Appendix

Concept of the Modelflow aortic age:

Langewouters et al have demonstrated a strong linear relationship between parameters of an arctangent model of human aortic pressure-area relationship vs. chronological age (1, 2). With this arctangent model of the aortic pressure-area relationship, Wesseling et al established the mathematical approach to compute aortic input impedance via a non-linear, time-varying, three-element Windkessel Model (3). Thus, this mathematically generated aortic input impedance is determined by chronological age, while aortic input impedance characterizes a dynamic relationship between aortic blood flow and pressure, and thus estimates stroke volume as an integration of aortic flow from any given arterial pressure waveforms (3). As a consequence, stroke volume is estimated from subject chronological age and any given arterial pressure waveform via the mathematical Windkessel model of aortic input impedance. This entire process is called the Modelflow system (Fig. A).

The critical point for the concept of the Modelflow aortic age is the fact that in the Modelflow system the estimated stroke volume (SV) can be considered as a function of subject age (Age) once arterial pressure waveforms are given, while the function itself is determined by the shape and value of the arterial pressure waveform; SV=F(Age) (Fig. B). If each SV value corresponds to exactly one Age value, the function is invertible; Age=F^{-1}(SV), and thus the Modelflow aortic age can be generated from stroke volume. In order to confirm a one-to-one relationship between Modelflow Age vs. SV, the Modelflow Age-SV relationships were plotted across a variety of arterial pressure waveforms obtained from young and elderly individuals including those during lower body negative pressures with Modelflow Age ranging 20-90 yrs. We found a strong negative linear relationship between the Modelflow Age and SV (SV=-

a*Age+b, a, b>0) for all arterial pressure waveforms. One representative relationship curve is shown in Fig. C. This result suggests that the linear relationship is universal at least in a healthy population while the slopes are individually different dependent on each arterial pressure waveform profile. This negative linear relationship implicates that as the Modelflow aortic age increases, that is, the aorta becomes stiffer, the Modelflow stroke volume becomes smaller at a given arterial pressure waveform. In the present study, the Modelflow aortic age was estimated by an inverse function, which was derived from each arterial pressure waveform, with an independent variable of stroke volume measured by the thermodilution;

$$\text{Modelflow aortic age} = (b - SV)/a \quad a, b>0$$

Conceptually, the Modelflow aortic age is the age which provides the aortic input impedance that best characterizes the dynamic relationship between measured aortic flow (i.e. stroke volume) and pressure waveform. The key difference between Modelflow stroke volume vs. aortic age estimation is that stroke volume calculation requires chronological age (true age) while aortic age calculation requires measured stroke volume (true stroke volume) at any given arterial pressure waveforms (Fig C).

References

1. **Langewouters GJ, Wesseling KH, and Goedhard WJ**. The pressure dependent dynamic elasticity of 35 thoracic and 16 abdominal human aortas in vitro described by a five component model. *Journal of biomechanics* 18: 613-620, 1985.

2. **Langewouters GJ, Wesseling KH, and Goedhard WJ**. The static elastic properties of 45 human thoracic and 20 abdominal aortas in vitro and the parameters of a new model. *Journal of biomechanics* 17: 425-435, 1984.

3. **Wesseling KH, Jansen JR, Settels JJ, and Schreuder JJ**. Computation of aortic flow from pressure in humans using a nonlinear, three-element model. *J Appl Physiol* 74: 2566-2573, 1993.

Figure A: The Schematic explanation for the Modelflow system to estimate ascending aortic flow and stroke volume. This system uses the aortic pressure-area relationship estimated from chronological age with the known age-related changes in the aortic properties. Nonlinear, time-varying three elements Windkessel Model generates aortic input impedance which estimates ascending aortic flow and thus stroke volume from the arterial waveforms. To summarize, the Modelflow system generates stroke volume as an output signal from arterial pressure waveform and chronological age as input signals.

Figure B: The Schematic explanation for the Modelflow system to estimate Modelflow aortic age. The Modelflow system generates "aortic age" as an output signal from arterial pressure waveform and directly measured stroke volume as input signals.

Figure C: One representative data for the relationship between Modelflow stroke volume and aortic age from one sedentary elderly subject. As seen in the figure, a strong linear relationship exists between Modelflow stroke volume and aortic age. Dot arrows show the pathway to estimate stroke volume from the chronological (true) age with given arterial waveform while straight arrows show the pathway to estimate aortic age from the measured (true) stroke volume. If the dot and straight lines are identical, it means that the Modelflow aortic age is equivalent to subject's chronological age, which consequently promises accurate stroke volume estimation with the Modelflow system.

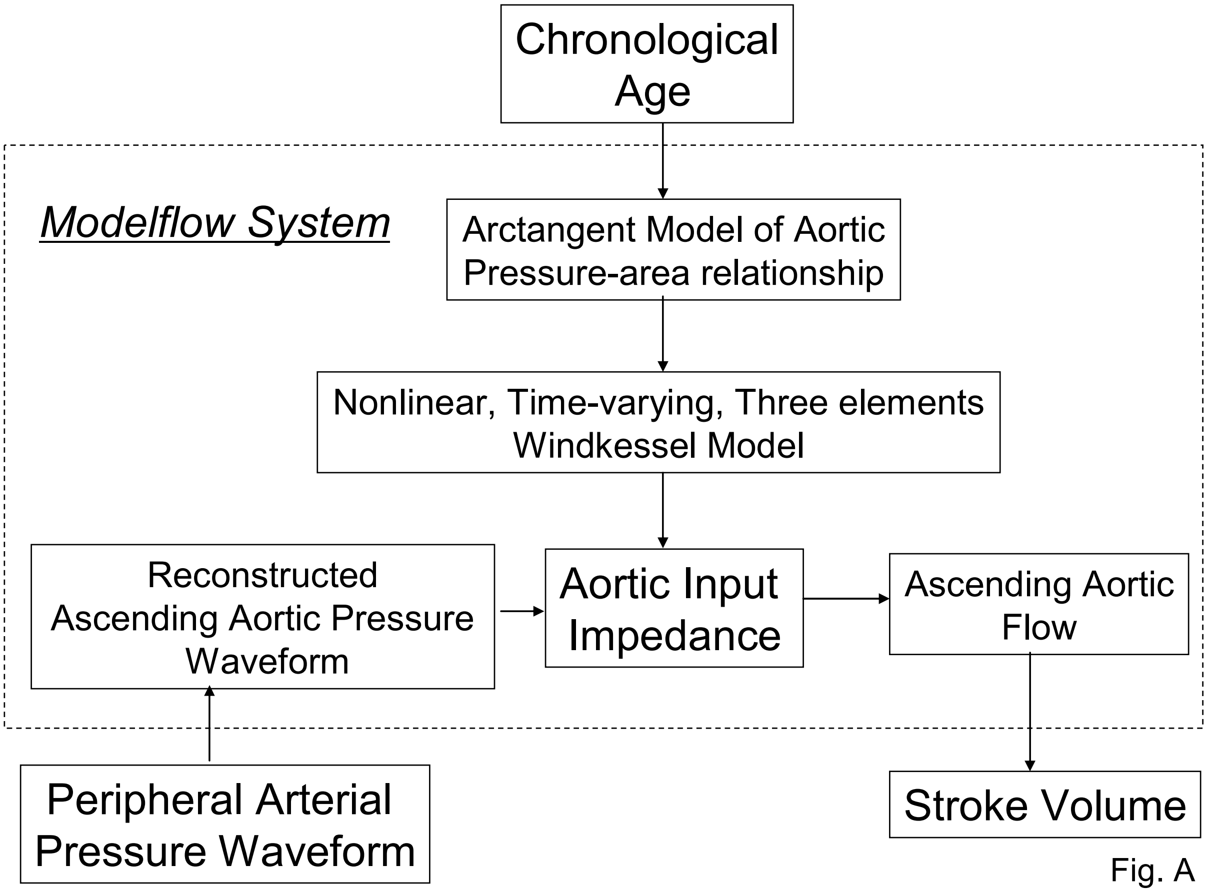
Chronological Age
Modelflow System
Arctangent Model of Aortic Pressure-area relationship
Nonlinear, Time-varying, Three elements Windkessel Model
Reconstructed Ascending Aortic Pressure Waveform
Aortic Input Impedance
Ascending Aortic Flow
Peripheral Arterial Pressure Waveform
Stroke Volume

Fig. A

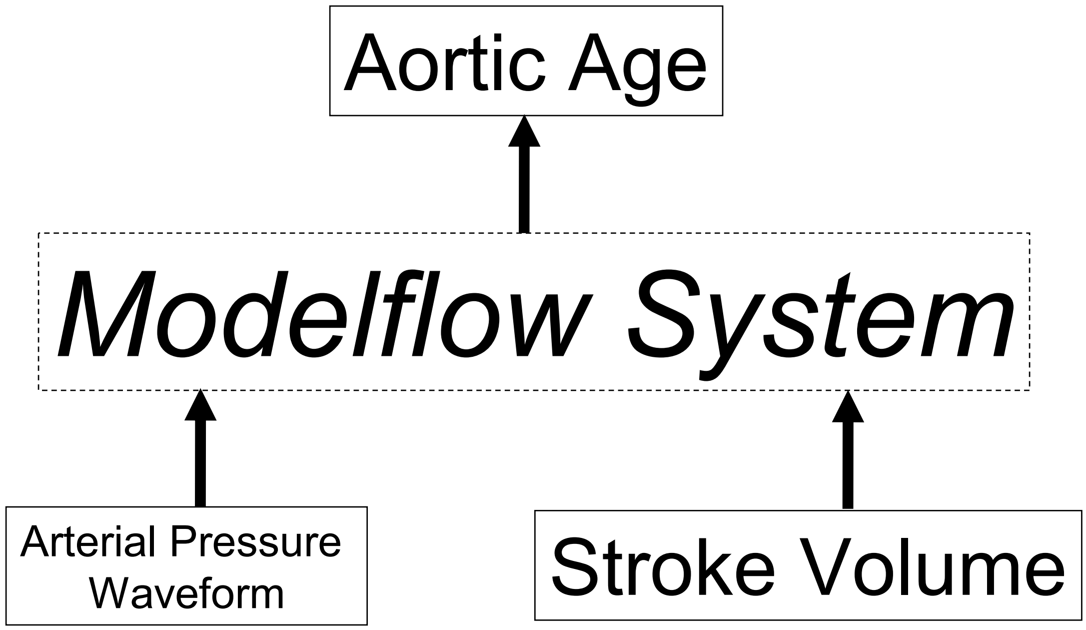
Aortic Age
Modelflow System
Arterial Pressure Waveform
Stroke Volume

Fig. B

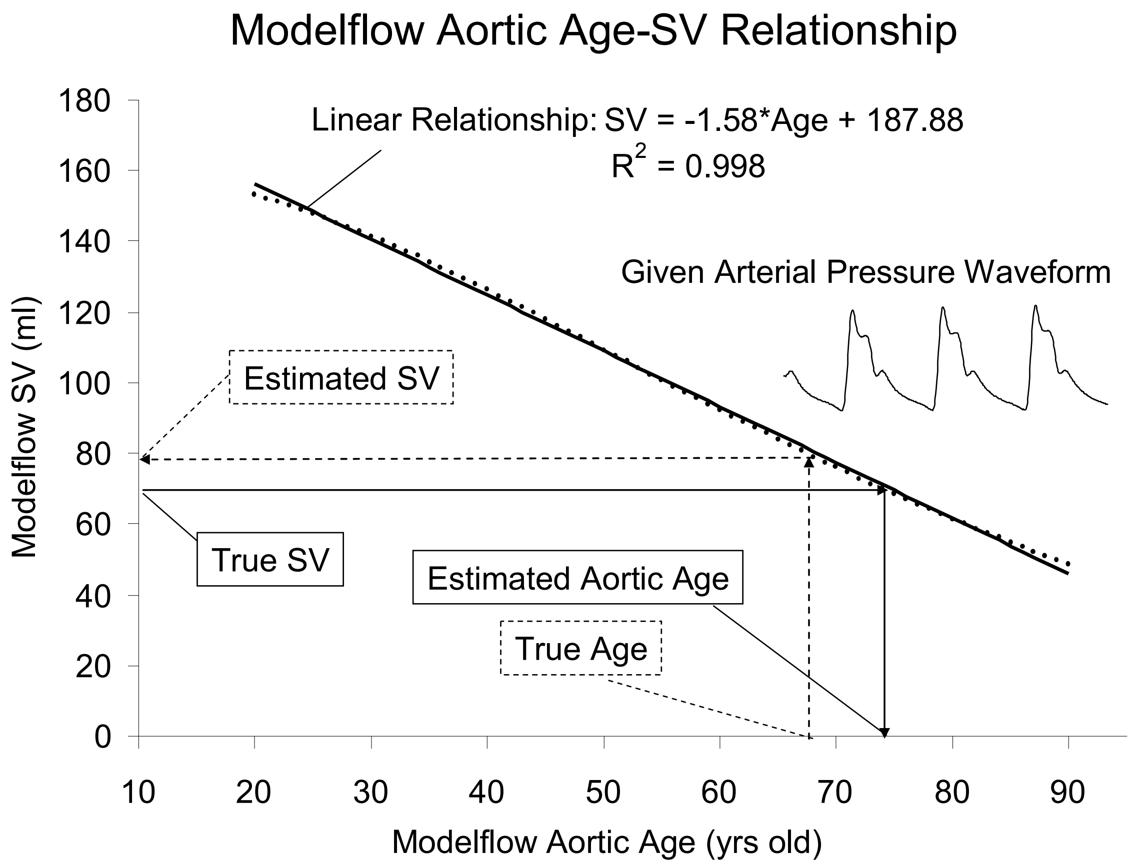
Modelflow Aortic Age-SV Relationship
Linear Relationship: SV = -1.58*Age + 187.88
R2 = 0.998
Given Arterial Pressure Waveform
Estimated SV
True SV
Estimated Aortic Age
True Age
Modelflow SV (ml)
Modelflow Aortic Age (yrs old)
0
20
40
60
80
100
120
140
160
180
10
20
30
40
50
60
70
80
90

Fig. C