

Supplementary information

Layers of interstitial fluid flow along a “slit-shaped” vascular adventitia

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Video 1 Illustration of the long-distance PACT pathways scanned by MRI at 10–15 min after hypodermic injection into the ankle dermis. Originating from the ankle dermis, the paramagnetic tracer of Gd-DTPA seemed to have enhanced visualization of the venous vessels of the limbs, the abdominal and thoracic cavities and some tissues of the heart. Due to the limitations of the MRI technique, whether Gd-DTPA was inside the venous cavity or in the PACT pathways outside the vessels cannot be determined. The pathways enhanced by Gd-DTPA coincided with the PACT pathways fluorescently stained by FluoNa from the ankle dermis.

Video 2 Illustration of dynamic flow of partially stained blood in a vein by fluorescence stereomicroscopy. After 20–30 μ L FluoNa solution entered and mixed with the blood in a small branch of the upstream veins in the third group, the intravascular blood was partially stained by FluoNa. Under real-time observation, a spiraling and rotating pattern of blood flow was clearly visualized inside the vascular vessel. The arch-shaped incision of the PACT pathway on the vein was not then stained. One flow circle of blood spiraling and rotating inside the vascular vessel was found to be 1.3–1.9 s. The flow length of one circle of the blood rotating was calculated to be 5.2–11.4 cm given a speed of femoral venous blood flow of 4–6 cm/s and a vessel diameter of 2 mm. We predicted that there would be a periodic internal spiral ridge-like structure along the tunica intima of vascular vessels. This needs verification.

Video 3 Illustration of the movement of FluoNa spots along the PACT pathway dynamically recorded by fluorescence stereomicroscopy. Around 50–60 min after the injection of FluoNa into the ankle dermis, a few FluoNa spots were found to emerge and move along the PACT pathway. The calculated speed of FluoNa spots was 3.6–15.6 mm/s and their size was about 10–20 μ m. This might represent fluid flow along adventitial fibers in tunica adventitia (Figs. 3a and 3b).

Video 4 Illustration of the movement of FluoNa clumps along the PACT pathway, dynamically recorded by fluorescence stereomicroscopy. Around 60–70 min after the injection of FluoNa into the ankle dermis, a few FluoNa clumps were continuously flushed away along the vessel wall. The calculated speed of FluoNa clumps was 0.1–7.6 mm/s and their size was about 50–400 μ m. This might represent a late stage of fluid flow between the tunica adventitia and its covering fascia (Figs. 3c and 3d).

Video 5 Illustration of a continuous ISF flow in an arch-shaped incision of the PACT pathway by real-time fluorescence stereomicroscopy. Dynamically observed after the injection of FluoNa into the ankle dermis, ISF was clearly seen to flow along the PACT pathway and emerge out of the arch-shaped incision and along the exposed outermost layer of adventitia. The dynamic processes of continuous and successive adventitial ISF flow are shown in Fig. 4.

Video 6 Illustration of a continuous fluid flow along the edge of an arch-shaped incision of the PACT pathway by real-time fluorescence stereomicroscopy. After ISF flow was clearly visualized in the arch-shaped incision (Video 5), fluid was found to flow down along the edge of the arch-shaped incision. It was clearly showed that the continuous ISF flow in the space between the adventitia and its covering fascia.

Video 7 Illustration of adventitial ISF flow converging into capillaries and a venule nearby. During adventitial ISF transport along the PACT pathway, FluoNa was found to converge into the capillaries and a nearby venule. Thus, the continuous ISF flow in a PACT pathway can exchange constantly with circulating blood via capillaries along the PACT pathways.