Contribution to the Hemodynamics of Arterial Venous Malformations

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Abstract:
In three cases of arteriovenous malformations (AVMs), and in one postoperative case, the passage of an I.V.-administered 99m-Technetium bolus through the brain and the 133Xenon clearance after intracarotid injection from different brain areas were observed, using a scintillation camera-1600 channel memory-digital magnetic tape unit. Regional cerebral blood flow values from contiguous areas down to 12 mm lateral lengths were calculated. In two cases computer-calculated cerebral blood flow maps are presented. Areas surrounding the AVMs revealed relatively high CBF values, while the blood flow in more distant parts of the hemisphere was decreased. Areas of low CBF values were detected also in the postoperative case with ligation of vessels. The initial part of the washout curves showed over all AVMs shunt peaks up to 88% of the initial activity. Shunt peaks detected also over most parts of the involved hemisphere are explained by arterio-arterial shunt connections. Their flow, centripetally directed to AVM, may cause the observed pattern of higher and lower flow values, indicating that the Xenon washout may be sensitive not only to capillary flow. Conclusions are drawn that the Xenon-clearance technique provides detection of the hemodynamic influence, but not of the shunt volume of AVMs.

ADDITIONAL KEY WORDS
Xenon clearance arterial shunts regional cerebral blood flow cerebral angiography

Introduction
Hemangiomas or arterial venous malformations (AVMs) are characterized, among other points, by bypasses or shunts between the arterial and venous parts of the circulatory system. Thus, a certain amount of the blood supply to the organ will not pass through the capillary bed, but will quickly reach the venous outflow through precapillary shunts of different diameters (shunt volume). This shunting may influence the blood supply to neighboring and even remote cerebral areas connected by arterial collateral channels to the AVM. This phenomenon is well known and has been proved qualitatively by many angiographical findings. Quantitative measurements of the hemodynamics of AVMs have provided mainly information about the shunt volume of the AVMs. The deleterious influence of AVMs on the blood supply of the entire hemisphere has not been determined.

This study reports CBF measurements on four cases, three with AVMs and one postoperative case. The postoperative case was not investigated preoperatively by our method.

Case Reports
CASE A
A 52-year-old female underwent three transient attacks of leftsided hemiparesis since her 30th year. On admission, one day after a further attack, the neurological examination showed a left hemiparesis and impairment of consciousness. Lumbar CSF was not hemorrhagic. The EEG showed a severe depression over both hemispheres, with a maximum of slow waves over the right frontotemporal region. Bilateral carotid angiography demonstrated a large AVM located in the right upper frontal region, supplied from the basal parts of the anterior cerebral arteries.
A. Right carotid angiogram of patient A, lateral view. B. Left carotid angiogram, sagittal view. Note complete filling of the right sided AVM from the left side.

From both the left and the right carotid arteries, the convolute could be filled (fig. 1). The patient died three days later. Autopsy findings showed a large, partially calcified AVM in the above-mentioned region, with some small bleedings of various ages.

CASE B
A 35-year-old male had leftsided headaches for the past 20 years. Admission followed a severe attack of headache, with stiffness of the neck. On neurological examination we found a slight right hemiparesis. EEG showed slow waves spread over the entire left hemisphere which were maximum over the temporal lobe. Carotid angiography of both sides indicated an AVM in the left middle frontal region supplied from the middle cerebral artery without functional connection to the other side (fig. 2). The patient was successfully operated upon.

CASE C
An 18-year-old female had a sudden attack of headache, right hemiplegia, and motor aphasia. Lumbar CSF was hemorrhagic. EEG showed severe abnormalities over the left hemisphere with a slow wave focus over the temporal region. Carotid angiography of both sides demonstrated an AVM of nut size in the left Sylvian fissure supplied from the middle cerebral artery. The AVM was surgically removed.

CASE D
A 22-year-old female had a three-year history of several bleedings from an AVM supplied by the middle cerebral artery and located in the right Sylvian fissure. After extirpation of the aneurism there was sustained increase of left hemiparesis, hemianesthesia, and hemianopia. The EEG showed disturbance over the entire left hemisphere, maximum in the temporoparietal region. The CBF was measured four months after operation. Carotid angiography at this time was nearly normal (fig. 3).

Methods
After intravenous injection of 4 mCi 99m-Technetium (Pertechnetate), the arrival of the tracer bolus in the brain and the initial

FIGURE 2
Left carotid angiogram of patient B.
Blood flow was calculated using the stochastic analysis:

$$f = \frac{(H_0 - H_{10}) \cdot \lambda}{A_{10} \cdot Bg}$$

and white matter, $H_0$ the initial activity, $H_{10}$ the activity after ten minutes, $\lambda$ the diffusion coefficient of gray and white matter, and $A_{10}$ the area under the washout curve represented by the sum of all counts registered during the ten minutes. $Bg$ is the average background over ten minutes.

Blood flow measurements have been conducted by injecting 4 mCi of $^{133}$Xenon dissolved in saline under local anesthesia into the internal carotid artery and registering the decrease of activity as a washout function over the brain ($Xe$-clearance method, Ingvar and Lassen6). Regional washout curves were obtained by means of a scintillation camera-1,600 channel store-unit, which provides blood flow measurements over multiple contiguous square areas of variable, but at least 12 mm, lateral lengths distributed over the entire brain.6 Concerning the resolution of the camera system, Anger7 specified the camera resolution with the lead bar phantom without collimator for $99m$ Technetium as $4''$. This measurement was repeated with our equipment and revealed the same result. The resolution for two different 2 mm sources measured with the 4,000-hole collimator and using Americium ($60$ KeV) and $133$-Xe was $20$ mm using the full-width-at-half-height definition, while the two sources could be discriminated optically at a distance of $15$ mm. Therefore, the size of the single areas is at the limit of resolution; by enlarging the areas, an improvement of accuracy cannot be achieved.
vestigation. The 1600-channel store provided a three-dimensional oscilloscope display and a digital printout. The tape was fed directly to a computer (IBM 360/30) for calculation and a final printout as a map of cerebral blood flow.8

A simple photographical summing-up of the Xenon activity over the brain during the first three minutes provides scintigraphical pictures, which deviate in some respects from the usual pictures obtained after intravenous administration of Per-technetate, Chlormerodrin, etc. First, the injection into the internal carotid artery brings out only cerebral structures. Second, the radiating blood volume and the local tracer penetration into the tissue does not determine the difference in local activity levels, as is the case in the above-mentioned radioisotopes. The difference in local activity levels is mainly caused by the regional blood flow which locally washes out more or less Xenon.

Counts: In the legend to figure 4 the counting statistics of the single areas in the computer evaluation are given. The actual countrates for the peaks were around 3,000 cpm, chosen in correspondence to the counting loss exceeding 2% with higher countrates than this. The regional washout functions are sufficiently defined by these countrates mainly due to the high signal-to-noise-ratio of our system (100:1 at the end of the curves). In figures 5 and 6 the computed areas are composed of multiple recording areas as shown on the photos from the memory oscilloscope; thus, the countrates are higher corresponding to this. On figure 7 the curve with the shunt
peak (right hemisphere) is written with 300 K/min for fullscale, while the curve of the left hemisphere is recorded with 1 M/min for fullscale. Due to deadtime of the gamma camera system at approximately 300,000 cpm a detectable counting loss of 2% begins to occur. Saturation of the camera, however, occurs at a much higher countrate (theoretically with 4 μs camera deadtime 15,000,000 cpm, actually measured in this system at approximately 6,000,000 cpm). The 300 ms for data transfer from the memory to the tape were interpolated according to the slope of the function.

Regional washout curves, representative of areas over, near, and distant to the AVM, were drawn manually from the digital printout in two cases. Attention was paid to the initial parts of the curves. The presence and, if so, the height of abnormal peaks of activity, disappearing after some seconds, were pursued.

**Results**

The rapid serial photographs, after the I.V. application of 99m-Technetium, show the sudden shooting in of a large amount of the tracer bolus into the AVM, which is depicted much earlier than the other structures. With a delay of approximately five to ten seconds to the filling of the AVM, the common shape of a brain scintigram comes out. Although all three cases showed this phenomenon, case B demonstrates it most clearly (fig. 8).

Blood flow measurements have been performed in case A from representative areas over the AVM and from angiographically indifferent areas over both hemispheres, indicated by black spots in figure 5. The cross-flow enabled simultaneous measurements from both hemispheres, placing the camera over the vertex. The tissue surrounding the AVM showed, with respect to the age and severity of the lesion, a relatively high perfusion (46 ml/100 gm min) in comparison to other regions; the parietal-occipital area had a significantly lower value (38 ml/100 gm min). Corresponding areas over the other hemisphere

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**FIGURE 6**

*Case B, left temporal view. Injections of 4 mCi 133Xenon into the left internal carotid artery. In the left upper corner Xenon-scintigram with decreased activity over the AVM (negative representation). On the right side presentation of one sampling period, taken from the oscilloscope of the core memory. The sites of the two areas of regional flow measurements are indicated as black spots.*

*On the bottom, scheme of carotid angiography, with sites of the AVM and regional areas, individual washout curves and values of shunt peaks (%) and blood flows (ml/100 gm min).*
Average clearance curves from both hemispheres in patient A, vertex registration. Both halves of the crystal of the camera are connected to ratemeter-recorder units. Note shunt peak over the right hemisphere while the left hemisphere shows no shunt peak but a delayed filling. Good separation between the shunt peak and the onset of the proper washout curve.

had uniformly low values in the range of 28 ml/100 gm min (fig. 5). Case B revealed 41 ml/100 gm min over the AVM region and 37 ml/100 gm min in the parietal occipital region (fig. 6). These two values, calculated from larger areas with higher count rates than from the units used in the computer-calculated blood flow maps, are significantly different.

In case C the computer-calculated blood flow may show (fig. 4) slightly but uniformly higher blood flow values over the temporal lobe than over other regions, mainly the parietal lobe, where markedly decreased values were registered. This slightly higher perfusion, in this particular frontotemporal region, seems not to be due to the AVM, since the same finding can occur in patients without an AVM and without cutting off any shunt peaks (fig. 9). This suggests that this finding represents a consistently higher tissue perfusion of the temporal lobe. An artifact caused by the quick bolus passage through the big branches of the middle cerebral artery in the Sylvian fissure or an insufficiently corrected A. V. shunting phenomenon must also be considered.

The blood flow may in case D (extirpation of an AVM in the Sylvian fissure) indicate a generally lowered perfusion in the region supplied by the middle cerebral artery (fig. 10). In the former region of the AVM there was no alteration of blood flow detectable. However, from this region, sector-shaped areas of decreased blood flow spread out to the parietal and basal-frontal lobes. A region of relatively high blood flow can be recognized over the upper frontal lobe, likely indicating blood supply from the anterior cerebral artery.

The scintigrams obtained from the Xenon radioactivity accumulated over the first three minutes showed, in all three cases, the position
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FIGURE 8
Scintiphoto in case B obtained 10 and 20 sec respectively after injection of 4 mCi 99m-Tc-Pertechnetate into the cubital vein. Exposure time three sec. Note the early and quick influx of the radioactive bolus to the AVM and the delayed presentation of other structures in this initial phase. On the right side usual brain scintigram showing the excellent depiction of the AVMs (200,000 cts).

and shape of the AVMs, but in a negative display. The region of the AVM in case A (fig. 5) shows almost no further Xenon activity, and in case B (fig. 6) less activity than the surrounding areas. The same phenomenon could be recognized in case C.

Investigating the initial parts of the regional washout curves, high peaks of activity (Hp), lasting only for approximately three to four seconds, could be recognized over all AVMs. As indicated in figures 5 and 6, similar peaks also could be recorded over most parts of the same hemisphere. The height of Hp decreased with the distance to the AVM. In no case were peaks detectable over the hemisphere opposite to the AVM. This is demonstrated in figure 7. This analog presentation of washout

FIGURE 9
Computer-calculated blood flow map from a patient with diffuse cerebral vascular disease. Blood flow values in ml/100 gm min. Note slightly generally lowered blood flow values. The higher values over the temporal lobe are similar to the AVM patient in figure 4.

FIGURE 10
Case D. Postoperative computer-calculated blood flow map, left temporal view. Same measuring conditions as in figure 4. Note areas of decreased flow (solid lines) and one area of relatively increased flow (dotted line).
curves from both hemispheres in case A, obtained by means of two ratemeter-recorder units, shows also that the intersection of the slope of the initial peak and the gentle slope of the proper washout curve were clearly determinable.

The difference between Hp and the height of this intersection has been called shunt peak (Sp). Over AVMs, its part on Hp runs up to 73% and 88% respectively (figs. 5 and 6).

Photographs taken from the display oscilloscope, after playback of single data-sets from the tape store to the core memory, show the initial phase of the Xenon distribution in the brain similar to the record of the I.V. 99m-Technetium injection. In figure 5 the first sampling period of 2.4 sec indicates the high degree of cross flow to the side of the AVM; the second sampling period indicates the quick disappearance of activity from the AVM and the delayed filling of both parietal-occipital regions.

Discussion

the delayed filling of both parietal-occipital pressure-resistance relation

\[ f = \frac{aPd}{\text{CVR}_{\text{tot}}} \]

where \( f \) equals the total cerebral blood flow, \( aPd \) the arterial pressure in the distal artery entering the organ minus sinus pressure, and \( \text{CVR}_{\text{tot}} \) the total cerebral vascular resistance. \( \text{CVR}_{\text{tot}} \) mainly depends on the diameter of the single vessels contributing to the total resistance and the total cross-section of all vessels in parallel arrangement. A variation in the diameter does not result in a linear but in an exponential change of the resistance, and, at a given \( aPd \), of the flow. The exponent determining this change in living pulsatile elastic systems may approach, but not reach, four, the theoretic exponent according to the law of Poiseuille.

The effects of a local decrease of CVR on the cerebral blood flow, as is the case in an AVM, can be derived from the Distribution Law of Kirchhoff. Provided parallel arrangements, the law defines the reciprocal value of the total peripheral resistance as the sum of the reciprocal values of the single partial resistances. At a given \( aPd \), the total perfusion rate and the perfusion rate of one single resistance unit respectively might be calculated from:

\[ \frac{1}{f} = \frac{1}{aPd} \left( \frac{1}{\text{CVR}_1} + \frac{1}{\text{CVR}_2} + \cdots + \frac{1}{\text{CVR}_n} \right) \]

\[ f = \frac{aPd}{\text{CVR}_{\text{tot}}} \]

(1)

\[ f_1 = \bar{f} - (f_2 + f_3 + \cdots + f_n). \]  (2)

Suppose an AVM causes a low resistance \( \text{CVR}_1 \). This leads to a high local flow \( f_1 \). As seen from equation 2, this may be provided by:

either an increase of the total flow \( f \) (positive factor on the right side of the equation) or a decrease of the flow in other segments of the vascular bed (negative factors), as well as by both reactions at the same time. Actually, the one reaction occurs in the form of an augmentation of the carotid flow \( f \). This has been proved by determination of increased cardiac output in cases with cerebral AVMs. The other reaction takes place as the increased \( f \) is distributed to the single resistance units, according to the varied relation of their resistances. However, since the diameter of AV shunts influencing the flow with an exponential function often reach the tenfold diameter and more of normal capillaries, the increased carotid flow \( f \) may not provide sufficient blood supply for the entire hemisphere in cases of large AVMs.

These theoretical considerations do not provide an approach for calculating the actual blood flow rates, but may help to understand the underlying hemodynamic mechanisms. How far our findings can prove them will be discussed in the same sequence as the data were presented.

(1) The visualization of the passage of a nondiffusible radioactive tracer bolus through the cerebral circulatory system by means of a scintillation camera has already been presented with considerable case material. However, just a few cases of AVMs have been briefly reported. In these cases, and in AV shunts of other origins (tumors of different types), observations similar to ours are described: early and quick influx of a considerable amount of the radioactive bolus to the shunt area and early disappearance into the venous outflow. These findings, together with obvious-
ly delayed filling of the other parts of the brain, make a negative influence on the entire brain circulation likely. However, quantitative data concerning this point are not deducible from this part of our investigations.

(2) The blood flow values obtained by the Xenon clearance technique in cases A, B, and C showed flow patterns which do not fit the common opinion of most lowered blood flow in brain tissue surrounding an AVM. These layers showed, on the contrary, the highest flow values in each case, although they did not approach to, or exceed, the normal CBF values (50 ml/100 gm min) determined in young healthy subjects by many investigators and also by us using our device. Low flow values were detectable in more distant parts of the brain supplied by the terminal branches of the affected artery.

This finding can be explained by a collateral blood flow involving the leptomeningeal network in the supply of the AVM. Some evidence for this superficial collateral flow, which does not come out in our angiographical pictures, is the presence of shunt peaks far away from the AVM. This cannot result from poor resolution of the recording system, since areas near to the AVM, but in the other hemisphere, do not show any shunt peaks while more distant areas of the same hemisphere present high shunt peaks (fig. 5).

One possible explanation for these shunt peaks distant from the AVM is the registration of the shunting bolus in big draining veins and in the sinuses. This accounts for a certain part of the shunt peaks registered. There are some points which make a further explanation likely: The shunt peaks not directly registered over the AVM are uniformly distributed over the hemisphere, and do not show a pattern similar to the venous drainage. They do not increase over the large occipital sinuses, but decrease with the distance to the AVM. This makes the assumption likely that shunt peaks distant from the AVM represent the quick passage of the radioactive bolus through arterio-arterial connections using the numerous arteriolar anastomosis of the leptomeningeal network for the supply of the AVM. These arteriolar anastomoses are small enough not to show on arteriograms.

Assuming these small arterio-arterial connections, the low flow values in the vascular periphery and the increasingly higher flow values centripetal to the AVM can be easily explained as an intracerebral steal mechanism which causes a decreased washout, where the blood fails to arrive, and an increased washout where a pressure gradient, caused by diminished vascular resistance, keeps the blood flowing.

Under these conditions the higher flow values near the AVM represent the washout activity of larger vessels carrying blood to the AVM rather than capillary perfusion. Whether washout curves under abnormal conditions reflect a true and regular tissue perfusion is questionable. The contribution made to the washout of Xenon by vessels larger than capillaries and by arteries which are extracerebral but close to the surface of the brain is not clearly understood. Similar questions concerning gas diffusion are raised by the pathophysiology of the luxury perfusion syndrome. The luxury perfusion syndrome may represent a kind of shunting phenomenon. From our findings we conclude that vessels larger than capillaries are important in washout though they may lie on the surface of the brain.

Fewer difficulties in the interpretation arise from the registered lower flow values. In some regions, for example in case C, this decrease reached a critical level (fig. 4) (normal flow values in our material were 50 ml/100 gm min; flow values under 25 ml/100 gm min usually were found over areas with ischemic damage). Electroencephalographical and clinical abnormalities in case C were appropriate to the location of reduced blood flow and made morphological damage caused by ischemia very likely.

The basal flow in case A led to a dangerous decrease of the perfusion of the entire left hemisphere (28 ml/100 gm min). The absence of shunt peaks results from the lack of direct connections from left hemispheric vessels to the AVM.

The blood flow map in case D (fig. 10), where all arteries connected to the malformations had been clipped, indicates the extent of the hemodynamic influence of the former AVM. The similarity of the parietal ischemic areas in cases C and D is remarkable considering that both patients had analogous AVMs.
The scintigrams obtained by summing up the Xenon activity from the first three minutes gave a negative presentation of the AVM regions. This is mainly due to two factors: (1) The AVMs have a large blood volume and are well demonstrated by tracers remaining inside the vessels (fig. 8). However, since there is no further Xenon in the arterial blood after the injection, the AVMs give a negative contrast to the surrounding tissue containing Xenon. (2) Since there is actually a high perfusion around the AVM, Xenon is washed out more rapidly from the surrounding brain tissue as mentioned above. This regional washout-contrast phenomenon has been predicted by Loken et al., relating to regional hyperemia after infarction, and is now proved in the model of AVMs. Case B had a smaller AVM and a lower difference in the regional perfusion rates measured (difference 4 ml/100 gm min in comparison to 8 ml/100 gm min in case A, figs. 5 and 6). Thus, the negative presentation of the AVM is less marked in case B than in case A.

The registered initial high peaks over AVMs representing the arterial-venous shunting have already been described by Haggendal et al. The height of these peaks, \( H_p \), at a given counting geometry depends on the Xenon concentration in the blood and on the blood volume within the field of registration. The slope of \( H_p \) depends on the amount of Xenon-carrying blood leaving the field of observation without having the opportunity of transferring Xenon to the tissue. There is good evidence that this is due to the thickness of the walls and the shortness of the shunt connections, to the high flow velocity in them, and finally because an increase in the diameter of a vessel results in a lesser increase of its contacting surface \( r^2 \) in comparison to the increase in flow (theoretically \( r^4 \)).

The height to which the quick slope falls and from which the proper washout curve starts indicates the Xenon content of brain tissue within the field of observation. The difference between \( H_p \) and this point, the shunt peak \( S_p \), should be proportional to the shunt volume.

Assuming this, Haggendal et al. have estimated the shunt volume directly from the ratio \( S_p/H_p \). The values obtained in this way were 70% to 90% and equal to figures which we could obtain in our cases by the same calculation.

However, a quantitative determination of the actual shunt volume \( S_v \) from this ratio is not possible. There is only a very rough correlation between them: \( S_v = S_p \times a \), where \( "a" \) represents an individual measuring variable, consisting of the ratio between blood volume and brain tissue in the field of observation and the other factors previously mentioned used to determine Xenon diffusion from the AVM to brain tissue. These variables differ in every patient and cannot be determined.

Considering these limitations, the Xenon-clearance method offers no quantitative measurement of shunt volume. For determining this, the 131-I-MAA method is useful.

However, preoperative measurements of regional cerebral blood flow in patients with AVMs, as described above, provide worthwhile information concerning the hemodynamic influence of such malformations on different parts of the brain.

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