Value of Routine Cerebral Radionuclide Angiography in Pediatric Brain Imaging

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In addition to static brain images, cerebral radionuclide angiograms (CRAGs) were performed in 1,051 children to determine the value of routine radionuclide angiography. The CRAG resulted in a statistically significant increase in detection of abnormalities ($p < 0.01$), as it provided the only evidence of confirmed abnormalities in 60 children (5.7%). The CRAG helped detect subdural fluid collections, cerebrovascular disease, and cerebral cysts, but it was of little value in detecting hydrocephalus. For maximum diagnostic yield, a CRAG should be performed with all pediatric brain-imaging studies.

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Cowan et al. (*1*) reviewed the static brain images and the cerebral radionuclide angiograms (CRAGs) of over 1,000 adults who underwent both procedures. Adding the CRAG increased lesion detection by 33% and nearly doubled the detection rate for cerebrovascular disease. Cowan et al. therefore recommended routine use of the CRAG in radionuclide brain imaging. However, only selective use of the CRAG has been advocated for children because of the low frequency of cerebrovascular disease in children compared to adults (*2,3*) and the need for higher tracer doses to obtain technically satisfactory studies (*3*). In the present study, in order to evaluate the CRAG as a routine procedure in pediatric brain imaging, CRAGs were performed as a routine part of radionuclide brain imaging in a large series of children. Standard doses of pertechnetate (approximately 215 μCi of ^{99m}Tc per kilogram) were used.

METHODS

A prospective evaluation was performed in 1,051 children at the Mallinckrodt Institute of Radiology (MIR; $n = 470$) and the Hospital for Sick Children (HSC; $n = 581$). The CRAG technique was identical at the two institutions. After pretreatment with oral perchlorate (10 mg/kg), an anterior or posterior CRAG was performed with approximately 215 μCi/kg of pertechnetate (minimum dose in neonates, 2 mCi). A saline-flush injection technique was used to ensure a compact bolus. Sequential 1-sec images of the cranial transit of the bolus were followed immediately by a 400,000-count blood pool image in the same projection. Standard four-view static images were performed (immediately at HSC, 1 hr after injection at MIR), with additional views 2–4 hr after injection (all children at HSC, only those with nondiagnostic early images at MIR). These additional views were performed either with a rectilinear scanner (maximum count density, 1,500/cm^2 at the periphery) or a scintillation camera (400,000-count images).

The CRAGs and static images obtained in this study were interpreted by visual inspection. To avoid misinterpretation caused by random fluctuations in count rate, asymmetric activity had to persist on at least three consecutive frames of the CRAG to be considered abnormal. Patients with bilateral regions of diminished or increased activity that persisted in the arterial, capillary, and venous phases were also considered abnormal. Unilateral or bilateral inward displacement of the convexity portion of the mid-

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dle cerebral artery territory was noted when present; this pattern suggested subdural disease (*4,5*). Conversely, uniform cortical perfusion on the CRAG indicated that a subdural problem was unlikely (*5*). Other patterns of diminished activity were not interpreted specifically. However, the sequence of decreased arterial and capillary phase activity, followed by a relative increase in activity during the venous phase ("flip-flop"), was considered evidence of cerebrovascular disease with collateral circulation.

The hospital record of each patient was reviewed before brain imaging and, based on the presenting neurologic signs and symptoms, the patients were classified as having either high or low a priori probabilities of organic brain disease. The high-probability group included children with a previous head injury or with abnormal enlargement of the head. Children who had abnormal cranial transillumination (*6*) and infants with a cranial bruit or congestive heart failure in the absence of known congenital heart disease were also included. Finally, children were placed in the high-probability group if they presented with focal neurologic signs (focal motor or cranial nerve deficits, visual field defects, aphasia, ataxia, focal seizures) or with signs of increased intracranial pressure. All the other children were placed in the low-probability group. The study was organized in this manner to provide data relevant to the possible preselection of children for the CRAG. Thus, if the results showed that preselection was the best way to utilize the CRAG, data on which to base this selection would be available.

Children with abnormal radionuclide studies were excluded from the analysis if the abnormality could not be confirmed by other radiologic or clinical studies. However, further evaluation was not obtained in many patients with normal radionuclide studies, and therefore the overall rate of true- and false-negative studies could not be derived. Results of angiography, pneumography, computerized cranial tomography (CCT), and subdural taps were used to evaluate the scintigraphic results. These techniques themselves are subject to error (especially false-negative subdural taps), but they represent the best indicators of true abnormality available in this group of children. The neuroradiologist who reviewed the CCT images was asked to evaluate the ventricular size in each case. Based on his subjective impression, ventricular enlargement was graded as mild, moderate, or severe. Tomography was only used to evaluate the accuracy of the radionuclide studies. An overall comparison of the value of CCT and radionuclide brain imaging in children was not attempted since only 131 patients in this study underwent CCT.

The results were analyzed to determine the frequency of additional lesions detected by routine use of the CRAG. This was determined by the number of cases in which the CRAG was needed to establish the correct diagnosis (i.e., when the diagnosis was uncertain or missed on the static images). In such cases the CRAG was termed "essential." This approach was used in order to eliminate the more subjective judgments needed to determine whether a confirmatory CRAG would be helpful when the diagnosis could be made from the static images alone. Statistical analyses were performed using the χ^2 test with Yates' correction.

RESULTS

Abnormal radionuclide images were obtained in 293 (28%) of the 1,051 children (Table 1). The CRAG was essential to the diagnosis in 60 children (5.7%), that is, it increased the number of confirmed positive studies by 20% (60 out of 293). This increase in detection of abnormalities is statistically significant ($p < 0.01$). The CRAG was more likely ($p < 0.001$) to be "essential" if a patient had a high a priori probability of neurologic disease. The CRAG was essential in 49 of these children (10.7%) and increased the number of confirmed positive studies by 21% (49 out of 232) (Table 2).

Displacement of convexity activity in the middle cerebral artery territory provided the only definite evidence of a subdural collection in 22 children (29% of the abnormal studies in children with a previous head injury). Eleven of these children had nor-

TABLE 1. RESULTS OF ROUTINE CRAG IN 1,051 CHILDREN

A priori probability of neurologic disease	No. of cases	Abnormal study*	Abnormal CRAG	Essential CRAG†	Yield
High	459	232 (50.5%)	148	49	10.7%
Low	592	61 (10.3%)	22	11	1.9%
Total	1,051	293 (27.8%)	170	60	5.7%

* Either the CRAG or the static images or both were abnormal.
† CRAGs that served to establish the correct diagnosis after normal or nonspecific static images are classed as "essential."

TABLE 2. UTILITY OF THE CRAG IN CHILDREN WITH A HIGH PROBABILITY OF BRAIN DISEASE

Presentation	No. of cases	Abnormal study*	Abnormal CRAG	Essential CRAG†	Yield
Focal signs	244	133	67	16	6.6%
Trauma	171	75	58	22	12.9%
Abnormal transillumination	37	24	22	11	29.7%
Other	7	0	0	0	
Total	459	232	147	49	10.7%

* Either the CRAG or the static images or both were abnormal.
† CRAGs that served to establish the correct diagnosis after normal or nonspecific static images are classed as "essential."

mal static images, but the others had skull fractures or scalp injuries that resulted in nonspecific superficially increased activity in the static images. The CRAG in these patients showed inward displacement of convexity activity. The CRAG was interpreted as positive for a subdural collection in only two patients who had no abnormality.

The ability of the CRAG to detect hydrocephalus was poor. Nineteen children had CCT evidence of hydrocephalus, and one additional child had markedly enlarged ventricles as shown by ^{111}In-DTPA cisternography. Only seven of these 20 children had an abnormal CRAG (Fig. 1) and each of these seven had moderate or marked ventricular enlargement (Table 3). In addition, three CRAGs were interpreted as positive for hydrocephalus in children with ventricles judged normal by CCT.

The CRAG revealed nine moderately large intracranial cysts. However, one small cyst was not detected and one study was a false positive. In three of the patients with cysts, the static images showed hemispheric lucency. In each case however, the cyst was more clearly shown by the CRAG (Fig. 2).

The CRAG provided additional information in 16 of the 244 children who presented with focal neurologic signs. These patients were generally referred to determine whether a focal brain lesion (e.g., tumor, abscess, arteriovenous malformation) was present. In nine children, asymmetric hemispheric perfusion during the CRAG provided the only evidence of cerebrovascular disease. Two additional children had arteriovenous malformations. Although the lesions were visualized on the static images, the characteristic arterial blush and the rapid

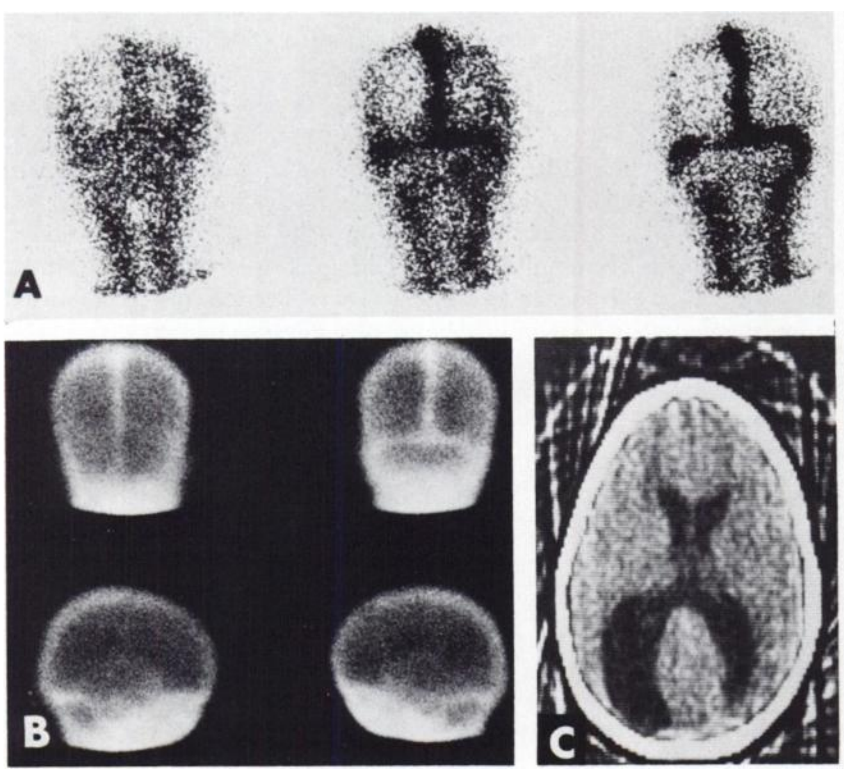

FIG. 1. This 5-year-old boy presented with psychomotor retardation. Arterial, capillary–venous, and late venous frames from posterior CRAG (A) reveal lucency of left hemisphere. Static images (B), obtained 1 hr after injection, were normal. Computerized cranial tomography (C) revealed hydrocephalus with moderate enlargement of posterior left lateral ventricle. Milder enlargement of right posterior ventricle was not well shown by CRAG.

TABLE 3. UTILITY OF THE CRAG IN DETECTING HYDROCEPHALUS

Degree of ventricular enlargement	No. of cases	Abnormal CRAG
Mild	6	0
Moderate	12	5 (42%)
Severe	2	2 (100%)
	20	7 (35%)

decrease in activity seen on the CRAG were diagnostic. All tumors visualized by CRAG were also seen on the static images, but the CRAG also revealed other abnormalities in five patients with tumors. In four children the CRAG showed decreased hemispheric activity due to secondary hydrocephalus. In another child CRAG showed an auricular rhabdomyosarcoma that had invaded the sigmoid sinus; the abnormal area was obscured by facial activity on the static images, but the CRAG revealed a sharply circumscribed defect in sinus activity.

The CRAG was also helpful in the 37 children (mean age 5.1 months, range 1 week to 30 months) who had abnormal cranial transillumination. Since transillumination is a nonspecific physical finding (*6*), several types of abnormality were discovered in these children. Eleven patients (30%) had abnormalities on both the CRAG and static images (seven subdural collections, three intracranial cysts, one hydrocephalus), and 11 (30%) had abnormalities revealed only by the CRAG (six intracranial cysts, four hydrocephalus, one subdural collection).

The CRAG did not significantly increase the diagnostic yield of radionuclide studies in children with low-probability presentations. The CRAG was abnormal in only 22 of these 592 children and was essential in only 11 (Table 1). This represents only a 1.9% yield, but it is still an 18% increase in the number of positive studies (11 out of 61). The characteristics of this population (90% had normal studies) account for these results. The CRAG revealed changes of cerebrovascular disease in five children and showed diminished hemispheric activity in four children who had hydrocephalus. In addition, two infants had subdural collections detected only by displacement of convexity activity during the CRAG.

DISCUSSION

Cowan et al. (*1*) state that radionuclide angiography is valuable for detecting and characterizing intracranial disease when used in conjunction with static radionuclide brain images. The results of the current study support this position by showing the utility of the CRAG in pediatric patients. Routine use of the

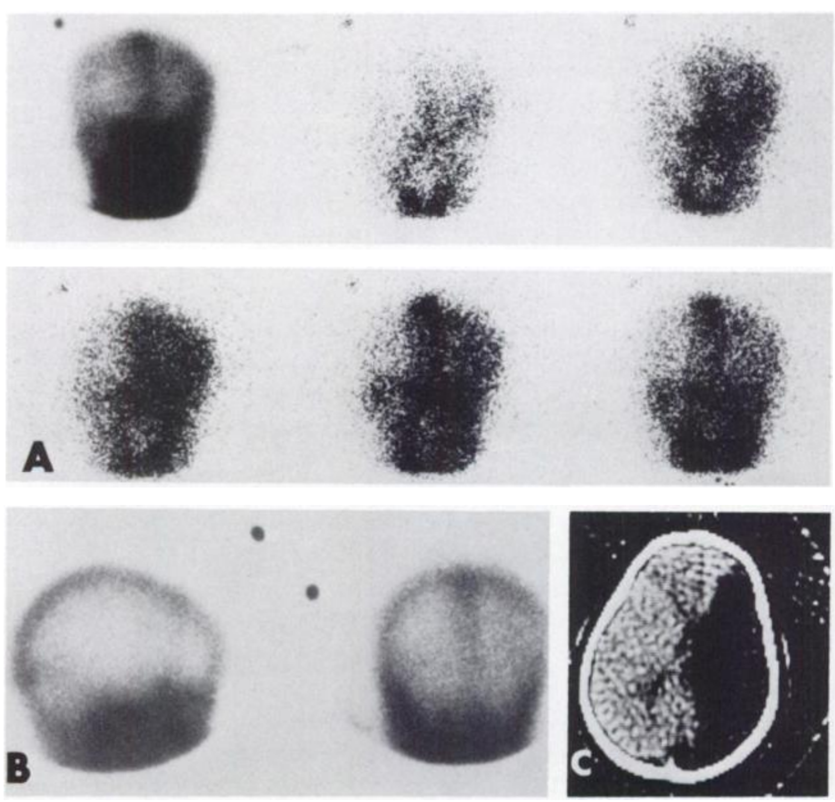

FIG. 2. This 18-month-old girl had congenital left hemiparesis and showed abnormal transillumination of right cranium. Markedly decreased activity in right hemisphere is shown by CRAG (A). Blood-pool image (A, upper left) and anterior and right lateral static images (B), reveal slight lucency of right hemisphere. Computerized cranial tomography (C) showed large right-sided intracranial cyst.

CRAG significantly ($p < 0.01$) increased detection of abnormalities. Confirmed positive studies increased nearly 6%, while false-positive interpretations rose by less than 1%. The increased yield obtained in this study exceeds the 3% reported by Yalaz and Treves (*7*), but they only used the CRAG in selected patients. Our increased yield was far less than the 33% increase in lesion detection reported by Cowan et al. (*1*), but the relative infrequency of cerebrovascular disease in children (compared to adults) accounts for much of this discrepancy.

The additional yield obtained by routine use of the CRAG in this study should not be misinterpreted as a recommendation for cerebral nuclear angiography per se. The CRAG image patterns are largely nonspecific, and correlation with immediate blood-pool and routine static images, as well as the patient's history and physical findings, is necessary for accurate assessment. The CRAG has other limitations. The poor statistical quality of the images make bilateral abnormalities harder to see; it works best in unilateral disease. For similar reasons it is likely to miss small lesions. These limitations help to explain the CRAG's inability to detect hydrocephalus. In the present study, ventricular dilatation was usually bilateral, the ventricles were often not markedly dilated, and the CRAG pattern of decreased activity seen with hydrocephalus was nonspecific. Thus, the 35% detection rate is readily explained. Radionuclide brain imaging (even with a CRAG) is not a useful test to determine the presence of hydrocephalus.

Despite these limitations, the CRAG was a useful addition to the blood-pool and static images in this study. It aided the diagnosis of cerebrovascular disease, but CRAG was even more important in the detection of subdural fluid collections. Using displacement of middle cerebral artery activity (*5*) as evidence of subdural disease, 22 additional children with subdural collections were detected. A recent study (*8*), in which both the CRAG and static images were used to detect subdural collections, showed similar results: the CRAG was essential to the diagnosis of subdural collections in 24% of those patients. These findings are of importance since subdural hematomas are common in infants (*9,10*) and may be difficult to detect in static images because they are often (70–80%) bilateral (*11*). The radionuclide angiogram increases the detection of these lesions, including those that are bilateral (*5*).

The CRAG was also helpful in detecting or confirming the presence of intracranial cysts. Although intracranial cysts are uncommon, they should be considered in the differential diagnosis of cerebral mass lesions in children (*12,13*). Large cysts may be shown as a lucency on static images (*14*), but the CRAG will reveal those and some smaller cysts as well.

Because of the greater than 10% increase in lesion detection in children with a high a priori probability of neurologic disease, the CRAG should be employed regularly in such patients, especially when subdural collections are suspected or when abnormal cranial transillumination is found. The limited additional yield (1.9%) from CRAGs in children with a low a priori probability of neurologic disease argues less strongly for routine use of the CRAG. However, this study purposely emphasized the "essential" CRAG. In practice, a CRAG that confirms normality is also valuable since several types of cerebral disease may occasionally be detected only by the CRAG. A normal CRAG is useful to help exclude subdural collections in patients with abnormal static images from scalp trauma. The CRAG can also aid interpretation of equivocal static images and provide information useful in differential diagnosis (e.g., the characteristic blush of an arteriovenous malformation). Furthermore, this information can be obtained without additional irradiation of the child. Accordingly, for maximum diagnostic accuracy a CRAG should be performed with all pediatric brain-imaging studies. In situations where camera or technologist time is limited and selective use of the CRAG is warranted, it should be restricted to children with a high a priori probability of detectable neurologic disease.

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