has permitted the modern neurosurgical attack on carotid and cerebral vascular lesions.\textsuperscript{4,16}

The initial report by Egas Moniz, which was presented to the Société de Neurologie in Paris on July 7, 1927, is reproduced below.

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ARTERIAL ENCEPHALOGRAPHY, ITS IMPORTANCE IN THE LOCALIZATION OF CEREBRAL TUMORS*

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The Sicard test of intraspinal injections of Lipiodol has rendered important services in the localization of medullary compression. At the same time it has constituted a big step forward in neurology, for the principle of putting into relief the radiographic opacity of the Lipiodol introduced into the cavities of the body has overtaken neurology and has become a general method which has progressed daily.

Recently the pathology of the gall bladder has been clarified considerably by the method of Graham, Cole and Copher. They have founded their experiments upon the action of certain preparations of phthalain and their selective elimination by bile, which was demonstrated by Abel and Rowestre for the study of the functional capacity of the liver. Graham, Cole and Copher started their work in 1923. They sought a compound with a phenolphthalein base with a fairly high atomic weight, such as, for instance, bromine or iodine, which, eliminated by the biliary channels, would show up the bladder as opaque to x-rays. They selected intravenous sodium tetradiodophenolphthalein and demonstrated the possibility of obtaining good pictures of the bladder in the dog. The American authors recognized at the beginning that the substance used was fairly toxic and replaced it with sodium tetrabromophenolphthalein. With bromine and iodine they obtained the desired results, except that the radiographic effects of iodine were more clearly visible than those of bromine.

After prolonged experimentation the authors decided upon phenoltetradiodophthalein as the most-to-be-recommended product, if it is pure. The undesirable effects on the animals, in some cases fatal, which were observed at the beginning with sodium tetradiodophenolphthalein were caused by impurities of the products. This was why they preferred the brominated compounds, which are less toxic but had to be used in larger quantities.

Having discovered the substance, it was now

necessary to study the means of entry. The gastric route, the intestinal, either by the introduction of coated substances or by using an Einhorn duodenal tube, and the rectal route have been practically abandoned.

Graham, Cole and Copher preferred the intravenous route, as being the most practical and the simplest, but taking special precautions with the manner of introducing the substance.

Phenolphthalein generally is used in a dose of 4 grams per 35 cc. of recently distilled water. The intravenous injection is pushed in very slowly, because the fall in arterial pressure is troublesome with rapid injections.

The method of the American authors shows the advantages of using opaque substances in the study of cavities normally not shown up by x-rays.

We used another route in the hope of obtaining visualization of the brain through the opacity of its vessels, particularly the arteries. This is the direction taken by our work.

Ventriculography has already been carried out to define the position of cerebral tumors. We believed that if we succeeded in visualizing the cerebral arterial network, it would also be possible to localize tumors on the basis of the alterations shown in the contexture of the arterial framework.

Before summarizing our experiments and our results in animals and humans, we should glance at the ventriculographic data obtained, as being an element in the diagnosis of cerebral tumors.

We are indebted to Dandy for the method of radiographic visualization of the lateral ventricles. His first note is dated 1918. Since then, Dandy and his associates have published other works and British and German neurologists have taken up this direction to obtain the localization of cerebral tumors by the study of the differences in appearance of the normal ventricles and those in brains with neoplasms.

The most commonly used substance for obtaining radiographic contrast was air. Oxygen or CO₂ has also been injected. Dandy has used thorium, potassium iodide, collargol, Argyrol and bismuth substrate, but the results were poor. Sicard used rising Lipiodol, that is iodinated oil with a lower percentage of iodine than the descending Lipiodol. Jacobaeus and Schuster also used Lipiodol. But air still remains the preferred substance. Resorption varies from a few hours to a few weeks. It is introduced into the ventricles either directly, or in cisternal or lumbar injections (Purves Stewart).

Most authors prefer direct puncture. This is performed by means of a cranial trepanation, either, for the anterior horn, 2 cm. from the median line, somewhat forward from the frontoparietal suture, or for the posterior horn at a point situated 3 cm. behind and 3 cm. above the external auditory orifice (Kocher). Other authors have given different points (Grant, Sicard, etc.).

In general 5 to 10 cc. of cerebrospinal fluid is drawn from the ventricle, and an equal quantity of air is injected, after which we wait for 2 to 3 minutes. Pressure becomes roughly equal to atmospheric pressure. Next we inject 90 to 120 cc. of air.

However, the methods are fairly variable (Dandy, Bingel, etc.). The radiographs are made with a Potter-Buckey diaphragm.

Ventriculography has often provided valuable information for the localization of tumors; but there are radiographs that show a deformation of the ventricles and it is still rather difficult to define the precise point at which the neoplasm is situated.

Recently, A. Elsberg and S. Sittler² have made studies on cadavers of subjects who died of cerebral tumors, and upon making comparisons between ventriculographs and moulages they arrived at the following conclusions:
1. In the case of a tumor of the right posterior fossa, one sees a displacement outside the posterior horn of the right ventricle, with a reduction in the capacity of the right ventricle.
2. In the case of a tumor of the frontal and right temporal lobes, radiography shows a considerable lengthening of the distance between the anterior and posterior horns on the side of the tumor, while on the opposite side they come closer to one another. In the case of an occipital tumor there is a distention of the two horns showing roughly the same appearance.

In his book Jüngling³ has shown a series of figures with fairly informative diagnosis. But interpretation often remains extremely difficult, and, at least in a large number of cases, does not provide an indisputable localization.

In a discussion of the Section of Neurology of the Royal Society of Medicine⁴ the question was presented by Sargent, who considered that ventriculography was a clinical aid in the diagnosis of tumors. But he warned against the method being used more than in doubtful cases or cases impossible to diagnose by neurological means. Two questions arise in connection with ventriculography: the danger of air injection and

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² Arch. of Neur. and Psych., October 1925.


⁴ Meeting held, April 16, 1924, *Brain*, 1924, p. 380.
the difficulty of a definite diagnosis even in cases with ventricular deformation.

Sargent makes ventriculographic interpretations dependent upon radiographic progress and upon generalization and perfectioning of radiological stereoscopy and the Potter-Buckey diaphragm.

The principal objection against ventriculography is the danger of air injections into the ventricles replacing cerebrospinal fluid. However, Sargent believes that this drawback could be modified with practice and experience. He even believes that such neurological exploration should be made by neurosurgeons, who, knowing the intracranial physiology, would, with their experience, be able to avoid surprises occasioned by such interventions.

At the end of 1924 he had made 18 injections in ten cases. One blind child with hydrocephalus died three days following the injection but the death could have been the result of natural causes.

Another patient, a woman with an unlocalized tumor who had undergone double puncturing of the posterior horns without yielding any cerebrospinal fluid, died seven days later. An autopsy was refused.

These two deaths made it clear to Sargent that the method should be used with caution.

McConnell has made ventriculographs in fifteen cases of cerebral tumors and in ten cases obtained the desired localization, which represents a fairly considerable percentage. He had two deaths, one eight hours, the other fourteen hours following the injection of air. In the two patients the tumor was situated in the posterior fossa of the cranium. In many cases he observed considerable reactions, which he attributed to the increased intracranial pressure. McConnell believes that the danger could be diminished by replacing the liquid with air in small quantities, 2 to 3 cc.

He recognizes that there are great difficulties in interpreting radiographs. For example, the posterior horn is often absent or cannot be distended. The absence of air does not signify that there is pressure at this point.

Wilfred Harris believes that ventriculography is so dangerous that it should only be used in very special cases. Jefferson is of roughly the same opinion. As to the method of injecting the air, most use direct introduction by cranial trepanation. McConnell always performs this at the Keen point; Sargent performs a double puncture of the posterior horns. James Stewart prefers the introduction of air by lumbar puncture. In his opinion this method is less severe and the results are the same. McConnell claims that this method is not preferable, since there is no assurance of filling the ventricles full of air.

From this discussion it may be deduced that there are two points upon which we must pause: 1. the danger of the method, and 2. the difficulty in interpreting the radiographs, for, as was stated by Purves Stewart, even in the most successful cases one does not invariably obtain an indication of the position of the tumor.

As to the danger of ventriculography opinions of surgeons and neurologists are not in complete accord. Dandy regards it as very slightly dangerous. In his first 100 cases of ventriculography he had 3 deaths. Burgel, out of 200 or more, had only 2 deaths. Weigeldt, Schott and Eitel, Wartenberg, did not have any deaths out of a large number of cases. On the other hand other authors had a higher percentage. Adson, Ott and Crawford had 6 out of 72 cases; Grant. 5 out of 40; Denk, 7 out of 67; Žüngling, 8 out of 60.

Regarding the localization of tumors by ventriculography, the authors once again are not entirely in accord. Out of 97 ventriculographies (1922-23) Dandy was able to make a diagnosis in 32 cases. Grant, out of 40 cases, was able to confirm the diagnosis in 15 cases, etc.

In other words ventriculography is a method to be utilized in the localization of cerebral tumors, but one which must be undertaken with care and carried out with prudence. There are certain dangers that must be avoided and reduced. The diagnosis is not always definite and in some cases it cannot be made; but in those cases in which there is no other means of clarifying the diagnosis, and since we are dealing with gravely ill subjects, ventriculography, with all its dangers and uncertainties, is a method to be used and perfected.

De Martel does not believe the injection of air into the ventricles to be harmless. He lost two patients and prefers the injection of a colored substance, also suggested by Dandy. These have been very useful to him without in any way harming any of the patients undergoing this procedure. De Martel punctures the posterior horns of the two lateral ventricles. He extracts from one of the two ventricles a certain amount of cerebrospinal fluid (a few cubic centimeters). This liquid is replaced by the same amount of methylene blue. After a quarter of an hour of waiting a few cubic centimeters of cerebrospinal fluid are drawn from the other ventricle. If this liquid is blue in color, one may conclude that the two lateral ventricles and the third ventricle communicate to a large extent with one another. After another quarter of an hour the inferior cerebellar cistern is punctured; if this liquid is not colored, one may suspect the existence of a tumor of the lower part of the cranium, which by compressing the walls of the fourth ventricle, obstructs the aqueduct of Sylvius and prevents the passage of the colored liquid outside the third ventricle, or even of a tumor in the region of the third ventricle. Sometimes one cannot puncture one of the two lateral ventricles, and the dye injected into the other.
ventricle passes freely across the third and fourth ventricles. In this case one must consider the existence of a tumor situated on the side of the lateral ventricle which has not been punctured and the cavity of which is probably obliterated by pressure from the tumor.

This method, according to De Martel, who is far from being infallible, has made it possible for him on several occasions to diagnose "roughly" the site of the tumor on one of the hemispheres. Such a localization, even though approximate, could be very useful for the surgeon.

All the above descriptions justify some further investigations, although these seem even more hazardous. While ventriculography and intraventricular injections of dye, which are fairly dangerous, only provide information regarding localization of cerebral tumors in certain cases, the method of arterial encephalography which we are about to propose might help in resolving certain problems of localization. We do not regard this problem as having been completely solved, but the knowledge acquired is the first step on a road which appears to promise good results.

Patients with cranial hypertension, as a rule, reach the neurologist very late, either through the fault of the general practitioner who does not interpret the headaches and vomiting correctly and postpones examination of the fundus of the eye, or because the patients reach the ophthalmologist voluntarily only when vision is lost or practically lost. Often patients come and ask for our care when they are blind. Clinical interest is much reduced in these cases, particularly when other symptoms of hypertension (headaches, vomiting, etc.) are attenuated. Surgical intervention could never restore the patients' vision and in view of the uncertainty in the diagnosis of localization, most prefer not to be operated on in these circumstances. We do not advise this intervention even if localization has been made, once the headaches have disappeared or only occur very rarely. Such cases are generally lost to any kind of intervention.

In the case of patients who come for consultation in the first phase of papillary edema, even if we do not have a diagnosis of probable localization, immediate cranial decompression is indicated. But if we were able to diagnose the site of the tumor, it would probably be possible to achieve a radical cure, and towards this end everything should be risked.

Ventriculography, intraventricular injections of dye, arterial encephalography on which we are pinning our hopes, are methods which should be used with the object of obtaining a localization which might guide the surgeon in a radical operation.

To achieve visualization of the arteries of the brain one needs an opaque, non-oily substance which can easily pass through the capillaries in such a way as to avoid any kind of embolism, and one which is harmless. This was our first task.

But since the substance had to be introduced through the internal carotid, it was necessary to know if this artery would allow its introduction without adverse effect and if the brain would accept the opaque substances selected without severe reactions.

Another question to be resolved was the avoidance of immediate dilution of the aqueous solution in the mass of the blood, which would cause a loss of visualization if it could not be introduced at the first attempt, in all probability by substituting blood. Each systole should spurt 160 cc. of blood into the organism. We have calculated that this quantity for each internal carotid should amount to between 3 and 4 cc. of blood. Thus, in a period of 5 cardiac rotations, the intracarotid injection made within this period (4 seconds) would be dissolved in 20 cc. of blood, which would eliminate the visibility of the liquid introduced.

At the same time it was necessary to have access to a very good x-ray installation—which we did not—to obtain photographs at the precise moment, so as to avoid dilution taking place too rapidly. In addition, temporary binding of the carotid would be indispensable for this operation.

Once a visualization of the arterial network has been obtained, one should have a fairly constant normal picture. If there is a cerebral neoplasm the network should present fairly appreciable modifications, at least in certain regions sufficient to allow a definition if not of the entire extent of the tumor, at least one point or another where it gives rise to a displacement of the arterial network. If we are dealing with a highly vascularized tumor, one could very probably obtain a visible spot by penetration of the opaque liquid by x-rays.

The outline presented above shows the course taken in our experimentation.

One cannot determine the size of tumors according to the intensity of the general symptoms of hypertension. All neurologists have encountered some surprises on this score. Large tumors, for instance tumors of the corpus callosum,9 may grow and develop without causing any appreciable disturbance.

On the other hand there are small tumors which give rise to a very remarkable hypertensive symptomatology. Sometimes they arise rapidly and give the impression of inflammatory processes. In other cases they appear slow and progressive. In other words it is impossible to correlate the symptoms observed with the volume of the tumor.

It would be very helpful if the radiographic methods of investigation of the brain would give

5 Egas Moniz. Tumeurs du corps calleux, a work which will appear in a future number of L'Encephale.
us all the information necessary for localization, spread, etc. of the intracranial neoplasm. But in solving this grave diagnostic problem the principal objective is the localization of at least a part of the tumor.

For example, in the case of a tumor of the corpus callosum, to which we referred earlier, the arteries, the callosal and the marginal callosal, should be changed. In the left hemisphere, in which the anterior horn of the much dilated lateral ventricle was invaded by neoplasm, the arterial circulation should also show considerable modifications.

We thought exclusively of the internal carotid and the arterial network derived from it because the internal carotid gives rise to the anterior cerebral and the sylvian, two strong arteries which irrigate the greatest part of the brain and particularly the silent part of the brain, that is the zone where the neoplastic invasion did not produce appreciable symptoms of localization.

The vertebral arteries nourish the diencephalon and the cerebellum where localization is relatively easy because it is manifested by disturbances which are well known to neurologists. Furthermore, they are not easy of access, and since they irrigate the bulb, the introduction of substances could give rise to grave and immediate consequences.

The internal carotid is localized in its own hemisphere. The anterior communicants between the two anterior cerebral arteries and the posterior communicants, which are branches of the basilar trunk, are the only possible passages to the opposite hemisphere. The injected substances will thus remain in the circulation of the internal carotid involved. Constant irrigation of the communicants by the blood of the internal carotid of the other side and the two vertebrals will prevent not only the entry of the opaque substance but will send blood to the carotid which is tied temporarily.

Of the opaque substances we preferred strontium bromide at the beginning. In another paper we have presented our conclusions on this subject.

Among bromides those of strontium and lithium are the most opaque. Sodium and potassium bromide also provide satisfactory opacity. Strontium bromide is somewhat less toxic than lithium bromide, but the latter is useful from this standpoint, since large quantities of it can be injected into veins without disturbance. However, lithium bromide is somewhat more irritating than strontium bromide. Their intravenous injection in a high concentration produces a painful sensation in the channel of the vein, but this is transient.

Strontium bromide, preferred by us, never gives rise to this phenomenon, but concentrated solutions from 30% and above cause a sensation of heat, at first localized in the head and later generalized throughout the body, which is transient but fairly uncomfortable. It is comparable to that produced by the intravenous injection of calcium chloride. Lithium bromide also produces these phenomena, but with a lesser intensity. These sensations of heat can be avoided if the injections are given slowly.

Strontium bromide in high doses gives rise to hardening of the veins which we corrected by adding 10% glucose.

Under these conditions we have been able to inject, without adverse effect, solutions containing up to 80% of strontium bromide and in very high quantities (10 to 15 cc.) without any discomfort on the part of the patients.

Parkinsonian postencephalitic patients have derived much profit from these injections. Despite the disagreeable sensation, they asked for them.

We have established that 70% solutions of strontium bromide were entirely harmless. At 80% we observed faintness in one patient, which led us to stop short of this amount.

We determined the opacities of the various bromides, notably 10 to 80% strontium bromide by placing a box of small rubber tubes full of progressive solutions of this salt into the cranium. We observed that the opacity starting from 30% is fairly considerable, but even the 10% solution is visible across the cranium (fig. 1). We experimented with this salt in animals and then in humans. We shall deal with the results obtained shortly.

After an accident had occurred, we took another direction. It seemed to us that bromides were less toxic, and particularly less irritating than iodides; we had selected them for this reason. However, we knew that iodides were more opaque than bromides, because opacity to x-rays is a consequence of the much higher atomic weight of iodine (127) than of bromine (80). One must also take into account the atomic weight of the associated metal; but the iodides, generally speaking, are much more opaque than the bromides. We repeated the experiments we made with bromides using iodides, and decided upon sodium iodide, which incidentally was already in clinical use, in intravenous injections. By injecting the cerebral arteries of cadavers with 30%, 20% and 10% and even 7.5% solutions it was observed that they were still visible across the cranium. We believe that this observation is so important that we are publishing four of the radioarteriographs obtained with these injections (figs. 2, 3, 4 and 5). In figure 2 (head preserved in formol) the penetration of the 30% solution of sodium iodide is not satisfactory. In figure 3 the arterial network ob-

tained with a 20% solution is fairly well visible. In figure 4, with a 10% solution, the arteries are still visible. The 7.5% solution, within the limits of visibility, shows some of the more important arteries. This fact, which was entirely unexpected, could be used in other clinical investigations outside neurology.

We have injected into the veins of humans 10–50% solutions of sodium iodide. It was observed that up to 30%, the injections, even when carried out at a certain speed, are not painful. At 30%, some patients complained of pains along the course of the vein. These are intensified and become constant when this percentage is exceeded. The addition of other substances (glucose, bromide, etc.) does not modify the painful reaction. We stopped at 25%, which still provides a very good opacity and does not give rise to any pain upon intravenous injection.

Iodides are less well tolerated by the tissues than bromides. Particular care must be taken in making the injections, to avoid their extravasia-

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Fig. 1. Opacity of strontium bromide in solutions ranging from 10% to 80%.

Fig. 2. Arterial network derived from the internal carotid. Injection of 30% NaI.
tion outside the vessels. However, iodides are harmless to arteries. Brooks, who injected them in cases of arteritis obliterans in 100% dosages, observed after the amputation of one of the limbs that the arteries did not present any macroscopic or microscopic lesions.

We have studied other iodides which we did not use. Most make up unstable solutions. Strontium and lithium iodide liberate iodine, even in low concentrations. Rubidium iodide, which is very opaque, is not toxic, but produces pains even at fairly low dosages.

Sodium iodide is not very stable either. Above 30% the liberation of iodine is almost constant, particularly if one keeps the ampules for some time and if they are exposed to light. As a precaution we use recent solutions, if possible sterilized on the day of application. When the ampules

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**Fig. 3.** Internal carotid injected with 20% NaI and vertebral with 10% NaI.

**Fig. 4.** Injection of the internal carotid with 10% NaI.
FIG. 5. In a live dog, visualization of some cerebral arteries. The internal carotid is visible, very thin, also the internal jugular and the vertebral veins.

appeared slightly yellow, we did not use them. One must also consider the chemical purity of the salts to be used.

The experiments performed by us on animals were numerous, and were made either to determine the toxicity of the drugs selected, or to establish the effects of the substances used on the brain, using intracarotid injections, or to detect the injected cerebral arteries in radiographs.

For the determination of toxicity we injected rabbits and dogs. The results for strontium bromide and lithium bromide and for sodium iodide were entirely reassuring in the doses to be administered to humans. Experiments made with intravenous and subcutaneous injections have shown their harmlessness at even high percentages. We obtained a confirmation of these results with intravenous injections in humans.

With intracarotid injections it was observed that dogs maintain a greater resistance to the substances introduced. We have two dogs alive, one weighing 8 kg. in which we injected 3 cc. of a solution of 100% strontium bromide into the carotid and a female dog in which we injected 1.5 cc. of a 25% solution of sodium iodide into the carotid.

The carotids of the dog are fairly resistant to the injections, although they behave variously. Sometimes they form hematomas, in others, blood spurts out after the injection, and in some the arteries showed no reaction. We never had any unfavorable complications here, nor were there any such in humans.

The dog was the animal selected for radiographic experiments. It was not a good subject for this, since the cranium presents lines in radiography caused by the bony rugosity of the muscular insertions which are very numerous and extensive in the head of the dog.

The internal carotid of the dog is very thin and cannot be reached directly. For this purpose we


FIG. 6. Arterial encephalography of the cerebral carotid network in a live human. Case of a large hypophysial tumor. The carotid is pulled forward, and the origin of the sylvian is also higher. The anterior cerebral, much reduced in volume, is deformed in its direction.
tied the common carotid above its point of origin, at the same time pressing the occipital artery which is as thick in the dog as the internal carotid and which originates above it and very close to it. But this was not sufficient to obtain a radiograph of the arteries of the dog brain. It was necessary to prevent the passage of blood from the common carotid, to avoid dilution of the opaque substance used. This lower ligature was therefore carried out and the opaque liquid was injected into the isolated segment, which forced the entry of the liquid into the internal carotid, without mixture of the carotid blood.

The first radiographs were negative. They were made with a Potter-Buckey and with a fairly long exposure. Thus we noticed that a condition which is indispensable for success is the radiograph to capture the progress of the substance across the arteries, now maintained by the blood of the collateral vessels. The photographs which we were able to obtain with the machine belonging to our hospital were very long—a quarter of a second—but we nevertheless succeeded in obtaining positive results. This radiological inadequacy was the most serious difficulty to overcome in all our experiments. It was even the indirect cause of other obstacles which we encountered and of the fact that we did not reach definite results rapidly. I hope that this situation will be improved shortly but do not know whether, solely with a more powerful instrument, we would obtain what is indispensable for us. We will return to this subject later.

In the dog we injected sometimes strontium bromide, sometimes lithium bromide in a 100% concentration into the carotid. We discovered the outlines of some cerebral arteries and veins of the neck in three cases. Figure 5 shows an injected head. The cerebral arteries are visible in the hemisphere and at the base (with some veins?). These results encouraged us to pursue the experiments on humans.

Before going further studies were made on cadavers in order to establish thoroughly the arterial tree of the brain and to confirm certain anatomical concepts by means of radioarteriographs. In fact we also used this work, which was carried out in collaboration with Almeida Dias and Almeida Lima,\(^8\) to present certain radioanatomical concepts and new ideas on the craniocerephalic topography. By means of stereoscopic radiography we were able to separate the two carotid systems of the brain: the internal, or anterior cerebral, and the external or sylvian.

These experiments were very informative. One can see very good networks by simultaneously injecting through the internal carotid and the vertebral artery on the same side, a 100% solution of sodium iodide under pressure.

We made a large number of radiographs on cadavers in order to obtain the normal picture of the distribution of the arteries seen with x-rays. We did everything possible to obtain cadavers of persons having died of cerebral tumors. These, with alterations in the arterial network, would provide a partial demonstration of the hypothesis suggested by us; but within six months of experimentation we were only able to obtain one cadaver which was of use from this standpoint.

The experiments underwent considerable changes according to the development of our work. There was always one great difficulty to overcome: the entry of the blood at the moment of injection of the opaque solution, which immediately lowered the concentration, in other words, the possibility of obtaining visualization of the vessels.

We had this difficulty with the dog and overcame it by tying the carotid. It should be noted that in the dog the communicating arteries are not comparable to those in humans. The problems appeared to be much more difficult to solve. But the opacities were well defined, well observable and consequently, in order to obtain the picture of the arteries, we had to have: 1. a solution which, when mixed with the existing blood, should still be opaque; 2. an apparatus which could give photographs rapid enough to capture the progress of the liquid in the vessels.

Our experiments can be divided into two stages, that of the injection of strontium bromide and the other the administration of sodium iodide. We began by attempting to inject the covered internal carotid in humans. The attempt was made in four cases. Before this we sought to reach the internal carotid at the point of entry into the carotid orifice, without result. It is possible that we did not succeed because we used very fine 0.5 and 0.6 mm. needles. The blood never spurting out because of their small diameter and length (5 cm.). Having abandoned this approach we were guided by the edge of the sternomastoid in the triangle formed by its border, the anterior surface of the digastric and the omohyoid.

In our first case we had the impression that we had reached the carotid, in a case of general paralysis. We had injected 7 cc. of a solution of 70% strontium bromide without consequences. It is probable that the injection was made into the internal jugular, since the patient did not experience any pain.

In the second case the injection was made into the internal carotid and since the patient was in a condition to allow the making of the first radiograph, the common carotid was compressed to prevent the entry of blood into the internal

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\(^8\) Egas Moniz, Almeida Dias et Almeida Lima. La radiartérioigraphie et la topographie cranio-encéphalique. *Journal de Radiologie*, 1927.
carotid during injection of the opaque liquid. The painful reaction was fairly violent following the introduction of 5 to 6 cc. of the solution. The patient rose suddenly and it was impossible to make the radiograph.

In the third case, that of a parkinsonian patient, who had greatly profited from the intravenous injection of strontium bromide, the sensation felt was again disagreeable but we decided to continue. This patient subsequently had a Claude Bernard-Horner syndrome which has since gone completely.

The fourth patient had a rather disagreeable surprise in store for us. The needle emerged from the artery and the greater part of the liquid (more than 10 cc.) was extravasated into the surrounding cellular tissue. There were no grave consequences. The patient had a temperature of around 88° for a few days, slow resorption, no abscess. The patient continued to have a Claude Bernard-Horner syndrome, from which he improved gradually. After this accident we decided to make the intervention on an exposed artery. The surgeon, Mr. Antonio Martins, was kind enough to undertake to expose and inject the internal carotid.

Fifth case. This was a female patient aged 20 years with an unlocalized cerebral neoplasm. She was blind. Once the right internal carotid was exposed the ligature was made and a 70% solution of strontium bromide was injected. The artery was punctured twice and approximately 4 cc. of the liquid were injected. At the beginning of the injection the patient complained. She had a neuropathic background and became highly agitated. Later she suffered from a type of anesthesia: disturbance in speech, and after one minute, cessation of speech. There were no other consequences. The radiographs were negative. They were taken somewhat late. The results of the injection were without adverse effect on the patient. She had some fever the following day (39°) and transient dysphagia. On the third day she was restored once more.

The sixth case was a progressive postencephalitic parkinsonian patient, very severe, aged 48 years. He had considerable muscular rigidity, trembling, transient diplopia, retropropulsion with repeated falls, blepharospasms, great difficulty in talking. Scopolamine was not beneficial. Intravenous injections of large quantities of strontium solution brought some improvement. We selected this patient with the double object of obtaining an arterial radiograph and to see the result of the direct action of strontium bromide on the brain. The carotid having been exposed, we injected 13 to 14 cc. of a solution of strontium bromide after tying the artery. The patient complained of severe pain. In order to obtain four radiographs we kept the ligature on for 2 minutes. The first radiograph, which is blurred, nevertheless shows the arterial penetration of the opaque fluid. Another radiograph, made immediately afterwards, shows only the internal carotid injected, and a small amount of opacity in the upper part of the anterior cerebral, which demonstrates that a thrombus immediately formed in this artery. Another radiograph made at the moment of removing the ligature of the carotid shows the sylvian and particularly the posterior cerebral, which showed us that the pressure of the carotid blood overcame the current originating from the vertebral. Since the blood was not able to pass through the anterior cerebral, pressure was exercised on one side, on an area of the vertebral, and on the other, on the ophthalmic. Then the patient exhibited a syndrome of thrombophlebitis and died eight hours after the injection. The state of this patient's arteries probably contributed to this accident; but we made a technical error by keeping the ligature of the internal carotid on for a prolonged period, and after the injection. The high dose of the drug may also have been the cause of trouble; but we are unable to explain the immediate formation of the anterior cerebral thrombus which we never observed in animals. Could the development of the vascular and perivascular lesions of severe encephalitides be explained by the action of bromides?

This accident led us to abandon bromide solutions and turned our attention to iodides in such a way as to obtain sufficient opacity with doses lower than those used with bromides.

At this point we began a study of the opacity of iodides and their action upon tissues and vessels. As has been stated, solutions of sodium iodide are visible across the cranium, even in very low doses, such as 10% and even 7.5%, and we were able to inject into the veins, without harmful effects, solutions of sodium iodide up to 30%. These injections are not painful up to 30%.

Under these conditions we took 22 to 25% solutions for intracarotid injections. We had to determine the dose to be injected without injury to the patient and sufficient to give the necessary opacity. For this we believe that large quantities of liquid are not necessary, for when they enter the arterial circulation of the communicants (the internal carotid being tied) the greater part of the substance will disappear. The quantity to be introduced had to be such that, mixed with the blood contained in the part of the carotid above the ligature, it should give a solution of about 20%, which is still fairly opaque. For this 3 to 5 cc. of a 25% solution of sodium iodide had to be

9 Histopathological examination of the brain, under the direction of Professor Parreira, is not yet complete.
Neurosurgical Classic—XVI

injected. Since the x-ray apparatus of our hospital makes ½ sec. pictures we were able to introduce up to 5 cc. of substance.

This liquid with a probable concentration of 20% comes into contact with the blood proceeding either from the anterior communicant or the posterior communicant. We do not know the amount brought in by the arteries into the hemispheric circulation as substitute for blood from the internal carotid. But we have calculated that for each cardiac revolution they would bring in the blood corresponding to the entry of the liquid injected in one second, that is, roughly one cubic centimeter. Even under these conditions—and the substances are not immediately dissolved, the two liquids, blood and iodide running side by side—we would obtain an opacity of 10%, which is sufficient to visualize at least a part of the largest arteries of the brain. However, it was necessary to capture the progress of the liquid with very rapid pictures.

We have tried intracarotid injections of 24% sodium iodide (first case) and 25%, without harm to the patient. These were carried out in 4 cases, one of which does not count because we were puncturing a bad artery and the experiment was abandoned without making radiographs. In the other three cases the injections were made without adverse effect into the internal carotid with solutions of sodium iodide in the dosages mentioned.

The first case, a patient with a cerebellar neoplasm, with a suspected right frontoparietal localization because of a slight opacity detected by radiography, and since he was blind in the right eye and saw very little with his left eye, received an injection of 3 cc. of 24% solution of sodium iodide. He received a local novocain anesthetic and also, in advance, an injection of morphine chlorhydrate with ½ mg. of atropine sulfate. At the instant of making the radiograph the ligature was removed from the internal carotid, hoping thus to profit from the entry into the cerebral circulation of the opaque mass which was stagnating in the carotid cisterna. The result should have been positive had we had very fast, instantaneous photographs at our disposal; but with ½ second and with the speed of the blood coming from the carotid the picture was taken without leaving even vestiges of opacity.

In the sixth case of the bromide series we obtained the outlines of the sylvian and posterior cerebral arteries by this method. Visualization was more pronounced in the posterior cerebral, possibly because opposition from the blood current coming from the basilar trunk briefly held up the current coming from the internal carotid, giving it an appreciable degree of visualization.

Radiography in the first case of the iodide series was entirely negative. There was no trace of any opacity in the arteries.

When the internal carotid was punctured the pulse slowed down from 90 to 56. The patient merely complained of a slight pain in the ear. The following day he revealed a certain degree of dysphasia and his temperature rose to 38°. On the third day he was up and has been in good health since.

The second case, a blind patient who has been in our service for some years because of cranial hypertension, did not show any obvious symptoms of localization. There were no cerebellar symptoms, but on the other hand, there was very pronounced nystagmus, even in the intermediate position of the eyeballs. The patient suffers from generalized epileptic attacks, which are more pronounced towards the left, which led us to make the sodium iodide test on the right. He has recently gained a fair amount of weight. No other symptoms. This being so, it appears to us impossible to determine any localization. Local anesthesia was with novocain and the carotid was exposed and injected before tying. Entry of blood into the syringe was very violent and to the 5 cc. of 25% solution, 3 cc. of blood were added, which lowered the concentration to about 15%. In other words if the solution finds 1 cc. in the communicating arteries, even if radiography was made between two cardiac revolutions, which did not in fact occur, the concentration would be reduced to 7.5%, which is the limit of visibility in cadavers.

However, in radiography the internal carotid is fairly well visible as far as the upper curve. It did not appear to us to be normal. We even suspected that it had assumed this shape because of pressure from a neoplasm but since the other arteries are not visible nothing can be claimed for certain.

Passage of blood from the communicating arteries dragged the contents along. The wave of blood probably pressed at the moment of making the radiograph, and the sodium iodide shadow, already much delayed, was lost during the time required to obtain the picture.

The patient complained during the injection of transient pain, not very intense, in the temples, to some extent in the eyes and in the right ear. The pulse fell from 95 to 60 during the injection. Slight dysphasia the following day. On the third day he was up and took his meals without difficulty.

Third case in the iodide series. Boy of 20 years with a hypophyseal tumor. A typical Fröhlich-Babinski syndrome. He was blind and had recently had severe attacks of vomiting and pronounced headaches. Grave condition.

In this patient for the first time a satisfactory method was followed: the internal carotid was
exposed and injected before tying, because once ligated it is very difficult to reach. The blood was not allowed to enter the syringe\footnote{A device with a stopcock may be used with two syringes, one full of physiological serum, communicating with the needle at the moment of puncturing the artery, and the other with the substance to be injected. This device was used with the first injections we made with the carotid covered.} and the artery was tied rapidly. Five cc. of a 25% solution of sodium iodide was injected. Then the artery was untied immediately. The patient experienced no pain. There was no fall in his pulse rate. There was some dysphasia the following day. After the third day he was in good condition.

He received two injections of 1 centigram of morphine and atropine during the 45 minutes preceding the injection.

The radiograph (fig. 6) shows the carotid pulled forward and without the upper curvature. The sylvian, very well visible, is also pulled forward and upward. The anterior cerebral shows a different arrangement from that which is seen in normal networks and it is very thin and blurred.

The tumor is the cause of the changes in position of the internal carotid and of the sylvian and probably of the modifications in the anterior cerebral, but on this point we cannot say anything positive. All of this demonstrated by comparison of normal radiographs with these.

Our problem has now been presented. In live subjects one can obtain radioarteriographs of the brain and it can furnish elements for the localization of tumors. But the experiments must be continued if we are to obtain information which cannot be furnished by one case alone.

The method is very simple but quite possibly many modifications will yet be made. It will even be possible to give the injection with the artery covered, with compression of the common carotid, either with the fingers, or with compressors of the type described by Dupuytren. This depends upon the percentage of liquid to be introduced. Morphine anesthesia should be replaced by ethyl chloride or nitrogen protoxide if high concentrations are used.

The meningeal arteries, derived from the external carotid, can also be explored by injection. In making the injection into the common carotid it will be possible to obtain both networks (meningeal and cerebral), which are very easy to separate in radioarteriographs.

But the great problem to be resolved now is not that of the carotid injection and the percentages to be used, which have already been established, more or less. The radiological method is much more important. It could provide considerable simplifications and new aspects in vascular encephalography, because we will be able to see not only the arterial network, but also the venous network and the sinuses.

A number of very quick photographs must be obtained, knowing that the progress of the blood is 10 meters per second. It is essential that these be successive pictures. It would be very interesting and very useful—since one would never lose the pictures—to make an actual cinematographic film of cerebral circulation with these opaque substances in motion. There is also another problem to be resolved: very rapid stereoscopic radiographs, so as not to lose the movement of the opaque liquids in the arteries. The solution of this problem appears somewhat more difficult, but stereoscopy would be a very valuable aid in showing the displacement of arteries caused by the pressure of tumors.

In summary, at the moment the problem has shifted to radiology which, we believe, will satisfy all our hopes before long. We will continue our experiments, but we will need a better x-ray apparatus. Without it no appreciable progress can be made.

For the time being, we advise the following method, which is harmless to the patients and able to provide a fairly satisfactory arterial encephalograph:

1. Preparing the patient with one or two injections of morphine and atropine.
2. Exposing the internal carotid.
3. Fixing the patient's head to the photographic frame by means of a bandage, to avoid movement of the head.
4. Making the injection into the carotid without allowing blood to enter the syringe.
5. Always taking good care to avoid the entry of air.
6. Immediately afterwards making the temporary ligation of the internal carotid with tweezers.
7. Immediately and rapidly injecting 5 to 6 cc. of a 25% solution of sodium iodide recently prepared and sterilized.
8. Making one or several radiographic pictures (as rapidly as possible), while continuing to inject the opaque fluid.
9. Immediately untying the temporary ligation of the internal carotid.

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