Neuroimaging in Patients with Head Injury

Andrew B. Newberg and Abass Alavi

Head trauma affects thousands of people every year. Neuroimaging techniques provide some of the most important diagnostic, prognostic, and pathophysiological information in the management of brain injury. Anatomical imaging modalities can help assess intracranial hemorrhage, fractures, and other structural lesions. Functional imaging has been shown to be helpful in assessing the areas of the brain affected by the trauma as well as determining long term prognosis and rehabilitation potential. This article will review the current uses of neuroimaging techniques in head trauma and delineate future applications.

HEAD TRAUMA AFFECTS several hundred thousand individuals in the United States each year. It has been estimated that as much as seventy-five thousand brain injuries (approximately 20% of all head injuries) each year result in long-term disability and neuropsychological dysfunction.[1] Motor vehicle accidents cause a large proportion of head injuries, particularly in the young male population. However, people in all age groups are subject to various causes of head trauma. In fact, the overall incidence of traumatic brain injury is similar to the incidence of stroke in the general population. The mortality associated with brain injury is the highest during the first 48 hours after trauma.[2] Since appropriate medical and neurological assessments of these patients plays an important role in initiating the needed therapies and determining prognosis, various neuroimaging methods have been employed in order to determine the extent and nature of brain injuries. The neuroimaging techniques include x-ray computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and single-photon emission computed tomography (SPECT). This review will consider the current and future applications of these imaging modalities as they pertain to the study and management of head trauma.

The development of modern tomographic anatomical imaging has had a major impact on the diagnosis and management of head trauma patients. While MRI is more sensitive and accurate in diagnosing cerebral pathology,[3,4] CT is considered the most critical imaging technique for the management of head injured patients in the first 24-48 hours.[5,6]

From the Division of Nuclear Medicine, Philadelphia, PA, USA.

Address reprint requests to Andrew Newberg, MD, Division of Nuclear Medicine, 110 Donner Building, H.U.P., 3400 Spruce Street, Philadelphia, PA 19104.

0001-2998/03/3302-0002$30.00/0

doi:10.1053/snuc.2003.127299

Importantly, CT imaging can be relatively easily performed while the patient is maintained by life support equipment. The ability to obtain images while on life support has been a more recent development with MRI, but usually presents some difficulty. Yealy and Hogan[7] indicated that CT is the procedure of choice for moderate to high risk head trauma patients. Low risk patients can often be observed without performing imaging studies at all. However, another study found that CT scans detected abnormalities in approximately 8% of patients with mild head trauma and less than one percent required neurosurgical intervention.[8] High-risk clinical variables such as the presence of cranial soft tissue injury, focal neurological deficits, signs of basilar skull fracture, and an age over 60 years, can be used to determine which patients require CT scanning.[8] A retrospective study by Reinus et al[9] indicated that patients with evidence of alcohol intoxication, a history of amnesia, or focal neurological deficits would most benefit from CT evaluation.

CT is superior to MRI in detecting bony fractures of the skull as well as epidural hemorrhage and subarachnoid hemorrhage.[7,10,11] CT is also an excellent imaging technique for distinguishing parenchymal hemorrhage from edema and is successful in detecting surgically significant lesion.[12] CT is typically more available, more cost effective, and requires a shorter period of time for scanning than MRI.

Today, MRI is still limited by its difficulty evaluating skull fractures, the degradation of MR images by motion artifact in agitated patients, and the difficulty in monitoring patients during MRI due to the need for nonferromagnetic monitoring equipment[12]. However, with the introduction of equipment which allows for better patient monitoring during MR imaging and short imaging times, MRI may become a more useful tool for the early evaluation of acute brain injury[13,14]. For now, it

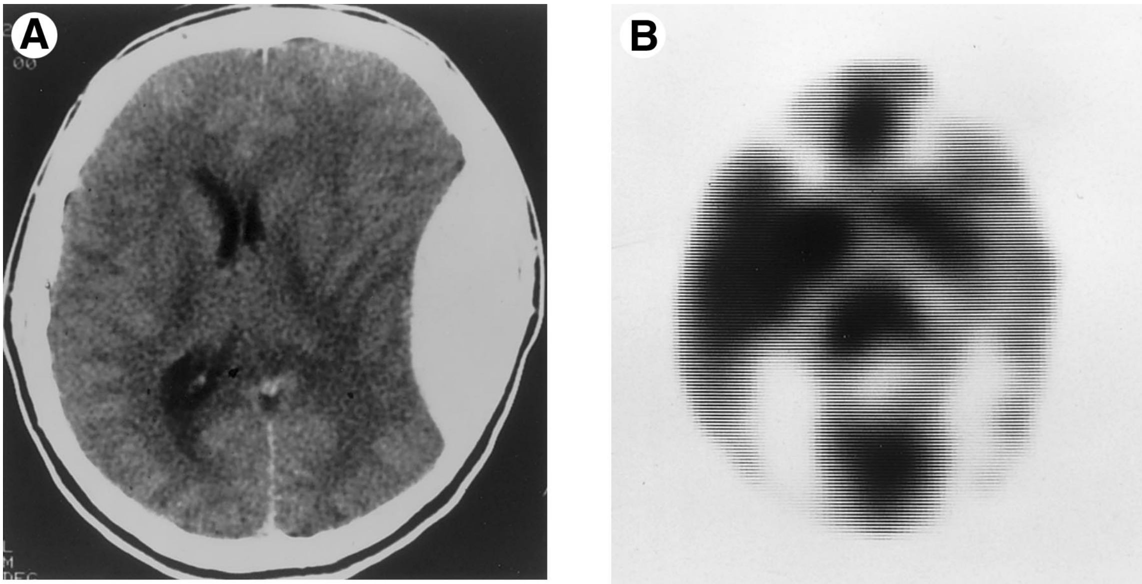


Fig 1. (A) CT image of a patient with head trauma who sustained a left sided epidural hematoma. (B) The corresponding FDG PET scan shows hypometabolism in the left hemisphere extending beyond the area directly affected by the hematoma and including the temporal and parietal cortices. (Reprinted with permission from Newberg A, Alavi A: Neuroimaging in patients with head trauma, Nucl Med Ann, 1996, pp 195-212).

appears that CT is still the imaging study of choice in the acute management of brain injury.

POSTITON EMISSION TOMOGRAPHY (PET)

A number of studies using PET for the evaluation of patients with head trauma have been reported in the literature. The major limitation of PET imaging is that it cannot distinguish between functional abnormalities specifically related to structural damage from those which are not associated with clear structural damage.[15] Therefore, it is essential that PET images are compared to the corresponding anatomical images generated by MRI or CT. In general, studies have found that cerebral dysfunction can extend far beyond the boundary of anatomical lesions and may even appear in remote locations from the trauma.[15,16] Alavi et al.[14] showed that approximately 33% of anatomical lesions were associated with larger and more widespread metabolic abnormalities. As much as 42% of PET abnormalities were not associated with any anatomical lesions.

Lesions such as cortical contusions, intracranial hematoma, and resulting encephalomalacia typically have metabolic effects that are confined primarily to the site of injury (Fig. 1). Subdural and epidural hematomas often cause widespread hypometabolism and may even affect the contralateral hemisphere or cerebellum.[17] Diffuse axonal injury (DAI) has been found to cause diffuse cortical hypometabolism as well as markedly decreased metabolism in the parieto-occipital cortex.[14] This is particularly true in the visual cortex of patients with DAI when compared to normal subjects and patients with other types of head injuries (Fig 2). The cause of this parieto-occipital hypometabolism is not completely known. However, it is believed to result either from disruption of callosal input into the visual cortex or from disruption of primary visual input due to the shearing axonal injuries of the optic and geniculo-calcarine tracts.[14]

Of particular relevance to the use of PET imaging in brain injury is that ischemic cell damage occurs in over 90% of these patients.[18] This ischemic cell damage is probably mediated by the release of various toxins in response to the molecular events associated with brain injury. This also leads to an ischemia-reperfusion type of injury.[19,20] Most ischemic changes in brain injury are observed in the fronto-parietal watershed regions and have been noted particularly in patients with severe brain injuries.[21] A study by Yamaki et al.[22] used PET scans to determine cerebral blood flow (CBF), oxygen metabolism and the oxygen extraction fraction (OEF) in patients with severe brain injury. The results suggested that patients with long last-

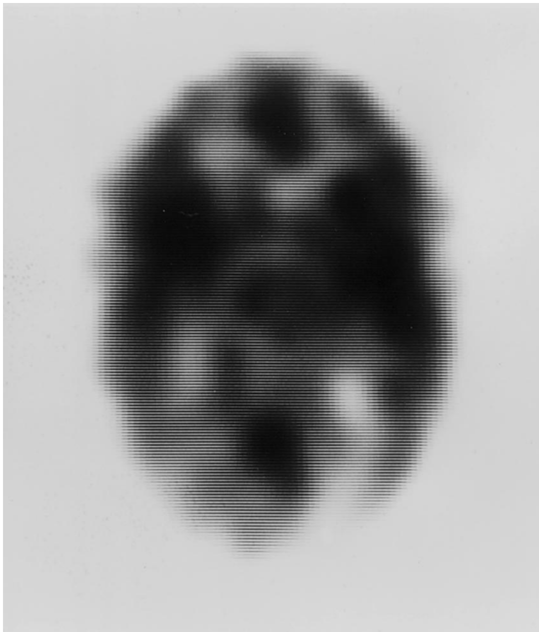
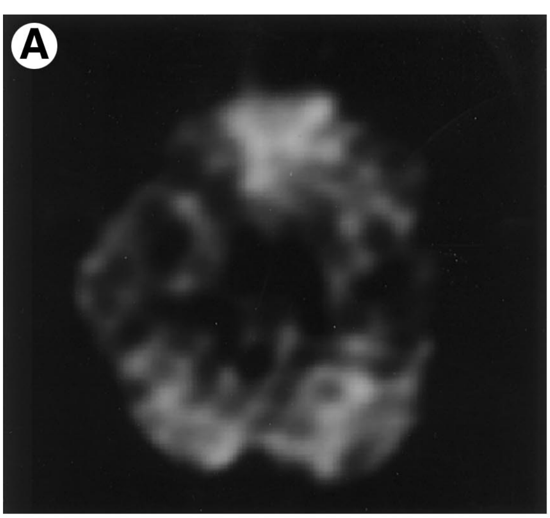


Fig 2. **FDG PET scan of a head injury patient demonstrating significant hypometabolism in the left visual cortex.**

ing anaerobic glycolysis with a high OEF and a relatively low metabolic ratio of oxygen metabolism to glucose metabolism were predictors for a poor outcome. Furthermore, it was suggested that the mechanism of these metabolic derrangements may not be related to protracted tissue hypoxia, but rather to the elevation of lactate levels. This study was performed with a small number of subjects and thus, more studies to corroborate the findings will be necessary.

Crossed cerebellar diaschisis, as well as ipsilateral cerebellar hypometabolism, has been reported in brain injury patients with supratentorial lesions (Fig 3). A study by Alavi et al.[23] showed that 40% of diffuse lesions observed in head trauma patients were associated with right sided cerebellar hypometabolism while only 20% were associated with left sided cerebellar hypometabolism. More importantly, 40% of focal unilateral lesions were associated with contralateral cerebellar hypometabolism. This was significantly greater than the 19% of the focal unilateral lesions that were associated with ipsilateral cerebellar hypometabolism. Similar results were found when comparing other types of brain injury such as cortical contusions, hemispheric penetration injuries, intracerebral hematomas, basal ganglia hemorrhages, and extraparenchymal lesions. The most pronounced contralateral hypometabolism for all categories of focal lesions was noted for those lesions ranked by a neurosurgeon as the patient's most severe injury. Of patients with focal injuries alone, virtually all had contralateral and none had ipsilateral cerebellar hypometabolism to the most severe lesion. Interestingly, patients with both focal and diffuse inju-



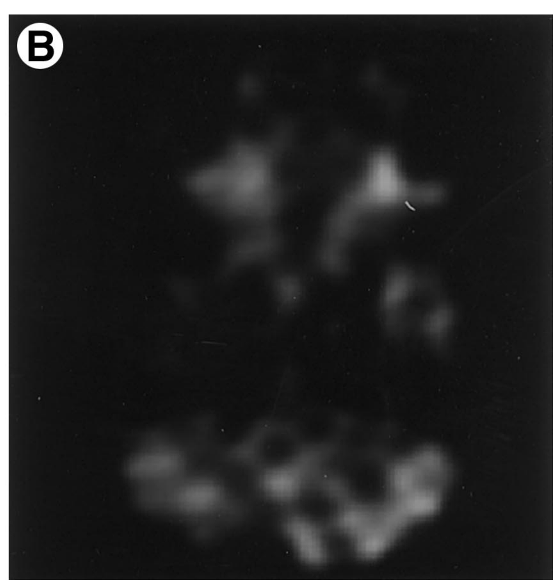


Fig 3. **FDG PET scan of a patient with a head injury that resulted in hypometabolism in the left temporal lobe (A) with associated crossed cerebellar diaschisis demonstrated by hypometabolism in the right cerebellum (B).**

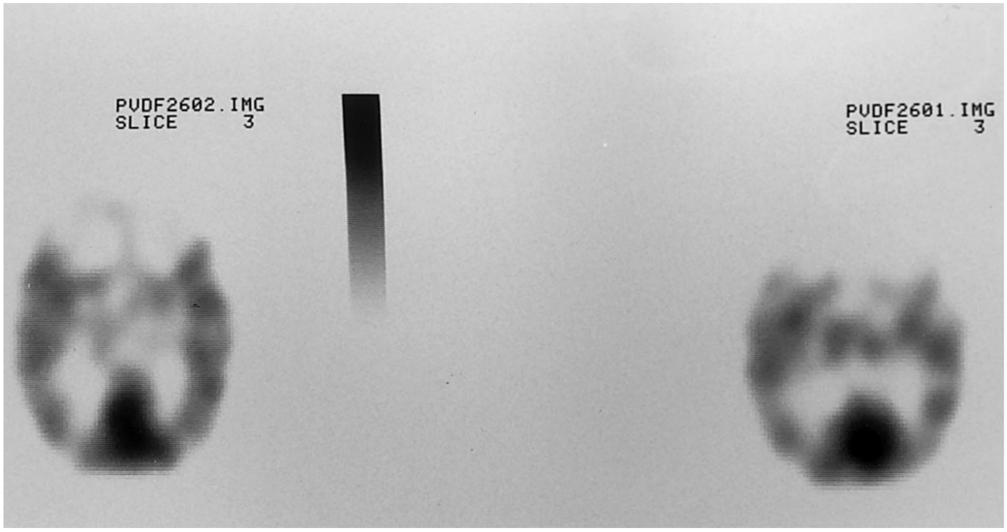


Fig 4. FDG PET scan of a head injury patient demonstrating significant hypometabolism in both frontal lobes.

ries did not show any predilection for the laterality of cerebellar hypometabolism. The results obtained from patients with serial PET scans showed that cerebellar hypometabolism is not consistent with time. This may be due either to the reversibility of cerebellar diaschisis resulting from acute brain injury or may be related to the competing effects of multiple lesions in the same patient. Another PET study of cerebellar diaschisis utilizing both FDG for glucose metabolism and 11C Flumazenil binding to benzodiazepine receptors demonstrated changes between children and adults with regard to changes in cerebellar function associated with cortical injury.[24] Children with injuries before 1 year of age were found to have significantly higher glucose utilization in the contralateral posterior quadrangular and superior semilunar lobules of the cerebellar cortex than did adults. In terms of benzodiazepine receptor activity in the cerebellum, half the children had increased benzodiazepine receptor binding in the dentate nucleus contralateral to the lesion. The other half had no increase in dentate nucleus, but showed increased binding in the lateral lobules of the cerebellar cortex contralateral to the lesion. On the other hand, adults had increased benzodiazepine receptor binding only in the contralateral dentate nucleus and not in the cerebellar cortex.

Alavi[14] found a good correlation between the severity of head trauma as measured by the Glasgow Coma Scale and the extent of whole brain hypometabolism as measured by FDG-PET. No significant differences in cerebral metabolism were observed between head trauma patients with a GCS of 14 or 15 and normal controls. Head trauma patients with GCS scores of 13 or lower did have significantly decreased cortical glucose metabolism. Therefore, cerebral metabolism is believed to be a good indicator of functional activity in patients with head trauma. However, a more recent study of 42 patients with head injury found a higher prevalence of metabolic abnormalities in the more severely injured patients even though the magnitude of the abnormality did not significantly correlate with the level of consciousness.[25] This finding suggests that while PET might be helpful in evaluating head injury patients, the metabolic abnormalities may be associated with a multifactorial etiology. Other studies have shown that hypometabolism measured by PET images correlates with neuropsychological and language testing. One study observed a significant correlation between cognitive and behavioral disorders and decreased cortical metabolism in the prefrontal and cingulate cortex in patients with severe traumatic brain injury.[26] Studies have shown that PET findings correspond well with the site and extent of cerebral dysfunction as determined by neurological and behavioral evaluations even though CT imaging did not.[27] Ruff et al.[28] studied six head trauma patients and found that five had decreased anterior frontal cerebral metabolism as measured by PET (Figs 4 and 5). This study also indicated that the hypometabolism correlated well with generalized

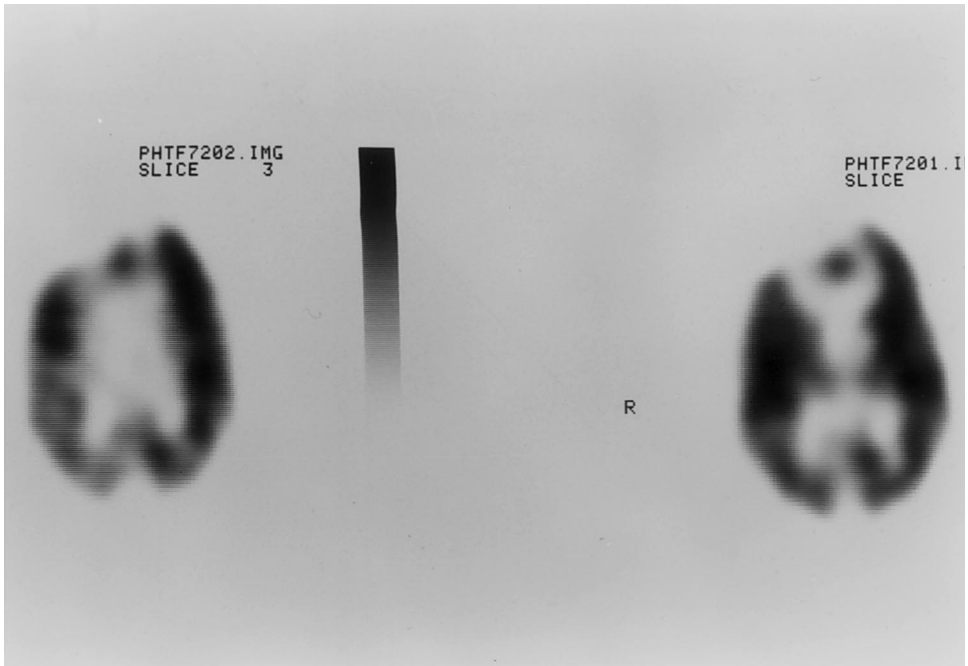


Fig 5. FDG PET scan of a head injury patient demonstrating significant hypometabolism in the right frontal lobe as well as diffuse hypometabolism throughout the posterior cortical areas consistent with diffuse axonal injury. (Reprinted with permission from Newberg A, Alavi A: Neuroimaging in patients with head trauma, Nucl Med Ann, 1996, pp 195-212).

cognitive dysfunction and behavioral changes in these patients as measured by neuropsychological testing. This study is somewhat difficult to interpret since there were not enough subjects for adequate statistical analysis. Furthermore, with the use of quantitative PET, more accurate correlations might be found. The relatively good correlation between PET and neuropsychological dysfunction may be related to the ability of PET to measure regional brain function regardless of structural damage observed on anatomical imaging of CT or MRI. This may explain why functional imaging may correlate better with neuropsychological dysfunction. Follow-up CT scans of head trauma patients did reveal structural abnormalities such as encephalomalacia and atrophy that were consistent with the PET images, neurologic examination, and behavioral assessment findings. Further, global and regional metabolic rates have been found to improve as patients clinically recover from head trauma.[16,17] Thus, PET imaging may have important implications for rehabilitation potential with regard to predicting which patients will be more likely to recover function.[27] However, more studies will be needed to clarify such assessments.

A study by Humayun[29] used FDG-PET to measure local cerebral metabolic rates for glucose (LCMRGlu) in three patients with mild to moderate closed brain injury. The brain injury patients were between 3-12 months post-injury and all had deficits in attention and recent memory as determined by neuropsychological testing and all had normal CT, MRI, electroencephalography (EEG) and drug screens. Subjects were scanned with PET while performing a vigilance task. While, there were no significant differences found in global cerebral glucose metabolism in brain injury patients compared to controls, the patients with brain injury had significantly decreased rCMRGlc in the medial temporal, posterior temporal, and posterior frontal cortices. They also had decreased metabolism in the left caudate nucleus compared to controls. The rCMRGlc was significantly increased in brain injury patients in the anterior temporal and anterior frontal cortices compared to controls. These results indicated that brain injury patients can have regional glucose metabolic abnormalities despite normal CT, MRI, or EEG results. While the number of subjects was small in this study, the results corroborate other reports regarding changes in cerebral metabolism despite normal anatomical findings. A more recent study suggested that frontotemporal damage from inertial strain might be associated with the disabling syndrome that may occur after head injury consisting of head, neck, and back pain; impaired short-term memory and concentration; fatigue and a loss of stamina; poor balance; and a change in personality.[30] PET findings might be particularly useful in evaluating patients with these symptoms after head injury.

It has also been found that after head injury, even though a patient may be in a persistent vegetative state, their brain actually responds to the emotional attributes of sound or speech. This was determined using PET to measure CBF changes when a story was told by a patient's mother.[31] During auditory presentation, there was increased activity in the rostral anterior cingulate, right middle temporal, and right premotor cortices.

An interesting PET study utilizing carbon-11-labeled diacylglycerol measured phosphoinositide turnover to observe the process of recovery from injury in human brain.[32] Patients with focal brain injury exhibited areas of increased activity in the association areas distant from the lesion. The investigators indicated that such a finding suggests initiation of reorganization of neural connections occurs in the remote association areas rather than in the area surrounding the brain injury. However, PET imaging may not be as helpful in determining overall prognosis in head injury patients, particularly children and adolescents, with respect to rehabilitation.[33]

The future goals of PET imaging in brain injury patients was recently delineated.[34] PET studies are required to detect ischemic lesions that develop soon after head trauma and help to clarify the significance of ischemia both clinically and pathophysiologically in these patients. PET can also be used to diagnose patients with diffuse axonal injury in order to determine the extent of damage and prognosis. PET studies may help delineate reversible and irreversible lesions in order to direct therapeutic interventions towards preventing further damage.

SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT)

SPECT studies have yielded results similar to those found with PET scans in patients with head trauma. SPECT is capable of detecting abnormalities in cerebral blood flow that indicate areas of dysfunction in brain injury. A large study of 228 patients with mild or moderate head injury who received SPECT imaging demonstrated a number of abnormalities.[35] The subjects in this study reported headache (60.9%), memory problems (27.6%), dizziness (26.7%), and sleep disorders (8.7%) as the most common symptoms. Subjects studied within 3 months of the injury demonstrated more lesions than those studied after 3 months. In patients with mild head injury and a normal CT, 68% had an abnormal SPECT study. Focal areas of hypoperfusion were seen in over three fourths of patients with head injury with the most frequent sites the basal ganglia and thalami, frontal lobes, temporal lobes, parietal lobes, and the insular and occipital lobes. This study helped to demonstrate the most common characteristics and findings in patients with head injury. Another study utilizing I^{123} iodoamphetamine demonstrated a good correlation between patient outcome and CBF values[36]. Quantitative and sequential CBF studies with I^{123} iodoamphetamine SPECT are promising for helping to determine the prognosis for patients with diffuse brain injury.

While it is well established that blood flow and metabolism are coupled in most disease states, acute states associated with brain injury can result in an uncoupling between these two functional parameters.[37] Therefore, the value of cerebral blood flow studies measured by SPECT in the acute phase of head trauma may be limited. In spite of this limitation, SPECT has generally been found to be more sensitive than CT for detecting lesions in patients with brain injury. Specifically, investigators have found a greater number of abnormalities detected earlier on HMPAO SPECT scans compared to CT.[38-42] Gray et al[43] reported that 80% of brain injury patients had cerebral blood flow deficits on SPECT while only 55% were found to have abnormalities on CT scans. The lesions found on SPECT generally are larger in size than those detected with CT. Roper et al.[44] found that while 39% of lesions in brain injury patients on SPECT were not seen with CT, 27% of lesions found on CT were not found on corresponding SPECT images. The results from this study led the authors to the conclusion that some types of cerebral contusions are associated with decreased blood flow while others are not. Not only can there be changes in blood flow, but there can also be defects in the blood brain barrier (BBB). One study reported that 75% of brain contusions were accompanied by an abnormality of the blood brain barrier.[45] A survey of 32 SPECT studies demonstrated a number of abnormal findings in patients with mild head injuries.[46] The authors concluded that brain perfusion imaging is valuable and sensitive for the evaluation of cerebral perfusion changes following mild traumatic brain injury; that these changes can occur without loss of consciousness; that SPECT is more sensitive than computed tomography in detecting brain lesions; and that the changes observed on SPECT imaging may explain a neurological component of the patient's symptoms in the absence of morphological abnormalities. Another study demonstrated that quantitative cerebral blood flow as determined by SPECT imaging may be useful in the clinical setting since such measures correlate with symptoms related to aphasia, dementia, and altered consciousness.[47]

Roper et al.[44] found that SPECT images indicated blood flow to injured areas was similar to that in the non-injured brain areas. This may have resulted from luxury perfusion to these areas with the subsequent uncoupling of cerebral blood flow with cerebral metabolism. Fumeya et al.[48] reported that lesions detected with CT ranged from hyperperfused to hypoperfused on SPECT. However, lesions not detected with CT were found to be only hypoperfused on SPECT. A more recent study found that 38% of patients with focal cerebral damage had areas of hyperemia primarily in the structurally normal tissue that was immediately adjacent to intraparenchymal and extracerebral lesions as determined by MRI or CT.[49] This same study reported that the incidence of brief or no loss of consciousness was significantly higher in patients with hyperemia than in those without hyperemia. Furthermore, patients with hyperemia were also found to have a lower mortality than those without hyperemia. While global hyperemia has been considered to be a more acute process associated with increased intracranial pressure, deep coma, and poor prognosis, this study suggested that those patients with focal hyperemia may actually have a better outcome.

Broich et al.[50] investigated cerebral blood flow in patients with severe brain injury using SPECT. SPECT imaging demonstrated similar, but more extensive, abnormalities than either MRI or CT. This was particularly the case in acute or subacute brain injury. Ten of the twelve patients studied with SPECT were found to have at least one region of hyperemia. In eight of these patients, the area of hyperemia correlated with the major neurological deficit. Follow-up SPECT scans more than six months after the trauma were obtained in four of the patients. The follow-up scans revealed that previously hyperemic areas now had hypoperfusion in two subjects, while two subjects had a normalization of blood flow in those areas. The hypoperfused areas corresponded to hypodense areas on CT images. The two patients with hypoperfusion had no clinical improvement while the patients whose CBF had normalized experienced clinical improvement. It was suggested by the authors that this hyperemia may represent "luxury perfusion" in the early phases of brain injury. Therefore, SPECT may be useful in detecting areas which correspond to chronic neurological dysfunction such as motor or visual field deficits (Fig 6). Another finding of this study was that patients with DAI had a widespread reduction in cortical activity. Additionally, SPECT scans in eight of ten patients with hemiplegia demonstrated crossed cerebellar diaschisis. Thus, both SPECT and PET are capable of detecting alterations in cerebellar function as the result of brain injury.

SPECT has been found to be better than CT in distinguishing lesions with a poor prognosis from those with a favorable prognosis. Patients with larger lesions, multiple defects and lesions involving the brain stem on SPECT tend to have a poorer overall outcome compared to patients with smaller, non-focal lesions.[51,52] Lesions detected by SPECT in the temporal lobes, parietal lobes, and basal ganglia have been found to be associated with a poorer outcome than other parenchymal lesions (Fig 7). Another study indicated that a negative initial SPECT scan after trauma is a good predictor for a favorable clinical outcome.[53] In a similar study, patients with the greatest disability were found to have the greatest number of lesions and the lowest cerebral blood flow as determined by SPECT[40]. These finding have been corroborated by other studies which have shown that SPECT scans more closely correlate with long-term outcome in head trauma patients compared to either MRI or CT.[52] Further, there is a strong correlation between the GCS and the global cerebral blood flow. Another study suggested that the combination of MR and SPECT studies might be able to better determine prognosis in brain injury patients.[54] This study

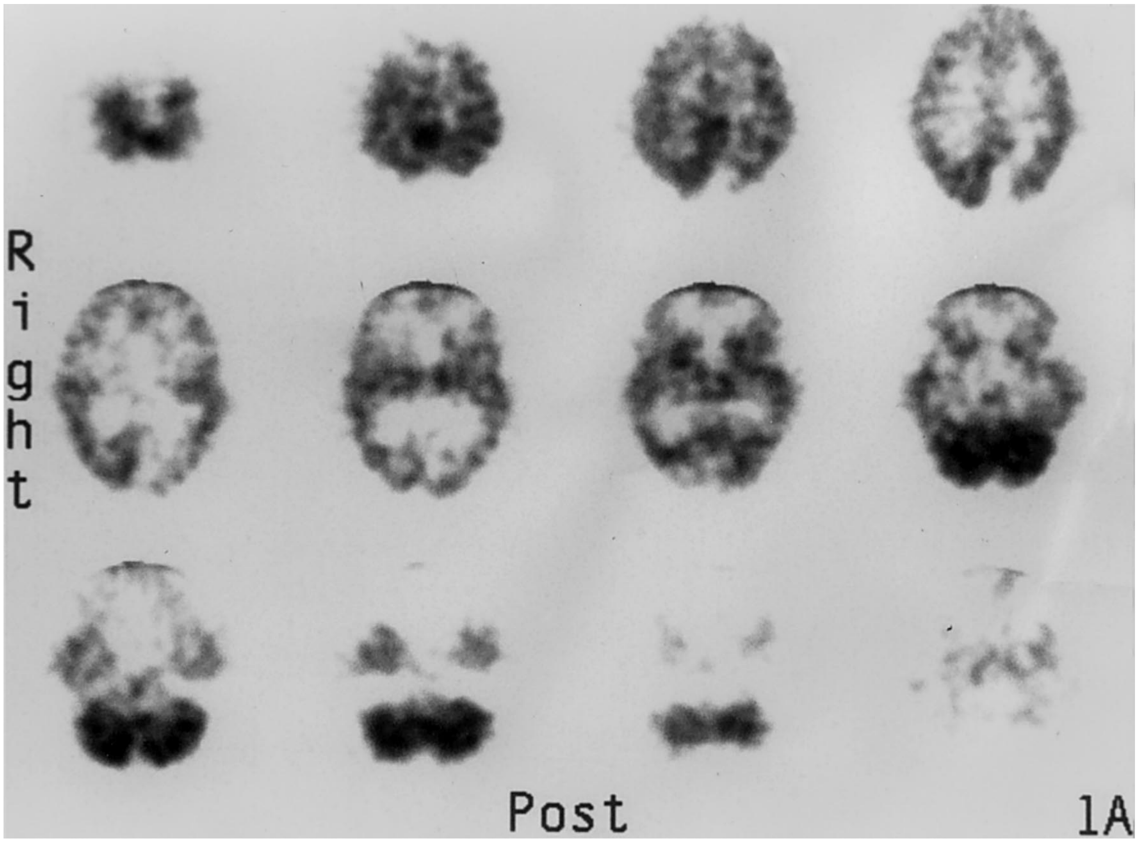


Fig. 6. HMPAO SPECT scan of a patient with head injury approximately 3 years prior to the scan, demonstrating a significant perfusion defect in the left medial occipital area extending to the visual cortex on the affected side. This finding corresponded to the clinical feature of a right homonymous hemianopsia (Reprinted with permission from Alavi A, Hirsch LJ: Studies of central nervous system disorders with single photon emission computed tomography and positron emission tomography: Evolution over the past two decades. Sem Nucl Med 21:58-81, 1991).

reported that the combination of cortical contusions and DAI on MR images with cortical and thalamic hypoperfusion on SPECT occurred in eight of twelve patients with an unfavorable outcome. Unfortunately, this was a small study, and studies with a larger number of patients comparing the use of MR and SPECT both separately and together will be needed to elucidate the ability of these modalities in determining prognosis in head trauma patients.

Oder et al[55] compared SPECT findings to behavioral and neuropsychological measures in patients who had suffered severe closed brain injury. The results from this study suggested that decreased blood flow to the frontal lobes was significantly correlated with disinhibitive behavior. There was also a significant correlation between decreased blood flow in the left cerebral hemisphere and increased social isolation. Interestingly, diminished cerebral blood flow in the right hemisphere was associated with increased aggressive behavior. The results from this study suggest that SPECT findings may help determine the behavioral and psychosocial sequelae of head trauma. Another study demonstrated that with improvement of clinical symptoms, SPECT findings similarly improve[56]. A SPECT study by Goldenberg et al.[57] showed that in patients with chronic neurological damage from brain injury, while there was a significant correlation between frontal lobe perfusion and executive functioning, the perfusion to the thalamus provided a stronger correlation. The relationship between thalamic perfusion and neuropsychological testing may be related to a deafferentation of cortical association areas secondary to damage to the thalamus. Alternatively, cortical damage may result in dysfunction of the thalami resulting in decreased thalamic perfusion. The

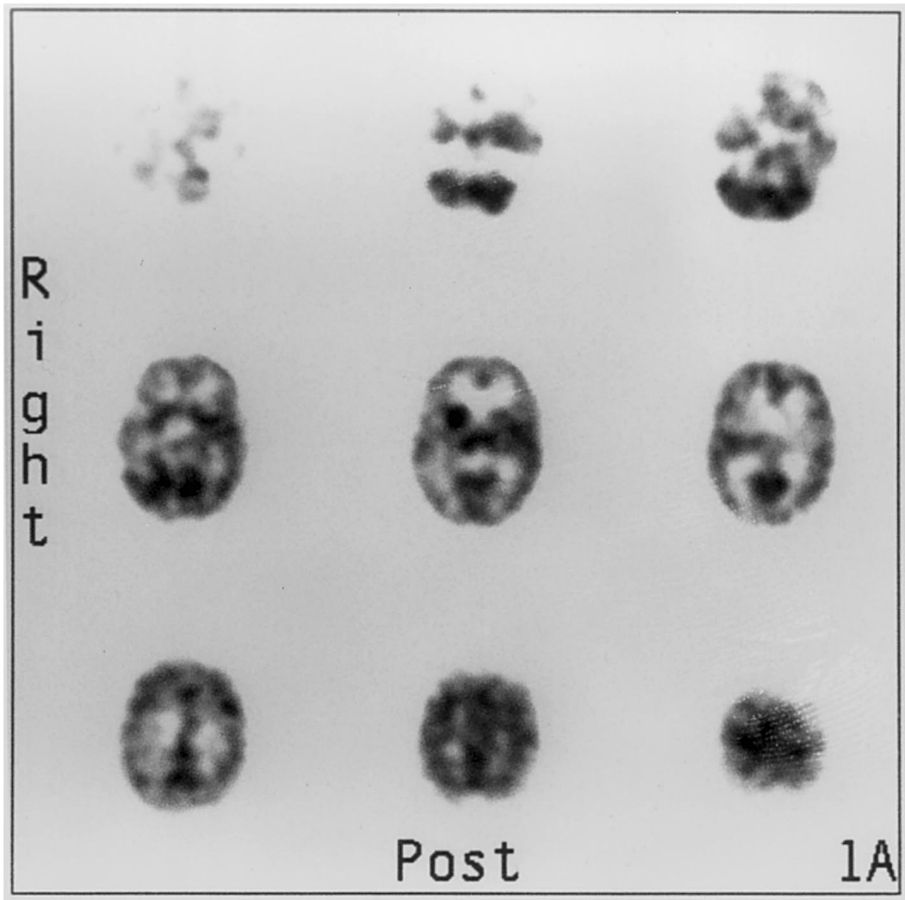


Fig 7. HMPAO SPECT scan of a patient with acute head injury demonstrating significant hyperemia in the right basal ganglia. The remainder of the cerebral perfusion is within normal limits (Reprinted with permission from Alavi A, Hirsch LJ: Studies of central nervous system disorders with single photon emission computed tomography and positron emission tomography: Evolution over the past two decades. Sem Nucl Med 21:58-81, 1991).

reciprocal effects of the thalami and the cortex are related to the heavy neuronal interconnections between the two. A case report of a subject with obsessive compulsive disorder that resulted from a brain injury to the frontal lobes reported hypoperfusion on SPECT images in both fronto-temporal regions and increased perfusion in the anterior striatum (both resolved upon resolution of the patient's symptoms) supporting the role of SPECT in evaluating behavior and psychological changes associated with brain injury.[58]

Gray et al.[43] used SPECT to study patients with a remote history of head trauma and found that 80% of brain injury patients had deficits of regional cerebral blood flow. By comparison only 55% of those same patients were found to have lesions on CT. This difference was similar for patients with both minor and severe head injuries. Patients with minor injuries were found to have deficits on SPECT in 60% of the cases while CT detected lesions in only 25% of the cases. However, this study did not demonstrate a relationship between clinical deficits utilizing neuropsychiatric testing and regional cerebral blood flow. One other limited study demonstrated that neurpsychologcal deficits could predict the perfusion abnormalities on SPECT, but SPECT findings could not predict the neuropsychological deficits.[59]

CONCLUSION

Neuroimaging is a crucial technique for evaluating and managing head trauma. CT is considered the imaging modality of choice in the management of acute brain injury. CT provides a rapid assessment of structural brain injuries, is readily available in most medical institutions, and is of relatively little cost. CT provides information regarding intracranial bleeds which may be associated with mass effect and which may require immediate surgical intervention. CT is also the most useful technique for detecting bone injuries such as fractures. However, CT is generally not as sensitive as MRI for detecting parenchymal lesions. Although MRI is more expensive, it is becoming widely available and is superior to CT for detecting intracranial lesions and hemorrhage. Despite the extensive use and significance of anatomical imaging techniques in the evaluation of patients with head trauma, it has yet to be determined whether the lesions seen on CT or MRI correlate well with cognitive dysfunction and overall outcome. In fact, studies to date show that this poor correlation may be one of the major limitations of MRI and CT.

The functional imaging techniques of PET and SPECT can play a complementary role to anatomical imaging by providing additional pathophysiological and clinical information. PET and SPECT can reveal areas of hypometabolism or hypoperfusion that are not associated with anatomical abnormalities. PET and SPECT have also been shown to be able to detect more lesions compared to CT. However, it has not yet been shown that PET and SPECT can detect more lesions than MR imaging. MRI is especially sensitive for detecting small lesions because of its excellent spatial resolution, however, the clinical relevance of these lesions remains to be fully evaluated. PET and SPECT do not have the resolution of MRI, but their ability to measure cerebral function may be more important for evaluating brain injury especially in the chronic setting. Studies to date have shown that PET and SPECT may correlate better with outcome and cognitive dysfunction compared to MRI or CT. Furthermore, even though neuropsychological testing is necessary to help guide rehabilitation, functional imaging may indicate the possibility for rehabilitation in terms of outcome. and can help identify areas involved other than those that specifically correlate with neuropsychological testing. Therefore, functional imaging can identify affected brain areas that may be missed by a particular neuropsychological battery as well as indicate which areas of decreased function may be more likely to normalize over time. Functional imaging can also be used to assess progress over time, even though it needs to be compared to neuropsychological testing. Until recently, PET has not been widely available for use in many medical centers and therefore its use for acute head trauma patients has been quite limited. However, with the wider availability of PET in the clinical setting, there may be renewed interest in utilizing PET to evaluate the acute and chronic phases of head trauma. SPECT generally has been more available and less costly than PET and thus is more practical than PET for the routine evaluation of brain injury. Despite continual improvement in the resolution of SPECT with the use of new software and improved cameras (such as those with triple or quadruple heads) SPECT is still limited by its poorer resolution and difficulty in obtaining quantitative data compared to PET. Furthermore, SPECT allows for the measurement of cerebral blood flow and does not provide metabolic information. This may be particularly relevant in the study of head injury which can frequently result in an uncoupling of blood flow and metabolism.

CT will likely remain the primary neuroimaging technique in the initial evaluation of the acute head trauma patient. However, MRI, PET, and SPECT each offer useful information for physicians in determining the pathophysiology, extent of injury, and outcome in patients with brain injury. Furthermore, as the need for the rehabilitation of patients with brain injury is emphasized, the role of functional neuroimaging may become significantly enhanced to help evaluate patients throughout their clinical course.

REFERENCES

1. Kraus JF: Epidemiology of brain injury, in Cooper PR (ed): Head Injury (ed 2) Baltimore; Williams and Wilkins, 1987

2. Langfitt TW, Gennarelli TA: Can the outcome from head injury be improved? J Neurosurg 56:19-25, 1982

3. Levin HS, Amparo E, Eisenberg HM, et al: Magnetic resonance imaging and computerized tomography in relation to the neurobehavioral sequelae of mild and moderate head injuries. J Neurosurg 66:706-713, 1987

4. Ogawa T, Sekino H, Uzura M, et al: Comparative study of magnetic resonance and CT scan imaging in cases of severe head injury. Acta Neurochir Suppl 55:8-10, 1992

5. Kelly AB, Zimmerman RD, Snow RB, et al: Head trauma: Comparison of MR and CT— experience in 100 patients. AJNR 9:699-708, 1988

6. Sklar EM, Quencer RM, Bowen BC, et al: Magnetic resonance applications in cerebral injury. Radiol Clin North Am 30:353-366, 1992

7. Yealy DM, Hogan DE: Imaging after head trauma. Who needs what? Emerg Med Clin N Am 9:707-717, 1991

8. Borezuk P: Predictors of intracranial injury in patients with mild head trauma. Ann Emerg Med 25:731-736, 1995

9. Reinus WR, Wippold FJ, Erickson KK: Practical selection criteria for noncontrast cranial computed tomography in patients with head trauma. Ann Emerg Med 22:1148-1155, 1993

10. Jennett B: Diagnosis and management of head trauma. J Neurotrauma 8:S15-S19, 1991 (Suppl)

11. Snow RB, Zimmerman RD, Gandy SE, et al: Comparison of magnetic resonance imaging and computed tomography in the evaluation of head injury. Neurosurgery 18(1):45-52, 1986

12. Ahmadi J, Destian S: Head trauma. Top Magn Res Imag 2(1):17-24, 1989

13. Crow W: Aspects of neuroradiology of head injury. Neurosurg Clin North Am 2:321-339, 1991

14. Alavi A: Functional and anatomical studies of head injury. J Neuropsychiatry 1:S45-50, 1989

15. Langfitt TW, Obrist WD, Alavi A, et al: Computerized tomography, magnetic resonance imaging, and positron emission tomography in the study of brain trauma. Preliminary observations. J Neurosurg 64:760-767, 1986

16. Alavi A, Fazekas T, Alves W, et al: Positron emission tomography in the evaluation of head injury. J Cereb Blood Flow Metab 7:S646, 1987 (suppl 1, abstr)

17. George JK, Alavi A, Zimmerman RA, et al: Metabolic (PET) correlates of anatomic lesions (CT/MRI) produced by head trauma. J Nucl Med 30:802, 1989 (abstr)

18. Adams JH: The neuropathology of regional cerebrovascular CO2 reactivity to blood pressure and regional resting flow, in Vinkin PJ, Bruyn GW (eds): Handbook of Clinical Neurology, vol 23. Amsterdam, North-Holland Publishing Co., 1975, pp 35-65

19. Ikeda Y, Long DM: The molecular basis of brain injury and brain edema: the role of oxygen free radicals. Neurosurgery 27:1-11, 1990

20. Schmidley JW: Free radicals in central nervous system ischemia. Stroke 21:1086-1090, 1990

21. Overgaard J, Mosdal C, Tweed WA: Cerebral attenuation after head injury. Part 3: Does reduced regional CBF determine recovery of brain function after blunt head injury? J Neurosurg 55:63-74, 1981

22. Yamaki T, Imahori Y, Ohmori Y, et al: Cerebral hemodynamics and metabolism of severe diffuse brain injury measured by PET. J Nucl Med 37: 1166-1170, 1996

23. Alavi A, Mirot A, Newberg A, et al: Fluorine-18-FDG evaluation of crossed cerebellar diaschisis in head injury. J Nucl Med 38:1717-1720, 1997

24. Niimura K, Chugani DC, Muzik O, et al: Cerebellar reorganization following cortical injury in humans: Effects of lesion size and age. Neurology 52:792-797, 1999

25. Bergsneider M, Hovda DA, Lee SM, et al: Dissociation of cerebral glucose metabolism and level of consciousness during the period of metabolic depression following human traumatic brain injury. J Neurotrauma 17(5):389-401, 2000

26. Fontaine A, Azouvi P, Remy P, et al: Functional anatomy of neuropsychological deficits after severe traumatic brain injury. Neurology 53(9):1963-1968, 1999

27. Rao N, Turski PA, Polcyn RE, et al: ^{18}F positron emission computed tomography in closed head injury. Arch Phys Med Rehab 65:780-785, 1984

28. Ruff RM, Buchsbaum SM, Troster AI, et al: Computed tomography, neuropsychology, and positron emission tomography in the evaluation of head injury. Neuropsych Neuropsychol Behav Neurol 2:103-123, 1989

29. Humayun MS, Presty SK, Lafrance ND, et al: Local cerebral glucose abnormalities in mild closed head injured patients with cognitive impairments. Nucl Med Com 10:335-344, 1989

30. Mamelak M: The motor vehicle collision injury syndrome. Neuropsychiatry Neuropsychol Behav Neurol 13:125-135, 2000

31. de Jong BM, Willemsen AT, Paans AM: Regional cerebral blood flow changes related to affective speech presentation in persistent vegetative state. Clin Neurol Neurosurg 99:213-216, 1997

32. Imahori Y, Fujii R, Kondo M, et al: Neural features of recovery from CNS injury revealed by PET in human brain. Neuroreport 10:117-121, 1999

33. Worley G, Hoffman JM, Paine SS, et al: 18-Fluorodeoxyglucose positron emission tomography in children and adolescents with traumatic brain injury. Development Med Child Neurol 37:213-220, 1995

34. Alavi A, Newberg AB: Metabolic consequences of acute brain trauma: Is there a role for PET? J Nucl Med 37:1170-1172, 1996

35. Abdel-Dayem HM, Abu-Judeh H, Kumar M, et al: SPECT brain perfusion abnormalities in mild or moderate traumatic brain injury. Clin Nucl Med 23:309-317, 1998

36. Shiina G, Onuma T, Kameyama M, et al: Sequential assessment of cerebral blood flow in diffuse brain injury by 123I-iodoamphetamine single-photon emission CT. Am J Neuroradiol 19:297-302, 1998

37. Abu-Judeh HH, Singh M, Masdeu JC, et al: Discordance between FDG uptake and technetium-99m-HMPAO brain perfusion in acute traumatic brain injury. J Nucl Med 39(8):1357-1359, 1998

38. Abdel-Dayem HM, Sadek SA, Kouris K: Changes in cerebral perfusion after acute head injury. Comparison of CT with Tc-99m HM-PAO SPECT. Radiology 165:221-226, 1987

39. Masdeu JC, Van Heertum RL, Kleiman A, et al: Early single photon emission computed tomography in mild head trauma. A controlled study. J Neuroimaging 4:177-181, 1994

40. Newton MR, Greenwood RJ, Britton KE, et al: A study comparing SPECT with CT and MRI after closed head injury. J Neurol Neurosurg Psych 55:92-94, 1992

41. Reid RH, Gulenchyn KY, Ballinger JR, et al: Cerebral perfusion imaging with technetium-99m HMPAO following cerebral trauma: initial experience. Clin Nucl Med 15:383-388, 1990

42. Kant R, Smith-Seemiller L, Isaac G, et al: Tc-HMPAO SPECT in persistent post-concussion syndrome after mild head injury: Comparison with MRI/CT. Brain Inj 11:115-124, 1997

43. Gray BG, Ichise M, Chung D-G, et al: Technetium-99m-HMPAO SPECT in the evaluation of patients with a remote history of traumatic brain injury. A comparison with x-ray computed tomography. J Nucl Med 33:52-58, 1992

44. Roper SN, Ismael MI, King WA, et al: An analysis of cerebral blood flow in acute closed-head injury using Tc-99m-

HMPAO SPECT in computed tomography. J Nucl Med 32:684-687, 1991

45. Bullock R, Statham P, Patterson J, et al: The time course of vasogenic oedema after focal human head injury—evidence from SPECT mapping of blood brain barrier defects. Acta Neurochir Suppl. 51:286-288, 1990

46. Abu-Judeh HH, Parker R, Singh M, et al: SPECT brain perfusion imaging in mild traumatic brain injury without loss of consciousness and normal computed tomography. Nucl Med Commun 20:505-510, 1999

47. Chang CC, Kuwana N, Noji M, et al: Cerebral blood flow measurement in patients with impaired consciousness: Usefulness of 99mTc-HMPAO single-photon emission tomography in clinical practice. Eur J Nucl Med 25:1330-1332, 1998

48. Fumeya H, Ito K, Yamagiwa O, et al: Analysis of MRI and SPECT in patients with acute head injury. Acta Neurochir Suppl 51:283-285, 1990

49. Sakas DE, Bullock MR, Patterson J, et al: Focal cerebral hyperemia after focal head injury in humans. A benign phenomenon? J Neurosurg 83:277-284, 1995

50. Broich K, Alavi A, Cruz J, et al: Evidence of "regional hyperemia" in patients with severe closed head injury using single-photon emission computed tomography. J Stroke Cerebrovasc Dis 4:271-274, 1994

51. Holman BL, Devous MD: Functional brain SPECT. The emergence of a powerful clinical method. J Nucl Med 33:1888-1904, 1992

52. Bavetta S, Nimmon CC, McCabe J, et al: A prospective study comparing SPET with MRI and CT as prognostic indicators following severe closed head injury. Nucl Med Comm 15:961-968, 1994

53. Jacobs A, Put E, Ingels M, et al: Prospective evaluation of technetium-99m-IIMPAO SPECT in mild and moderate traumatic brain injury. J Nucl Med 35:942-947, 1994

54. Prayer L, Wimberger D, Oder W, et al: Cranial MR imaging and cerebral 99mTc-HM-PAO SPECT in patients with subacute or chronic severe closed head injury and normal CT examinations. Acta Radiol 34:593-599, 1993

55. Oder W, Goldenberg G, Spatt J. et al: Behavioral and psychosocial sequelae of severe closed head injury and regional cerebral blood flow. A SPECT study. J Neurol Neurosurg Psych 55:475-480, 1992

56. Laatsch L, Jobe T, Sychra J, et al: Impact of cognitive rehabilitation therapy on neuropsychological impairments as measured by brain perfusion SPECT: A longitudinal study. Brain Inj 11(12):851-863, 1997

57. Goldenberg G, Oder W, Spatt J, et al: Cerebral correlates of disturbed executive function and memory in survivors of severe closed head injury: A SPECT study. J Neurol Neurosurg Psych 55:362-368, 1992

58. Hendler T, Goshen E, Tadmor R, et al: Evidence for striatal modulation in the presence of fixed cortical injury in obsessive-compulsive disorder (OCD). Eur Neuropsychopharmacol 9(5):371-376, 1999

59. Umile EM, Plotkin RC, Sandel ME: Functional assessment of mild traumatic brain injury using SPECT and neuropsychological testing. Brain Inj 12(7):577-594, 1998