RAPID SERIAL ANGIOGRAPHY: PRELIMINARY REPORT

BY

J. B. CURTIS*

From the Nuffield Department of Surgery, Oxford

Egas Moniz (1927) originated the method of visualizing the cerebral arteries in the living human by radiography of an injected radio-opaque substance. In addition he has been associated with many subsequent advances. According to Sanchez-Perez (1941) the first phlebogram was obtained by Egas Moniz on Dec. 19, 1931, accidentally from a technical error in making a late exposure. Moniz was quick to realize its implications and from this time angiography, which is the visualization of both arteries and veins, may be said to have replaced arteriography. The practice of making repeated exposures during an injection was then developed, and by 1934 the Portuguese school had elaborated the technique of taking six films in six seconds at one-second intervals (Egas Moniz, Lima, and Caldas, 1934). The apparatus used, called the "radio-carousel," consisted of a circular table on which six cassettes were fixed equidistantly. Mechanical rotation of the table brought the cassettes into position for serial exposure. By this means they were able to make crude studies of the cerebral circulation (Egas Moniz, 1934), and little has been added to their findings since that time.

The value of phlebograms in addition to arteriograms is now well established. For routine work most centres gradually evolved simple mechanical contrivances enabling two, three, or more films to be exposed over a period of about four to six seconds (Sanchez-Perez, 1943; Engeset, 1944; Lindgren, 1947; Boardman and Vickers, 1947). Such methods, satisfactory for routine diagnostic use, are subject to the criticism that they give pictures representing only isolated parts of a cycle of events. A study of the full circulation was not possible, and on these isolated pictures some unwarranted conclusions have been reached in reference to variations in circulation rate, the filling of vessels, arterial spasm, and even blockage.

Further development was possible along two lines.

Cineradiography depended on a cinematographic record of the image projected on a fluorescent

screen. Holm (1944) first reported its use in cerebral angiography. However, by this method at present there is great loss of definition. Lysholm and his assistants (1947) were fully aware of this drawback, and sought improvements in the definitive quality of the fluorescent screen and in the lens system of the camera.

Rapid Serial Exposures.—An alternative approach to the problem was by means of rapid serial exposures on a length of x-ray film. It was felt that this method could provide clearer pictures although the sensation of movement would be sacrificed. Exposures at a rate of up to two per second would then be adequate, at this stage, to study changes in the circulation, provided that the full period of the circulation could be covered. This paper is concerned with the results obtained by means of an apparatus developed along these lines.

Apparatus

Only a brief account of the apparatus will be given here. A prerequisite to its design and construction was x-ray equipment with the following characteristics:

1. An x-ray tube of the requisite power output with sufficient heat capacity to enable it to withstand exposures at half-second intervals over a period of 10 to 15 secs.
2. Film and intensifying screens which, used in combination with such a tube, would give sufficient penetration of the skull to obtain a clear image with an exposure as short as 1/5 sec.

A Machlett Dynamax, Type D, rotating anode fine focus x-ray tube, Kodak ultra-speed intensifying screens, and Ilford's Red Seal film were found to be suitable.

It was decided that the machine would need to fulfil the following requirements:

1. The size of each image should be 10 in. wide by 8 in. long, as this was the minimum size necessary to obtain a picture of the cerebral vascular tree.
2. It should be capable of taking twenty-five successive images entailing a total length of film of about 20 ft. This would cover adequately possible variations in the circulation time.
3. It should have three available rates of exposure: two per sec., three in 2 secs., one per sec.

* Nuffield Dominions Scholar from the University of Melbourne.

4. There should be a mechanism for the opposition of intensifying screens to the film at the time of exposure, as this is essential to obtain the necessary definition with such a short exposure.

5. The film should stand vertically, as by this means lateral views could be taken with the head in the brow-up position. This would facilitate percutaneous arterial puncture and accurate positioning.

6. The machine should fit the standard Lysholm-Schönander skull table which was available to us.

The considerable problems arising from these requirements were brilliantly solved by Dr. E. Schuster, O.B.E., who designed and constructed a machine based on the following principles:

1. The movements are driven by a constant-speed electric motor.

2. The timing devices depend on electrical circuits.

3. The film is taken up on a spool which is rotated by a transmission rod. This is timed to engage, rotate, and disengage automatically between exposures.

4. The intensifying screens are clamped to, and disengaged from, the film before and after the exposure by a system of electro-magnets.

5. The electrical impulse to set off the exposure mechanism of the x-ray tube is synchronized with the movement of the film.

Difficulty was experienced in developing a strip of film 20 ft. long and 10 in. wide, but was overcome by utilizing the principle of the "spiral holder," used to develop the lengths of film used in aerial photography during the 1939-45 war. The holder was modified to take film 10 in. wide.

Results

The results obtained by this method are illustrated by the records obtained from the following cases.

Case 1.—The record of this case has been used to illustrate the appearances in a normal angiogram (Figs. 1 to 18).

A man aged 40 years was admitted to hospital on Jan. 27, 1949. One week before, after a shivering attack on the previous night, he suddenly developed right-sided headache, and this was followed by a fairly rapid and progressive left hemiparesis affecting the arm more than the leg. Examination showed also left-sided sensory loss of cortical type affecting mainly the hand. His blood pressure was 135/85 mm. Hg, and examination of the cardiovascular system revealed no abnormality.

During the ensuing month there was marked improvement. On March 2 a right-sided routine percutaneous angiogram showed non-filling of the main branches of the middle cerebral artery, and a diagnosis of thrombosis was made.

On March 4 a lateral serial angiogram was carried out on the healthy left side. The percutaneous method described by Lindgren (1947) was used

with local anaesthesia and Omnopon-Scopolamine premedication. Twelve ml. of 35 per cent. diodone were injected, of which a residuum of 2 ml. remained in the tubing connexion, making a total of 10 ml. entering the artery. Twenty exposures were made at intervals of $\frac{2}{3}$ sec., the first exposure coinciding with the beginning of the injection. The tube was set at 150 MA and 85 kV and the exposure time was 0.2 sec.

Figs. 1 to 18 reproduce the exposures made in 11½ secs. and the legends attached interpret the various stages of the circulation.

Case 2.—The following case illustrates the special value of this method in the diagnosis of a pathological circulation.

A girl (No. 95,121/48) aged 19 years had suffered from attacks since the age of 7 years. In these there was a transitory loss of consciousness preceded by a sensation of numbness in the left hand. Examination showed slight motor weakness and a slight sensory loss of the cortical type in the left hand. Otherwise there was no abnormality on clinical examination, and there was no evidence of cutaneous hæmangiomas. X-ray examination of the skull showed a patch of irregular calcification in the right parietal region (Fig. 19). Examination of the cerebrospinal fluid showed no abnormality.

On Jan. 21, 1949, a right lateral serial angiogram by percutaneous puncture of the internal carotid artery was carried out with the same technique.

ILLUSTRATIONS

KEY TO LETTERING OF ARTERIES

Sy.	=	Carotid Syphon.
P.C.	=	Posterior Cerebral A.
A.C.	=	L or R Anterior Cerebral A.
F.P.	=	Fronto-Polar A.
Pre.Ro.	=	Pre-Rolandic or Candelabra. A.
P.P.	=	Posterior Parietal A.
P.T.	=	Posterior Temporal A.
A.A.	=	Artery of Angular Gyrus.
P.Cal.	=	Peri-Callosal A.
M.Cal.	=	Marginal Callosa A.

KEY TO LETTERING OF VEINS

I.L.S.	=	Inferior Longitudinal Sinus.
S.S.	=	Straight Sinus.
T.S.	=	Transverse Sinus.
G.V.G.	=	Great Vein of Galen.
I.C.V.	=	Internal Cerebral Vein.
B.V.	=	Basilar Vein.
V.L.	=	Inferior Anastomatic Vein of Labbé.
V.T.	=	Superior Anastomatic Vein of Trolard.
S.P.S.	=	Spheno-Parietal Sinus.
V.A.	=	Ascending Vein.
S.V.	=	Sylvian Veins at "Venous crossroads."
Si.S.	=	Sigmoid Sinus.

FIGS. 1 to 18.—Left angiogram to illustrate the normal appearances (Case 1).

FIG. 1 (at onset).—Left lateral view. There is no rotation in either plane, and centring is above and slightly behind the pituitary fossa.

FIG. 2 (at $\frac{2}{3}$ sec.).—The diiodone is seen faintly in the internal carotid and its branches. It has reached the genu of the anterior cerebral, the beginning of the ascending part of the middle cerebral in the sylvian fissure, and has filled the posterior communicating and the early part of the posterior cerebral (P.C.).

FIG. 3 (at $1\frac{1}{2}$ secs.).—There is filling to the periphery of the branches (P.Cal., M.Cal., F.P., Pre-Ro., P.P., A.A., and P.T.) of the anterior cerebral and middle cerebral arteries, with faint filling of the posterior communicating and posterior cerebral. The right anterior cerebral (R.A.C.) shows very faint filling indicating overflow to the opposite hemisphere. Anatomical variations are : (1) The carotid syphon (Sy.) has a "squashed" appearance ; (2) The early ascending portion of the anterior cerebral takes an unusual upward and backward course.

FIG. 4 (at 2.0 secs.).—The small unnamed branches have filled to the periphery. The diodone is now faint in the posterior cerebral (P.C.) and even fainter in the right anterior cerebral (R.A.C.). Diodone is still present in the internal carotid in the neck. In the usual angiographic procedure the first exposure would be made at about this stage.

FIG. 5 (at 2½ secs.).—There is now no diodone in the internal carotid in the neck or in the region of the syphon. It is fainter in the proximal parts of the anterior and middle cerebrals. One may conclude that it has taken a little over 2.0 secs. and slightly under 2½ secs. for the injection of 12 ml. of diodone. A diffuse cloudiness is now developing, indicating filling of the capillary bed. Careful comparison with Fig. 6 will show that the internal cerebral vein (I.C.V.), great vein of Galen (G.V.G.), and the posterior end of the inferior longitudinal sinus (I.L.S.) show very faint filling.

FIG. 6 (at 3¼ secs.).—The diffuse cloudiness is now marked. There are widely scattered very small vessels, and these are probably veins as they do not correspond with the peripheral small arteries shown in earlier exposures. The veins mentioned in Fig. 5 now show more definite filling. There is early venous filling at the Sylvian point (S.V.), and the sphenoparietal sinus (S.P.S.) is faintly filled.

FIG. 7 (at 4.0 secs.).—More definite venous filling is seen and the capillary haze has commenced to clear. There are numerous superficial ascending veins (V.A.) in the frontal and parietal regions and faintly in the occipital region. One of these, larger than the rest, is at the posterior end of the parietal lobe and is probably the superior anastomotic vein of Trolard (V.T.). Proceeding backwards and downwards from the region where this vein arises, is another smaller vein which in later films is identified as the inferior anastomotic vein of Labbé (V.L.). The sphenoparietal sinus is more clearly seen. No basilar vein is seen. The usual first phlebogram taken 2 secs. after the arteriogram would show this picture.

FIG. 8 (at 4 $\frac{3}{4}$ secs.).—There are no new details but the veins previously mentioned show better filling and are clearer. It is seen that the anterior end of the internal cerebral vein (I.C.V.) curls back on itself.

FIG. 9 (at 5 $\frac{1}{2}$ secs.).—The diffuse cloudiness due to the capillary haze has now almost gone. There is marked filling of the larger veins. No single Sylvian vein runs in the direction of the fissure of that name, and only a very small basilar vein (B.V.) can be made out. The small inferior anastomotic vein of Labbé is seen running into the transverse sinus (T.S.), and posterior to this there is an occipital vein.

FIG. 10 (at 6.0 secs.).—There is marked filling of the large veins. In some clinics which take their second phlebogram 4 secs. after the arteriogram this picture would be seen. The structures can be identified from the labelling in the previous figures.

FIG. 11 (at 6½ secs.).—This shows the maximal venous drainage. The superficial venous system is well seen and there is a full anastomosis of veins in the region of the Sylvian fissure (S.V.). Moniz called this the “venous cross-roads.” Arising from this region are the anastomotic veins of Trolard and Labbé and smaller veins passing down to the sphenoparietal sinus. Passing into this region is a vein from the frontal region. Do not confuse the superimposition of the shadows of these veins on the anterior end of the deep internal cerebral vein (I.C.V.) and its tributaries. The internal cerebral vein is clearly seen. It may be traced back to join the basilar vein to form the great vein of Galen (G.V.G.) which combines with the inferior longitudinal sinus to form the straight sinus, S.S.

FIG. 12 (at 7½ secs.).—This is a clear phlebogram.

FIG. 13 (at 8.0 secs.).—There are signs of slight fading of diiodone in the smaller veins. Where the second phlebogram is taken 6 seconds after the arteriogram, this picture would be seen. All the named veins stand out clearly. The superior longitudinal sinus, transverse sinus (T.S.), and sigmoid sinus (Si.S.) are well filled. The cavernous sinus cannot be made out with certainty.

FIG. 14 (at 8½ secs.).—There are the first signs of fading of contrast in the larger veins. The sphenoparietal sinus is only faintly filled and the internal cerebral vein and great vein of Galen have faded a little. The inferior longitudinal and straight sinuses and the smaller veins have disappeared.

FIG. 15 (at 9½ secs.).—The fading is more marked. The venous drainage around the temporal lobe no longer shows. There are only a few frontal and parietal ascending veins.

FIG. 16 (at 10.0 secs.).—There is further fading of the contrast.

FIG. 17 (at 10 $\frac{2}{3}$ secs.).—There is further fading.

FIG. 18 (at 11 $\frac{1}{3}$ secs.).—There is still very faint filling in some posterior frontal and parietal ascending veins. Exposure 19 at 12.0 secs. showed only the slightest trace of contrast, and exposure 20 showed no contrast.

FIGS. 19 to 34.—Right angiogram to illustrate an unusual type of angioma (Case 2).

FIG. 19 (at onset).—Right lateral view. There is no rotation in either plane and centring is in the region of the pituitary fossa. There is visible calcification in the right parietal region.

FIG. 20 (at $\frac{2}{3}$ sec.).—The contrast medium is seen in the following arteries : (1) internal carotid artery ; (2) right and left anterior cerebral arteries (R.A.C. and L.A.C.) ; (3) The posterior communicating artery* ; (4) right and left posterior cerebral arteries (P.C.). There is also slight but definite retrograde filling of the basilar artery (B.A.). The small vessels outlined beneath the posterior cerebrals are almost certainly the anterior superior cerebellar arteries. The anterior choroidal artery is also seen. The wider sweep of the right anterior cerebral may indicate some hydrocephalus on the right side, which is the side of the angiomatous malformation.

FIG. (21 at $1\frac{1}{2}$ secs.).—This is a full arteriogram and no abnormal vessel can be seen. The arteries are well filled with contrast to the periphery. The contrast is now fainter in the left anterior and posterior cerebral arteries. The main branches of the anterior cerebral artery and of the middle cerebral artery can be seen.

* It is a larger vessel than the posterior communicating seen in Figs. 2 and 3.

FIG. 22 (at 2.0 secs.).—This is a late arteriogram. It would be difficult now to detect contrast in the left anterior and posterior cerebral arteries. No abnormal vessels are seen, particularly in the region of calcification. The end of the column of diodone can be seen in the neck and it is missing in the next picture. Thus, the time of injection of the diodone was about 2 secs.

FIG. 23 (at 2½ secs.).—A diffuse cloudiness is now becoming evident. There is no diodone in the internal carotid or proximal arteries but there is still fairly good filling of the larger branches distally. The first veins can be distinguished if a careful comparison is made with Fig. 24: the internal cerebral vein (I.C.V.) and the posterior end of the inferior longitudinal sinus (I.L.S.).

FIG. 24 (at 3¼ secs.).—There is more definite venous filling. The inferior longitudinal sinus (I.L.S.), internal cerebral vein, great vein of Galen (G.V.G.), and straight sinus (S.S.) are seen. There is early venous filling at the Sylvian point and in the anterior temporal region.

FIG. 25 (at 4.0 secs.).—This corresponds to the usual first phlebogram, taken 2 secs. after the end of the injection. There is now more obvious venous filling of the vessels noted in Fig. 24. There are numerous thin-calibre ascending veins in the frontal region and superficial veins at the Sylvian point. No large veins are seen. Slightly below and in front of the calcified area a small collection of contrast is indicated by an arrow. It indicates the site of filling of the angiomatous malformation.

FIG. 26 (at 4.4 secs.).—The capillary haze has commenced to clear. There is widespread filling of small veins and the larger veins show more clearly. The straight sinus (S.S.) is clearly seen. The superficial veins are noticeably of much smaller calibre than usual. No anastomotic veins of Trolard or Labbé can be identified.

FIG. 27 (at 5.4 secs.).—This is a clearer phlebogram. The sphenoparietal sinus (S.P.S.) is seen. The angiomatous collection of contrast previously seen is now more plainly visible and has increased in size.

FIG. 28 (at 6.0 secs.).—This corresponds to the second phlebogram of most clinics, which is taken 4 secs. after the end of the injection. There is marked venous drainage of both the deep and superficial veins. All these vessels appear normal but small in calibre. In the area of calcification no definite abnormality is detected but there is venous drainage by vessels of small calibre. The collection of diodone in front and below it is now quite clearly seen. It measures about 1.0 cm. by 0.5 cm. Passing upward from it there is very faint filling of a large vein (V.) and passing forwards from it are two small veins.

FIG. 29 (at 6½ secs.).—Venous drainage is marked. The angiomatous collection of contrast has increased in size and the veins draining it are better filled. In the calcified area there are some fine vessels faintly filled lying parallel to each other.

FIG. 30 (at 7½ secs.).—The venous drainage of the rest of the hemisphere has commenced to fade. The small veins cannot be seen and the large veins are fainter. By contrast, the angiomatous area is now showing denser filling and more marked venous drainage. The vessels in the calcified area are also better filled.

FIG. 31 (at 8.0 secs.).—The general venous drainage has faded considerably. The venous drainage of the angioma has increased in density and the lesion is now clearly shown.

FIG. 32 (at 8½ secs.).—There is scarcely perceptible filling of the normal veins but the angioma is most marked.

FIG. 33 (at 9½ secs.).—The angioma shows marked drainage. There is still very faint filling of the internal cerebral vein and a posterior vein.

FIG. 34 (at 10.0 secs.).—The angioma still shows marked venous drainage.

FIG. 35 (at $10\frac{2}{3}$ secs.).—The same. Exposure 18 at $11\frac{1}{3}$ secs. showed the same appearance.

in Case 1. Figs. 19 to 34 reproduce the exposures made in 10 secs. at intervals of $\frac{2}{3}$ sec. These show an angiomatous malformation in the right parietal lobe. It is unusual in showing no abnormal arteries, and in possessing a very slow circulation, a finding which would have been missed in routine angiography.

Discussion

The Normal Angiogram (Case 1).—The normal arterial pattern is well illustrated in Fig. 3, while the appearances during early venous filling are seen in Fig. 7 and the details of later venous filling in Figs. 11 and 12.

The injection of diodone took slightly over 2.0 secs. During the first $\frac{2}{3}$ sec.* the contrast passed

* All times are measured from the first exposure which is taken at the beginning of the injection.

down the tubing connexion and up the artery to reach the genu of the anterior cerebral artery (Fig. 2). It has thus travelled about 20 cm. up the artery and a rough estimate of the minimum velocity of the contrast in the artery therefore would be 30 cm./sec.

The first veins showed filling after $2\frac{2}{3}$ secs., and it is of interest to note that they are parts of the deep venous drainage (Fig. 5). Previously it has been held that the deep venous drainage is slower than the superficial: the internal cerebral vein, the great vein of Galen, and the inferior longitudinal sinus are generally shown filled on the phlebogram of the second phase, and not on the first phlebogram (Moniz, 1934; Sanchez-Perez, 1941; Engeset, 1944). In Case 1 the sequence of venous filling is clearly shown to be the opposite of this, for, as

Fig. 5 shows, the deep veins fill first, and the superficial venous drainage appears in later exposures (Figs. 6 to 8), starting in the region of the sylvian point and then spreading upwards. The same order of venous filling was seen in Case 2. There is a rough relation between the time of appearance of diodone in the veins and their distance from the internal carotid artery.

The time taken from the beginning of the injection to the end of the venous drainage was 12.0 secs., the major portion of which was occupied with venous drainage, the time taken for the contrast to traverse the arteries, arterioles, capillaries, and venules being just under 3 secs. After $8\frac{2}{3}$ secs. the deep venous drainage could no longer be seen. The last veins to be seen were the posterior frontal and parietal superficial ascending veins, which had first shown filling at about 4.0 secs. Thus, diodone had been passing through the deep veins for about 6.0 secs. and through the superficial veins for about 8.0 secs.

Overflow.—There are several illustrations of overflow in these two cases. In Case 1 contrast from the left internal carotid could be seen in the left posterior cerebral and the right anterior cerebral arteries (Fig. 3). However, it quickly became fainter (Fig. 4). Overflow occurring at such an early stage ($1\frac{1}{3}$ secs.) may easily be missed in angiography by previous techniques when the arteriographic picture is taken at the end of the injection.

In Case 2 with injection through the right carotid there is also the unusual example of filling of the right and left anterior cerebral, the right middle cerebral, the right and left posterior cerebral arteries (Figs. 20 and 21, taken at $\frac{2}{3}$ sec. and $1\frac{1}{3}$ secs.). In addition, in the same figures, there is seen retrograde filling of the basilar and anterior superior cerebellar arteries. The overflow has faded considerably by Fig. 22 (at 2 secs.), and it would be difficult to detect by the ordinary arteriographic timing.

The Angiomatous Malformation.—In Case 2 the visualization of the angiomatous malformation, seen best at $9\frac{1}{3}$ secs. (Fig. 33), demonstrates the value of this technique in pathological diagnosis. The usual first and second phlebograms, corresponding to Figs. 25 and 28 of this series, would not have given the diagnosis, though the slight unusual collection of contrast seen in these pictures might have aroused suspicion. A second phlebogram 6 secs. after the end of the injection, corresponding to Fig. 31, would have been more informative, but

a diagnosis of some form of angiomatous malformation would be all that was possible and the true nature of the lesion would still be obscure. In this case, unlike most angiomas, there are no abnormal arteries and the venous drainage, except from the angioma, is normal. Instead of extremely rapid filling and emptying of the angioma which is seen in other cases, there is here a slow accumulation of contrast in one site followed by an equally slow venous drainage from it. To account for this slow filling of the angioma, the site of the lesion must be distal to the arterioles. There is no evidence of any abnormal arterio-venous communication and this would appear therefore to be a true capillary or small cavernous angioma. This is an unusual type of angioma and, as far as I know, has not been previously demonstrated by angiography, except possibly by Green and Arana (1948). The slow circulation of the malformation was adequately visualized only by the serial films over a long period.

Summary

1. A method of rapid serial angiography has been described which will take twenty-five full-size x-ray pictures at intervals of $\frac{1}{2}$, $\frac{2}{3}$, or 1 second.
2. The results obtained by this method in the normal and in a case of angiomatous malformation are demonstrated.

This work would not have been possible without the help of Dr. E. Schuster, O.B.E., who invented and made the apparatus. I wish to thank also Dr. C. de Andrade who assisted in the technique of the percutaneous carotid angiography; Mr. A. F. Nicholls, M.S.R., for the technical skill with which he solved many of the early problems; and Miss D. Haigh, M.S.R., who provided excellent radiographic assistance. Special lengths of x-ray film and the photographic reproductions have been supplied by Messrs. Ilford Ltd. The expenses have been met by a research grant from the Nuffield Committee for the Advancement of Medicine, University of Oxford.

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FIG. 1.—The needle and tubing.

FIG. 2a and b.—Case 1.

FIG. 3.—Case 2.

FIG. 4.—Case 3.