention.

[0032] FIG. **13** illustrates a flow diagram of steps associated with converting contrast CT angiographic imaging data into TAFE-ready TAG information for a selected arterial network.

[0033] FIG. **14** illustrates a flow diagram of steps associated with obtaining CFV from TAFE for a selected area of interest of an arterial network.

[0034] FIG. **15** illustrates a flow diagram of steps associated with determining coronary flow reserve from TAFE for arteries in the selected arterial network.

[0035] FIG. **16** illustrates a flow diagram of steps associated with obtaining pressure gradient (PG) and loss coefficient (K) from TAFE for arteries in the area of interest in the selected arterial network.

[0036] FIG. **17** illustrates a process of obtaining FFR from TAFE for arteries in the area of interest of the selected arterial network.

DETAILED DESCRIPTION

[0037] The presently disclosed subject matter now will be described more fully hereinafter with reference to the accompanying Drawings, in which some, but not all embodiments of the inventions are shown. Like numbers refer to like elements throughout. The presently disclosed subject matter may be embodied in many different forms and should not be construed as limited to the embodiments set forth herein; rather, these embodiments are provided so that this disclosure will satisfy applicable legal requirements. Indeed, many modifications and other embodiments of the presently disclosed subject matter set forth herein will come to mind to one skilled in the art to which the presently disclosed subject matter pertains having the benefit of the teachings presented in the foregoing descriptions and the associated Drawings. Therefore, it is to be understood that the presently disclosed subject matter is not to be limited to the specific embodiments

disclosed and that modifications and other embodiments are intended to be included within the scope of the appended claims.

[0038] An embodiment in accordance with the present invention provides a method for non-invasively determining the functional severity of arterial stenosis in a selected portion of an arterial network. The method includes gathering patient-specific data related to concentration of a contrast agent within an arterial network of a patient using a coronary computed tomography angiography scan (CCTA). The patient specific data can be gathered from rest or under stress. Alternately, the use of the estimation of a loss coefficient (K) can be used to eliminate the need for data gathered under stress. The patient-specific data is used to calculate a patient-specific transluminal attenuation gradient (TAG) for a selected portion of the arterial network of the patient. The data may be corrected for imaging artifacts at any stage of the analysis. The patient specific TAG is used to determine an estimate of the arterial flow velocity, pressure gradient, arterial flow reserve, and/or fractional flow reserve for the patient. Arterial flow velocity, pressure gradient, arterial flow reserve, and fractional flow reserve can then be used to estimate the functional severity of stenosis.

[0039] More particularly, Equation (1) represents a one-dimensional advection equation for the cross-sectional averaged contrast concentration C which is generally proportional to the arterial attenuation measured in CTCA by HU (Hounsfield Unit):

$$\frac{\partial C}{\partial t}+\frac{Q}{A}\frac{\partial C}{\partial s}\approx 0\Rightarrow \frac{\partial C}{\partial \xi}+Q\frac{\partial C}{\partial \eta}\approx 0, \tag{1}$$

$$\xi=\int Q(t)dt=\overline{Q}\cdot t,$$

$$\eta=\int A(s)ds=\overline{A}\cdot s$$

where $C_{(t,s)}$ is a function of time (t) and axial location (s) in the artery. Assuming $\overline{Q}$ is constant, the solution of Eq. (1) can be approximated as:

$$C(t,s)\approx C_{ostium}(t-V(s)/\overline{Q}) \tag{2}$$

where C_{ostium} is the time variation of concentration at s=0, i.e. coronary ostium, and we call $C_{ostium}(t)$ as an arterial input function (AIF), and V(s) is the vessel volume given by $V(s)=\int_0^s A(s)ds$. Based on Eq. (1) concentration gradient between two axial locations s_1 and s_2 in an artery, which is in fact the TAG, results in:

$$TAG=\frac{\overline{C}_{s_2}-\overline{C}_{s_1}}{s_2-s_1}\approx -\overline{A}\cdot\frac{\partial \overline{C}}{\partial \xi}\approx -\frac{\overline{A}}{\overline{Q}}\cdot\frac{\partial}{\partial t}C_{ostium}(t-V(\hat{s})/\overline{Q}) \tag{3}$$

where $\overline{A}=V_{vessel}/L_{vessel}$ is the average cross-sectional area and ŝ is the axial distance in the artery to the point between the two axial locations. Thus TAG is inversely proportional to the average flow rate, $\overline{Q}$, but also related to the arterial input function (AIF), $C_{ostium}(t)$. FIGS. **1**A and **1**B show two particular types of AIF models that we have considered. AIF profiles are available from CT scans and other representative profiles may also be employed.

[0040] The simplest approximation of the AIF is a linear ramp function (FIG. **1**A);

$$C_{ostium}(t)=C_{min}+(C_{max}-C_{min})\left(\frac{t-t_s}{T_d}\right) \tag{4}$$

where C_{max} and C_{min} are the maximum and minimum concentrations at the ostium, t_s is the arrival time of the bolus, and T_d is the time-delay between the arrival of the bolus and the maximum enhancement. Substituting Equation (4) into Equation (3), the TAG at $t=t_s+T_d$ is estimated as:

$$TAG^*(\mathrm{cm}^{-1})=\frac{TAG}{C_{max}-C_{min}}\sim -\frac{\overline{A}}{\overline{Q}\cdot T_d} \tag{5}$$

where TAG* is TAG normalized by the density rise at the ostium with units of cm^{-1}. Solving for $\overline{Q}$ we arrive at a simple expression for arterial flow (ml/min) as a function of TAG*, the average cross sectional area ($\overline{A}$):

$$\boxed{\overline{Q}=\frac{\overline{A}}{(-TAG^*)\cdot T_d}} \tag{6}$$

In some cases, the AIF can be described by a non-linear function, such as for instance, a cosine function (FIG. **1**B) as:

$$C_{ostium}(t)=C_{min}+1/2(C_{max}-C_{min})[1-\cos(\pi(t-t_s)/T_d)] \tag{7}$$

where C_{max} and C_{min} are the maximum and minimum concentrations at the ostium, t_s is the arrival time of the bolus, and T_d is the time-delay between the arrival of the bolus and the maximum enhancement. Substituting Equation (7) into Equation (3), the TAG at $t=t_s+T_d$ is estimated as:

$$TAG^*(\mathrm{cm}^{-1})=\frac{TAG}{C_{max}-C_{min}}\sim -\frac{1}{2}\frac{\overline{A}}{\overline{Q}}\frac{\pi}{T_d}\sin\left(\frac{\pi V(\hat{s})}{T_d\overline{Q}}\right) \tag{8}$$

$$\approx -\frac{1}{2}\left(\frac{1}{\overline{Q}^2}\right)\left(\frac{1}{T_d^2}\right)\pi^2\overline{A}V(\hat{s})$$

where TAG* is TAG normalized by the density rise at the ostium with units of cm^{-1}. Solving for $\overline{Q}$ we arrive at a simple expression for arterial flow (ml/min) as a function of TAG*, the average cross sectional area ($\overline{A}$), vessel volume (V(ŝ)) and the bolus duration T_d;

$$\boxed{\overline{Q}=\frac{\pi}{T_d}\sqrt{\frac{\overline{A}V(\hat{s})}{-2(TAG^*)}}} \tag{9}$$

[0041] All of the parameters in the above equation are readily available using current conventional CTA exams. The calculation of $\overline{Q}$, as in Eqs. (6) and (9) (as well as other related equations) can also be referred to as transluminal attenuation flow encoding (TAFE). FIG. **2** illustrates a schematic diagram of a blood vessel, labeled with the above parameters. As illustrated in FIG. **2**, the vessel segment (**10**) has a proximal end (**12**) and a distal end (**14**) and a vessel length ŝ extending

at least partially there between. The average cross sectional area $\overline{A}$ can be calculated with the total vessel volume and the vessel length. Vessel volume V can also be determined for the entire vessel, and particularly over vessel length ŝ (**16**).

[0042] By way of example, CFD simulations of contrast dispersion dynamics were performed with the cosine AIF (Eq. 7) in simple models of coronary artery stenosis under physiologic flow conditions to confirm the proposed relationship between TAG and AIF and the fundamental relationship between flow and TAG, as illustrated in FIGS. **3**A-**3**B. These data demonstrate the effect of AIF duration (T_d) on TAG and confirm the linear relationship between TAG and $1/Q^2$ detailed in Equation (8).

[0043] In order to formulate TAFE for an arterial network, first the connectivity of segments of the selected portion of the arterial network, should be identified. FIG. **4** illustrates an exemplary schematic diagram of a selected portion of an arterial network, segmented, according to an embodiment of the present invention. As illustrated in FIG. **4**, the arterial network (**100**) includes segments labeled with (1)-(5). For the linear ramp function AIF (Eq. 4), Eqs. (5) and (6) can be applied to any segments without modification. For the cosine function AIF (Eq. 7), the retarded time for each segment should be considered. Equation (10) shows the representation of TAG for an arbitrary segment (n) in the arterial network for the cosine AIF.

$$TAG_n \approx -\frac{A_n(\hat{s})}{Q_n}\cdot\frac{\partial}{\partial t}C_{ostium}\left(t-\frac{V_n(\hat{s})}{Q_n}-\sum_{upstream}\frac{V_j}{Q_j}\right) \tag{10}$$

Here the summation for the upstream segments should include all the segments up to the coronary ostium. Equation (11) shows the representation of TAG for the segment labeled (3) in the exemplary arterial network. Note that the upstream segments of (3) up to the coronary ostium are (1) and (2).

$$TAG_3 \approx -\frac{A_3(\hat{s})}{Q_3}\cdot\frac{\partial}{\partial t}C_{ostium}\left(t-\frac{V_3(\hat{s})}{Q_3}-\frac{V_2}{Q_w}-\frac{V_1}{Q_1}\right) \tag{11}$$

[0044] Based on the above representation, TAFE based Q can also be determined for a selected portion of an arterial network, as described in the equations below. From Eq. (10), TAG for the segments (n) is given by Equation (12),

$$TAG_n^{*} \approx -\frac{A_n(\hat{s})}{2}\frac{\pi^2}{T_d^2}\frac{1}{Q_n}\left(\frac{V_n(\hat{s})}{Q_n}+\sum_{upstream}\frac{V_j}{Q_j}\right) \tag{12}$$

Here we define scaled TAG which has units of (sec^2/mL),

$$TAG_n'' = \frac{-2\cdot TAG_n^{*}}{A_n(\hat{s})}\frac{T_d^2}{\pi^2} \tag{13}$$

and the branch retarded time, τ (sec)

$$\tau = \sum_{upstream}\frac{V_j}{Q_j}. \tag{14}$$

Finally, the flow rate through the specific arterial segment is given by

$$Q_n = \frac{\tau+\sqrt{\tau^2+4\cdot TAG_n''\cdot V_n(\hat{s})}}{2\cdot TAG_n''}. \tag{15}$$

Equation (12) represents the formula for flow estimation in the segment, n of the selected portion of the arterial network.

[0045] If the detailed information on the cross-sectional area variation, A(s), is not available, vessel volumes can be estimated with only proximal and distal cross-sectional areas by assuming linear tapering. For a tapered vessel schematically illustrated in FIG. **2**, the entire vessel volume can be estimated by

$$V_{vessel} = \frac{L_{vessel}}{3}\times\left(A_{proximal}+A_{distal}+\sqrt{A_{proximal}A_{distal}}\right), \tag{16}$$

where $A_{proximal}$ and A_{distal} are cross sectional areas at the proximal end (**12**) and distal end (**12**), respectively. The vessel volume only up to halfway in the axial direction V(ŝ) is given by

$$V(\hat{s}) = \frac{L_{vessel}}{2}\times\left(\frac{1}{2}A_{proximal}+\frac{1}{12}A_{distal}+\frac{1}{3}\sqrt{A_{proximal}A_{distal}}\right), \tag{17}$$

[0046] Here examples of coronary flow rate estimation are given for an exemplary arterial network illustrated in FIG. **4**. For the linear ramp function AIF, the flow rate through each segment can be estimated by using the same formulation with Eq. (6);

$$Q_n = \frac{\overline{A}_n}{(-TAG_n^{*})\cdot T_d}, \tag{18}$$

For the cosine function AIF, the flow rate is estimated by applying Eq. (15). Since the first segment labeled (1) has no upstream segments, the flow rate Q_1 is given by TAFE as

$$Q_1 = \sqrt{\frac{V_1(\hat{s})}{TAG_1''}}, \tag{19}$$

where $V_1(\hat{s})$ can be determined using Equation (14) and TAG_1'' is determined using Equation (13). Note that Eq. (19) is derived from Eq. (15) with τ=0. Now Q_2 for the segment labeled (2) is given by directly from Eq. (15) as

$$Q_2 = \frac{\tau_1 + \sqrt{\tau_1^2 + 4 \cdot TAG_2'' \cdot V_2(\hat{s})}}{2 \cdot TAG_2''}, \tau_1 = \frac{V_1}{Q_1} \quad (20)$$

where τ_1 is determined using Equation (14) using V_1 and Q_1, as the first vessel segment labeled (1) precedes the second vessel segment labeled (2). Similarly, Q_3 for the third segment labeled (3) is determined by

$$Q_3 = \frac{\tau_2 + \sqrt{\tau_2^2 + 4 \cdot TAG_3'' \cdot V_3(\hat{s})}}{2 \cdot TAG_3''}, \tau_2 = \frac{V_1}{Q_1} + \frac{V_2}{Q_2} \quad (21)$$

τ_2 is calculated using a summation of V_j and Q_j, as both the first segment (1) and the second segment (2) precede the third segment (3). Q_4 for the segment labeled (4) is determined by

$$Q_4 = \frac{\tau_1 + \sqrt{\tau_1^2 + 4 \cdot TAG_4'' \cdot V_4(\hat{s})}}{2 \cdot TAG_4''}, \tau_1 = \frac{V_1}{Q_1} \quad (22)$$

Since the upstream segment to the ostium for the segment (4) is only the segment (1), the branch retarded time for the segment (4) is the same with τ_1. Finally, Q_5 for the segment labeled (5) is given by

$$Q_5 = \frac{\tau_2 + \sqrt{\tau_2^2 + 4 \cdot TAG_5'' \cdot V_5(\hat{s})}}{2 \cdot TAG_5''}, \tau_2 = \frac{V_1}{Q_1} + \frac{V_2}{Q_2} \quad (23)$$

Note that the upstream segments for the segment (5) are (1) and (2).

[0047] FIG. **5** illustrate a quantitative example of determining Q for the real coronary artery model simulation. FIG. **5**A shows the computational fluid dynamics (CFD) simulation results for the flow and contrast dispersion in the real coronary artery model made with CT-scan data. The main LAD (left anterior descending) branch (**400**) includes four segments S1~S4 with 3 bifurcations. FIG. **5**B shows the normalized contrast dispersion along the LAD branch (**400**). FIG. **5**C is the table showing the estimation of flow rate through each segments (S1~S4) using the formulation (**12**), and the estimated flow rates, Q_{TAFE} are compared with the actual flow rate obtained by full CFD simulation, Q_{CFD}.

[0048] FIG. **6** illustrates a flow diagram detailing steps in accordance with a method (**500**) of the present invention. Step (**502**) includes determining at least one section of interest of an arterial network of the patient. In turn, step (**504**) includes identification of at least one upstream segment for each arterial segment in the arterial network. The average areas and volumes for each selected segment are determined using the coronary angiography data in step (**506**). The flow rate in each segment should be determined sequentially from the most upstream branch with Eqs. (13), (14), (15) in step (**508**). The pressure gradient in each segment can be calculated by using the flow rate and the geometrical information in step (**510**). Pressure gradient can be used to determine the functional significance of the arterial stenosis. These steps can be carried out for a given patient in rest and stressed conditions and the flow rate and/or pressure information obtained from these two conditions provides another measure of functional significance of the stenosis. These steps can also be carried out using a computer, non-transitory computer readable medium, or alternately a computing device or non-transitory computer readable medium incorporated into the CT scanner. Indeed, any suitable method of calculation known to or conceivable by one of skill in the art could be used. It should also be noted that while specific equations are detailed herein, variations on these equations can also be derived, and this application includes any such equation known to or conceivable by one of skill in the art. A non-transitory computer readable medium is understood to mean any article of manufacture that can be read by a computer. Such non-transitory computer readable media includes, but is not limited to, magnetic media, such as a floppy disk, flexible disk, hard disk, reel-to-reel tape, cartridge tape, cassette tape or cards, optical media such as CD-ROM, writable compact disc, magneto-optical media in disc, tape or card form, and paper media, such as punched cards and paper tape.

[0049] In CT angiography, the spatial resolution of the CT image is limited by the voxel size of the scanner, which for a modern multi-detector CT scanner is about 0.5 mm^3. This implies for instance that the lumen of a 2 mm diameter section of an artery would be resolved by only about 12 voxels, as illustrated in FIG. **7**B. The voxels at the outer edges of the lumen may be partially located outside the lumen leading to errors in the estimation of the average attenuation factor at any given cross-section. This "mixing" of densities from different structures into the same voxel is known as partial volume-averaging (PVA) and is an inherent limitation for all tomographic imaging modalities.

[0050] To assess these effects from CFD data, the simulation domain is embedded in a virtual voxel lattice and the mean attenuation value is reevaluated at a given axial location (s), as illustrated in FIG. **7**. This procedure mimics the estimation of attenuation in CTCA and HU_{voxel}^* incorporates the effect of PVA inherent in these measurements. Using this approach a simple initial simulation is performed to estimate the effect of PVA and its effect on TAG for a case with area constriction of 70%, as illustrated in FIGS. **5**A and **5**B. More particularly, FIGS. **7**A-**7**B illustrate a method for assessing partial volume averaging effect from CFD data. FIG. **7**A illustrates multiple cross sectional slices in a CFD modeled vessel with a decreasing luminal area. The two cross sectional views illustrated in FIG. **7**B represent simulated CT attenuation according to equations for the theoretical attenuation result considering a 0.5 mm^3 voxel size without and with partial volume averaging, respectively using the following equations.

$$HU_{voxel}(s) = \frac{1}{N_{lumen}(s)} \sum_{i=1}^{N_{lumen}} HU_i, \quad HU_i = \frac{1}{V_i} \int C d\mathrm{V}, \quad (24)$$

$$HU_{voxel}^* = HU_{voxel}(s) / HU_{voxel,ostium}$$

where $HU_{voxel}(s)$ is the mean attenuation value at a given axial location, s. N_{lumen} is number of voxels covering the lumen at the axial location, s, and HU_i is the average attenuation for the i-th voxel, V_i is the volume of the voxel, HU_{voxel}^* is the normalized mean attenuation value and C is the iodine concentration. Results indicate that PVA effect combines with vessel taper to increase the measured TAG and the com-

bination of PVA and vessel curvature/tortuosity generates spurious fluctuations in the attenuation profile. However CFD modeling, which may be coupled with ex-vivo phantom studies can be used to compensate TAFE formulations for PVA effects, described further, herein.

[0051] FIG. **8** illustrates CFD simulated normalized attenuation profiles for 70% area constriction for voxel resolutions of 0.5 mm^3, 0.25 mm^3, and the case for the theoretical profile with infinite spatial resolution. Decreasing spatial resolution (increased partial volume averaging) tends to cause overestimation of TAG. To account for the artificially higher TAG values that result due to partial volume effects as shown in FIG. **8**, a correction factors, δ_1, and δ_2 can be implemented that accounts for the CTA voxel resolution. From computational simulations at multiple spatial resolutions and fixed taper, δ_1 is approximately equal to 3.5 for the voxel resolution most typically used (approximately 0.4×0.4×0.4 mm).

$$\bar{Q} = \frac{\delta_1 \bar{A}}{-(TAG^* + \delta_2)\cdot T_d} \text{ (for linear } AIF\text{)}, \qquad \bar{Q} = \frac{\pi}{T_d}\sqrt{\frac{\delta_1 \bar{A} V(\hat{s})}{-2(TAG^* + \delta_2)}} \text{ (for cosine } AIF\text{)} \tag{25}$$

[0052] By way of example, this section will outline the process of applying Eq. (25) to real-world CT angiography data for absolute flow measurement in a patient with LAD disease, as illustrated in FIG. **9**. As indicated in Equation (25), after the 3D CT acquisition there are a total of 4 variables that need to be extracted from the CT data for flow calculation. Three of these variables ($\bar{A}$,V(ŝ), TAG*) come directly from static CTCA images of the vessels, as illustrated in (**704**) and (**706**), and one variable (T_d) is derived from the AIF (temporal contrast concentration) following contrast injection shown in (**708**) and (**710**). To summarize the process in FIG. **9**, following 3D isotemporal acquisition of the whole heart is illustrated in (**702**), multiplanar reformations of the three primary coronary vessels are generated that provide a straight vessel view as illustrated in (**704**). Software is then used to measure the luminal density as a function of vessel length between two user-defined proximal and distal boundary locations. The variable V(ŝ) is defined as the vessel volume from the ostium to the user-defined points and $\bar{A}$ is defined as the average cross-sectional area over the length of the vessel. TAG is defined as the slope of the normalized luminal density versus distance plot, as illustrated in (**706**). The temporal element of contrast dispersion needed for Equation (21) is taken from the time-density curve shown in (**710**) that is measured in the descending aorta, as illustrated in (**708**) prior to scanning to allow optimal timing or triggering of the CTA acquisition. While it is usually not used in standard CTCA, this temporal AIF data can be stored in the CT raw data and is easily reconstructed for the determination of T_d. The parameters for PVA correction, δ_1 and δ_2 which depend on the scanner and voxel resolution, may be determined by doing calibration test. Once all parameters have been isolated, Equation (25) can be used to calculate arterial flow.

[0053] In addition to CFD simulations to guide the formulation above, Equation (25) can also, for example, be used to calculate absolute blood flow in an ischemic canine model of LAD stenosis and in patients with obstructive and non-obstructive coronary artery disease. However, these applications are simply examples and are not to be considered limiting.

[0054] By way of example, the approach described in [0035] was applied to canine CT measurements. This data set consisted of 4 canine models of LAD stenosis that underwent CT imaging using a prototype 256-CT scanner with simultaneous microsphere injections. Despite the limited temporal resolution of this prototype scanner, image analysis and application of Equation (25) demonstrated resting coronary blood flow (LAD+LCx) of 29±10 ml/min. While coronary flow probes were not used in this study, this result is quite similar to direct probe-derived measurements in similar sized canines previously published, 31±8 ml/min.

[0055] Furthermore, there was a good correlation between flow derived from Eq. (25) and microsphere MBF ($R=0.89$, $p<0.001$). Thus, in the limited preclinical pilot data set, Equation (21) appears to provide the ability to accurately determine territorial flows supplied by the LAD and LCx and provides absolute total coronary flow values that are in agreement with those reported in the literature.

[0056] By way of example, the approach described in [0035] was applied to patient datasets. This clinical data set consisted of 9 patients enrolled in the CORE320 multicenter trial conducted at Johns Hopkins University. Patients in CORE320 underwent coronary CTA, stress CT and SPECT myocardial perfusion imaging. All AIF data was collected. FIG. **1** shows an AIF function for a patient included in this analysis demonstrating a perfect match of the linear or cosine AIF models, which gave further confidence to apply Equation (25) to the data set. Average total coronary flow (LAD+LCX+RCA) was 123.4±66 ml/min. When corrected for myocardial mass, total myocardial flow was 0.86±0.39 ml/g/min. These data are nearly identical with resting MBF seen in humans by O15-PET. When comparing patients with normal vs. abnormal perfusion by the reference standard (SPECT myocardial perfusion imaging), TAG alone showed no significant difference between ischemic and non-ischemic territories ($p=0.93$). However, when TAG was normalized by the density rise at the ostium and Equation (25) applied, there was a statistically significant difference in total coronary flow, 142 ml/min vs. 71 ml/min in normal and ischemic patients, respectively ($p=0.04$, See FIG. **9**). Results from these preliminary data in human CT studies indicate Eq. (25) accurately measures coronary blood flow and can predict myocardial perfusion abnormalities determined by SPECT; while TAG, without accounting for the AIF, cannot.

[0057] Equation (25) has been derived for the specific types of AIF from simplified computational models and preliminary assessment of this expression against limited sets of canine and human data are highly promising and demonstrate feasibility. However, the expression can be further generalized to incorporate effects of arbitrary AIF and flow wave form function. In general the solution of the convection equation, Eq (1) can be given by

$$\bar{C}(t,\eta) = C_{ostium}(t-\tau)\int_{t-\tau}^{t} Q(t)dt = \eta \tag{26}$$

where τ is a retarded time and Q(t) is arbitrary time varying flow rate. One can express the time varying flow rate and its time integral by the following forms;

$$Q(t) = \bar{Q}\cdot q(t), \int Q(t)dt = \bar{Q}\int q(t)dt = \bar{Q}\cdot g(t), \tag{27}$$

where $\bar{Q}$ is average flow rate. From Eqs. (3), (26) and (27) we can obtain the following expressions for the average flow rate;

$$\bar{Q} = \frac{\eta}{g(t) - g(\tau')}, \qquad (28)$$

$$\bar{Q} = \frac{\bar{A}}{-TAG \cdot q(\tau')} \frac{\partial}{\partial t} C_{ostium}(\tau'),$$

where $\tau'=t-\tau$. Since the above system of equations has two unknowns; $\tau', \bar{Q}$ if TAG is measured, it can be solved to find the average flow rate $\bar{Q}$ for any AIF and flow wave form. Thus the system of equations, Eq. (28) is the general TAFE formula for arbitrary AIF and flow wave form.

[0058] While FFR is considered the gold standard in assessment of stenosis, the methods described above could be applied to obtain other metrics of stenotic severity. In particular an estimate of the pressure gradient (PG) within the section of interest of the arterial network of the patient could be obtained using the arterial flow velocity, the arterial input function, information on the arterial luminal area, position and location within the artery; and once the pressure drop across the stenosis and the flow velocity are determined using the above method, the functional severity of the stenosis could also be determined in terms of a loss coefficient defined as

$$K = \frac{\Delta P}{\frac{1}{2}\rho\left(\frac{Q}{A}\right)^2} \qquad (29)$$

where Q is the flow rate upstream of the stenosis (obtained from TAFE) and A is the lumen area upstream of the stenosis. The advantage of the above measure is that it is virtually flow-rate independent and can be obtained with a single scan at rest condition (i.e. no need for a second scan at maximal hyperemia). The estimates of pressure drop across the stenosis may also be converted to FFR.

[0059] A method according to the present invention provides for obtaining a patient specific transluminal attenuation gradient (TAG) over a calcium-free section of the artery and determining a time variation of a contrast at a predetermined vascular or ventricular location (called the arterial input function or input bolus profile). The method also includes calculating an estimate of the fractional flow reserve (FFR) within the artery using the TAG and AIF and using the FFR to determine the functional significance of the arterial stenosis in vessels with severe calcification. The technique can include a method for correcting the TAG values for the effects of CT spatial resolution and partial volume averaging. The technique also includes a method for correcting the TAG values for the effects of vessel tortuosity, curvature and partial volume averaging. The method can also include protocol for determining a functional significance of arterial stenosis includes obtaining contrast concentration versus time data via a dynamic CT acquisition to calculate flow velocity.

[0060] The flow velocity may be obtained in the main artery as well as all of the sub branches for which contrast measurements are available. Thus, the method can provide the relative magnitude of the flow rate in the various branches and this information may be combined with other information or mathematical models to develop alternate measure of the functional significance of the coronary stenosis.

[0061] The flow velocity obtained from TAG (via TAFE) may be used to provide boundary or initial conditions for computational models (for example computational fluid dynamics (CFD) models) of the vasculature. The computational model could then be used to predict the pressure distribution and associated metrics such as FFR and PG. This eliminates the need for modeling of upstream (aorta, etc.) and downstream vasculature and reduces the computational expense and complexity of CFD based modeling. FIGS. **10** and **11** show an embodiment of this approach: TAFE takes contrast dispersion data from CTA and coverts it into flow-rate for all relevant vessels. These flow rates then generate inflow and outflow boundary conditions for a computational model.

[0062] The method described here could be used in normal vessels, in abnormal vessels as well as vessels subject to medical therapies such as medication, stents, grafts. The method can be applied in rest as well as other conditions such as stress (induced via exercise or medication).

[0063] The measurement of the contrast may be triggered by variety inputs including simultaneously measured ECG.

[0064] FIG. **12** illustrates a summary of the process for implementation of the current method for computational modeling (i.e. CFD calculation) according to an embodiment of the present invention. Step **800** is determining a lesion or arterial segment of interest from CTA. In step **802** adjoining arteries in a local arterial network that effect flow or pressure in a segment of interest are determined. Step **804** includes using TAFE to determine inflow and outflow boundary conditions for the local arterial network identified above. In step **806** boundary conditions are used to simulate blood flow in the local arterial network, and in step **808** the pressure in the local arterial network is determined and FFR, PG, loss coefficient are determined for each segment or lesion of interest.

[0065] FIG. **13** illustrates a flow diagram of steps associated with converting contrast CT angiographic imaging data into TAFE-ready TAG information for a selected arterial network.

[0066] Step **902** illustrates a region of interest **904** and an arterial network **906** disposed within the region of interest. The arterial network **906** is identified for TAFE analysis. In step **908** a centerline is identified for the arterial network identified for analysis. A luminal analysis is done in step **910**. In step **912** this information is used to calculate a TAG estimation, and in step **914** a TAFE analysis is executed on the data.

[0067] FIG. **14** illustrates a flow diagram of steps associated with obtaining CFV from TAFE for a selected area of interest of an arterial network. In the flow diagram **1000**, a CT scan is performed in step **1002** in order to gather data related to the patient. In step **1004** an angiogram is produced with the data related to the patient, and in step **1006** AIF is calculated and graphed using the data related to the patient. In step **1008**, contrast distribution and TAG is calculated from the angiogram. TAG and AIF are used to calculate the TAFE analysis in step **1010**. The TAFE analysis of step **1010** can also include input based on scanner characteristics, such as resolution, as noted in step **1012**. The TAFE analysis is used to determine coronary flow velocity in step **1014**.

[0068] FIG. **15** illustrates a flow diagram of steps associated with determining coronary flow reserve from TAFE for arteries in the selected arterial network. In the flow diagram **1100**, data must be obtained from the patient for the arterial network of interest, at both rest and stress. In step **1102**, the patient is brought to a rest condition. In this state, coronary flow velocity is obtained from a TAFE analysis, as described

above, in step **1104**. In step **1106**, Q_{rest} is determined, also as described above. In step **1108**, the patient is brought into a stress condition. In the stress state, coronary flow velocity is obtained from a TAFE analysis, as described above, in step **1110**. In step **1112**, Q_{stress} is determined, also as described above. Coronary flow reserve (CFR) is determined in step **1114**, as the ratio between Q_{stress} and Q_{rest}.

[0069] FIG. **16** illustrates a flow diagram of steps associated with obtaining pressure gradient (PG) and loss coefficient (K) from TAFE for arteries in the area of interest in the selected arterial network. In the flow diagram **1200**, the TAFE analysis process described above, is executed in step **1202**. In step **1204**, the TAFE analysis is used to determine coronary flow velocity, also as described above. In step **1206**, inflow and outflow rate boundary conditions are determined for the area of interest in the selected arterial network. 3D arterial lumen geometry is calculated from the angiogram and in step **1208**, the 3D arterial lumen geometry and the information about CFV and inflow and outflow rate boundary conditions are used to execute computational fluid dynamics (CFD) modeling of the arterial network of interest, in step **1210**. A computing device, server, tablet, smartphone, or other computer can be used to execute these steps, as illustrated in step **1212**. Pressure gradient (ΔP) is calculated in step **1214** and loss coefficient is calculated in step **1216**, using EQ. 29.

[0070] FIG. **17** illustrates a process of obtaining FFR from TAFE for arteries in the area of interest of the selected arterial network. In the flow diagram **1300**, the TAFE analysis process described above, is executed in step **1302**. In step **1304**, the TAFE analysis is used to determine coronary flow velocity, also as described above. In step **1306**, inflow and outflow rate boundary conditions are determined for the area of interest in the selected arterial network. 3D arterial lumen geometry is calculated from the angiogram and, in step **1308**, the 3D arterial lumen geometry and the information about CFV and inflow and outflow rate boundary conditions are used to execute computational fluid dynamics (CFD) modeling, in step **1310**. A computing device, server, tablet, smartphone, or other computer can be used to execute these steps, as illustrated in step **1312**. Pressure gradient (ΔP) is calculated in step **1314**. In step **1316**, physiological pressure measurements, such as brachial pressure are obtained. The pressure gradient (ΔP) and the physiological pressure measurements are used to estimate absolute pressure at the coronary ostium and combined with the CFD modeling to calculate absolute arterial pressure in the artery of interest in step **1318**. In step **1320**, FFR is calculated as the ratio between P_{distal} and $P_{proximal}$.

[0071] The many features and advantages of the invention are apparent from the detailed specification, and thus, it is intended by the appended claims to cover all such features and advantages of the invention which fall within the true spirit and scope of the invention. Further, since numerous modifications and variations will readily occur to those skilled in the art, it is not desired to limit the invention to the exact construction and operation illustrated and described, and accordingly, all suitable modifications and equivalents may be resorted to, falling within the scope of the invention.

What is claimed is:

1. A method for determining functional significance of an arterial stenosis or lesion in a patient comprising:

determining an area of interest an arterial network of the patient;

obtaining a CT scan of the patient during an angiogram procedure, resulting in data on the area of interest;

using the data obtained from the CT scan to calculate an arterial input function (AIF) for the area of interest;

using the data obtained from the CT scan to determine contrast distribution and transluminal attenuation gradient (TAG) for the area of interest;

calculating transluminal attenuation flow encoding (TAFE) using contrast distribution, TAG, and AIF; and,

modeling flow velocity using TAFE.

2. The method of claim **1** further comprising augmenting the calculation of TAFE with data related to characteristics of the scanner used to obtain the CT scan.

3. The method of claim **1** further comprising programming a non-transitory computer readable medium to execute the method.

4. The method of claim **1** further comprising bringing the patient to a rest condition before obtaining the CT scan of the patient during the angiogram.

5. The method of claim **4** further comprising calculating the coronary flow velocity for the area of interest for the patient at the rest condition.

6. The method of claim **1** further comprising bringing the patient to a stressed condition before obtaining the CT scan of the patient during the angiogram.

7. The method of claim **6** further comprising calculating the coronary flow velocity for the area of interest for the patient at the stress condition.

8. The method of claim **1** further comprising obtaining a CT scan of the patient during an angiogram with the patient at rest and obtaining a CT scan of the patient during an angiogram with the patient under stress.

9. The method of claim **6** further comprising calculating flow rate for the patient at rest and under stress.

10. The method of claim **7** further comprising calculating coronary flow reserve for the area of interest as a ratio of Q_{stress} to Q_{rest}.

11. A method for determining functional significance of an arterial stenosis or lesion in a patient comprising:

determining an area of interest an arterial network of the patient;

obtaining a CT scan of the patient during an angiogram procedure, resulting in data on the area of interest;

using the data obtained from the CT scan to calculate an arterial input function (AIF) for the area of interest;

using the data obtained from the CT scan to determine contrast distribution and transluminal attenuation gradient (TAG) for the area of interest;

calculating transluminal attenuation flow encoding (TAFE) using contrast distribution, TAG, and AIF;

modeling flow velocity using TAFE;

using the coronary flow velocity to determine inflow and outflow rate and boundary conditions for the area of interest;

determining 3D arterial lumen geometry;

performing CFD modeling for the area of interest using the boundary conditions, inflow and outflow rates, and the 3D arterial lumen geometry;

calculating a pressure gradient for the area of interest using the CFD model; and,

using the pressure gradient to determine a loss coefficient for the area of interest.

12. The method of claim **11** further comprising augmenting the calculation of TAFE with data related to characteristics of the scanner used to obtain the CT scan.

13. The method of claim **11** further comprising programming a non-transitory computer readable medium to execute the method.

14. A method for determining functional significance of an arterial stenosis or lesion in a patient comprising:

determining an area of interest an arterial network of the patient;

obtaining a CT scan of the patient during an angiogram procedure, resulting in data on the area of interest;

using the data obtained from the CT scan to calculate an arterial input function (AIF) for the area of interest;

using the data obtained from the CT scan to determine contrast distribution and transluminal attenuation gradient (TAG) for the area of interest;

calculating transluminal attenuation flow encoding (TAFE) using contrast distribution, TAG, and AIF;

modeling flow velocity using TAFE;

using the coronary flow velocity to determine inflow and outflow rate and boundary conditions for the area of interest;

determining 3D arterial lumen geometry;

performing CFD modeling for the area of interest using the boundary conditions, inflow and outflow rates, and the 3D arterial lumen geometry;

calculating a pressure gradient for the area of interest using the CFD model;

using the pressure gradient to determine a loss coefficient for the area of interest;

measuring brachial pressure;

calculating an absolute arterial pressure; and,

calculating fractional flow reserve at rest for the patient.

15. The method of claim **14** further comprising augmenting the calculation of TAFE with data related to characteristics of the scanner used to obtain the CT scan.

16. The method of claim **14** further comprising programming a non-transitory computer readable medium to execute the method.

17. A system for determining functional significance of an arterial stenosis or lesion in a patient comprising:

a CT scanner configurable to obtain patient specific data related to an area of interest of an arterial network of the patient;

a non-transitory computer readable medium programmed for:

determining an area of interest an arterial network of the patient;

obtaining the patient specific data on the area of interest;

using the patient specific data obtained from the CT scan to calculate an arterial input function (AIF) for the area of interest;

using the patient specific data obtained from the CT scan to determine contrast distribution and transluminal attenuation gradient (TAG) for the area of interest;

calculating transluminal attenuation flow encoding (TAFE) using contrast distribution, TAG, and AIF; and,

modeling flow velocity using TAFE.

18. The system of claim **17** further comprising obtaining patient specific data during an angiogram with the patient at rest and obtaining patient specific data during an angiogram with the patient under stress.

19. The system of claim **18** further comprising calculating flow rate for the patient at rest and under stress.

20. The system of claim **17** further comprising calculating coronary flow reserve for the area of interest as a ratio of Q_{stress} to Q_{rest}.

21. The system of claim **17** further comprising:

using the coronary flow velocity to determine inflow and outflow rate and boundary conditions for the area of interest;

determining 3D arterial lumen geometry;

performing CFD modeling for the area of interest using the boundary conditions, inflow and outflow rates, and the 3D arterial lumen geometry;

calculating a pressure gradient for the area of interest using the CFD model; and,

using the pressure gradient to determine a loss coefficient for the area of interest.

22. The system of claim **21** further comprising:

measuring brachial pressure;

calculating an absolute arterial pressure; and,

calculating fractional flow reserve at rest for the patient.

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