The Hemodynamic Importance of the Geometry of Bifurcations in the Circle of Willis (Glass Model Studies)

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Abstract:
The critical Reynolds number, $Re_c$, at which turbulence developed in glass model bifurcations was measured with an Evans blue indicator for bifurcations with a branch/trunk area ratio of unity, and bifurcation angles of 45°, 90°, 135°, and 180°. The $Re_c$ dropped from 2,500 in a straight tube to 1,200 in the 180° bifurcation. Further drops occurred with pulsatile flow (if the mean flow rate was used to calculate the velocity). Three sizes of aneurysms at the apex of the 90° bifurcation lowered the $Re_c$ to between 400 and 500 with a slight difference between steady and pulsatile flow. Reverse flow through the same bifurcation produced a more radical drop in the $Re_c$ at small bifurcations, and less in the 180° ones. The curves for steady and pulsatile flow crossed at 135°. We did qualitative, but not quantitative, assessments of axial stream impingement on the apex of the bifurcation in the site of aneurysm formation, and of boundary layer separation and vortex shedding at the lateral angles. Both appeared to vary with the angle of the bifurcation and the Reynolds number. We also studied flow profiles in glass models of anterior cerebral-anterior communicating artery bifurcations and the posterior communicating artery origin from the internal carotid. The relevance of these studies to localization of intimal cushions, aneurysms, and atherosclerosis was discussed.

Additional Key Words: atherosclerosis, aneurysms, turbulence, vortex shedding, boundary separation layer, Reynolds number, intimal cushions

Introduction

Hemodynamic forces may be important in the pathogenesis of localized vascular lesions such as aneurysms and atherosclerosis. The circle of Willis provides some advantages as a place to study the role of hemodynamics in arterial disease because: (1) The vessels are thin-walled so that atherosclerotic plaques and erosions can be seen through the wall, and flow profiles assessed. (2) The importance of bifurcations, where many lesions occur, can be studied geometrically as many sizes of angles are available with both symmetrical and asymmetrical branches. (3) Forward and reverse flow can occur at the same site at different times (e.g., with a subclavian steal), so that the role of constancy of hemodynamic forces might be studied.

The disadvantages are: (1) the small size of the vessels which makes it difficult to insert wire probes without distorting the flow, (2) the depth of the vessels inside the skull so that in vivo experiments are almost impossible, and...
The effect of bifurcation angle (between the side branches) on the critical Reynolds number ($Re_c$). The solid circles are for steady flow and the open circles for pulsatile flow with the $Re$ calculated for the trunk. The solid triangles are for steady flow with the $Re$ calculated in the branch. Note that the larger the angle, the lower the $Re$ (or flow) at which turbulence develops in the branches.

With aneurysms, turbulence develops at a much lower flow rate. The points were obtained by averaging the results from all three types of aneurysms since no difference was found between them.

The effect of reverse flow through bifurcations on the $Re$ for turbulence. The solid circles are for steady flow and the open circles for pulsatile flow. The $Re$ was calculated for the trunk. Note that there is no difference in the two curves for angles above 120°.

The variation of the circle both within species and between species.

Model studies should suggest where hemodynamically generated lesions might occur. A careful pathological study of these regions at autopsy might prove whether these regions have the predicted incidence of different types of lesions. This study should include distending the vessels to normal pressure, and doing three-dimensional mapping of lesions in terms of the tube diameters (see below).

Several studies have attempted to study the alterations in flow profiles at bifurcations. However, none of these have tried to assess systematically the importance of the angle of the bifurcation on the resulting flow profiles if other parameters such as flow, Reynolds number, and geometry are kept constant. Our study has attempted to do this in glass model bifurcations.

We have tried to assess the following variables. (1) The effect of the apical angle on the development of turbulence since Fry has provided evidence that turbulence, with its associated increased shear rate, can damage the endothelium of canine aorta, and possibly cause atherosclerosis. Roach and Boughner and Roach have also shown that turbulence can alter the elastic properties of a variety of arteries from dog and man. (2) The location of boundary layer separation with different sizes of angles. This has been studied previously, although not systematically, by several authors. (3) The effect of pulsatile and steady flow on (1) and (2). (4) The importance of special geometries, e.g., models of the anterior communicating artery joining the two anterior cerebral arteries with and without occlusion of one side of the circulation. (5) The effect of flow reversal in a bifurcation on the presence or absence of turbulence.

We have done some preliminary studies on the location of aneurysms in the circle of Willis, and also on the location of atherosclerotic plaques and intimal cushions. However, we had difficulty comparing these with the model studies because of lack of information.
Flow within the large, unilocular, saccular aneurysm. (a) The axial stream flows rapidly into the sac with little deflection until it reaches the apex of the aneurysm when it is deflected back. (b) Turbulence within the aneurysm and side branches. The flow appears to remain more on the side of injection. Some backflow is seen at the left-hand side of the origin of the lower branch. (c) Several laminae are shown in the parent trunk. The upper area shows boundary layer separation at the origin of the top branch. (d) Similar to (c) but with less dye. The differential streaming (i.e., lower side of parent to lower branch) is apparent, although at least one lamina appears to cross from the aneurysm to the opposite branch. N.B.—rapid clearing of the aneurysm.

on how the geometry of bifurcations changes with age, blood pressure, and other variables. These questions must be answered before the real relevance of model studies can be determined. However, answers to the first questions can be obtained, at present, only from model studies.

Methods
Glass models of bifurcations with smooth angles were blown by an expert glassblower from Pyrex. We used the following. (1) Five straight tubes of internal diameter (i.d.) 0.7 cm and lengths of 12.5, 25, 50, 75, and 100 cm to assess the importance of the length of the parent tube on flow before the bifurcation was reached. (2) Four symmetrical bifurcations with stems of 0.7 cm i.d. and 20 cm long, with branches 0.5 cm i.d. and 15 cm long, but bifurcation angles of 45°, 90°, 135°, and 180°. These were designed so that the total area of the branches was approximately equal to the area of the parent tube so that neither acceleration nor deceleration would occur at the branch point. (3) A model of an asymmetrical 90° bifurcation with the same 0.7 cm trunk, but branches of 0.6 cm and 0.3 cm i.d. (4) A model of the anterior communicating artery complex with stems 15 cm long and 0.5 cm i.d., a cross-piece 2 cm long and 0.3 cm i.d., and branches 15 cm long and 0.4 cm i.d. Each stem was offset 45° to the axis of the branches. (5) A model simulating the origin of the posterior communicating artery (PCA) from the trunk of the internal carotid artery. The branch (PCA) was 10 cm long with 0.5 cm i.d. and arose at an angle of 105° from the main stem which was 0.7 cm i.d. proximal to the branch and 0.5 cm i.d. distal to it.
Three types of aneurysm—(a) and (b) are small, (c) large unilocular, and (d) large bilocular. 
(a) Small aneurysm with injection into axial stream. Flow is turbulent in branches, and clears rapidly from aneurysm. Little differential streaming of central stream. 
(b) Small aneurysm with small axial stream injection. N.B.—backflow out of aneurysm with turbulence at origin of branch, and cross-over of stream so left side (upper) of axial stream goes to right branch (lower part of photograph). 
(c) Large unilocular aneurysm. Central stream went to apex of aneurysm and then cleared rapidly into the branches. 
(d) Large bilocular aneurysm. Circulation in the sac is not as rapid as in (c). There is little deviation of axial stream. Flow in branches is unstable, and sometimes turbulent (lower branch).

(6) Three glass aneurysms blown at the apex of a 90° bifurcation, but of varying diameter. The "minute" one had a neck diameter of 0.7 cm and a sac diameter of 0.5 cm. The large spherical aneurysm had a neck diameter of 1.0 cm and a sac diameter of 2.0 cm; the large bilocular aneurysm had a neck diameter of 1.0 cm and a sac diameter of 2.3 cm.

We used a modification of Stehbens' apparatus toperfuse the bifurcations. Essentially this consisted of a constant pressure reservoir filled from the taps, with the pressure kept constant by an overflow. This was connected by tygon tubing of 1 cm diameter to the glass model and the outflow went via a resistance to a stopcock and the sink. The stopcock could be used to divert flow into a graduated cylinder to measure the flow. All bifurcations were horizontal to avoid gravity effects. Descriptions in the legends of "lower" and "upper" branches are for interpretation from the photographs. Evans blue dye was injected into the tygon proximal to the glass tube in order to study the flow profiles, and to determine if turbulence was present. A 26-gauge needle was used and caused minimal flow disturbance.

The viscosity of the water was obtained from the Handbook of Physics and was temperature-dependent. With the flow rates used, we found no temperature difference between the reservoir and the outflow. Measurements with an Ostwald viscometer showed that the amount of Evans blue dye used did not alter the viscosity.

Reynolds numbers were calculated for the parent trunk using the measured mean flow rate, the diameter of the tube, and the viscosity and density of water at that temperature. The Reynolds number, Re, is expressed as Re =
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**Figure 5**

Boundary layer effects in 90° bifurcation. (a) Boundary layer separates from wall just distal to lateral angle of bifurcation. (b) Boundary layer separates on both sides, and does not re-attach at this low rate, but stays away from the edge of the tube. (c) A thicker dye injection shows that the boundary layer is quite thick (top of photograph), and that the more central components are more apt to re-attach (return to the wall) than the peripheral ones. (d) The boundary layers, or those close to them, tend to generate a small vortex near the apex. The apical zone remains clear, and represents a stagnation point. (e) Early turbulence in the upper tube, and vortex shedding in the lower one on the photograph, although the Re is still 500. Note the minimal damping of the vortices compared to (f) at Re = 1,500. (f) Re = 1,500. Here the boundary layer separates more, but rapidly (i.e., a short distance downstream) reattaches and generates vortices which have a progressively greater spacing as they are swept downstream. Attempts to quantitate this to compare it with the Re failed.

\[ \frac{\rho \cdot \bar{v} \cdot d}{\eta} \]

where Re = Reynolds number, \( \bar{v} \) = mean velocity = flow/unit area, d = diameter, \( \rho \) = density, and \( \eta \) = viscosity. Reynolds\(^1\) found that turbulence occurred in a long straight tube if this number exceeded 2,000. Since then there have been many debates in the biological literature about whether this value can be reached in the circulation. Stehbens\(^2\) was one of the first to point out that bifurcations lowered the critical Reynolds number, \( \text{Re}_c \), at which turbulence first developed, but did not provide sufficient data to allow predictions of the \( \text{Re}_c \) for different bifurcation angles. We have done this with angles from 45° to 180°.

Comparable studies were done with reverse flow. Here the two branches of the bifurcation were joined with long equal lengths of tygon tubing to the inlet tygon tubing via a Y-tube. The “parent” trunk was attached via a variable resistance to the outflow. Thus flow went from the branches into the parent trunk. This situation is analogous to flow in veins, or to flow from the vertebrais into the basilar artery. It will also occur in certain of the “steal” syndromes.

Finally, the effect of pulsation was assessed by feeding the inflow tubing through a sigma-motor pump (model T8) at 70/minute. The mean flow was used for calculation of the Re.

Photographs and movies were made of the flow profiles to assess the extent and location of...
Axial stream effects in a 90° bifurcation. (a) Injection in the axis of the trunk produced apical impingement with deflection into the side branches, and some separation paracentrally. (b) Same as (a) but with pulsatile flow. Note that there is more "back flow" in the apical region, and that the axial stream in the trunk becomes the boundary layer in the branches. (c) Similar to (b) but slightly off center, and some nonlaminar flow is seen in the top branch. (d, e and f) With higher Re of 1,500, vortex shedding occurs in the branches. The pitch or spacing of the vortices varies with the lamina injected. The closer to the central stream the injection is made (f), the shorter is the original vortex.

Results

**Tube Length**

All of the tubes gave an Re, for steady flow of 2,500 ± 30 (SEM)* and 2,090 ± 10 (SEM) for pulsatile flow. These values exceeded Reynolds' value of 2,000 for a long, straight tube, far from the inlet, and so we concluded that our connections would not produce turbulence in the region of the bifurcation. All subsequent experiments were done with tube lengths of approximately 20 cm.

*SEM = standard error of the mean.

The effect of bifurcation angle on turbulence

In all cases of forward flow the branches developed turbulence at much lower flow rates (Re) than occurred in the parent trunk or in a straight tube. The critical value at which flow just became turbulent in the branches was determined by varying the flow and watching the dye patterns. The results are shown in figure 1. The values plotted are the lowest ones at which we felt turbulence (as opposed to eddy shedding) occurred. The values varied with the angle of the bifurcation even though the tube sizes were identical, thus indicating that geometry must be considered as well as other parameters. The solid circles show the Re, in the trunk, and the triangles the Re, in the branches at which branch turbulence occurred with steady flow. While some authors
suggest that pulsatile flow has a stabilizing influence, we found it lowered the $Re_c$ appreciably (fig. 1). With forward flow, the effect of the angle of the bifurcation was similar for both steady and pulsatile flow. However, with reverse flow (fig. 2) the curves for steady and pulsatile flow intersected. We are unable to explain this.

Aneurysms at the apex of the bifurcation developed turbulence at very low Reynolds numbers (about 400), and this was more marked with pulsatile than with steady flow (fig. 1). The circulation within the aneurysm was rapid (fig. 3a and b), and fitted with the angiographical observation that aneurysms, unless thrombosed, tend to clear at the same time as their feeding vessels. The boundary layer within the aneurysm often cleared slowly. The boundary layer from the artery was not pulled into the aneurysm (fig. 3c). There was a suggestion from some studies (fig. 3d) that dye from one side of the parent trunk tended to go to the ipsilateral side of the aneurysm, but this was not consistent, and probably is flow-dependent. In view of the degree of turbulence seen, it is not surprising that Ferguson\(^1\) found clinical evidence of turbulence in human intracranial saccular aneurysms studied with phonocardiography. There was very little difference for the $Re_c$ in the three types of aneurysms, but the different sizes of aneurysm seemed to have slightly different effects (fig. 4) on the flow in the branches. All aneurysms caused flow distortion at the neck and at the origin of the branches. The minute aneurysm, on the whole, caused more flow distortion in the branches than the large ones did. Ferguson\(^1\) has demonstrated that human intracranial saccular aneurysms produce turbulent flow. Except in one or two cases the turbulence (murmur) was localized to the aneurysmal sac. In one a murmur was also recorded in the branches, but it was not clear if this was due to transmission of the murmur to the branches from the sac or due to distortion of the flow in the branches. No murmurs were recorded at normal intracranial bifurcations. It seems unlikely from available measurements of cerebral artery flow that Reynolds numbers in the circle will exceed 600 to 700 at most.\(^{10-21}\) Anemia will raise the $Re$ some, but not enough to generate the $Re_c$ of 1,200 to 1,500 needed to produce turbulence at normal bifurcations, while it will aggravate the chance of turbulence in aneurysms.

THE EFFECT OF THE BIFURCATION ON THE BOUNDARY LAYERS

These results were less consistent (fig. 5) and did not appear directly related to the angle. The size and shape of the lateral angle, as well as its smoothness, were important, but much harder to measure accurately than the angle of the apex. The patterns observed included: (1) boundary layer separation (fig. 5a to f), (2) eddy shedding (fig. 5e and f), and (3) turbulence (fig. 5e). All of these varied with the angle of the bifurcation and to a lesser extent with the Reynolds number. Some of the variations are shown in figure 5 for a 90° angle at different Reynolds numbers. In most cases the dye was injected into only one lamina and so the patterns were sharp. However, it is obvious from figure 5 that the different laminae behaved differently. Since we are able to

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**FIGURE 7**

Asymmetrical bifurcation. The large branch has twice the area of the smaller one. (a) Shows that the boundary layer forms helices in the large branch, but not in the small one. (b) Shows the rapid clearing of the apical area with the same branch patterns as before even though there is now both axial and boundary injection.
Model of the anterior communicating artery (ACCA) joining the two anterior cerebral arteries (ACA). (a) Flow in both anterior cerebral arteries. There is little boundary layer separation, and minimal flow in the communicating artery. (b), (c) and (d) Have no flow in the upper branch of the anterior cerebral artery. (b) and (c) Illustrate the stagnation point produced at the junction of the ACCA with the lower ACA. This is a common site of aneurysm formation with occlusion of the opposite ACA. (c) Shows the lag in flow in the occluded ACA compared to the patent one. (d) Shows that back flow occurs eventually into the occluded artery, although it never goes back to the origin.

Since aneurysms appear always to develop at the point where the axial stream impinges in the wall,10 a number of studies were made with central injections. Figure 6a illustrates that the central stream, at Re 500, may be deviated at the apex without appreciable back flow. This is analogous to the observations of others6 with sharper flow dividers. In other injections in apparently the same position (fig. 6b and c) there was significant back flow, or “bouncing” off the apex. This was very marked with pulsatile flow. With higher Reynolds numbers (e.g. 1,500), eddy shedding occurred in the branches (fig. 6d, e and f). The frequency of shedding varied with the lamina studied, and to a lesser extent with the angle of the bifurcation and the Reynolds number.

**ASYMMETRY**

Figure 7 illustrates how branch diameter affects the flow. In this case, one branch was twice the diameter of the other. Comparison of the pattern here with that in a symmetrical 90° bifurcation (fig. 5) shows that flow in the small branch is more stable. This would suggest that lesions due to high shear would be more likely to occur in large branches than in small ones. This has been observed for atherosclerosis in some series.22

**ANTERIOR COMMUNICATING ARTERY SIMULATION**

With flow in both “anterior cerebals,” there was little flow in the “anterior communicating” at Re of 500 to 1,000 (fig. 8a). However, if one of the “anterior cerebals” was blocked, flow occurred through the anterior communicating, hitting the apex of the junction as shown in figure 8b, and slowly reflecting...
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This term we have used to describe flow from two branches into a single tube. It is the usual situation in veins, and occurs also at the junction of the vertebral arteries with the basilar. It may occur if flow is altered in the circle of Willis.

Figure 2 illustrates that turbulence occurs in the trunk at much lower Re than with forward flow. This is not surprising since two streams meet. With acute angles there was little flow distortion even at a high Re (fig. 10a and b), but with wider angles (fig. 10c and d) dye from the branches is shot across to the opposite side of the trunk. By injecting different colors of dye into the two branches, a peculiar pulsation was observed in the trunk even though the branches were perfused from the same reservoir via a common tube with steady flow. This “whiplash” effect is almost certainly due to very slight differences in resistance of the two branches, and has been used in various fluidic devices as a means of generating pulsation. With a low Re (about 500) there was no mixing of the two types of dye, even though both traversed the trunk. This phenomenon was most marked in the 180° bifurcation, but occurred with all of the bifurcations studied. Figure 10a and b illustrates how the dye tends to remain at the “apex” of the bifurcation in this situation, in contrast to forward flow where this area cleared (fig. 5c and d). With high flow (Re 2,000) the branch flow is more apt to “stick” to its side of the trunk (fig. 10b), while the pattern is quite different as it is due to the bend if flow in one branch is occluded (fig. 10d).

Discussion

These observations should be confirmed biologically. There has been much debate about streaming, e.g., of platelet or tumor emboli. This makes it important to know if the laminae are as stable in distensible, pulsating arteries and veins as they are in the model. Brain vessels are transparent enough that these studies should be possible, at least in the larger arteries during brain surgery.

Since there is doubt whether atherosclerosis is shear-dependent, and whether it occurs in areas of high shear due to endothelial damage as proposed by Fry, or in areas of low shear due to diffusion problems as proposed by Caro et al., the exact localization of plaques and...
Reverse flow. (a) and (b) Show a 45° bifurcation with rapid flow (Re 2,000). The dye tends to stagnate or accumulate at the apex, which is filled largely from the "inner" boundary layer. There is little boundary layer separation. Dye tends to stay on the same side of the trunk as the branch from which it came (b). (c) and (d) Show reverse flow through a 180° bifurcation at low Re of 500. Even though the flow was laminar in the branches, a peculiar whiplash effect occurred in the trunk with interplay before the two streams. With dye injection of different colors in the two branches there appeared to be little mixing in the trunk (c), although grossly the flow appeared turbulent. However, with a large dye injection (d) the separation of the two streams was obscured and it appeared turbulent in the trunk.

cushions, with reference to cerebral artery bifurcations, may help to solve this problem, since this is one of the few places where the wall is thin enough (100-200μ) that intimal lesions can be seen through the intact artery wall, and their relationship to boundary layer separation (low shear) and reattachment (high shear) studied.

Rodbard17 has demonstrated that drag forces can alter the contour of silicone putty lining tubes through which water is flowing. Thus the loosely attached endothelium might also be altered. Hassler6, 14, 25 suggests this is the mechanism of production of intimal cushions. He feels these are precursors of atherosclerosis. Haust and More26 have suggested that muscle cells can generate collagen and elastin. These tend to occur in plaques, and their increasing size would create a diffusion barrier with subsequent lesions at the base, and thence the development of a plaque.

Figure 11 shows a low-power photomicrograph of the bifurcation of a brain artery. A small cushion is seen on the right, and a plaque on the left. The latter contains less muscle, although there is some near the lumen (figs. 12a and b). However, the depth of the plaque shows cholesterol clefts (fig. 12a). These lesions occur over a greater distance than that predicted for the boundary layer separation at normal flow rates (they are about 1.3 tube diameters long compared to a helix of 0.4 tube diameters at this site in the model). This does not say if the initial lesion occurred at a site of boundary layer separation or reattachment. We
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FIGURE 11
A low-power photomicrograph of the bifurcation of a middle cerebral artery from a 58-year-old woman. The direction of flow is shown with an arrow. There is a large atherosclerotic plaque on the left (shown with high power in fig. 12a) and an intimal cushion or small plaque (fig. 12b) on the right. These lesions at the lateral angles are typical. Lesions at the apex are usually aneurysms.

FIGURE 12a
A higher power view of the lesion shown on the left of figure 11. Cholesterol clefts were seen in the depth of the plaque and a few muscle filaments near the lumen. Flow is from bottom to top.

FIGURE 12b
A high-power photomicrograph of the lesion shown in the right branch in figure 11. There is some fixation artifact between the cushion and the vessel wall. Most of the lesion is made up of muscle cells histologically, and so is felt to be a cushion rather than a plaque.

are still looking for very early lesions to answer this question.

Also, we do not know if the vessel geometry changes with pulsation since brain vessels are quite distensible. Work on this is in progress. This would affect the boundary layer primarily, and it is difficult to predict whether the viscosity of the blood would allow the boundary layer to follow the change in vessel size with or without a phase lag. The former seems more likely, and adds greatly to the complexity of the problem.

The pulse contour may have some effect, although it is likely to be small. Our pulsatile pressures were produced by a sigma-motor pump and were almost sinusoidal. For technical reasons it is likely to be impossible to determine the exact shape of the waveform at the bifurcation of intracranial vessels, but it should be possible (with hot wire or hot film probes) to obtain it at larger bifurcations and to compare this with the waveform in the parent truck.

How valid are glass models? If properly made, and with proper flows (determined by the value that gives a comparable Reynolds number), they are useful. If the geometry is found to be crucial (as appears true at the apex here), then the rigid tube analogy must be questioned. We cannot find information on whether the geometry of vessels at the bifurcation changes with pressure, or if the distension of all parts of the bifurcation is equal so that only the size and not the...
geometry would vary. Preliminary experiments suggest that the geometry changes.

Model experiments such as ours can suggest physiological experiments (illustrated by Ferguson's analysis of murmurs in aneurysms). We now feel that comparable studies should be made looking at shear rate at the wall, and also at areas of boundary layer separation. These are difficult in brain vessels because the smallest size of probe available is about 1 mm long. This would produce a significant stenosis, and hence alter the flow profiles. Velocity profiles have been studied at aortic bifurcations, but all of these groups had trouble ensuring that the probe remained in the same position relative to the wall. Since we are still not sure how much the wall moves, the magnitude of this error cannot be predicted at present. However, we can say with considerable certainty that the hemodynamic forces at the apex of a bifurcation and at the lateral angle are different, and that both vary with the angle of the bifurcation. Thus a detailed analysis of flow at bifurcations may explain the cause of aneurysms, intimal cushions, and atherosclerotic plaques.

Conclusions

1. Glass model bifurcations of 45°, 90°, 135° and 180° angle were studied with forward and reverse flow under steady and pulsatile flow conditions. Dye injection showed that the critical Reynolds number for branch turbulence depended on the angle of bifurcation, the direction of flow, and whether the flow was steady or pulsatile.

2. Aneurysms of three sizes at the apex of the 90° bifurcation developed turbulence at very low Reynolds numbers (400).

3. The relevance of these observations was discussed with respect to the localization of aneurysms, intimal cushions, and atherosclerotic plaques in the circle of Willis.

4. The true geometry of the circle of Willis in vivo should be determined, and also its effect on the localization of lesions.

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