Appendix A

Determination of k_{TM}

When $w_0 > w_N$, the fiber matrix in the TM is in tension, and k_{TM} is assumed to be constant and equal to $k_{TM,N}$, the elastic constant at $w = w_N$. $k_{TM,N}$ is estimated to be 7.35×10^{-3} cm H_2O/nm and is determined by requiring that the initial thickness of the TM, w_0, in its fully hydrated high filtration state be 500 nm when P_L = 60 cm H_2O. P_0 counterbalances the elastic restoring force and causes the fluid to drain out of region TM into the much larger tissue space through the cleft and region E.

When $w_0 < w_N$, the fiber matrix in the TM is in compression, and k_{TM} follows the non-linear elastic law described by the theoretical predictions and experimental measurements in refs. 1 and 2 for the compression of the thin subendothelial intimal matrix layer beneath rat aortic endothelium due to pressure loading. Fig. 4 in ref. 2 shows the relationship between its dimensionless thickness w as a function of P_L. This relationship is well described by a third-order polynomial, from which one obtains the elastic constant k_{TM} by evaluating dP/dw as a function of w. The compression pressure, P, in the subendothelial arterial intima is $-P_L$.

$$P = k_I(w - w_{IN}), \quad [\mathbf{A1}]$$

where w_{IN} is the neutral position of the fiber matrix in the subendothelial intimal layer, and k_I is the elastic constant of the intimal layer under compression. k_I is a function of (w-w_{IN}).

$$k_I = \frac{dP}{dw}. \quad [\mathbf{A2}]$$

One assumes that

$$\bar{P} = \frac{P}{P_{\max}}, \text{ and } \bar{w} = \frac{w - w_{IN}}{w_{IN}},$$

where $-P_{max}$ is the maximum P_L applied in ref. 2, 150 mm Hg. Therefore,

$$k_I = \frac{d\bar{P}}{d\bar{w}}, \text{ [**A3**]}$$

and

$$\frac{k_I}{k_{IN}} = \left(\frac{d\bar{P}}{d\bar{w}}\right) \Bigg/ \left(\frac{d\bar{P}}{d\bar{w}}\right)_N, \text{ [**A4**]}$$

where k_{IN} is the elastic constant at w_{IN}, and $\left(\frac{d\bar{P}}{d\bar{w}}\right)_N$ is $\left(\frac{d\bar{P}}{d\bar{w}}\right)$ evaluated at $w = w_{IN}$. The ratio of $\frac{k_I}{k_{IN}}$ as a function of $\bar{w}$ is shown in Fig. A1. One notices that the increase in k_I with $\bar{w}$ is non-linear.

Due to the similarity of the subendothelial matrix in the TM beneath the ECs in our microvessels and that in the aortic intimal layer, we assume that the change in the elastic constant of the TM under compression, k_{TM}, follows the same relation as for the aortic intimal layer, which is shown in Fig. 4 in ref. 2 and described in Eq. **A4**. Therefore, when $w<w_N$,

$$\frac{k_{TM}}{k_{TM,N}} = \left(\frac{d\bar{P}}{d\bar{w}}\right) \Bigg/ \left(\frac{d\bar{P}}{d\bar{w}}\right)_N, \text{ [**A5**]}$$

where $k_{TM,N}$ is the elastic constant when $w = w_N$, 7.35×10^{-3} cm H_2O/nm, and $\left(\frac{d\bar{P}}{d\bar{w}}\right)_N$ is $\left(\frac{d\bar{P}}{d\bar{w}}\right)$ evaluated at $w = w_N$. $\left(\frac{d\bar{P}}{d\bar{w}}\right) \Big/ \left(\frac{d\bar{P}}{d\bar{w}}\right)_N$ as a function of $\bar{w}$ for the TM follows the curve in Fig. A1. One finds that at the maximum compaction of the TM, w = 40 nm, or $\bar{w} = 0.6$, $\left(\frac{d\bar{P}}{d\bar{w}}\right) \Big/ \left(\frac{d\bar{P}}{d\bar{w}}\right)_N$ is 2.7 and $k_{TM} = 2.01 \times 10^{-3}$ cm H_2O/nm.

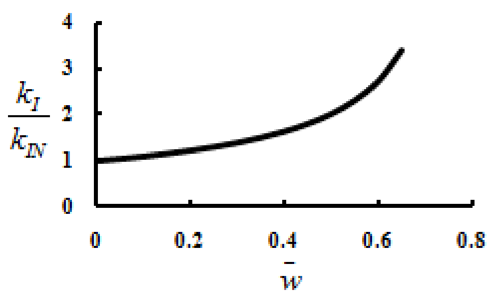

Fig. A1. Non-linear function for $\frac{k_I}{k_{IN}}$ as a function of $\bar{w}$ derived from Fig. 4 in ref. 2.

1. Huang Y, Jan KM, Rumschitzki D, Weinbaum S (1998) Structural changes in rat aortic intima due to transmural pressure. *J Biomech Eng* 120:476-483.
2. Guyton AC (1963) A concept of negative interstitial pressure based on pressures in implanted perforated capsules. *Circ Res* 12:399-414.