Neurocrit Care
https://doi.org/10.1007/s12028-023-01912-0

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The First Cerebral Angiograms: Imaging to Find Displacement

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Although he won the Nobel Prize for a different reason, António Egas Moniz has received universal acclaim for the discovery of the cerebral angiogram. It opened a new world, just as the computed tomography scan did a couple of decades later. But initially, cerebral angiogram was another way to demonstrate displacement and not to specifically look at the vasculature.

It replaced two previous techniques: the pneumoencephalogram and the ventriculogram. American neurosurgeon Walter Dandy first described the injection of air into the cerebral ventricles and later intraspinous injection of air, with the intent to look for changes in its normal anatomy, which would indicate a new mass. These studies were associated with major side effects, including seizures, bradycardia, and apnea, and the procedure itself was so dangerous that it was contraindicated whenever a diagnosis could be made by other means. By injecting arteries, Egas Moniz's technique also looked for a change in the normal anatomy of the cerebral vasculature that could be indicative of a mass lesion. He injected carotid arteries in cadaveric human heads and several animals before he resorted to humans. His original 1927 article also has a cerebral angiogram of a dog [1]. He then asked Dr. Almeida Lima, a neurosurgeon, to perform the procedure by surgically cutting down the carotid artery, including placement of a ligature.

Egas Moniz published his discovery in 1927, titled *L'encéphalographie Artérielle, Son Importance Dans la Localisation des Tumeurs Cérébrales*, indicating in the title that it was indeed used to localize tumors rather than to look for arterial pathology. He tried several contrast materials, but eventually Egas Moniz preferred *le bromure de strontium*; this created opaque arteries. Several attempts were necessary to obtain a successful study, but images remained hard to interpret because of shadows resulting from over projection (Fig. 1). This article also revealed that his multiple attempts resulted in multiple complications, including extravasation of contrast medium and two patients developing Horner syndrome. In two patients, he also encountered bradycardia. One patient with parkinsonism died. Eventually, Egas Moniz returned to direct injection into the carotid and chose the common carotid artery instead of the internal division. He also changed the contrast agent to iodine. In 1931, he used thorium dioxide (Thorotrast), which remained the preferred contrast agent until the 1950s, when it was found to be extremely carcinogenic, resulting in a multifold increase in liver cancer and leukemia decades later [2]. Egas Moniz did not ignore the anatomy and is also responsible for naming the carotid siphon and sylvian fissure arteries. Egas Moniz first presented his cerebral angiogram at a meeting of the Société Neurologie [3, 4].

In 1949, James Bull reviewed the status of cerebral angiography [5]. He reported 500 procedures, with three patients who died, explained by herniation of large frontal astrocytomas. He described arterial puncture that took a few seconds, followed by normal saline injection before 10 cm^3 of contrast injection.

Other indications became apparent, such as subarachnoid hemorrhage, to detect the ruptured aneurysm as early as 1947. Negative angiograms could occur if no good filling of the basilar artery and its branches were obtained. At that time, there was certainly concern about aneurysms not filling with contrast.

Other reasons were arterial occlusion, demonstration of cranial cerebral injury, such as subdural hematoma, and finding angiomas that had not bled. Egas Moniz was already under the impression that carotid artery thrombosis, as it was called, could be considered an "obscure case of hemiplegia." Interestingly, the

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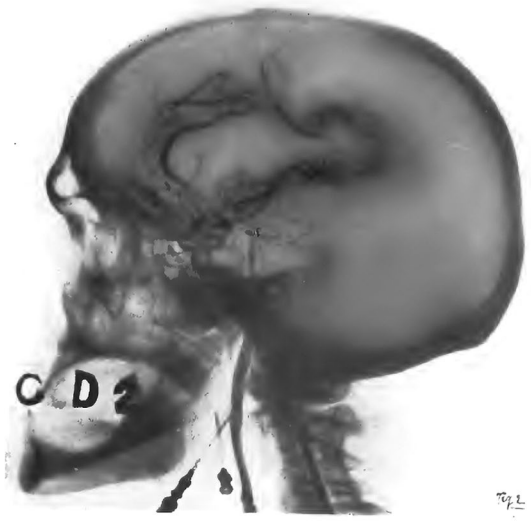

Fig. 2. — Réseau artériel dérivé de la carotide interne. Injection de NaI à 30 %.

Fig. 1 One of the very first cerebral angiograms, as reported by Moniz in 1927. Note the syringe entering the carotid artery

progressive weakness over time was originally interpreted as a growing tumor (although, in many cases, either the aphasia and hemiplegia came on acutely after), and then a carotid occlusion was found. Egas Moniz was surprised by the findings and concluded carotid occlusion was likely more common than commonly thought, as his patients were referred because of a strong suspicion of a brain tumor ("*la thrombose de la carotide interne, bien qua rare, est, cependant, plus fréquente qu'on ne l'avait pensé*"). He related the progression to failure of collateral circulation, a mechanism we still use today, and reported it in a separate communication [6]. Egas Moniz also suggested, "One should not forget the help that may come from the external carotid and its anastomosis with the internal carotid…it may be possible to perform surgery in these cases in order to increase the auxiliary blood flow to the internal carotid." He switched focus on imaging the carotid artery before he became invested in psychosurgery [7].

Surgical exposure of the carotid artery was a drawback, but in 1947, Stig Radner from Lund University introduced the catheter in the brachial axillary and subclavian arteries, which extended cerebral angiogram to vertebral artery angiogram, and published findings in more than 200 patients [5, 8]. Commonly, infiltration of the skin of the neck with procaine preceded percutaneous puncture of the carotid artery. If cannulation of the vessel could not take place within a reasonable time, they made an incision and injected the vessel.

Sven-Ivar Seldinger, a radiologist at Karolinska in Stockholm, introduced a major innovation [9] in 1953 by introducing the catheter through the puncture hole on a flexible "metal leader"; after withdrawal of the puncture needle, this technique allowed insertion of a larger polyethylene tube.

As computers improved, catheter-based cerebral angiogram using digital subtraction angiography reduced the amount of dye, and the subtraction showed only the filled vessels and no other structures. Cerebral angiogram made a revolutionary change, becoming more therapeutic than diagnostic. Cerebral angiogram involves 3D reconstructions that allow full imaging of arteriovenous malformation, aneurysm morphology, and, of course, large vessel occlusion.

If you want to see how it was done at the time, you can find it in an unusual place. The film *The Exorcist* depicts the original cerebral angiogram done through a direct carotid puncture, which emphasized medical technology, with all its discomfort and clanking mechanical (diabolical) noise. The cerebral angiogram with carotid puncture squirting blood caused distress in the cinemas, and viewers called the imagery—not unreasonably—graphic (Fig. 2). Filming took place at Bellevue Hospital (New York), with radiologists as consultants on the film while working at the hospital in August 1972. The late director William Friedkin claimed he spent many hours with them to get it exactly right. The angiography scene was derided by critics for being unnecessarily gory, but it has gone on to receive praise from medical professionals, particularly radiologists, for showing the procedure and drawing attention to it.

The Consequences of Finding Displacement

Physicians used the ventriculostomy and cerebral angiogram sparingly in the 1930s, and it took nearly four decades for the procedure to gain acceptance (similarly with computed tomography, which took not decades but years). Most neurosurgeons did not feel that these studies were better than a good neurologic examination. In the first decade following his discovery, Egas Moniz claimed to have done more than 500 cerebral angiograms. The initial publication showed barely noticeable cerebral arteries, but the images were much improved in a publication 10 years later [6]. Egas Moniz did note several vascular abnormalities that were then linked to presentation, with not always convincing

Fig. 2 Direct carotid puncture angiogram in *The Exorcist* (licensed by Photofest)

associations. Egas Moniz was the first to point out later the angiographic features of angiomas, meningiomas, and certain vascular gliomas. They also recognized a conspicuous absence of vascularity in cysts, abscesses, and cholesteatomas [10, 11]. Common findings were (1) hydrocephalic sweep of the anterior cerebral artery; (2) diffuse displacement of cerebral vessels (which is less profound than is the case in meningiomas of comparable size because of infiltrating manner of growth); and (3) the angiographic examination of astrocytoma revealing extensive stretching and spreading of the larger and medium-sized cerebral arteries. The finer arterial branches, however, could have been entirely absent. The angiographic picture of most glioblastomas showed increased vascularity in the margin of the tumor and sinuses, irregular dilatations, and vascular loops within the tumor [12, 13]. Moreover, finding an artery-displacing mass may have indicated a substantial tumor, which, certainly in the 1930s and heyday of neurosurgery, would need a brave (or brazen) neurosurgeon to perform surgery. Most would not even attempt it, certainly not if it appeared to be a glioblastoma with a hopeless prognosis. Some of this concern was noted in an article from the 1950s:

In planning a craniotomy, angiography helps the surgeon by indicating the position of major arteries irrigating the neoplasm. This is of value in vascular meningiomas and in some gliomas. This information is important in tumors about the sella turcica, where the internal carotid arteries are frequently involved in the tumor. With the knowledge that the internal carotid artery runs through a tumor, the surgeon is spared the humiliation of having a casualty from exsanguination and the patient, a fatal outcome [12].

Epilogue

Egas Moniz won the Nobel Prize for Medicine in 1949 (together with Walter Rudolf Hess) for the prefrontal leucotomy, rather than for the practice-changing discovery of cerebral angiography, and became known as "the neurologist awarded as a psychiatrist." He had a broad interest in neurology and psychiatry. His interest in leucotomy started a decade later, as he saw the effects of frontal lesions and made the connection to psychosurgery for severe depression and obsessive–compulsive disorders [14].

Egas Moniz was a celebrity in Portugal, with his name on a postage stamp, and he was commemorated with a statue in front of the Hospital de Santa Maria in Lisbon. He was known as a friendly, humble, humane, and highly intelligent neurologist. He also served as Minister of Foreign Affairs, Portuguese Ambassador to Spain, and president of the Portuguese delegation to the Versailles Peace Conference after World War I. He was also a gastronome, a gambler, and the author of a book on card games.

Egas Moniz later came under attack for the practice of leucotomy ("that barbaric procedure"). Criticized for understating the complications and providing inadequate documentation and poor patient follow-up, he nevertheless retained his prize because the Nobel Prize Committee does not revoke prizes.

On March 14, 1939, a psychiatric patient with a paranoid psychotic break shot Egas Moniz multiple

times in his Lisbon clinic. Five shots lodged in his right hand, one in his chest, and one in the spine, which could not be removed. Characteristically, Egas Moniz worried more about the patient's safety than his own, fearing that the authorities would treat the patient as a criminal, when in fact he was in a mental health crisis. Unlike his colleague Miguel Bombarda, who died from a similar attack by a patient, Egas Moniz recovered. Rumors that Egas Moniz had become paraplegic and wheelchair-bound and that the patient had previously undergone leukotomy have never been corroborated [15, 16].

Acknowledgments
I thank Dr José M. Ferro and Dr Rui Araújo for their insights, fact-checking, and translation of Portugese text.

Source of support
No extramural funding supported this effort.

Declarations

Conflicts of interest
There are no conflicts of interest.

Publisher's Note

Received: 1 December 2023 Accepted: 7 December 2023
Published online: 22 January 2024

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