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Structural MRI findings in head injury at acute and sub acute stages

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TEL : +33 (0)4 76 63 71 44
FAX : +33 (0)4 76 63 71 70

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RESUME

Les traumatismes crâniens représentent une large cause de handicaps et de décès. Ces dernières années, les techniques d'imagerie ont beaucoup évoluées, permettant d'approfondir les connaissances sur leur physiopathologie et d'apporter des données diagnostiques et pronostiques.

L'objectif de ce travail consiste à faire une revue de la littérature sur l'intérêt de l'imagerie structurale par résonnance magnétique.

Après une description des principales lésions cérébrales primaires (lésion axonale diffuse, contusion corticale et saignements extra axiaux) et secondaires, nous avons discuté des apports diagnostiques et pronostiques des séquences conventionnelles IRM (en pondérationT2, T1, FLAIR, T2* Echo de gradient et de diffusion).

Puis nous nous sommes intéressés aux techniques IRM récentes permettant la détection accrue des lésions hémorragiques (séquence de susceptibilité magnétique, SWI), des atteintes structurales de la substance blanche (tenseur de diffusion, DTI) et des anomalies métaboliques (spectroscopie par résonance magnétique).

En résumé, l'IRM est un outil diagnostique et pronostique majeur dans les traumatismes crâniens. Son manque de disponibilité et les difficultés de monitoring de patients instables représentent les principaux facteurs limitant son utilisation au stade hyper aigu du traumatisme crânien.

Mais au stade aigu d'un traumatisme crânien léger à modéré, et au stade sub aigu d'un traumatisme crânien grave, l'IRM permet la détection de lésions subtiles et de facteurs pronostiques.

Structural MRI Findings in Head Injury at Acute and Sub acute Stages

A. Delouche, A. Attyé, S. Grand, F. Carpentier, and A. Krainik

From Clinique Universitaire de Neuroradiologie et d'IRM-CHU de Grenoble

ABSTRACT

SUMMARY: Head injury is a leading cause of disability and death. Significant developments in imaging techniques have contributed to the knowledge of its pathophysiology.

In this review, we focus on structural magnetic resonance imaging techniques. We discuss the interest of each sequence including Susceptibility Weighted Imaging, Diffusion Tensor Imaging and MR spectroscopy.

The advantages and limitations of these various techniques in initial assessment, identification of brain abnormalities and prediction of outcome is covered.

ABBREVIATIONS: TBI = Traumatic Brain Injury; GCS = Glasgow Coma Scale; DAI = Diffuse Axonal Injury; GRE=Gradient-recalled echo, FA= fractional Anisotropy.

Traumatic brain injury (TBI) represents a significant public health burden around the globe and is a major cause of disability and death in adults.

Using the Glasgow Coma Scale (GCS), patients identified as mild (GCS 13-15) (80%), to moderate (GCS 9-12) (10%), and severe injury (GCS<8) (10%)(1).

In France, the incidence of mild TBI is estimated at 150 to 300 for 100000 inhabitants(2).

It has been reported that most of the patients referred for a mild head injury recover within 3 to 12 months. However, some studies suggest that a significant proportion report distressing persistent symptoms(3) as a combination of physical, emotional, and cognitive symptoms, collectively known as post-concussion syndrome(3) that hinders their return to work or resumption of social activities.

Severe TBIs involve an extended stay in intensive care units and may cause subsequent functional disability that needs long-term follow-up and rehabilitation.

At admission, CT is routinely performed after TBI, to evaluate and manage these patients. Yet CT is limited to depict subtle intracranial abnormalities.

Furthermore, MRI has become a major tool of neurological diagnosis in acute brain injury and has been proposed to better estimate prognosis.

In this review, we remind the pathophysiology of TBI lesions and then we discuss the interest of MRI in clinical practice.

PATHOPHYSIOLOGY OF TBI LESIONS

Brain lesion can arise from disruption of brain tissue at the time of initial trauma (primary injury) as a result of both direct external contact forces and movement of the brain within the skull(4) or can be subsequent to initial trauma (secondary injury).

PRIMARY BRAIN INJURIES

PRIMARY PARENCHYMA INJURIES

Diffuse Axonal injury (DAI) : These lesions are the most common type of primary traumatic injury in patients with moderate and severe head trauma(5,6), around 48% of all primary traumatic lesions in some series(5,6).

DAIs may reflect the selective vulnerability of WM axons during rapid head accelerations and decelerations. Because differential inertia across brain structures, shear lesions may occur in case of high rotational accelerations or decelerations forces. They are responsible for disorders of the conscience and often of gravity proportional to the initial clinical condition(7). Furthermore, many authors use the term traumatic axonal injury to refer to more limited axonal injury which appears to result from traumatic inertial forces and tissue strains in the WM(8). Traumatic axonal injury referred to DAI when damage is extensive with microscopic injury that occurs even in the absence of tissue disruption(9).

After a TBI, axonal degeneration arising from DAI is usually recognized as progression from disruption in axonal transport leading to axonal swelling followed by secondary disconnection and finally Wallerian degeneration.

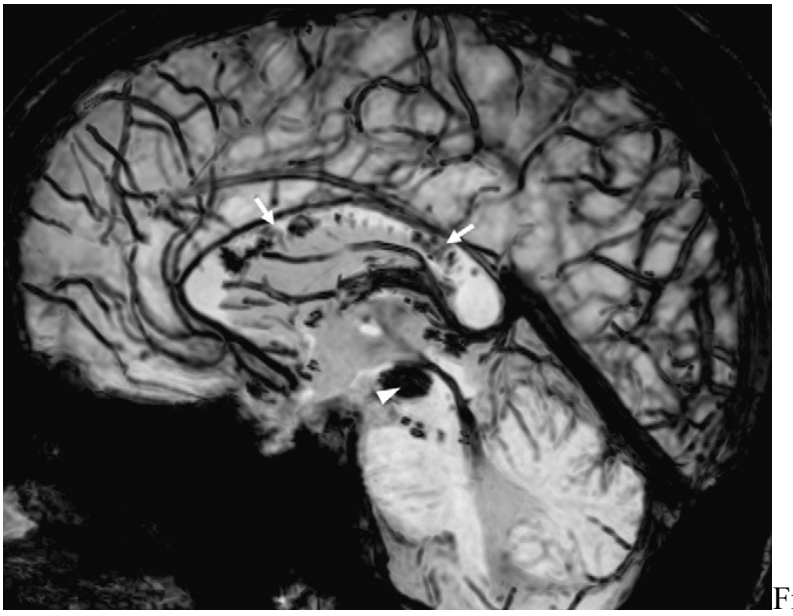
At autopsy, there are seen as multiple, small, focal traumatic lesions typically found in the peripheral lobar of the WM, in the junction WM-GM at the level of the arched fibbers, along the corpus callosum, and also in dorsolateral fibbers of upper brainstem(10) (Fig.1).

Although evidence exists in the literature that DAI is typically accompanied by small haemorrhages, or so called *tissue tear haemorrhages* (10,11), most MR imaging studies suggest that numerous DAI could be non hemorrhagic(12,13).

Brain microbleeds have been defined as lesions of less than 5mm without connection to the brain surface or ventricular system(14).

DAI are better identified between 24 to 48 H after the trauma when the oedema and disruption of the blood-neural barrier manifest themselves. The more severe the trauma is, the more extended, deeper and numerous brain DAI are(7).
The sequelae of DAI are one of the most frequent causes of poor clinical outcome in patients with head injury(10,15), particularly hemorrhagic DAI, which are reported to be a poor prognostic sign(16,17).
Lesions of the corpus callosum, basal ganglia, hippocampus and especially of the ponsmesencephalic junction and the protuberance are recognized as unfavourable(18).
Indeed, bilateral lesions of the upper part of the ponsmesencephal are more highly predictive of a fatal outcome(19), whereas superficial lesions of the brainstem would be of good prognosis.
Brain stem injuries have a poorer prognosis than corpus callosum lesions, and these, in turn, have a worse prognosis than sub cortical lesions(20).
According to their location, volumes of lesions were determined as prognostic factors, independently of the location of lesions(21,22).

Furthermore, with the current wars in Afghanistan and Iraq, some authors studied blast-related TBI, defined as primary injury from blast exposure with or without additional mechanisms of injury. Recently, two seminal studies have been published that described tau pathology and axonal injury in US military personnel with blast-related TBI(23,24).


Fig.1: A lot of DAI (arrows) in TBI after a motorcycle accident on SWI: multiple hypo intense, diffuse, small, focal lesions in corpus callosum and midbrain.

Cortical contusion is the second most common primary traumatic parenchyma injury(7). These lesions involve primarily the superficial parenchyma close to skull.
Oedematous haemorrhagic contusions are due to the impact of the brain on the skull and the intracranial septas. Indeed, intracranial displacements of the brain can lead a compression of parenchyma surface against: 1) the inner table of the skull such as short curvatures radius of the temporal fossa (temporo-polar contusion) and orbito-frontal angle (orbito-frontal contusion), 2) intracranial sharpened edges such as the upper ridge of the petrous bone (temporo-basal contusion), the tent of the cerebellum (postero-lateral aspect of mesencephalon), the posterior edge of cerebral falx (splenial callosal contusion). (Fig. 2)
Besides these lesions, contusion might be detected opposite to the cranial impact (contrecoup contusion) and in case of penetrating skull fracture. Acute compression of the brain parenchyma leads to micro vascular lesions with focal BBB dysfunction, focal oedema and extra vascular haemorrhages. According the severity of the lesions, pre-existing vascular lesion (angiopathy) and the coagulation status, oedematous haemorrhagic contusions may appear as a haematoma, an oedema or the association of both.
Compared with DAI, contusions tend to be larger and more superficial.
These lesions are better detected within 24-48 hours after the trauma, probably due to BBB dysfunction following initial trauma(25).

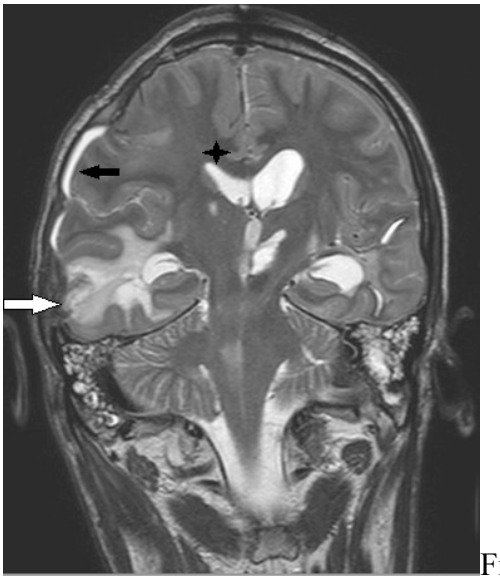


Fig. 2: Severe TBI after traffic accident, in coronal T2-WI: oedematous haemorrhagic temporo-basal contusion (white arrow) responsible for an effect of mass on the ventricular system (star) and extra dural collection next to flap craniectomy (black arrow).

PRIMARY EXTRAPARENCHYMAL HAEMORRHAGES

On a MR scan, the appearance of haemorrhage undergoes complex signal intensity changes, which are determined foremost by the age of the bleeding. Haemorrhage can be classified as hyper acute (first few hours), acute (1-3 days), early sub acute (3-7 days) and late sub acute (4-7 days to 1 month)(26).

Subdural hematoma affects 10 to 20% of the TBI and may appear after several hours or days. After a trauma, the veinous disruption leads to blood extravasation into the subdural space, between arachnoid and inner layer dura, mainly located at the level of supra tentorial convexity (Fig.3).

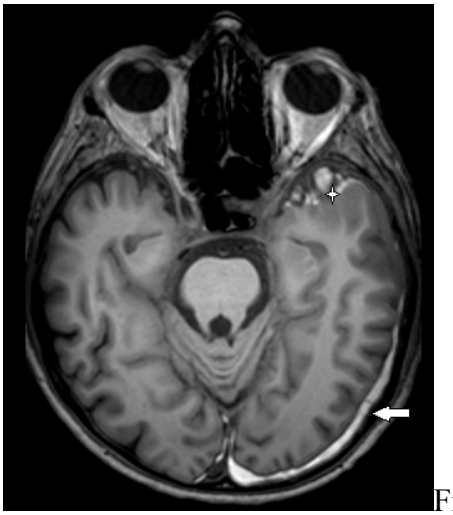


Fig. 3: Transverse MR T1-WI in an 18-year-old female patient in the late subacute stage of TBI secondary to motor vehicle crash: subdural haematoma (arrow) and haemorrhagic temporo-polar contusion (star) appear hyperintense on T1-weighted images.

Extra dural hematoma is a collection of blood, between the skull and dura, typically seen as a biconvex lens, which may result from either arterial (90%) or venous (10%) injury(5).
In less than 4% of traumatic brain injury, it is located next to the impact and is associated to a skull fracture in 90% of cases. MRI can be helpful to differentiate extradural from subdural haematoma in depicting directly the displaced dura mater as a thin line of low signal intensity separating the brain from the haematoma(5).

SAH may be seen in 33% with moderate TBI and 60% with severe TBI, diffuse or localized, most often following to a cortical parenchyma haemorrhage(7).
In hyper acute stages, the sensitivity and specificity of the FLAIR sequence are excellent,

even if flow artefacts can be problematic(27).

Intra ventricular haemorrhage is rare (less than 10 %) and secondary to a parenchyma peri ventricular haemorrhage, to a shear-strain under ependymary layer or under callosum veins. The diagnosis is easy in CT or MRI because the signal from the blood differs from that CSF signal (7).

SECONDARY BRAIN INJURIES

The most frequently secondary brain lesions include territorial arterial infarction, global anoxia and ischemia, pressure necrosis, brain herniation syndromes, delayed haemorrhages, and secondary brain stem injuries(5). They occur in the early post traumatic period.
They are mainly due to the natural evolution of the first impact but can be secondary to systemic failure, metabolic disorders, changes of cerebral blood flow and increasing in brain pressure.
Edema refers to an abnormal accumulation of water in the intracellular and/or extracellular spaces of the brain and can be divided in fours types: cytotoxic, vasogenic, interstitial, and osmotic. Intra cranial hypertension is a serious complication, due to edema which is reflected by the erasing of cortical spaces and the compression of the ventricles(7).
Territorial arterial infarctions most commonly result from sequelae of prolonged transtentorial and subfalcine herniation. For example, ischemic lesions can be found after compression of the posterior cerebral artery during a transtentorial herniation or after compression of the anterior cerebral artery during a subfalcine herniation against the rigid dural structures.

The secondary lesions of the brainstem are due to systemic anoxia or intracranial hypotension, as well as arterial thrombosis. They can occur from a mechanical compression after transtentorial herniation. Duret hemorrhages are small areas of bleeding in the ventral and paramedian parts of the upper brainstem. They are secondary to raised intracranial pressure with formation of a transtentorial pressure cone involving the cerebral peduncles and other midbrain structures caused by raised pressure above the tentorium. The mechanism is uncertain(28) but is probably caused by the displacement of the brainstem stretching and lacerating pontine perforating branches of the basilar artery; venous infarction may play a role.

CLINICAL APPLICATION OF MR IMAGING

Most conventional MR methods, including T1WI, T2WI and T2-FLAIR may show structural changes missed on CT scan.

As good as these methods are, there are more advanced MRI methods that offer more sensitive measures of blood products, micro structural WM integrity and metabolic activity. After a short recall on conventional MR sequences, we focus on these methods in both a diagnosis and prognosis view.

CONVENTIONAL MRI TECHNIQUES:

T2WI.

The T2 weighted imaging presents the best signal-to-noise ratio and may be useful to visualize changes in water content, particularly helpful in the posterior fossa.

T2-weighted imaging play an important role in the distinction of early (3-7 days) and late (4-7 days to 1month) subacute haemorrhages(26) and seem to be more sensitive in detecting contusions as a hyperintensity lesion compared with T1-weighted spin-echo sequences which show only an inhomogeneous isointensity and mass effect.

T2WI can also detect DAI lesions that are beyond the sensitivity of CT scans. Gentry and Al.(6) define non hemorrhagic DAI as T2-hyperintense, diffuse, small (5-15mm), focal abnormalities limited to WM tracts. Haemorrhagic DAIs appear like hypointense lesions.

T1-WI.

Conventional T1-weighted spin echo is useful in the distinction of acute and subacute haemorrhages(26).

In the acute stage (1-3 days) on T1-weighted images, hematomas appear iso to hypointense to brain. In the late subacute stage, haemorrhage appears hyperintense on T1-weighted images. The lesions of haemorrhagic DAIs may be visible in hypersignal, whereas non-haemorrhagic DAIs are usually not visible.

T1WI is more sensitive than the CT scan to detect thin subdural hematomas in subacute stages and especially allows the detection of pseudo rapid resolution of haematomas in showing their dispersion and redistribution(7).

T2 FLAIR.

This sequence is recognized as a fundamental sequence at all stages of the trauma(29,30) and is recommended to be performed in sagittal slices or 3D in order to detect the lesions of the trigone including corpus callosum(29).

It is particularly sensitive for detecting oedema within brain parenchyma, which has a strong correlation with outcome, probably due to the likelihood that most patients with significant oedema are more likely to have increased intracranial pressure(31).

The oedematous DAI appear as ovoid images of high signal, located at the junction between WM and GM, aligned in the oval center, in the corpus callosum and the mesencephalic region (7). The lesions of DAI can be transient, even in the corpus callosum, with gradual regression signal anomalies on the FLAIR sequence(32). FLAIR lesion volume in the early stages correlates with clinical outcome(33–35).

Cortical contusions are often difficult to identify on initial CT, the oedema within contused brain may be so minimal that the lesions are only faintly seen.

MR FLAIR imaging is considerably more sensitive than CT for initial detection and the extent of contusions(13,36).

Some studies have demonstrated that FLAIR MRI is equal to or even more sensitive than CT for detection of acute or sub acute SAH(27,37).

FLAIR is more sensitive for superficial convexity SAH than for the detection of intra ventricular blood products(38). Furthermore, in the posterior fossa, CSF pulsations, vascular pulsation or supplemental oxygen may cause FLAIR artifacts in the form of hyperintense signal of the subarachnoid spaces(39).

T2-weighted gradient-recalled echo (GRE).*

Magnetic susceptibility differences resulting from the presence of paramagnetic blood breakdown products create local magnetic field inhomogeneities, which manifest as marked hypointensity on T2*-images. The T2* signal intensity loss is wider with higher magnetic field strength (40,41).

However, T2*GRE sequences are artifacted near brain interfaces, e.g. air and bones with difficulty to study the cortical lesions and the peripheral haemorrhagic collections(7).

With the magnetic susceptibility effect, can be dated a bleeding precisely.

Indeed, the signal of hematomas changes according to haemoglobin products: it appears as a hyperintensity in the hyperacute stage (oxyhaemoblobine), a hypointensity in the acute and

early subacute stage (deoxyhaemoglobin and intracellular methaemoglobine) and a hyperintensity in the late subacute stage (extracellular methaemoglobin).
T2*WI allows better detection of intra cranial haemorrhage compared to other conventional MR sequences (14,40,42). In head injury of varying severity, the number of lesions on T2*-weighted GRE sequences would be positively correlated with poor outcome, whereas it would not on T2-WI (40).
Indeed, T2*GRE imaging has been used to reveal very small haemorrhages on the order of several millimeters or smaller (referred as "microbleeds")(43).
These haemosiderin deposits are possibly due to DAI(22,40) and occur in 10%-30% of patients with DAI(22,42).
A T2*gradient echo sequence is more reliable for detecting the size, number, volume, and distribution of micro haemorrhagic lesions than other more classic MRI sequences(44).
T2*-weighted GRE images is more sensitive than DWI for detecting haemorrhagic DAI lesions(45).
Besides, T2*-weighted GRE sequences are less sensitive than T2-weighted fast SE, FLAIR, and diffusion-weighted sequences for depicting non haemorrhagic lesions(46).

DWI.
In few studies including mild head injury, diffusion abnormalities were seen within days of injury(47,48).
In severe head injury, DWI can be used to identify DAI as hyperintense lesions that are not visible on T2-weighted spin echo, T2*GRE, or FLAIR sequences(45,46).
DAI lesions can be transient with full ADC normalization in 6 months(49).
The volume of lesions depicted with DWI show a stronger correlation with clinical outcome in patients with head injury than FLAIR, T2 WI, or T2*WI(46).
Most of these DAI lesions show decreased diffusion probably due to cytotoxic oedema with swelling of astrocytes(50) within days to weeks of injury lesions(45,51,52).
Although cytotoxic oedema predominates, vasogenic edema is also involved in the process of DAI(53,54) in the acute phase, which may lead to increased extracellular water associated with increased water diffusion. At this point, a DAI lesion is likely to be mildly hyperintense due to the T2 component on DWI.
Hergan et Al.(51) have classified DAI into three groups on their signal characteristics on DWI and ADC maps: type 1, DWI-and ADC-hyperintense most likely representing lesions with

vasogenic edema; type 2, DWI-hyperintense, ADC-hypointense indicating cytotoxic edema; type 3, central hemorrhagic lesions. (Fig. 4)
As EPI is also intrinsically sensitive to magnetic susceptibility effect, b0 acquisition also reveals low-intense hemorrhagic DAI lesions. However, some studies showed that GRE imaging was more sensitive than b0 acquisition in the identification of haemorrhage in DAI lesions(45,55).
Therefore, DWI has T2-weighted contrast as well as contrast due to differences in ADC (T2 shortening), susceptibility effects could be related to the decreased signal intensity on DWI(56,57).
Some of the hemorrhagic DAI lesions do not show high-signal intensity on DWI and cannot therefore be a substitute to the sequence in T2*GRE.

ADC measurements are useful in detecting DAI in pediatric traumatism brain injury. Before DWI, it was difficult to detect axonal ischemia or damage in pediatric brain due to the relatively high water content of the developing WM tracts. DWI allows improved differentiation between the uninjured immature brain and injured area because the immature WM tracts have less water restriction than mature brain or hyperintense ADC values compared to the adult brain. Opposite, injured brain regions usually have increased water restriction with hypointense ADC values relative to the uninjured immature brain(58).
In recent studies, ADC values in the peripheral WM tracts were significantly reduced in children with severe TBI that had poor outcomes(59) and acute ADC values were inversely correlated with long term neurocognitive outcomes(60).

The post traumatic cortical contusions have been studied in diffusion imaging: quantification of the ADC have shown an area of cell necrosis and vasogenic edema surrounded in the first 2 days by a zone of cytotoxic edema likely limiting the extension of lesions(61).

With DWI, the ischemic lesions secondary to vascular compression by a brain herniation can be detected at an early stage. They show areas in hypersignal systematized to an arterial territory with a decrease of the ADC. Indeed, DWI is also useful to separate cytotoxic oedema, indicating potentially irreversible cellular injury due to trauma and/or ischemia, from reversible vasogenic oedema(45).

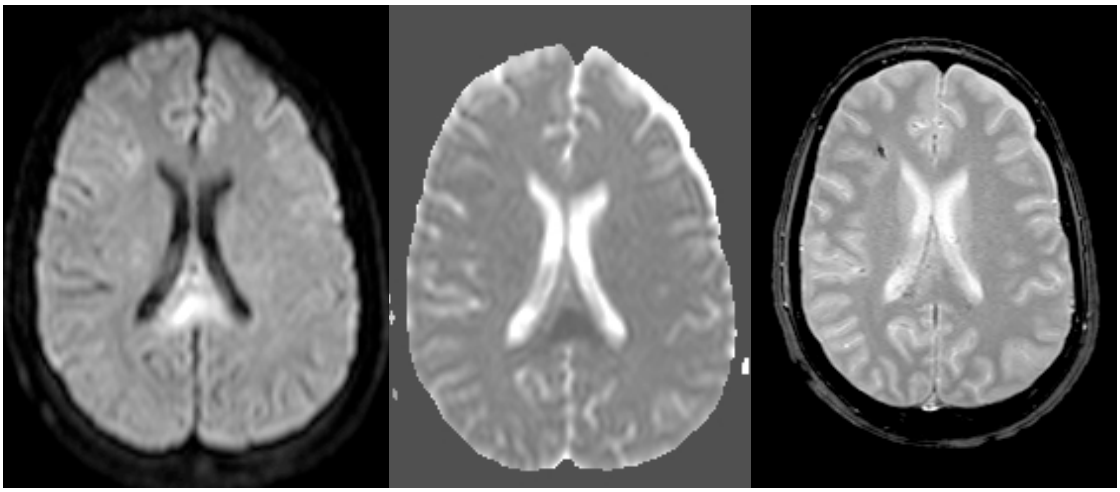


Fig. 4: Transverse MR images in a 17-year-old male patient after TBI secondary to a skiing accident. Total lesion extent, with abnormality involving splenial callosum, is better depicted on diffusion-weighted images (first column: DWI-hyperintense and second column: ADC-hypointense) than on T2-weighted images (third column).

ADVANCED MRI METHODS :

Susceptibility Weighted Imaging:

SWI is fully velocity-compensated high resolution 3D gradient-echo sequence that uses magnitude and filtered-phase information, both separately and in combination with each other, to create new sources of contrast(44).

SWI is very sensitive to differences of the magnetic susceptibility properties between blood products including deoxyhemoglobin, methemoglobin and hemosiderin.

However, the most common artefact is at the air-tissue interface and manifests as concentric hypointensities, which is problematic for interpretation of periphery of the brain. A local field of inhomogeneity due to metallic implants is another possibility of artifact. The differentiation of physiologic versus pathologic mineral deposition can be difficult. Phase inhomogeneity continues to be reduced by the applications of advanced filtering techniques(62).

An artefact of “blooming” (extension and hyposignal of the vein) because of the venous deoxyhaemoglobine stase can be found in the veins of drainage located in the circumference of the haematomas.

Although larger haemorrhages are visible on CT and standard diagnostic MRI sequences, Tong et Al.(17) have shown that numerous small hemorrhagic shearing lesions are only visible by using SWI.

SWI sequences are able to depict better microbleeds than T2*-weighted sequences(14,63,64). Indeed, in children with diffuse posttraumatic DAI, SWI depicts 4 to 6 times more micro-haemorrhages as does T2*-GRE (14). Significant correlations have been found between number and volume of SWI lesions, global clinical outcomes(65) and cognitive variables in children(17,66–68).
SWI has 3 to 6 times the sensitivity of conventional T2* GRE sequences for detecting the size, number, volume and distribution of hemorrhagic lesions in DAI(14,17,66,69).
In adults, cerebral microbleeds are related to GCS and neurologic deficits in the patients with DAI(14), and JH Park et al.(64) suggested that their presence and number were closely related with initial GCS and clinical outcome in TBI.

SWI is very sensitive to small amounts of SAH which appear in the acute stage like a triangular discontinuous hyposignal because aliasing on phase image, which is easy to differentiate from veinous signal. (Fig. 5) It is a performing tool to identify interhemispheric and supracerebellar haemorrhage and SWI has a high detection capacity for intraventricular hemorrhage(70).
However, SWI is not a reliable tool in detecting basilar cistern SAH(70) and does not identify SAH if imaging is performed too early due to short time for haemorrhage decomposition(38).



Fig. 5: SAH at early sub acute stage of a TBI, in axial SWI (MinIP: minimum intensity projection): linear hypo intensity easy to differentiate with vein because of its discontinuity and its triangular form (arrow).

DTI.

The clinical pathology underlying TBI related impairment is traumatic axonal injury(71), that is a microscopic injury occurring even the lack of frank tissue disruption.

Increasing evidence suggests that novel advanced neuroimaging techniques may be useful in the assessment of WM tracts in vivo. In particular, DTI is now a well-documented technique for assessing WM integrity via the measurement of the anisotropic diffusion of water molecules(72).

The degree of diffusion is characterized by 3 eigenvectors representing the diffusion in each orthogonal direction. Diffusion in WM is particularly limited and anisotropic because of physical obstacles to water diffusion imposed by the myelin and axon membranes(73).

DTI can be used to study brain structure either on a regional or a whole-brain level. In these approaches, average diffusion value such as fractional anisotropy (FA) or mean diffusivity (MD) are extracted from voxels within the ROIs or tracts for subsequent analysis.

Unfortunately, the degree of anisotropy is influenced by many factors such as axon diameter, inter-axon spacing, membrane permeability, myelination and the coherence of axon orientations(74).

Abnormally low FA is widely held to represent alterations of WM microstructure consistent with traumatic axonal injury(75).

Despite significant variability in patient demographics, differences in data acquisition parameters and a multiplicity of data analysis techniques, the consensus of studies is that low FA is associated with TBI(9).

In animal studies, DTI would be able to detect populations of degenerating axons in the absence of amyloid precursor protein pathology(76), an integral membrane protein which has been considered a “gold standard” for identifying traumatic axonal injury(77).

DTI can detect microstructural WM injury early after TBI, and there is a correlation with reduced FA, the number of affected tracts, and cognitive deficits even in mild TBI(8). The decrease in the values of FA would be correlated to the neurological unfavourable prognosis, among the brain injury seen early after the cerebral aggression(78,79).

Whole brain WM and regional DTI measures are sensitive markers of TBI, and correlate with neurological status. The addition of DTI measures adjusted for age, gender, and admission GCS score significantly improved prognostic models(80).

DTI reveals changes in the WM that are correlated with both acute GCS and Rankin scores at discharge(78).

The corpus callosum, frontal lobe, internal capsule, and cingulum are among the most commonly identified regions of abnormality in DTI studies of TBI, perhaps because these structures are particularly vulnerable to injury due to their anatomic relationship to the skull and other structures such as falx cerebri.
The corpus callosum is the most commonly identified region of abnormal FA and MD.
The corona radiata and the brain stem are locations where abnormal FA has commonly been identified by using ROI analysis. The superior longitudinal fasciculus is the most commonly identified location with abnormal FA by using whole-brain analysis(9).

In addition, little is known about the effects of blast exposure on the human brain in the absence of head impact. DTI findings in U.S. military personnel support the hypothesis that blast-related mild TBI can involve axonal injury(81), particularly in cerebellar WM(82). Unique aspects of TBI sustained by military personnel include blast injuries and the high rate of post-traumatic stress disorder(83). The relationships among blast-related TBI, axonal injury, and outcomes that include post-traumatic stress disorder are topics of active research. However, variability in outcome measures limits our ability to extract useful information from DTI data in relation with clinical outcome(9).

In vivo 1H MR Spectroscopy.
Cellular changes to neurons and glia following TBI are complex and dynamic. Proton (1H) spectroscopy has the advantage of measuring brain metabolism in vivo, and is able to detect various biochemical processes of brain injury such as loss (or dysfunction) of neuronals cells. The field strength, the type of sequence and the parameters used such as TR (repetition time) and the echo delay time (TE) determine the appearance of the spectrum and the metabolites that can be detected.
TBI is known to induce changes in N-Acetyl-Aspartate (NAA) (a neuronal marker), choline (Cho) (a marker for membrane disruption, synthesis or repair), lactate (a result of anaerobic glycolysis), and glutamate (an excitatory aminotransmitter, known for potential neurotoxicity)(84).
Prior studies using single-voxel techniques (SVS) have shown a significant correlation between unfavourable clinical outcome and reduction in the neuronal and axonal marker NAA(85,86) and increases in Cho(86,87).
Reduction of NAA in visibly-injured brain is often caused by the primary injury, whereas reduction of NAA in normal-appearing brain may reflect DAI and Wallerian degeneration(87).

Elevated Cho may be detect in WM as a breakdown product after damage to myelin(88) and the presence of lactate in brain suggests hypoxic/ischemic injury.
Several studies suggest that the report NAA/Cr would be the most reliable prognostic factor for predicting a bad neurological evolution(21,85,88,89).
Another technique, magnetic resonance spectroscopic imaging (MRSI) or chemical shift imaging (CSI) has an advantage over single-voxel MRS because spectra from multiple regions can be acquired simultaneously using two-dimensional or three-dimensional techniques. MRSI provides more information than SVS but also requires more acquisition time, which must always be considered when imaging children.
Many studies of metabolic changes after TBI have proven MRS to be a sensitive tool to predict neurologic(85,90,91), cognitive(92,93), and functional outcome(94). However, the post-processing and analysis of MRS is complicated and the expertise needed to etablish an MRS program may not be available at all institutions.

Perfusion MRI

Based on the passage of a contrast agent through the brain, perfusion-WI is sensitive to microscopic tissue-level changes in CBV, CBF or MTT. Some studies(95,96) found low CBV in regions of focal pathology in patients at the sub acute phase of TBI with contusions and oedema visible on conventional MRI and transient hypo perfusion was also observed in non injured contro lateral hemisphere although there was no evidence of oedema formation(97).
An important limitation of this technique is that quantification remains difficult, together with the limited application in the emergency setting. Moreover, standard perfusion is based on T2* weighted imaging and may then be artifacted by bleeding through susceptibility effect.

IMPLICATIONS, LIMITATIONS, AND POSSIBILITIES

If the performance of the MRI to detect hemorrhagic brain injury in acute phase are well-etablished (98), MRI remains less efficient for highlighting skull lesions and foreign body when compared to CT scan.
Moreover, MRI is difficult to achieve in emergency because of its lack of availability, difficulties in monitoring and of the need of resuscitation non-magnetic equipment.
Finally, the susceptibility to motion artifacts related to the relatively long exposure time and the difficulty to obtain stationary position of the patient discourage the use of MRI in the acute stage of head injury. For these reasons, MRI should not achieve today at the initial imaging evaluation of a polytrauma patient.

Therefore, in the case of mild or moderate TBI, the use of MRI should be more important and MRI initially recommended, because of its performance and the frequent medical-legal implications. In fact, it is already recommended in patients having presented a transitional amnesia of 30 minutes even with a Glasgow Coma Scale score to 15(99).
Finally, MRI should be indicated at least in second intention in case of severe trauma. It will show the volume and location of the lesions and it provides prognostic elements(7).

Other advanced MRI techniques have not been discussed in this review.
Functional imaging can provide useful information for determining the extent of ischemic and metabolic injury in patient with head injury. The main imaging techniques dedicated to brain hemodynamics and metabolism in head injury are functional MRI, SPECT and PET.
Whereas SPECT uses radioactive tracer materials (Tc ^{99}m) that emit gamma radiation directly, PET tracers (Fluoro-Desoxyglucose) emit two gamma photons at 180 degrees to each other. SPECT and PET have limited availability and are mainly used in a research setting.
Functional MRI combines a good spatial resolution with information on brain function and metabolic state of the brain. fMRI is currently rather used in the chronic phase after injury. Recently, resting functional MRI using the BOLD techniques permitted to show disruption on thalamic resting state networks in patients with mild TBI(100).
In addition, Han et al. demonstrated a disrupted modular organization of the resting-state cortical functional network in U.S. military personnel with concussive blast-related TBI(101).
Finally, there is growing evidence suggesting that the release of selected biomarkers of brain injury, especially protein S100B, adequately mirrors the severity of concussion(102) and may also be predictive of main outcomes after mild TBI(103,104). This biological approach will be of great interest in future research area and shall be always well-informed in advantages and limits of MR management for traumatic patients.

These findings in patients with TBI suggest that advanced neuroimaging techniques could play a meaningful role in establishing the degree of injury more accurately, providing valuable prognostic information, and guiding the management and rehabilitation of patients with head injury.

THESE SOUTENUE PAR : Aurélie DELOUCHE

TITRE: STRUCTURAL MRI FINDINGS IN HEAD INJURY AT ACUTE AND SUB ACUTE STAGES

CONCLUSION

L'objectif de ce travail consiste à faire une revue de la littérature sur l'intérêt de l'IRM dans les traumatismes crâniens à leur stades aigus et sub aigus.

Ils représentent une cause majeure de handicap et de décès et leur incidence en France est estimée à 150 à 300 pour 100000 habitants.

Les lésions cérébrales primaires, survenant au stade initial du traumatisme crânien, sont largement représentées par les lésions axonales diffuses (48%) et les contusions corticales.

Les premières sont la conséquence de la fragilité de la substance blanche aux mouvements d'accélération/décélération de la tête et sont de gravité proportionnelle à l'état clinique initial.

Les secondes sont la conséquence d'une contrainte mécanique directe sur le parenchyme cérébral.

Les lésions cérébrales secondaires apparaissent de manière différée par rapport au traumatisme crânien et incluent les lésions ischémiques, l'œdème et les engagements cérébraux.

La détection de lésions non vues en imagerie tomodensitométrique fait partie des nombreux apports diagnostics des séquences conventionnelles IRM.

La séquence pondérée en T2 est sensible à la présence d'œdème et aux lésions axonales diffuses, tout comme la séquence FLAIR qui détecte également les hémorragies sous arachnoïdiennes. La séquence pondérée T1 peut déceler de petit hématomes sous duraux passés inaperçus au scanner.

La séquence T2* est plus sensible que les autres séquences IRM conventionnelles dans la détection des saignements intra parenchymateux et notamment des lésions axonales diffuses hémorragiques.

La séquence de diffusion a une forte sensibilité pour les lésions axonales diffuses œdémateuses.

Récemment, de nouvelles méthodes d'imagerie IRM ont permis la détection accrue des lésions hémorragiques, des atteintes structurales de la substance blanche et des anomalies métaboliques.

La séquence de susceptibilité magnétique (SWI) est 4 à 6 fois plus sensible que le T2* dans la détection de lésions axonales diffuses hémorragiques.
Le tenseur de diffusion (DTI) permet de repérer l'altération de la substance blanche, en montrant une chute de la fraction d'anisotropie.
La spectroscopie par résonance magnétique montre des variations biochimiques secondaires à une dysfonction des cellules nerveuses suite à un traumatisme crânien.

L'IRM apporte également des données pronostiques. Les lésions situées dans le tronc cérébral, l'importance de leur volume et la présence de lésions axonales diffuses sont des facteurs de mauvais pronostic.
Les lésions œdémateuses détectées sur les séquences FLAIR et de diffusion, les saignements visibles sur les séquences T2* et SWI et l'altération structurale de la substance blanche retrouvée sur la séquence DTI sont corrélées avec la mauvaise évolution clinique d'un traumatisé crânien.

En résumé, l'IRM est un outil diagnostique et pronostique majeur dans les traumatismes crâniens.
Son manque de disponibilité et les difficultés de monitoring de patients instables représentent les principaux facteurs limitant son utilisation au stade hyper aigu du traumatisme crânien.
Mais au stade aigu d'un traumatisme crânien léger à modéré, et au stade sub aigu d'un traumatisme crânien grave, l'IRM permet la détection de lésions subtiles et de facteurs pronostiques.

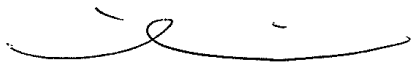
VU ET PERMIS D'IMPRIMER
Grenoble, le 30 Mars 2014

LE DOYEN



J. P. ROMANET

LE PRESIDENT DE LA THESE



PROFESSEUR Alexandre Krainik

CENTRE HOSPITALIER UNIVERSITAIRE
DE GRENOBLE
POLE IMAGERIE
Clinique Universitaire de Neuro-Radiologie et IRM
Professeur Alexandre KRAINIK
RPPS 10001409167

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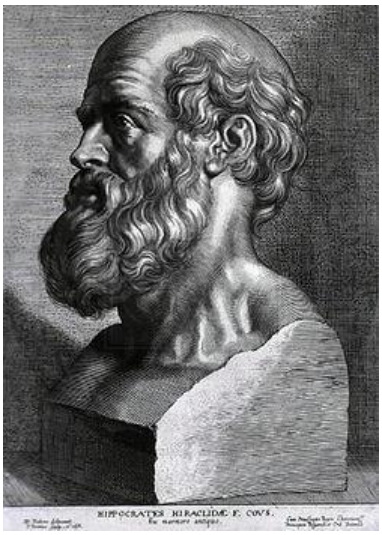
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SERMENT D'HIPPOCRATE

En présence des Maîtres de cette Faculté, de mes chers condisciples et devant l'effigie d'HIPPOCRATE,

Je promets et je jure d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la Médecine.

Je donnerais mes soins gratuitement à l'indigent et n'exigerai jamais un salaire au dessus de mon travail. Je ne participerai à aucun partage clandestin d'honoraires.

Admis dans l'intimité des maisons, mes yeux n'y verront pas ce qui s'y passe ; ma langue taira les secrets qui me seront confiés et mon état ne servira pas à corrompre les mœurs, ni à favoriser le crime.

Je ne permettrai pas que des considérations de religion, de nation, de race, de parti ou de classe sociale viennent s'interposer entre mon devoir et mon patient.

Je garderai le respect absolu de la vie humaine.

Même sous la menace, je n'admettrai pas de faire usage de mes connaissances médicales contre les lois de l'humanité.

Respectueux et reconnaissant envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime si je suis fidèle à mes promesses.

Que je sois couvert d'opprobre et méprisé de mes confrères si j'y manque.