

## Appendix E1

### Scaling Power Laws

We defined a proximal vessel segment as a stem and the tree distal to the stem as a crown, as shown in Figure E1. A tree structure (eg, the epicardial coronary artery tree) has many stem-crown units. In a stem-crown unit, the crown volume ( $V_c$ , in milliliters) is defined as the sum of the intravascular volumes of each vessel segment and the crown length ( $L_c$ , in centimeters) as the sum of the lengths of each vessel segment in the crown from the stem to the most distal vessels. Here, the smallest stem-crown unit corresponds to a terminal bifurcation (ie, Stem<sub>n</sub> and Crown<sub>n</sub> in Fig E1) of the epicardial coronary arterial tree obtained from CT angiography with the diameter of terminal vessels in the range of 0.6–1 mm.

To derive the volume-length scaling power law, a cost function for an integrated system of stem-crown units was proposed, which consists of two terms: viscous and metabolic power dissipation. The cost function,  $F_c$  (in ergs), is written as follows (22):

$$F_c = Q_s \cdot \Delta P_c + K_m V_c, \text{ [A1]}$$

where  $Q_s$  and  $\Delta P_c = Q_s \cdot R_c$  are the flow rate through the stem (in milliliters per second) and the pressure drop in the distal crown (in dynes per square centimeter), respectively.  $K_m$  is a metabolic constant of blood in a crown (in dynes/cm<sup>2</sup> · sec). Two important structure-structure scaling power laws as well as a flow-structure scaling power law are needed to perform the minimum energy analysis in the cost function. First, we have shown that the resistance of a crown (in dynes · sec/cm<sup>5</sup>) has the following form (22):

$$R_c = K_R \frac{L_c}{D_s^4}, \text{ [A2]}$$

where  $D_s$  is the stem diameter (in centimeters) and  $K_R$  a flow resistance constant in a crown (in dynes · sec/cm<sup>2</sup>), which depends on the branching ratio and total number of tree generations in a crown. Second, the crown volume is found to scale with the stem diameter, as follows (21):

$$V_c = K_{VD} D_s^3, \text{ [A3]}$$

where  $K_{VD}$  is a morphometric constant in a crown. Finally, the flow-length scaling power law is given as follows (21):

$$Q_s = K_{QL} L_c, \text{ [A4]}$$

where  $K_{QL}$  is a functional constant in a crown (in square centimeters per second).

When resistance (Eq [A2]), volume-diameter (Eq [A3]), and flow-length (Eq [A4]) scaling power laws are substituted into the energy cost function, Equation [A1] can be written as follows:

$$F_c = Q_s^2 \cdot R_c + K_m V_c = \left( K_R \cdot K_{QL}^2 \cdot K_{VD}^{4/3} \right) \frac{L_c^3}{V_c^{4/3}} + K_m V_c. \text{ [A5]}$$

Similar to the approach used by Murray (31), we minimized the cost function with respect to crown volume at a fixed crown length to obtain the following equation (21):

$$\frac{\partial F_c}{\partial [V_c]} = 0 \Rightarrow -\frac{4}{3} \left( K_R \cdot K_{QL}^2 \cdot K_{VD}^{4/3} \right) \frac{L_c^3}{V_c^{7/3}} = -K_m \cdot [A6]$$

Equation [A6] can be written as follows:

$$L_c = \sqrt[3]{\frac{3K_m}{4K_R \cdot K_{QL}^2 \cdot K_{VD}^{4/3}} V_c^{7/9}} = K_{LV} V_c^{7/9}, [A7]$$

where

$$K_{LV} = \sqrt[3]{\frac{3K_m}{4K_R \cdot K_{QL}^2 \cdot K_{VD}^{4/3}}} [A8]$$

is a constant (in  $\text{cm}^{-4/3}$ ). Equation [A7] provides the length-volume scaling power law, which forms the theoretic basis for the diagnosis of diffuse CAD. Moreover, a combination of Equations [A3] and [A7] results in

$$L_c = K_{LA} A_s^{7/6}, [A9]$$

where  $A_s$  is the cross-sectional area of the stem (in square centimeters) and  $K_{LA}$  is a constant (in  $\text{cm}^{-4/3}$ ). Equation [A9] refers to the length-area scaling power law.

## Reference

31. Murray CD. The physiological principle of minimum work. I. The vascular system and the cost of blood volume. Proc Natl Acad Sci U S A 1926;12(3):207–214.