An Analysis of Cerebral Blood Flow in Acute Closed-Head Injury Using Technetium-99m-HMPAO SPECT and Computed Tomography

Steven N. Roper, Ismael Mena, Wesley A. King, Jeffrey Schweitzer, Karen Garrett, C. Mark Mehringer, and Duncan McBride

Divisions of Neurosurgery, Nuclear Medicine, and Neuroradiology, UCLA-Harbor Medical Center, Los Angeles, California

Technetium-99m-hexamethylpropyleneamine (HMPAO) SPECT and x-ray CT were compared in 15 patients with acute closed-head injury. There were 44 focal lesions in all. Fifteen (34%) lesions were seen on both x-ray and SPECT. Seventeen (39%) lesions were seen only on SPECT. Twelve (27%) of the lesions were seen on x-ray tomography only. Of the lesions seen on x-ray tomography but not on SPECT, two were subarachnoid hemorrhage, two were thin subdural hematomas, and eight were contusions. This study shows that SPECT can detect focal disturbances of cerebral blood flow that are not seen on x-ray tomography. It also suggests that there are two types of contusions: those with a decreased cerebral blood flow (i.e., detectable on SPECT) and those with a cerebral blood flow equal to that of the surrounding brain.

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The role of cerebral blood flow (CBF) in closed-head injury has been studied for many years but is still poorly understood. The most common methods for determining CBF in patients are based on the washout of ^{133}Xe administered via various routes and recorded directly with scintillation detectors placed extracranially (*1–5*). These give reliable numerical values for regional and averaged hemispheric CBF but have a very coarse spatial resolution. The development of SPECT combined functional radionuclide imaging with computed tomography. Xenon-133 and [^{123}I] iodoamphetamine were the first radionuclides used with SPECT, but both of these had significant drawbacks (*6,7*). More recently, another radionuclide, ^{99m}Tc-hexamethylpropyleneamine oxime (^{99m}Tc-HMPAO), has become available for use in SPECT scanning. It has a high first-pass extraction fraction, its deposition is proportional to CBF, and there is a near constant maintenance of the regional distribution of the radionuclide over several hours (*6–8*). Several investigators have already demonstrated the ability of ^{99m}Tc-HMPAO SPECT to determine relative changes in CBF in cerebrovascular disease, epilepsy, extrapyramidal disorders, and trauma (*6,8–10*). Recent work by Abdel-Dayem et al. has demonstrated focal decreased perfusion in a significant number of patients with traumatic contusions. They also found a reversal of the normal fronto-occipital flow gradient (slope reversal) in one patient with acute head injury and raised the question whether this might be a non-focal SPECT finding associated with traumatic brain injury (*9*). In this study, we compared ^{99m}Tc-HMPAO SPECT and x-ray computed tomography (XCT) scans in 15 patients with acute closed-head injury in an attempt to further elucidate the role of CBF in this process.

MATERIALS AND METHODS

Fifteen patients (14 male, 1 female, age 16–66 yr, mean age 32 ± 13) with acute closed-head injury admitted to Harbor-UCLA Medical Center from March 17, 1988 to September 20, 1988 were studied. In all instances except two, patients requiring surgery for intracranial mass lesions were excluded from the study to rule out possible effects of surgery and anesthesia on CBF. The two exceptions were patients who had epidural hematomas emergently evacuated but who also had significant contusions in areas remote from the site of surgery.

Nine patients sustained a mild head injury (Glasgow coma scale = 12–15), one had a moderate head injury (Glasgow coma scale = 8–11), and five suffered severe head injuries (Glasgow coma scale = 3–7). The mean Glasgow coma score was 11 ± 4.3. All patients with severe head injuries were intubated, hyperventilated, and underwent intracranial pressure monitoring via a fiberoptic subdural catheter. Intravenous mannitol (0.3–1.0 mg/kg) was given periodically for intracranial pressures greater than 20 mm Hg lasting 5 min or longer. No patients died during follow-up. All patients received an initial neurologic exam and follow-up exams by neurosurgery staff. Duration of follow-up ranged from 4 to 135 days with a mean follow-up of 22 days. Both XCT and SPECT were performed within 72 hr of injury in all patients except one who presented five days after his injury.

XCT scans were performed immediately on all patients and follow-up studies were performed as indicated. They were performed on a Picker 1200SX high-resolution scanner using routine 1-cm slices. All XCTs were read by a single neuroradiologist (MM). They were evaluated for the presence of focal lesions in

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For reprints contact: Steven N. Roper, MD, Division of Neurosurgery, UCLA School of Medicine, 10833 LeConte Ave., Los Angeles, CA 90024.

the form of epidural hematoma, subdural hematoma, subarachnoid hemorrhage, intraparenchymal hematoma, and contusion. A comment on the presence or absence of diffuse swelling was made for each XCT. If present, it was classified subjectively as mild, moderate, or severe, based on sulcal patterns, ventricular size, midline shift, and the status of the perimesencephalic cisterns.

For the SPECT studies, each patient received 20 mCi of HMPAO injected intravenously within 20 min of reconstitution. All patients were injected in the supine position with low ambient light and noise. SPECT scanning was started 2 hr after injection to clear soft-tissue background activity. A large field of view rotating gamma camera (Elscint, ECT Apex 415) with a truncated detector was used. The camera was equipped with a high-resolution parallel-hole collimator and operated on a step and shoot mode. The orbit was circular, over 360°. Sixty images were gathered every 6° steps for 20 sec each. Total acquisition time was 20 min. The matrix size was 64 × 64. The counts per image were in the range of 50,000–90,000, with a total number of counts for the whole series between 3 and 5 million. The 60 raw data images were corrected for decay and smoothed. For uniformity correction, a special sensitivity map was used consisting of a 120-million count flow field image. The acquisition zoom used was 1.6 and the reconstruction zoom was 1.33. Reconstruction was performed by means of the backprojection algorithm using a Hanning filter. Attenuation correction using Chang's method was applied and the attenuation correction coefficient was 0.11/cm. Each set had 14 to 16 images depending on the volume of the brain. The images were 1-cm thick (=2 pixels) and were displayed using a Harbor-UCLA color scale that denotes abnormal diminished uptake defined by a drop below 60% of maximal encephalic activity.

All SPECT scans were read by a single nuclear medicine radiologist (IM). They were evaluated for focal abnormalities in perfusion. Each SPECT scan was also evaluated for the presence of nonfocal lesions in the form of slope reversal or differences in blood flow between the two hemispheres. The radiologist that read the XCTs was blinded to the findings on SPECT and vice versa. Both radiologists were blinded to the patients' Glasgow coma scores.

Statistical analysis was used to evaluate relationships between slope reversal on SPECT, diffuse swelling on XCT, and intial Glasgow coma core. The chi-square test was used to test for a correlation between the degree of swelling on XCT and slope reversal on SPECT. The Student's t-test was used to test for correlation between initial Glasgow coma score and the degree of swelling on both XCT and slope reversal on SPECT.

RESULTS

Focal Lesions

Focal lesions detected by XCT were tabulated and compared to the focal lesions found on SPECT. XCT findings in this category included epidural hematoma, subarachnoid hemorrhage, subdural hematoma, intraparenchymal hematomas, and contusions. SPECT findings in this category consisted of focal areas of hypoperfusion and one instance of an extrinsic mass. There were no instances of focal hyperperfusion. These findings are presented in Table 1. There were 44 focal lesions in all. XCT and SPECT concurred in 15 (34%) of these. SPECT showed focal lesions not seen on XCT in 17 (39%) instances. Figures 1 and 2 show examples of lesions where SPECT and XCT concurred as well as lesions that were seen on SPECT but not on XCT. There were 12 (27%) focal findings on XCT with no corresponding abnormality on SPECT. Table 2 represents a breakdown of the types of focal lesions detected by XCT but not by SPECT. Two of these lesions were subarachnoid hemorrhage, two were small (<5 mm) subdural hematomas, and eight were contusions. Using XCT as the accepted standard, SPECT detected 56% of the focal lesions found on XCT. Of the 20 contusions demonstrated by XCT, 12 were seen on SPECT and eight were not. The lesions seen only on SPECT were evaluated with respect to the site of initial impact of the injury. Seven out of 17 (41%) of these lesions were found to represent contra coup injuries.

Diffuse Lesions

Diffuse lesions on XCT fell into the categories of mild, moderate, or severe swelling. The only diffuse change seen on SPECT was slope reversal. Diffuse swelling and fronto-occipital slope reversal were therefore compared. Diffuse swelling was present in 12 of the 15 patients. It was mild in seven, moderate in four, and severe in one. Slope reversal on SPECT was present in four patients. Three of these patients had mild swelling and one had moderate swelling. There was no significant correlation between the presence of slope reversal on SPECT and the degree of swelling on XCT. The mean Glasgow coma scores for absent, mild, moderate, and severe swelling were 14 ± 0, 13 ± 2.7, 8 ± 5.2, and 5 (n = 1), respectively. There was a significant difference ($p < 0.025$) between the Glasgow coma scores of those patients with absent and mild swelling and those with moderate and severe swelling. The four patients who had slope reversal on SPECT had initial Glasgow coma scores of 3, 8, 14, and 14. There was no significant difference between the Glasgow coma scores of those patients with slope reversal on SPECT as compared to those without it.

DISCUSSION

The understanding of CBF and its relationship to the pathophysiology of traumatic brain injury in humans has closely followed advances in nuclear medicine technology. Results from xenon washout studies showed that after

TABLE 1
A Comparison of Focal Lesions on XCT Versus SPECT (n = 15 Patients)

Lesions seen on XCT and SPECT	15 (34%)
Lesions seen on XCT only	12 (27%)
Lesions seen on SPECT only	17 (39%)
Total	44

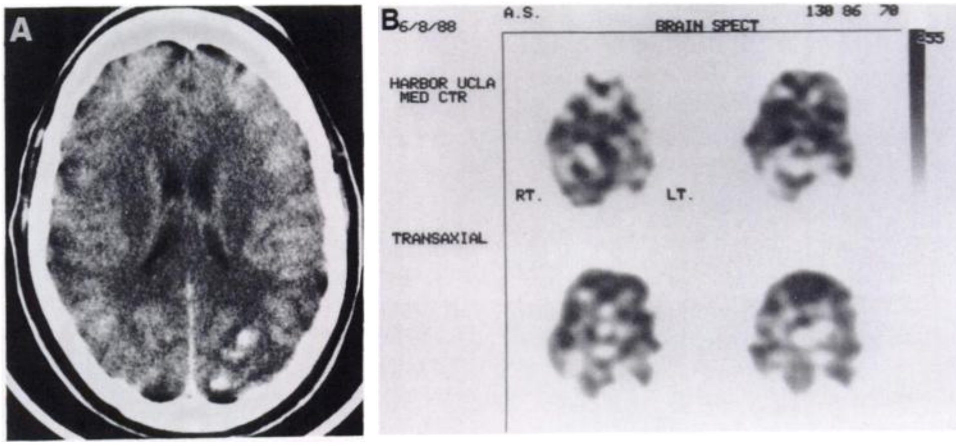

FIGURE 1. Imaging studies from a 19-yr-old male who suffered a non-penetrating gunshot wound to the left temporal area. XCT (A) shows a left frontotemporal contusion. SPECT (B) shows decreased CBF in the left frontotemporoparietal, right frontal, and right occipital areas.

severe closed-head injury about one-half of the patients have hyperemia (CBF in excess of the metabolic demands of the tissue) and the other half show decreased CBF (*4*). This reduced CBF was found to be appropriate for the reduced metabolic demands of the injured tissue. When ipsilateral hemispheric arteriovenous gradients were taken into account, actual ischemia was documented in only 1 of 55 patients (*4*). They also found that the gross evaluation of CBF did not correlate well with clinical outcome (*1,3,4*). Both animal (*11–14*) and human (*2,5,15,16*) studies have demonstrated a temporary loss of autoregulation, CO_2 reactivity, and metabolic coupling of CBF in traumatized cortex. It is not clear, however, how these findings based largely on mean hemispheric CBF apply to the focal disturbances addressed in this study. Studies of focal CBF changes with trauma in animals have generally shown decreased flow in the first few hours after injury (*17–19*). Results vary, however, between species, experimental model, and severity of injury (*17–20*).

With the development of SPECT technology, we now have a method that couples physiologic monitoring with a spatial resolution approaching that of XCT. We can see changes in CBF with much better anatomic definition than before. An earlier study found that SPECT detected 73% of these lesions (focal and diffuse) seen on XCT (*9*). In our study, SPECT detected 55% of the focal lesions found on XCT. It is easy to understand why some of the lesions were not detected by SPECT. Subarachnoid hemorrhage and very thin subdural hematomas would not produce a mass effect within the spatial resolution of the SPECT scanner. There were, however, eight contusions seen on CT but not on SPECT. This raises the question of whether the contusions were simply missed by SPECT or whether there are two hemodynamically different subsets of traumatic contusion: those with flow equal to that of surrounding brain and those with a decreased blood flow. Although the numbers in this study are small, a review of the contusions showed some to be well within the spatial resolution of the SPECT scanner and of equal or greater size than many of those contusions which showed up as areas of decreased perfusion.

If there are two subsets of contusions, the significance of those with flow equal to the surrounding brain becomes an important question. Langfitt et al. compared PET to XCT in three head injury patients and found decreased metabolism in all areas with focal lesions on XCT as well as other areas of decreased metabolism which showed no abnormalities on XCT (*21*). Another recent study utilizing PET in 11 patients found that contusions on XCT consistently had decreased rates of oxygen metabolism. This investigation demonstrated no incidents of relative hyperemia in contusions in the subacute or chronic stages of

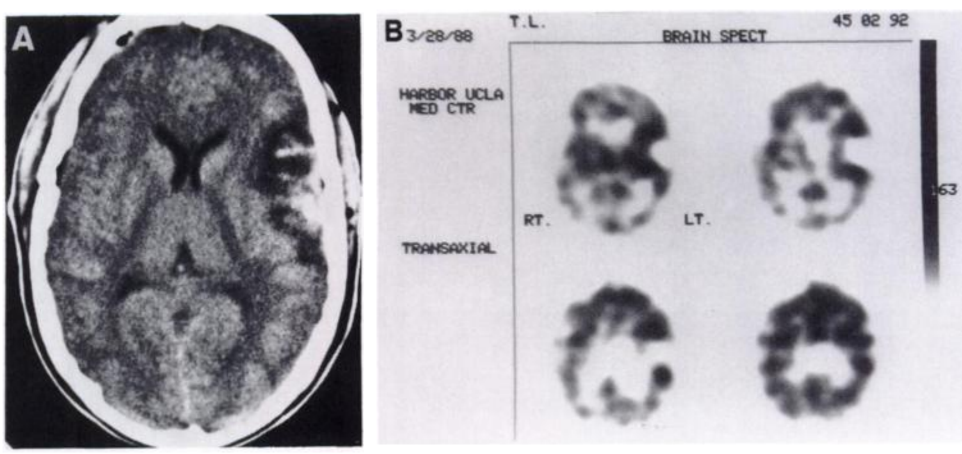

FIGURE 2. Imaging studies from a 45-yr-old male who was thrown from a horse. XCT (A) shows a left occipital contusion and SPECT (B) shows decreased CBF in both occipital lobes.

TABLE 2
Nature of Lesions Found on XCT Only

Subarachnoid hemorrhage	2
Subdural hematoma (<5 mm)	2
Contusion	8
Total	12

closed-head injury; however, acute studies (<8 days post-injury) were not performed (*22*). Since these articles suggest that most or all contusions are hypometabolic, it is probable that CBF and metabolism in the eight contusions from the current study have become dissociated and that they are actually in a state of hyperemia relative to a decreased metabolic demand. The factors that determine whether a contusion has reduced or unaltered CBF and whether these subsets evolve differently with time are interesting questions for future study.

The areas of decreased CBF on SPECT with no abnormalities on XCT demonstrate that changes in CBF after closed-head injury need not produce detectable structural changes. Repeat SPECT scans were performed on four patients who initially had areas of decreased CBF that were not seen on XCT. Two of these cases clearly showed that such lesions may normalize with time. Two other cases, however, showed either no change or increase in size on repeat SPECT. These persistent lesions correspond to areas of encephalomalacia on repeat XCT. But the factors that determine those areas of decreased CBF that normalize with time and those that will not have yet to be elucidated. There was one instance of a patient with altered consciousness, a normal XCT, and decreased CBF in both parietal lobes. This suggests that abnormalities seen only on SPECT can significantly influence a patient's clinical status.

Using traditional ^{133}Xe determination of CBF, several investigators have found that increased CBF correlated well with diffuse swelling and increased ICP (*3,4,23*). This study does not show a SPECT finding that correlates well with diffuse swelling on XCT or clinical outcome. This may be largely due to the fact that our SPECT studies gave only relative comparisons of CBF and not absolute values. Although slope reversal occurred in four patients, it did not correlate with the degree of swelling on XCT or initial Glasgow coma scores.

In conclusion, this study suggests that HMPAO SPECT will be most useful in the context of closed-head injury for examining focal rather than diffuse lesions. It demonstrates the ability of SPECT to define physiologic changes that are undetectable to XCT and shows that these lesions can significantly influence cerebral function in some cases. It also identifies two hemodynamically divergent subgroups of traumatic contusion. Larger studies with SPECT and PET are needed to more clearly define the natural history of these contusions and further our understanding of the pathophysiology of traumatic brain injury.

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