Microcirculation of Left Atrial Muscle, Cerebral Cortex and Mesentery of the Cat

A Comparative Analysis

BING-LO CHANG, TAKASHI YAMAKAWA, JILL NUCCIO, RON PACE, AND RICHARD J. BING

SUMMARY

By means of transillumination (microtransilluminator and light pipe), comparative analyses were carried out on geometry, topography, and morphometry of microcirculation in the cerebral cortex, left atrial muscle, and mesentery of the cat using computer analysis. In addition, specific types of capillary distribution (concurrent, countercurrent, and asymmetric distribution) in these three organs were ascertained from images visualized on films. These parameters were related to their role in tissue oxygen supply. It was found that mean capillary diameter, mean intercapillary distance, total capillary length, and total capillary surface area differed significantly among the three organs. Differences in mean capillary tortuosity between cerebral cortex and left atrial muscle and between left atrial muscle and mesentery also were significant. Mean capillary tortuosity in mesentery and cerebral cortex was of equal magnitude. In the cerebral cortex, a high degree of tortuosity and asymmetric capillary distribution favor tissue oxygenation. A similar situation exists in left atrial muscle, although some concurrent and countercurrent distribution could be detected. In the mesentery, the combination of high capillary tortuosity and concurrent capillary arrangement is unfavorable for tissue oxygenation.

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IT IS the function of the capillaries to maintain tissue oxygenation constantly and to respond rapidly to changing oxygen demands (Hall, 1831; Krogh, 1919a, 1919b; Opitz and Schneider, 1950; Thews, 1960; Diemer, 1965; Grunewald, 1973a; Lubbers, 1976; Pawlik et al., 1981). Some of these demands are met by dynamic factors such as changes in cardiac output and systemic blood pressure, or by the tone of arteriolar smooth muscle. In addition, morphological and geometric factors such as capillary arrangements and topography play an important role in tissue oxygenation (Krogh, 1919b; Opitz and Schneider, 1950; Thews, 1960; Diemer, 1965; Grunewald 1973a; Lubbers, 1976; Pawlik et al., 1981). These factors are well adapted to the specific demands of individual organs. The organ specificity of individual microcirculatory beds has been demonstrated for a number of organs. Utilizing both histological and in vivo methods, capillary diameter, capillary segment lengths, total capillary length, total capillary volume, total capillary surface area, and intercapillary distance have been determined previously for skeletal muscle, myocardium, omentum, small intestine, and cerebral cortex (Pawlik et al., 1981). In addition, the influence of different capillary arrangements on oxygen pressure fields of brain and heart have been studied by Lubbers (1976) and by Grunewald (1973) for determinations of oxygen histograms. These workers differentiated between capillary arrangements with concurrent, countercurrent, and asymmetric patterns. It is the purpose of this report to analyze and compare the topography, geometry, and distribution of capillary circulation in cerebral cortex, left atrial muscle, and mesentery of the cat, and to relate these patterns to tissue oxygen demands. This involved analyses of capillary distribution of topography and geometry. These goals were accomplished from microcirculatory patterns obtained by high-speed cinematography and transillumination.

Methods

Transillumination

A pulsed short gap 300-W xenon illuminator (AVL300HXC-75, modif., Varian/Eimac Division) served as a light source. The xenon illuminator contained a series of heat filters (Schott KG) to cut down infrared radiation and a gelatin filter (Kodak Wratten 2A) to cut down UV radiation. A custom-built power supply (John Power, California Institute of Technology) boosted the xenon arc to an output of 5000 lm (=20 watts) of visible radiation at a color temperature of 5400°K. The power supply provided strobe impulses at rates between 25 and 400 flashes per second for TV monitoring. The strobe was triggered by the operation of the cine-camera.

Two different light-conducting systems were used. A microtransilluminator was employed for...
the illumination of the cerebral cortex and a light pipe for the illumination of the atrial muscle and mesentery (Figs. 1 and 2). The microtransilluminator was first used to study the coronary microcirculation in ventricular muscle (Tillmanns et al., 1974). Several changes were made in order to adapt the transillumination system to the cerebral cortex. These changes were recently published in detail (Pawlik et al., 1981). They involved optimized light gain for the illumination of the cerebral cortex. The microtransilluminator (Robert Hamilton, UC Berkeley) consists of two main components, an outer piece of seamless steel tubing (outer diameter 0.7 mm, length 45 mm) and an inner coated optical fiber (diameter 381 μm, Valtec 0.56) (Pawlik et al., 1981) (Fig. 1). One end of the tubing was cut at a right angle and the other end was ground to a 20° bevel. One end of the optical fiber was cut at a right angle and the other end at 45°. The angled end was aluminized to reflect light upward through the tissue through a window (diameter 390 μm) that was drilled on the shorter side of the outer tubing. The window and bevel of the tubing were sealed with clear epoxy (Epo-Tek 301-2, Epoxy Technology Inc.). The light pipe (Thurston Le Vay, Glass Instruments) used for the transillumination of the atrial muscle and mesentery also has been described in a previous publication (Hellberg et al., 1971). The one used for the current experiments consists of an outer glass sheath (outer diameter 4.5 mm, inner diameter 3.5 mm, length 70 mm) and an inner-coated optical fiber (diameter 3.0 mm, length 76.5 mm). The sheath was made from a hollow glass tube that was cut at a right angle at one end and closed and rounded at the other end (Fig. 2). The closed end has a flat upper surface (2.5 mm X 4.5 mm). One end of the inner optical fiber was cut at a right angle and the other end at 45°. The angled end was aluminized to reflect light upward through the tissue toward the objective of the microscope (Fig. 2). All light transmitted through the transillumination system resulted in a transmitted spectrum that produced optimal contrast (Pawlik et al., 1981). Temperature of the cerebral cortex above the light exit point of the microtransilluminator increased at a maximum of 0.1°C after 40 seconds of high light intensity (Pawlik et al., 1981). Using the light pipe, the temperature of the atrial muscle above the light exit point increased less than 1°C during a 10-minute observation (Hellberg et al., 1971). For both systems, a high light intensity was needed only during filming (approximately 3 seconds).

Intravital Microscope

This consisted of the animal stage, microscope, TV, and camera system (Hellberg et al., 1972 and Wayland, 1975). The telescopic microscope was equipped with 10X (UM10), 32X (UMK32), and 50X (UMK50) objectives with long working distance (Leitz). A beam splitter directed 20% of the image intensity into a low light level TV system and 80% into a cinecamera. The diameter of the illuminated field visible on the TV monitor was 375 μm, of which an area of 185 × 137 μm (32X objective) could be recorded on film. The depth of field of the medium power objective, which was used for all experiments, was 52 μm (Pawlik et al., 1981). A 16-mm Milliken camera (DBM 54, Teledyne Camera System) synchronized with the xenon lamp was used to take color pictures (Ektachrome film 7250, Kodak) at a rate of 400 frames/sec.

Procedure

Sixty cats of either sex weighing 2.3-4.5 kg were sedated with ketamine hydrochloride (18 mg/kg body weight) followed by intramuscular injection of 0.4-0.5 mg atropine sulfate. Cats used for the study of the cerebral cortex also received an intramuscular injection of 1 mg dexamethasone. Heparin (100 IU/kg body weight) was given intravenously to cats used for observation of the atrial muscle. Sodium pentobarbital, not exceeding a total dose of 25 mg/
kg body weight, then was injected intravenously at intervals required to maintain a medium level of anesthesia. The combination of ketamine and sodium pentobarbital was chosen because ketamine increases cerebral blood flow (Lassen, 1976), thus counteracting the effect of sodium pentobarbital, which causes a slight decrease (Goodman and Gilman, 1980). Atropine is known to have little effect on peripheral circulation or blood pressure when given without choline esters (Goodman and Gilman, 1980). A flexible catheter (4.0 FR., Malinckrodt) was inserted into the aorta through the femoral artery to monitor blood pressure. A second flexible catheter was placed into the femoral vein for injection of drugs. A tracheotomy was performed in order to artificially ventilate the animals with room air (Infant Ventilator LS104-150, Bourns Inc.).

When the coronary microcirculation was observed, the animals were ventilated with room air to which oxygen was added. The amount of oxygen added depended on the analysis of the arterial blood gases. Body temperature was determined by an intrarectal thermocouple and maintained at about 37.5°C by means of a heating pad. A polygraph (Electronics for Medicine, Honeywell Inc.) recorded heart rate (151.17 ± 22.2 beats/min) and arterial blood pressure (Statham P231D) (95.36 ± 19.0 mm Hg). Arterial blood gases and pH were measured with a microanalyzer (Radiometer). Values were within the range of awake cats (pH 7.37 ± 0.07, Po2 94 ± 12.8 mm Hg, and Pco2 30 ± 3.1 mm Hg) (Herbert and Mitchell, 1971).

Experiments on the cerebral cortex were carried out on 30 cats. After anesthesia, the head was fixed in a surgical head holder (David Kopf Instruments). Craniotomy was performed by means of a turbine drill at 40,000 rpm. After the dura was radially incised and folded back, the cerebral surface was kept moist with frequent applications of Ringer-Tyrode solution gassed with 5% CO2 and 95% O2 and warmed to 37°C. The light pipe was inserted parallel to the cerebral surface (supraventricular and subcortical) at a depth of up to 1 mm by means of a multiple joint manipulator. The possible damaging effect of this procedure has been carefully evaluated in a previous publication (Pawlik et al., 1981). Histological specimens were obtained from a series of cats to assess the degree of tissue damage induced by the experimental procedure. After the animal’s had been killed with an overdose of sodium pentobarbital, in situ fixation with the microtransilluminator in place was accomplished by constant suffusion of the cerebrum with 10% buffered formalin over 24 hours. The hematoxylin and eosin- (H-E) and Nissl-stained slides showed the expected narrow zone (up to 180 μm) of distortion and compression with signs of slight edema (Pawlik et al., 1981), more marked below than above the microtransilluminator. Some erythrocytes and cellular debris could be seen at the edges of the needletrack. Preparation of the left atrium was carried out in 26 cats. A left side thoracotomy was performed while bleeding was controlled with an electrocauter (Bantam Bovie Unit, Hanley Equipment Co.). After the ribs were retracted, the pericardium was incised. The heart was kept moist with frequent applications of Krebs-Henseleit solution warmed to 37°C. A small portion of the tip of the left atrial appendage (3 mm) was clamped with a Potts clamp. A small incision was made in the tip of the atrial appendage and the light pipe then was inserted through this opening. A suture was quickly tightened around the light pipe to prevent leakage of blood. The light pipe was inserted so that the flat surface of the sheath lies against the upper surface of the atrial wall. Care was taken to exert the proper amount of tension on the atrial wall to prevent the interference of the blood supply or the entrance of blood between the light pipe and atrial wall.

Microcirculation of the mesentery was observed in seven cats. Since visualization of the microcirculation in the mesentery offers no particular difficulties, this number of observations was deemed sufficient. The peritoneal cavity was opened by an abdominal midline incision (length 8 cm) through the umbilicus. A single loop of the small intestine was gently exteriorized into a chamber that was irrigated with Ringer-Tyrode solution, warmed to 37°C. The light pipe was positioned just underneath the tissue and stabilized with a multiple joint manipulator. The mesentery was placed on the upper flat surface of the light pipe for observation. The small intestine and mesentery were covered with moistened gauze to prevent drying.

Image Analysis
Twenty tissue observations on each organ (cerebral cortex, left atrial muscle, and mesentery) were recorded on film and used for analysis. The data were collected with a photo-optical analyzer (224-A, L-W International) at 3000X for the medium power objective (32X), which was used exclusively. For computer analysis of vascular topography and geometry, the image was projected on drafting paper (17 × 22 inches). The projected images were copied by tracing the center of the vessel walls on the paper (Fig. 3). Capillaries were differentiated from venules and arterioles by diameter size. Any vessel with a diameter of less than 8 μm was considered to be a capillary. The average diameter for each capillary was determined from the drawn picture by taking 10 or more random measurements with a reference scale. For further identification of capillaries, the criteria of Chambers and Zweifach (1946) were used. Accordingly, we used as true capillaries only those vessels which arose from pre-capillaries and represented direct branches of the distal portion of the control channel and of the non-muscular venule.

The drawing described above was used for obtaining the raw data for computerization. To accom-
Calculations

The formulas for calculations of topographic and morphometric parameters of cerebral cortex, left atrial muscle, and mesentery have been previously described in principle (Underwood, 1970; Pawlik et al., 1981). They include determinations of total capillary length per tissue volume ($L_V$), total capillary surface area per tissue volume ($S_V$), and total capillary volume fractions ($V_V$). In all three systems, it was determined that random orientation of capillaries did not obtain, hence slightly different formulas had to be used to infer true capillary length from the observed projected capillary length. For a subset of the images for heart, cerebral cortex, and mesentery, the average angular orientation and distribution of the capillaries were determined, and these values were assumed to be applicable to all of the images studied.

To determine the orientation of capillaries or subsegments of capillaries to the projection plane, the degree of deviation from the projection plane ($\theta$) had to be known. $\theta$ depends on whether or not the subsegments of capillaries are parallel to the projection plane. If the capillaries are parallel to the projection plane, $\theta = 0$. However, the value for $\theta$ is not established for capillaries of heart, brain, or mesentery.

To determine $\theta$, we have chosen a procedure which, by optical means, determines this angle. In order to accomplish this, the depth of field had to be determined. This was accomplished by focusing first on the television screen on one point of a relatively straight capillary. The objective of the microscope was then moved until the other end of this capillary was in focus. The degree of rotation of the micrometer adjustment of the microscope was recorded and the projected length between the two points was measured on the screen. $\theta$ then is calculated as follows:

$$\tan \theta = \frac{\text{depth of field}}{\text{projected capillary length}}$$

If, as in the cerebral cortex, the projected capillary length in focus was short, several points of this capillary were brought consecutively into focus to obtain different depth of field for calculation of $\theta$. In the mesentery, the projected length could be readily obtained, since the total length of the capillaries was clearly visible on the TV screen. In the heart muscle, images were not as clear. For that reason, the heart was arrested with potassium chloride and, following this, capillaries were injected with India ink from the aorta. In the cerebral cortex, capillaries were outlined without the help of contrast material. Table 1 summarizes the results.

The calibration factor ($F$), which converts the degree of rotation of the micrometer screw of the microscope into $\mu m$, was obtained as follows: a micrometer scale with 10-, 50-, and 100-$\mu m$ divisions (Bausch & Lomb, no. 31-16-90) was placed under the objective at an angle of $30^\circ$. After bringing one of the divisions of the scale into focus on the screen, the micrometer screw was turned until a distant point on the scale was clearly seen. The degree of

![Figure 3](http://circres.ahajournals.org/)

**Figure 3** Example of a drawing of projected image of capillaries. The picture is drawn on drafting paper and overlaid with a transparent grid. Each square is equal to 5 $\mu m$ of the projected image. Four capillaries are represented. The $x$ and $y$ coordinates for each successive square are determined. The vascular diameter and coordinates for each capillary provide the input for computer analysis.
rotation was determined on a protractor attached to the micrometer screw. This was first read in degrees and then converted to μm. For example, if the projected length of the capillary on the TV screen was 5 cm (200 μm), and the degree of rotation to necessitate focusing on the 2nd point of the capillary was 187° on the protractor, then

\[
F = \frac{200 \times \tan 30}{187} \quad \text{OR} \quad F = \frac{200 \times 0.58}{187} = 0.62.
\]

This is the factor (F) which is used to convert the degrees of rotation in μm and to measure the depth of field. Depth of field = degree of rotation × F.

\[
\tan \theta = \frac{\text{depth of field}}{\text{projected length}}
\]

Projected capillary length was measured on the TV screen directly in centimeters by means of a ruler. This was converted into micrometers as follows: The micrometer scale previously used was placed horizontally under the microscopic objective and the projection of the division of the micrometer scale on the screen was determined in centimeter and converted into μm (1 cm = 40 μm).

We assume that the average of the true capillary length (\(L_i\)) is given by

\[
L_i = \frac{L'_i}{\cos \theta}
\]

Total capillary length per tissue volume (\(L_V\)) was computed from the total projected length of capillaries (\(\sum L'_i\)) within a space of projection (\(V_A\)):

\[
L_V = \frac{\sum L_i}{V_A} = \frac{\sum L'_i}{\cos \theta V_A}
\]

**Table 1** Topographic and Morphometric Parameters of Cerebral Cortex, Left Atrium, and Mesentery

<table>
<thead>
<tr>
<th>Structure</th>
<th>n</th>
<th>Projected length ((L'_i) μm)</th>
<th>Depth of field (μm)</th>
<th>Angle (θ)°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral cortex</td>
<td>32</td>
<td>17.94 ± 7.30</td>
<td>70.63 ± 41.49</td>
<td>69.49 ± 14.15</td>
</tr>
<tr>
<td>Left atrium</td>
<td>36</td>
<td>360.44 ± 132.36</td>
<td>112.17 ± 35.94</td>
<td>19.14 ± 8.70</td>
</tr>
<tr>
<td>Mesentery</td>
<td>31</td>
<td>558.7 ± 34.92</td>
<td>90.26 ± 28.97</td>
<td>9 ± 2.73</td>
</tr>
</tbody>
</table>

All results are expressed as mean ± SD.
Total capillary surface area per tissue volume \((S_v)\) and total capillary volume fractions \((V_v)\) were computed from Equation 2 and mean capillary diameter \((D_i)\), respectively.

\[
S_v = \frac{\pi \sum (L_i \cdot D_i)}{V_A} = \frac{\pi D_i \sum L_i}{V_A \cos \theta}
\]

\[
V_v = \frac{\pi \sum (L_i \cdot D_i^2)}{4V_A} = \frac{\pi D_i^2 \sum L_i}{V_A \cos \theta}
\]

To determine the variance in the true capillary length and related quantities, the variance in both \(L_i'\) and \(\theta\) must be considered. We note from Table 1 that the standard deviations in both \(L_i'\), projected length and \(\theta\) are typically approximately one-third or less of the mean values. Hence we may linearise Equation 1 and write, for \(\Delta L_i\), the variation in \(L_i\) about its mean value.

\[
\Delta L_i = \frac{\Delta L_i'}{\cos \theta} + \frac{L_i'}{\cos^2 \theta} \sin \theta \cdot \Delta \theta
\]

where \(\Delta L_i'\) and \(\Delta \theta\) are the variations in \(L_i'\) and \(\theta\) about respective mean values. Assuming then that \(L_i'\) and \(\theta\) are normally distributed, one has

\[
\Delta L_i^2 = \frac{\Delta L_i'^2}{\cos^2 \theta} + \frac{L_i'^2}{\cos^2 \theta} \tan^2 \theta \cdot \Delta \theta^2
\]

The determination of intercapillary distances \((d)\) was measured from capillary center to center for the cerebral cortex, as previously described (Pawlik et al., 1981):

\[
d = \sqrt{c^2 + d'^2}
\]

where \(d'\) represents the projected distances between contiguous capillary walls and \(c\) is a median likelihood correction term for the missing information on the spatial position of any two capillaries within a known depth of field. Assuming that all capillary segments are distributed with equal probability along the depth axis of the field of view, the probability distribution of the difference in depth \((\delta)\) between any two projected points is a beta distribution.

\[
P(x) = \frac{(1 - x)^{\alpha - 1}}{B(\alpha, \beta)}
\]

with parameters \(\alpha = 1\) and \(\beta = 2\), and

\[
x = \frac{\delta}{\delta_{\max}}
\]

where \(x\) is the relative difference in depth. The probability integral of Equation 8 up to \(x\) is an incomplete beta function ration \((I_x)\)

\[
I_x = \frac{1}{B(1, 2)} \int_0^x (1 - t) \ dt = 2x - x^2
\]

Solving Equation 10 for physically plausible root of the quadratic equation of \((x)\) with \(I_x = 0.5\), it follows from Equation 9 that

\[
c = \delta_{0.5} = \delta_{\max} (1 - \sqrt{0.5})
\]

Measurement of capillary tortuosity as a morphometric parameter of a capillary pathway was introduced by (Pawlik et al., 1981). It was defined as inversely proportional to both the radius of the curvature corresponding to the average deviation from a straight line and the relative average length of a monotone curving vessel segment. The axis of a capillary was approximated by a number of chords \((N)\) of uniform length \((s)\) that permitted a satisfactory representation of the vascular axis even in the narrowest curves. Five micrometers were used as a uniform length \((s)\). The mean tortuosity of individual capillaries \((T_i)\) was determined accordingly:

\[
T_i = \frac{\pi N \sum \alpha_j}{(N - 1)(n + 1)}
\]

where \(\alpha_j\) represents the angle between the straight-line extension of one chord and the next chord and \(n\) represents the number of zero crossings of \(\alpha\).

**Computer Programming**

The Picture Analysis System is designed to run on a PDP 11-03 minicomputer (Digital Equipment Corp.) with two flexible disc drives. All data input and output occurs through the printer terminal. The system is comprised of two main programs which operate in conversational mode. These are: A, an input program which accepts capillary coordinate and diameter data for numbered pictures, performs on line checking for continuity of successive coordinate pairs, and writes the data on disks. B, a data reduction program which calculates the capillary geometry parameters (see Calculations) from the above coordinate and diameter data. This program produces a terminal listing of the calculated parameters for each picture analyzed and a corresponding disk file of these reduced data.

**Results**

Data collected from cerebral cortex, left atrial muscle, and mesentery are listed in Tables 2 and 3. Table 2 shows the mean values and standard deviations obtained by computer analysis for mean capillary diameter (\(\mu m\)), mean intercapillary distance (\(\mu m\)), total capillary length/volume (\(mm/mm^3\)), total capillary surface area/volume (\(mm^2/mm^3\)), and mean capillary tortuosity (\(mm^{-2}\)). The inferred standard deviations for quantities derived from the projected length were calculated using Formula 6. The data on the brain are subject to uncertainty, as the capillary segments tend to be aligned along the depth axis of the field of view. Table 3 represents the statistical analysis of these parameters. Table 4 contains data
on capillary distribution (concurrent, countercurrent, and asymmetric). All data were collected from individual frames of films of the microcirculation of the heart, cerebral cortex, and mesentery with techniques described above.

Tables 2 and 3 show that the left atrial muscle has the highest values for total capillary length/volume, total capillary surface area/volume, and total capillary volume fraction. The mean intercapillary distance in the atrial muscle was low. On the other hand, mean capillary tortuosity was greatest in the cerebral cortex. The mesentery has high values for intercapillary distance, low values for total capillary surface area, total capillary volume fraction and total capillary length (Tables 2 and 3). All of these parameters are unfavorable for tissue oxygenation. Only the relatively high capillary diameter is of benefit for tissue oxygenation in the mesentery. Additional factors of importance for tissue oxygenation are capillary distribution (Lubbers, 1976; Gunewald, 1973b) (Fig. 4). The most efficient system in these theoretical models was found to be asymmetric distribution (Fig. 4). Symmetric distribution was thought to be relatively inefficient. Table 4 and Figures 5 and 6 illustrate that both atrial muscle and gray matter possess primarily asymmetric distribution. In atrial muscle, a small percent of countercurrent and an even smaller degree of concurrent circulation were visualized (Fig. 5). In the cerebral cortex, capillary distribution was entirely asymmetric (Fig. 6). In that organ, the high degree of tortuosity is of additional benefit since it coexists with asymmetric capillary distribution (Fig. 4). In contrast, the mesentery has symmetric capillary distribution (Fig. 7). For this reason, the high degree of tortuosity is of little benefit in maintaining high tissue oxygen tension. This agrees with the limited O2 demands of this organ (Frasher and Wayland, 1972).

**Discussion**

Capillary morphometry and topography and O2 supply to the tissue are intimately related. This relationship has been studied by a number of investigators (Krogh, 1919a, 1919b; Opitz and Schneider, 1950; Thews, 1960; Diemer, 1965; Grunewald, 1973a, 1973b; Lübbers 1976). Krogh (1919a) defined the oxygen field around the capillary as a cylindrical space. This concept was refined, taking into consideration the effect of capillary spacing, capillary flow, and the influence of the O2 dissociation curve (Opitz and Schneider, 1950). In the schema devised by Krogh, the tissue with the lowest O2 tension, the jeopardized area (the lethal corner of Lübbers), lies at the venous ends of the capillaries (Krogh, 1919a and Lübbers, 1977) (Fig. 4). Thews (1960) concluded that additional longitudinal diffusion of flow can raise the O2 pressure in this endangered region. The system of Krogh may be defined as one with concurrent flow in which input is symmetrical and parallel (Lübbers, 1976). Diemer (1965) later demonstrated that, besides capillary length and intercapillary distance, the relative direction of flow in capillaries is of importance (parallel vs. countercurrent flow. Lübbers (1976), on the basis of studies on models obtained by means of accumulation of O2 histograms in various tissues, defined two additional patterns of capillary distribution: one with

**Table 2** Comparison of Capillary Topography: Cerebral Cortex, Left Atrial Muscle, and Mesentery

<table>
<thead>
<tr>
<th>Structure</th>
<th>Capillary diameter (μm)</th>
<th>Intercapillary distance (μm)</th>
<th>Total capillary length/volume (mm/mm³)</th>
<th>Total capillary surface area/volume (mm²/mm³)</th>
<th>Total capillary volume fraction (%)</th>
<th>Capillary tortuosity (mm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral cortex</td>
<td>6.03 ± 1.516</td>
<td>23.8 ± 7.51</td>
<td>1568.49 ± 475.72</td>
<td>30.07 ± 7.85</td>
<td>4.87 ± 1.37</td>
<td>695 ± 318</td>
</tr>
<tr>
<td>Left atrial muscle</td>
<td>5.23 ± 0.863</td>
<td>5.22 ± 0.31</td>
<td>1917.58 ± 305.05</td>
<td>32.95 ± 5.16</td>
<td>4.51 ± 0.84</td>
<td>228 ± 119</td>
</tr>
<tr>
<td>Mesentery</td>
<td>7.2 ± 0.779</td>
<td>81.0 ± 22.8</td>
<td>398.98 ± 116.26</td>
<td>9.09 ± 2.47</td>
<td>1.71 ± 0.56</td>
<td>516 ± 243</td>
</tr>
</tbody>
</table>

All results are expressed as mean ± SD.

**Table 3** Statistical Analyses (Cerebral Cortex, Left Atrial Muscle, and Mesentery)

<table>
<thead>
<tr>
<th>Structures</th>
<th>Mean capillary diameter (μm)</th>
<th>Mean intercapillary distance (μm)</th>
<th>Total capillary length/volume (mm/mm³)</th>
<th>Total capillary surface area/volume (mm²/mm³)</th>
<th>Total capillary volume fractions (%)</th>
<th>Mean capillary tortuosity (mm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral cortex and left atrial muscle</td>
<td>P &lt; 0.05</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.05</td>
<td>P &lt; 0.1</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Left atrial muscle and mesentery</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Mesentery and cerebral cortex</td>
<td>P &lt; 0.005</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.1</td>
</tr>
</tbody>
</table>
Table 4  Relationship of Capillary Morphometry, Topography, and Distribution to Tissue Oxygenation

<table>
<thead>
<tr>
<th>Left atrial muscle</th>
<th>Cerebral cortex</th>
<th>Mesentery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distribution of capillaries</td>
<td>A +, COUNT. C and CON. C</td>
<td>A +, CON. C</td>
</tr>
<tr>
<td>Mean capillary tortuosity</td>
<td>L-</td>
<td>H+</td>
</tr>
<tr>
<td>Mean intercapillary distance</td>
<td>L+</td>
<td>H+</td>
</tr>
<tr>
<td>Total capillary surface area/volume</td>
<td>H+</td>
<td>L+</td>
</tr>
<tr>
<td>Total capillary volume fraction</td>
<td>H+</td>
<td>L+</td>
</tr>
<tr>
<td>Total capillary length/volume</td>
<td>H+</td>
<td>L+</td>
</tr>
<tr>
<td>Mean capillary diameter</td>
<td>L-</td>
<td>H+</td>
</tr>
</tbody>
</table>

Definitions: + = advantageous for tissue oxygenation, − = disadvantageous for tissue oxygenation, A = asymmetric capillary distribution, COUNT.C = countercurrent capillary distribution, CON. C = concurrent capillary distribution, L = low value, and H = high value.

* Negative because of combination with symmetric capillary arrangement.

Symmetrical antiparallel input and output (the countercurrent flow) and another with asymmetric arrangement in which the arterial inflow is opposite to the middle part of an adjoining capillary. The countercurrent arrangement has a definite advantage over the concurrent capillary pattern, since arterial Po2 is more efficiently used. However, O2 can be shunted by diffusion directly from the arterial inflow to the opposite venous outflow, depriving more distal tissue of O2. The most efficient system appears to be the asymmetric capillary structural pattern, since the O2 diffusing out of one capillary is still available to a second, adjoining capillary, a distance away from the jeopardized area of the capillary venous outflow (Fig. 4). There is still another capillary morphometric pattern favoring the maintenance of tissue oxygen fields: Asymmetric distribution with a high degree of tortuosity. This pattern is outlined in Figure 4. Tortuosity, together with asymmetric distribution, reduces intercapillary distance and can maintain O2 tension in the jeopardized area, particularly if the intercapillary distance is lowest at the venous end of the capillary. The effective intercapillary distance can be changed by the presence of unperfused capillaries as has been shown in the cerebral cortex (Pawlik et al., 1981). It is possible that in some organs, such as the cerebral cortex, a change in capillary distance produced in this manner permits a more economic O2 supply. These factors also have been discussed (Bourdeau-Martini and Honig, 1973).

Increased capillary surface area and capillary volume fraction may also maintain higher tissue O2 fields around the jeopardized area, but only as long as there is asymmetric capillary pattern. Otherwise, an increase in capillary surface area and volume fraction results in shunting of O2 from one capillary to adjacent venous outflow of a neighboring capil-
The ideal capillary pattern is one in which there is asymmetric arrangement, together with a high degree of tortuosity with multiple arterial inputs.

Of additional importance for tissue oxygenation are mean capillary diameter, mean intercapillary distance, and total capillary length (volume). Capillary diameter determines resistance to flow. Therefore, a large capillary diameter as observed in the mesentery maintains a relatively high oxygen tension at the venous end (the jeopardized area). Short intercapillary distance as found in heart muscle reduces distance the oxygen must diffuse, maintaining a relatively high oxygen tension in the center between the two adjoining capillaries. Total capillary length per tissue volume is the sum of the length of individual capillaries visualized in one field. A large number of short capillaries is advantageous, since the area of diffusion is large.

These concepts are of importance in the comparative evaluation of the microcirculatory pattern in various organs and in the relationship between morphology in vivo and tissue O\textsubscript{2} transport. Tables 2 and 3 illustrate comparisons in topography and morphometry between portions of the cerebral cortex, the atrial muscle, and the mesentery. It appeared unnecessary to fit distribution curves to the data represented in Table 3, since the morphological conclusions drawn are not sensitive to the precise nature of the statistical distribution of the parameters measured.

Capillary diameter, intercapillary distance, total capillary length, and capillary surface area differ significantly from organ to organ. There is no significant difference in total capillary volume fraction between cerebral cortex and left atrial muscle. The difference in capillary tortuosity between cerebral cortex and left atrial muscle and between left atrial muscle and mesentery are significant. In contrast, no significant difference exists between capillary tortuosity in mesentery and cerebral cortex. According to Table 4, tissue oxygenation in left atrial muscle is favored by large total capillary surface area and high total capillary volume fraction, by large total capillary length/volume, and by low mean intercapillary distance. In the cerebral cortex, high mean capillary tortuosity is also advantageous. In the mesentery, only large mean capillary diameter favors tissue oxygenation. In addition, in both atrial muscle and cerebral cortex, asymmetric capillary distribution is advantageous (Table 4). In heart muscle, although countercurrent arrangements can occasionally be seen in the presence of general parallel arrangement, most capillaries are arranged in asymmetric pattern (Hellberg et al., 1972) (Table 4). The relatively low metabolic demand of the mesentery is reflected mainly by concurrent capillary arrangement. Therefore, high tortuosity does not offer any particular advantages.

It would be erroneous to conclude from this discussion that the relationship of capillary topography, morphometry, and arrangement is solely responsible for the maintenance of adequate tissue oxygenation. Capillary flow related to these parameters plays an important role. Regional capillary flow is dependent on arterial P\textsubscript{O\textsubscript{2}}, which may have opposite effects on capillary flow in different areas (Lubbers, 1978).

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