

USE OF ^{99m}Tc -LABELED ALBUMIN MICROSPHERES IN CEREBRAL VASCULAR DISEASE

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The intracarotid injection of radioalbumin microspheres (15 and 30 μm) is followed by scanning procedures that permit the description of the cerebral bloodflow distribution. The method is reproducible. Injection can be made into the internal and common carotid arteries, as well as into the aortic arch or the left ventricle. This last procedure makes it easy to examine patients with severe extracranial vascular stenosis or thrombosis and permits comparison of the two hemispheres. Most patients (88%) injected on the affected side showed one or more local vascular deficits. The method therefore is more efficient than pertechnetate scanning or arteriography.

The intracarotid injection of macroaggregated human serum albumin has been suggested for the investigation of cerebral tumors (1) and for the meas-

urement of intracerebral arteriovenous shunting (2). This method was used in cerebral vascular diseases and compared favorably with diffusible gas measurements (3). Macroaggregates or microspheres of human serum albumin are distributed in the brain according to the distribution of regional arteriolar blood flow. The present study deals with the same group of patients with cerebral infarctions presented previously in Ref. 4.

MATERIALS AND METHODS

Fifty-three patients with brain infarcts and three patients admitted for coronography were submitted to one or more slow intra-arterial injections of ^{99m}Tc -

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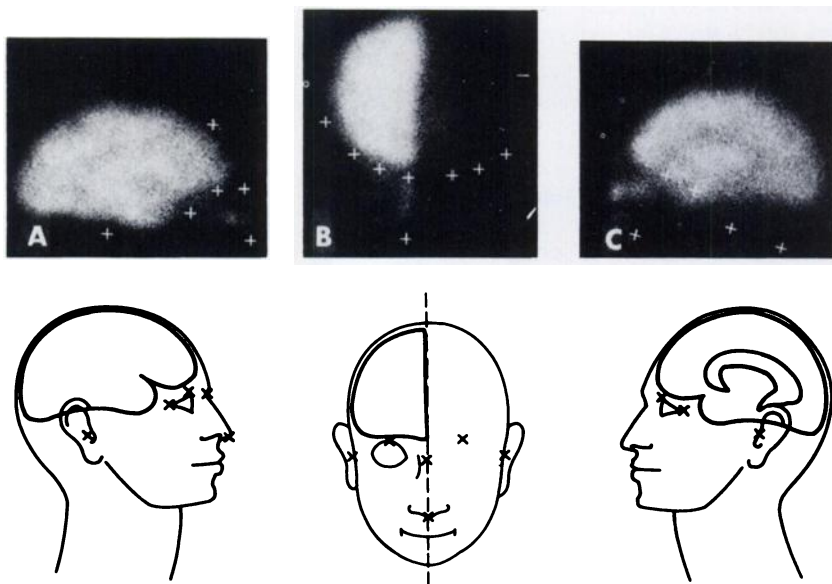


FIG. 1. Right lateral (A), anterior (B), and left lateral (C) views of normal cerebral hemisphere after injection of ^{99m}Tc -microspheres in right internal carotid artery.

labeled microspheres.* Spheres $30 \pm 5 \mu\text{m}$ in diameter were used for the 53 brain studies and $15 \pm 5 \mu\text{m}$ for the coronary studies. Reproducibility of particle size distribution from batch to batch was found to be excellent. Approximately 100,000 particles were injected into the carotid artery and up to 500,000 into the left ventricle, amounting to 5 mCi of $^{99\text{m}}\text{Tc}$.

In the group with brain infarcts, 61 tests were carried out, 55 of them on the affected side. The injections took place 5–211 days after infarction (the average delay was 43 days). In 50 cases the injection was made into the internal carotid artery, in seven cases into the common carotid artery, in three cases into the aortic arch, and in one case into the left ventricle.

In each case, local anesthesia was sufficient. The procedure was accompanied by a conventional cerebral arteriogram and was followed by a four-view scan made with the Searle Radiographics Pho/Gamma III scintillation camera using a high-resolution parallel-hole collimator. Scans were studied on a descriptive basis.

RESULTS

Biologic half-life of 15- μm microspheres in brain.

In two patients without cerebral disease, the count rate over the brain, corrected for radioactive decay, was found to be consistent with a biologic half-life of 12 hr.

Morbidity. In the group with brain infarcts (average age 69 years), the whole procedure (arteriography and microsphere injection) was followed by clinical deterioration in four cases (7%), transient aggravation of the neurologic deficit in two cases, pneumonia and permanent neurologic aggravation in one case, and death in one patient 2 days after injection due to an intraventricular hemorrhage on the contralateral side.

In a similar population of 70 patients submitted to arteriography without microsphere injection in 1971 through early 1973, the morbidity was found to be 8.5%. Transient obtundation occurred in two cases, persistent obtundation in one case, transient aggravation of the neurologic deficit in two cases, and permanent neurologic aggravation in one case.

Normal distribution after microsphere injection into internal carotid artery. *The anterior view* is characterized by homogeneous radioactive distribution over the hemisphere. Two neighboring structures also

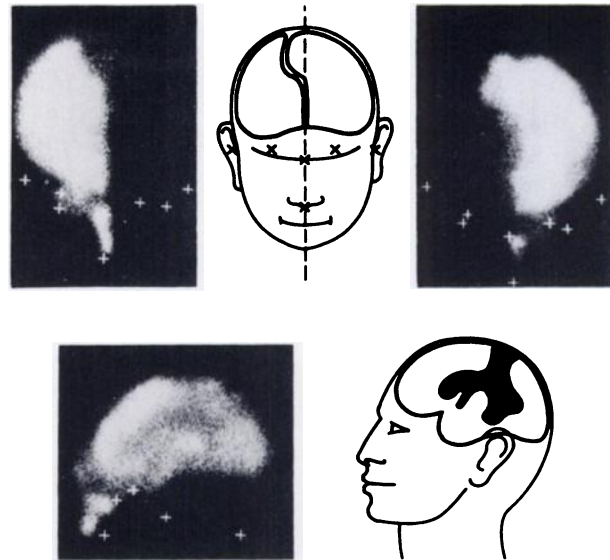


FIG. 2. Normal cerebral scans after microsphere injection into each internal carotid artery. Part of field of anterior cerebral artery is injected through contralateral artery. Medial view of right hemisphere (below) shows discontinuity of peripheral radioactive corona due to faulty injection of anterior cerebral artery.

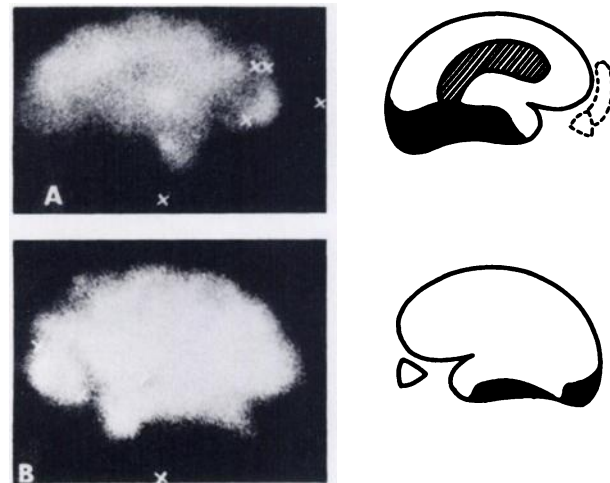


FIG. 3. Scan of normal left hemisphere after microsphere injection into ipsilateral internal carotid artery. Medial (A) and lateral (B) views show characteristic pattern for nonpathologic partially uninjected field of posterior cerebral artery.

appear: the eye and part of the skin from nose and forehead (Fig. 1). In 11 patients (21%) this projection showed some crossover of vascular supply into the field of the opposite anterior cerebral artery (Fig. 2).

The lateral view usually shows homogeneous activity (Fig. 1), but occasionally the distribution appears patchy. When the field of the posterior cerebral artery is not perfused, the inferior portions of the temporal and occipital lobes present a typical pat-

* Microsphères d'albumine humaine Kit TCK-5, IRE-MOL-DONK-Belgique. Preparation by heat gelification of a concentrated HSA emulsion in oil phase. Size range obtained by mechanical sieving (5).

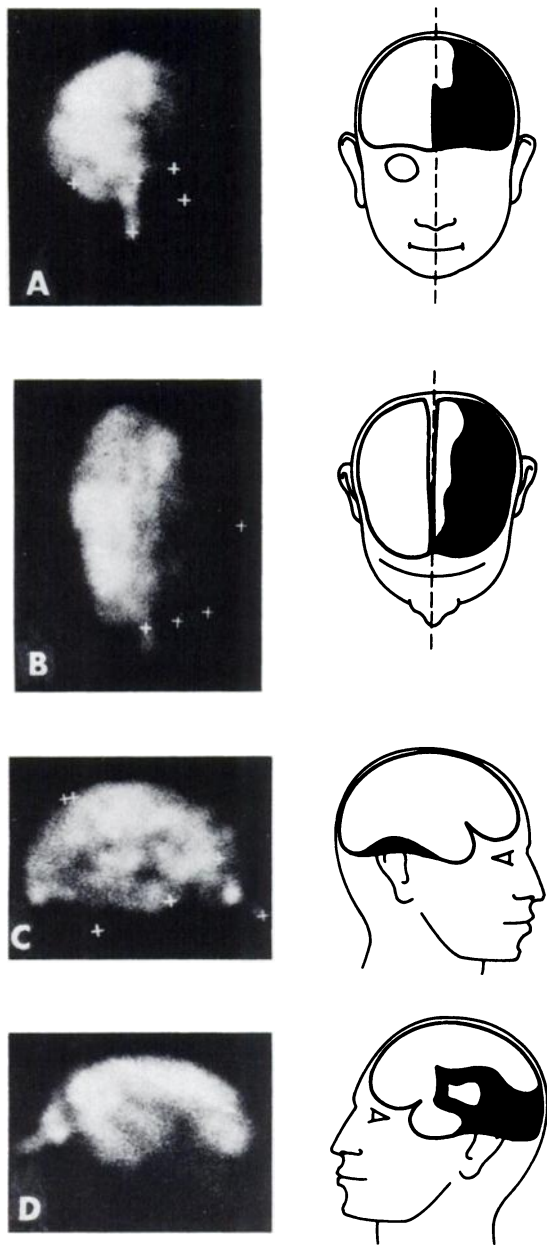


FIG. 4. Scan of right hemisphere after injection of microspheres into ipsilateral internal carotid artery. Anterior (A) and vertex (B) views show partial injection of field of contralateral anterior cerebral artery. Lateral view (C) shows multiple lesions in field of sylvian artery. Medial view (D) shows characteristic pattern of partially uninjected field of posterior cerebral artery. Carotid arteriogram is normal.

tern (Fig. 3). This last situation was encountered in 51% of the patients.

The medial view is characterized by an active peripheral border, a less-active intermediate zone, and a highly active inner nucleus. The peripheral active zone corresponds to the medial cortex, as shown when part of this cortex is not perfused by the ipsilateral anterior cerebral artery (Fig. 2). The intermediate zone probably corresponds to the less-

vascularized white matter and to the cerebral ventricles. The inner nucleus was found to correspond to the thalamus and striatum, a region that was cut off in a patient with a cystic thalamic lesion. This interpretation was supported by the examination of a frontal brain section of a patient injected ante mortem.

Pathologic patterns. Eighty-eight percent of patients injected on the affected side showed one or more local vascular deficits (Fig. 4). In the same clinical sample, arteriograms visualized 18% of the infarcted regions and pertechnetate scanning showed 58%. This examination proved very useful in the demonstration of accessory vascular supplies (Fig. 5).

Injection into the common carotid artery, the aortic arch, or the left ventricle. The quality of the scans remained good in spite of the neighboring activity in the field of the external carotid artery (Fig. 6). This

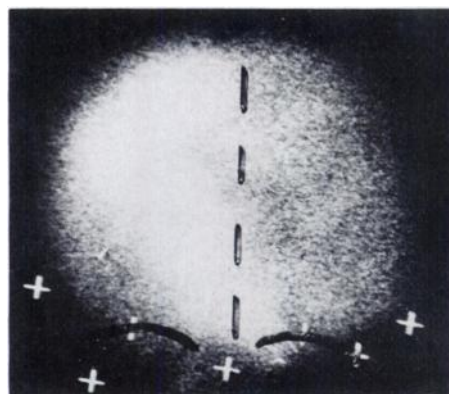


FIG. 5. Anterior view after microsphere injection into right internal carotid artery. Scan shows substantial vascular supply to left hemisphere in patient with occlusion of left carotid artery.

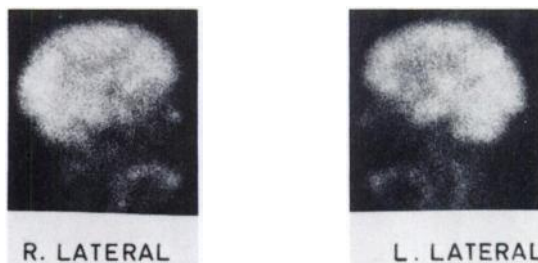
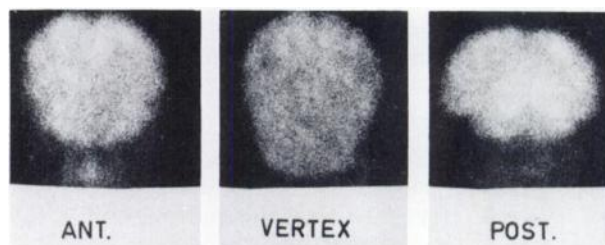


FIG. 6. Scan after microsphere injection into left ventricle. Hemispheres and cerebellum are clearly shown in spite of simultaneous injection of field of external carotid.

method proved particularly valuable in showing accessory vascular supply from the external carotid artery in the presence of an occluded internal carotid artery. It also evaluates cerebral blood flow when both carotids are occluded (Fig. 7). The vertex and the anterior views proved to be more useful than the profiles for studying the relative bloodflow distribution for both hemispheres.

Reproducibility. From two to three injections were made on the affected side in three patients. The results proved to be similar (Fig. 8).

Correlation of microsphere scans and arteriograms. Arteriography permitted the description of six triangular hypovascularized regions. All of them were found again on microsphere scans. In three cases, scans revealed nonpathologic conditions: lack of perfusion in part of the field of the anterior cerebral artery (one case) and in that of the posterior cerebral artery (two cases).

Correlation of microsphere scans and pertechnetate scintigraphic data. Twenty-one patients with positive serial pertechnetate brain scans were also submitted to microsphere injections. A normal arteriolar vascularization was found at the site of the lesion in eight patients, four of them presenting abnormalities of the vascular pattern elsewhere. In this group, the injections took place 19–55 days (average 37 days) after infarction.

DISCUSSION

The only specific hazard related to the intra-arterial injection of albumin microspheres is the exceptional incidence of anaphylactoid reaction (6). The injection in small animals of radioactive albumin macroaggregates in doses 5–500 times the absolute dose injected in human patients did not produce any

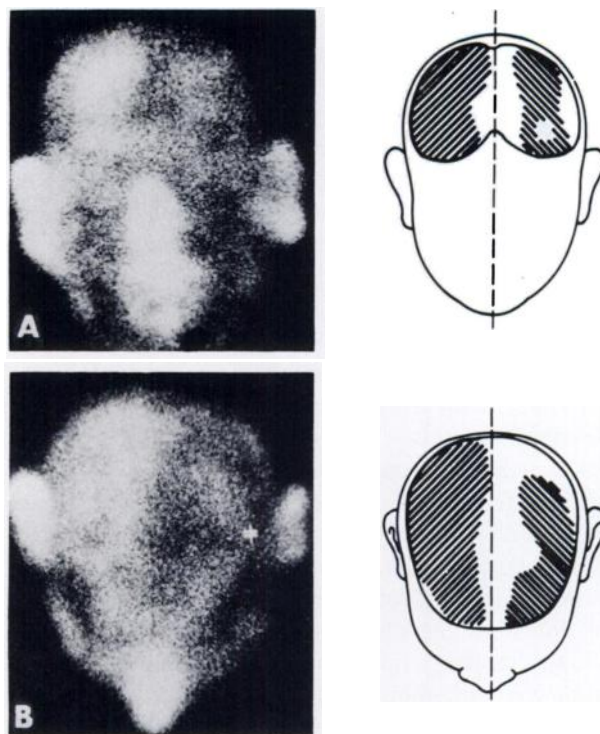


FIG. 7. Anterior (A) and vertex (B) views after injection of microspheres into aortic arch. Right hemiplegia had occurred following thrombosis of both internal carotid arteries. Note relatively homogeneous right hemispheric activity and much weaker supply to left hemisphere.

clinical, gross pathologic, or microscopic alterations (7,8). Likewise the safety of the direct coronary injection of radiolabeled microspheres has been assessed on humans (9).

However, the method in association with arteriography leads to a significant morbidity; this was unchanged when carotid arteriography alone was

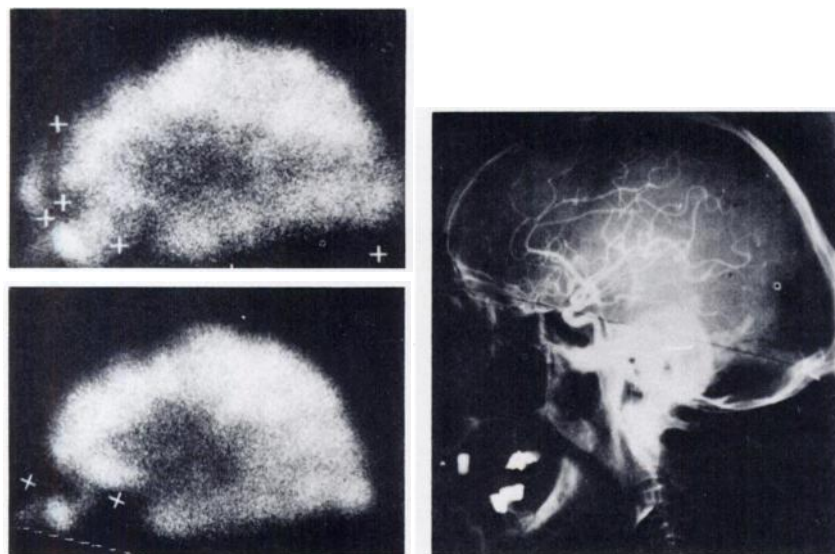


FIG. 8. Two lateral views of left hemisphere in same patient made 84 days apart, showing vast sylvian lesion. Comparison attests to reproducibility of microsphere scan. Carotid arteriogram shows diffuse atheromatosis but does not show infarcted region.

practiced in a similar elderly population with brain disease. We hope to reduce the morbidity by limiting the procedure to a slow injection of microspheres into the common carotid artery or into the left ventricle without concomitant arteriography. At present, the safety of the technique cannot be claimed with certainty until it has been applied to a larger population with mixed symptoms for which the morbidity rate of arteriography manipulation is more in accordance with published data.

The size of microspheres was initially $30 \pm 5 \mu\text{m}$. Since these spheres are temporarily stopped in the arterioles, their distribution represents the bloodflow distribution at the arteriolar level. Since physiologists are mainly concerned with capillary blood flow, we now feel that the use of particles of about $15 \mu\text{m}$ in diameter is more appropriate. Smaller particles pass freely through the brain (10).

A preliminary comparison of the simultaneous use of diffusible gases and microspheres in six patients shows that the normal bloodflow distribution appears somewhat different for each technique used. With ^{133}Xe , blood flow is greater in a peripheral band and in the region of the sylvian fissure, whereas with microspheres the activity is homogeneously distributed on the external profile. Nevertheless, the two approaches give very similar delineations of pathologic areas.

Microspheres are particularly valuable for the assessment of blood flows when one or both carotid arteries are occluded. On the other hand, it may be possible to express regional flows of both hemispheres in absolute terms (milliliters per unit time) by adapting the reference flow technique (11-16). This modification of the method should be valuable for studying the effects of drugs on the cerebral circulation, on the normal as well as on the affected side.

It was not possible in this study to use the microsphere examination at some standard time after the onset of hemiplegia. Nevertheless, it is noteworthy that eight out of 21 lesions shown by conventional scanning had a normal local arteriolar vascularization when examined 19-55 days after onset.

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