The Role of Diffusion Weighted and Diffusion Tensor Imaging in Epilepsy

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2.1 Introduction

Epilepsy is a chronic neurologic disorder characterized by unpredictable, recurrent, unprovoked seizures. It is the fourth most common neurologic disorder and affects people of all ages. A substantial number of epilepsies are well controlled with the administration of suitable antiepileptic medication. However, approximately 20–30% of epilepsy cases can be medically intractable, and hence there is an increasing interest in surgical approaches for seizure abolition [1]. It follows that accurate lateralization and localization of the epileptogenic focus are significant prerequisites for determining surgical candidacy once the patient has been deemed medically intractable.

Neuroimaging and especially magnetic resonance imaging (MRI) play a very important role in the identification and localization of the seizure focus. MRI with high-resolution structural imaging has become the modality of choice, and it is essential in detecting hippocampus and temporal pole atrophy as well as structural abnormalities such as cortical dysplasias [2]. Nevertheless, the detection of structural lesions is not always feasible, and the true extent of the abnormality may not be reflected using exclusively conventional MRI [3]. Advanced MR based imaging techniques such as diffusion weighted imaging (DWI), diffusion tensor imaging (DTI), and diffusion MR tractography may also be used as multimodal approaches for the purpose of detection of abnormalities and investigation of the microstructural alterations.

Since these advanced neuroimaging techniques are increasingly established in the clinical routine, the objective of this chapter is to analyze and discuss the meaningful role of diffusion MRI in epilepsy, both in the diagnosis, treatment, and research of the disorder.

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2.2 Diffusion Imaging

2.2.1 Diffusion Weighted Imaging (DWI): Basic Principles

Water molecules placed inside a medium are in continuous motion because of their thermal energy. Their collisions with other water molecules combined with their motion describe a random walk which is called Brownian motion originating from the Scottish botanist Robert Brown. The phenomenon of diffusion can be observed when a drop of ink is added to a glass of water. Human tissue and especially the human brain has a more complex structure; it contains neuronal axons, macromolecules, and cell membranes, which hinder and restrict water diffusion. As a result the water mobility is anisotropic. When a wealth of neuronal axons are located in a brain area, then the water molecules are forced to move along their axes rather than perpendicular to them.

Additionally, Brownian motion is the natural occurrence on which DWI is based. The insertion of a patient into the MR scanner, namely, into its homogeneous magnetic field, induces alignment of nuclear spins in the same direction of the static magnetic field. The application of a radiofrequency pulse induces protons to spin, while the duration, the strength, and the direction of the pulse define the rate of the spin. If an equal and opposite gradient is applied, protons will be refocused, and thus the signal of the stationary protons will be null in contrast to mobile protons, which will display a signal loss. The factor that reflects the strength and duration of the gradients used to generate diffusion-weighted images is called the b-value [4]. In order to determine the direction of diffusion, the signal from mobile protons should be measured.

Nevertheless, the spin alignment will be ruined because of the different effect the magnetic field will have on every spin. This misalignment of the spins leads to a decline of the total signal, which arises as the sum of signals from every individual spin [5]. The most common pulsed-gradient spin-echo pulse sequence for diffusion imaging is illustrated in Fig. 2.1.

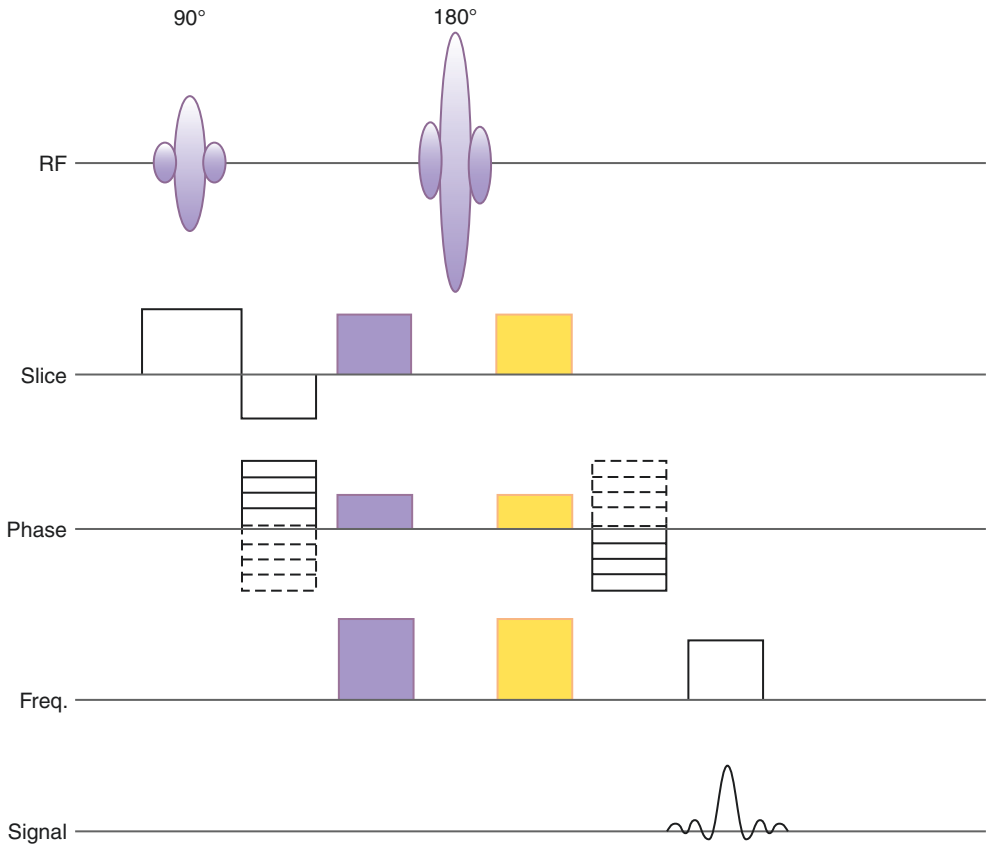

Fig. 2.1 A pulsed-gradient spin-echo pulse sequence for diffusion imaging

The parameter that adequately characterizes DWI is called apparent diffusion coefficient (ADC). The term "apparent" shows that there is often an average measure of a number of complex processes within the tissues and does not always represent the magnitude of the inherent self-diffusivity of water [6, 7].

ADC can measure the magnitude of diffusion within every voxel, and this constitutes the aim of DWI. After processing a number of DWIs with different b-values, a parametric map is created. More specifically, in this parametric map of ADC values the intensity of every pixel represents the strength of the diffusion in it. The interpretation of the ADC values shows that a bright signal corresponds to a high ADC value and reflects free diffusion, while a dark signal corresponds to a low ADC value and denotes restricted water movement [8]. Figure 2.2 depicts a typical ADC parametric color map.

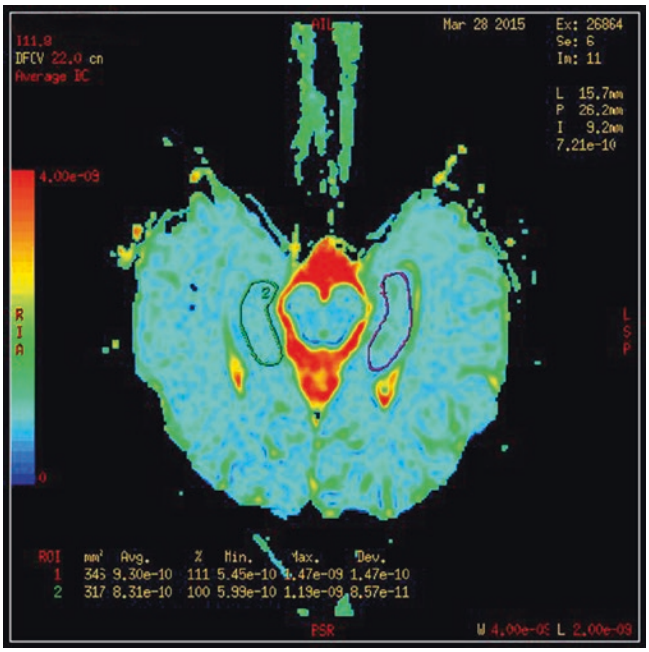

Fig. 2.2 ADC parametric color map

2.2.2 Diffusion Tensor Imaging (DTI): Basic Principles

DWI is undoubtedly a very useful clinical tool, but unfortunately it suffers from a serious limitation. It is only a qualitative type of examination and depends on the direction of the applied diffusion encoding gradient. This means that in certain regions of the brain, ADC will be different, depending on the applied gradient. In other words, ADC is directionally dependent [9, 10], and it follows that an infinite number of ADC measures should be obtained to characterize anisotropic tissue. Inside the brain, the presence of neuronal axons and macromolecules, cell membranes, and several intracellular subunits hinders and limits the diffusion of water. In particular, the preferable direction of water diffusion is along the white matter axons compared to the direction perpendicular to them, and in the first case the diffusion is called anisotropic (Fig. 2.3) [4]. In that sense, different tissue structures affect the diffusion profile of water in different ways.

DTI evolves from DWI and was developed to remedy the aforementioned limitations of DWI, exploiting the preferential water diffusion inside the brain tissue [11, 12]. Diffusion tensor (DT) is a mathematical model that can summarize the measurements of both the magnitude and direction of proton motion, which correspond to individual voxels [8]. Assuming that the probability of molecular displacements follows a multivariate gaussian distribution over the observation diffusion time, DT is defined as a 3 × 3 matrix of numbers corresponding to several diffusion rates for different diffusion directions. The mathematical formulation below represents the DT matrix of an anisotropic and a perfect isotropic diffusion, and it contains nine elements.

$$D = \begin{bmatrix} Dxx\ Dxy\ Dxz \\ Dyx\ Dyy\ Dyx \\ Dzx\ Dzy\ Dzz \end{bmatrix} D_{isotropic} = \begin{bmatrix} D\,0\,0 \\ 0\,D\,0 \\ 0\,0\,D \end{bmatrix}$$

Assuming that the directional motion of water within a voxel can be depicted by an ellipsoid (*see* Fig. 2.3), it can be

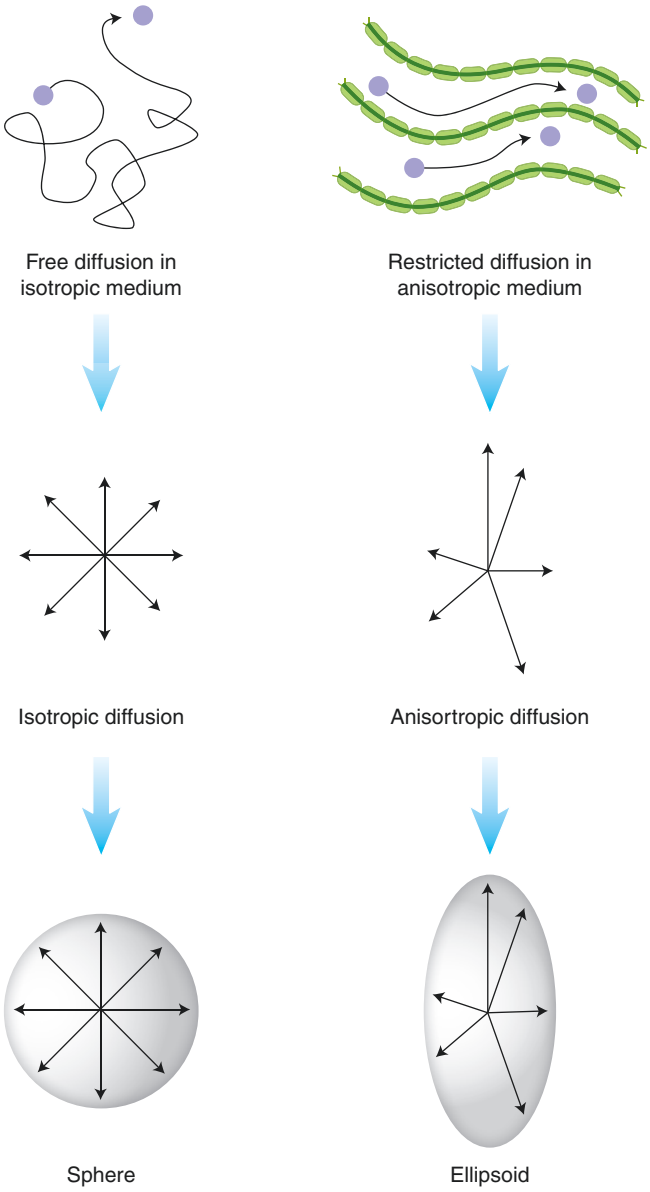

Fig. 2.3 The diffusion of water molecules in an isotropic and in an anisotropic medium

described by the tensor in that particular voxel. This tensor practically is a 3 × 3 matrix derived from measurements of water diffusivity in at least six different directions. The tensor matrix demonstrates diagonal symmetry (Dij = Dji), and that means the complete determination of the matrix by six parameters. If the diffusion tensor is totally aligned with the anisotropic medium, the off-diagonal elements are all zero and the tensor is diagonalized. The outcome of this diagonalization is three eigenvectors—v1, v2, and v3—that describe the orientation of the three axes of the ellipsoid. Additionally, three eigenvalues (λ1, λ2, and λ3) arise and represent the magnitude of the axes (apparent diffusivities) in the corresponding directions (Fig. 2.4). The direction of the major axis is considered to coincide with the direction of maximum diffusivity (λ1) and with the orientation of the tract [4, 13]. Therefore, a conversion occurs from the x, y, z coordinate system defined by the geometric characteristics of the scanner to a new coordinate system where axes are prescribed by the directional diffusivity information.

Local diffusion defines the shape of the ellipsoid, namely, prolate, oblate, or spherical. There are many diffusion parameters offering specific information, but the most common and widely used are the fractional anisotropy (FA) and mean diffusivity (MD). FA is calculated from the standard deviation of the eigenvalues λ1, λ2, and λ3, while MD is the mean of the eigenvalues describing the directionally measured average of diffusivity of water molecules.

The degree of anisotropy, which refers to a particular voxel, is represented by the signal brightness as it is displayed on a FA map. The microarchitecture of the tissue affects the value of FA; it fluctuates between 0 (isotropic diffusion) and 1 (highly anisotropic diffusion). Typical examples of isotropic and anisotropic diffusion are the cerebrospinal fluid (CSF) (value closer to 0) and the corpus callosum (value closer to 1) [4]. In Fig. 2.5, a T2 weighted image, an ADC, an FA map, and a color-coded orientation map are illustrated.

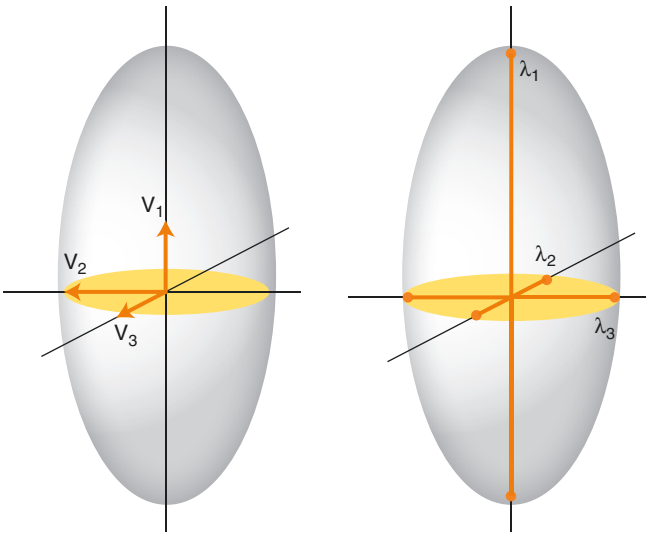

Fig. 2.4 The orientation of the three axes of the ellipsoid is described by three eigenvectors: v1, v2, and v3. The magnitude of the axes of the ellipsoid is represented by three eigenvalues: λ1, λ2, and λ3

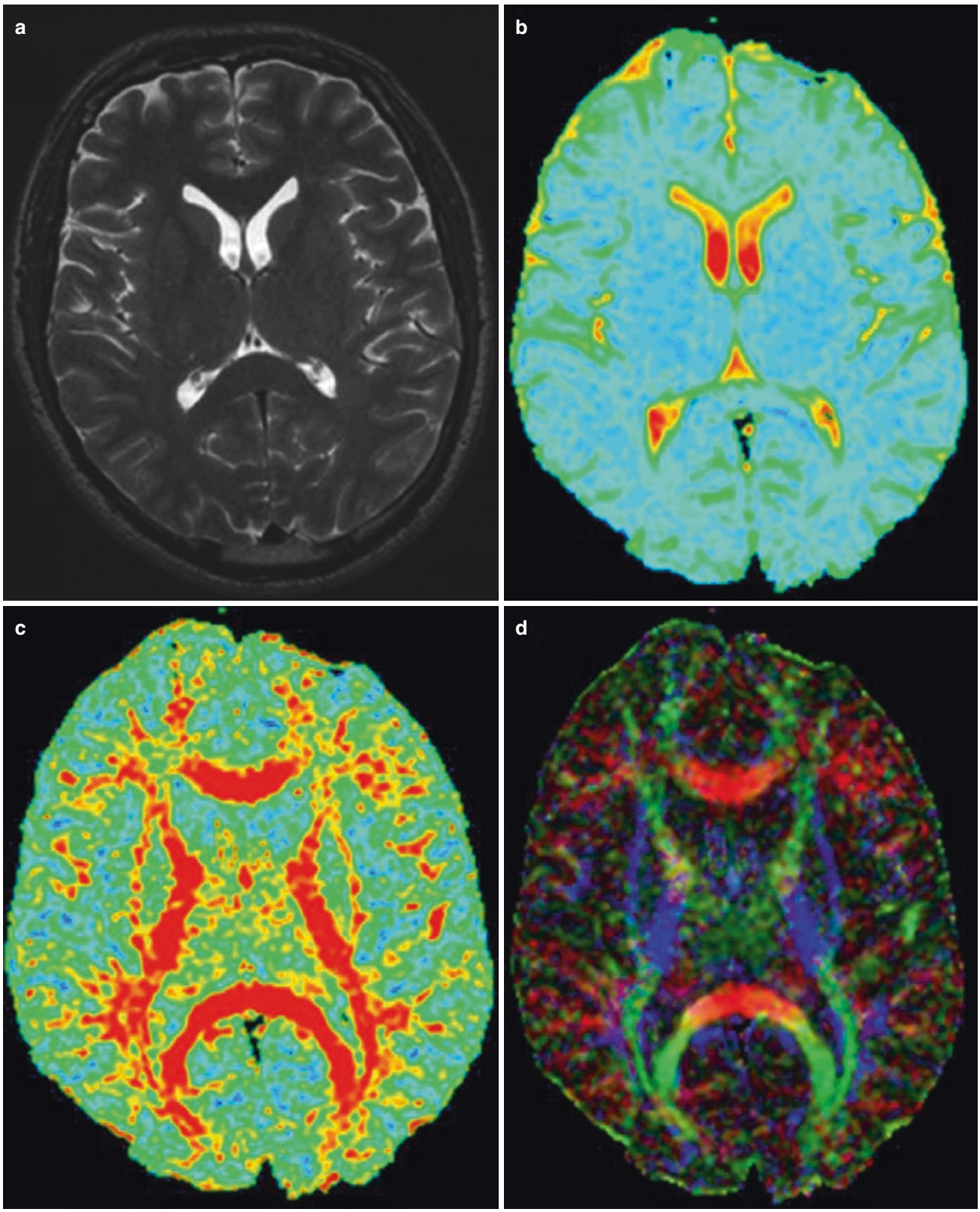

Fig. 2.5 (**a**) T2-weighted image; (**b**) Average DC; (**c**) FA map; (**d**) Color-coded orientation map. Images were acquired using a 3.0 T scanner. The colors (red, green, blue) correspond to different orientations of fibers; red: right–left, green: anterior–posterior, and blue: superior–inferior

2.2.3 Diffusion-Based MRI in Epilepsy

DTI provides information regarding the microstructural arrangement of a tissue and can improve understanding of the structural pathology that induces epilepsy. Epileptic seizures fail to come under control with seizure medication in about one third of cases. A number of terms such as "refractory," "intractable," or "uncontrolled epilepsy" are used to describe this situation. However, the International League Against Epilepsy has proposed the term "drug-resistant epilepsy." According to the League, drug-resistant epilepsy occurs when a person has failed to become seizure free with adequate trials of two seizure medications [14]. This type of epilepsy can be treated with surgical intervention when the seizures are focal and the epileptogenic area can be removed safely. Hence, the detection of a structural brain lesion or/and abnormality is of paramount importance for the presurgical work-up [15]. Advanced MRI techniques offer a noninvasive method for the investigation of underlying neurobiological abnormalities that cause epileptic seizures.

Epileptic seizures are classified into three main types: focal, generalized, and unknown onset. Focal seizures refer to those that affect only one hemisphere of the brain; generalized seizures indicate that both sides of the brain are affected at the start of a seizure; and unknown onset are seizures with no clear seizure focus from the beginning of the event [16].

There is also a list of terms such as epileptogenic zone, status epilepticus (SE), and temporal lobe epilepsy (TLE) that need to be defined because there is a large body of literature on diffusion-based analysis in cases with one of the aforementioned categories of epilepsy. The epileptogenic zone is defined as the area of cortex indispensable for the generation of clinical seizures [17], and SE is defined as a continuous seizure lasting more than 30 min or two or more seizures without full recovery of consciousness between them [18]. TLE is the most common form of partial or localization-related epilepsy, where seizures begin in the temporal lobe.

Especially during SE (prolonged seizures), there is a breakdown of the sodium-calcium pumps on brain cell membranes (cytotoxic edema), which leads to a rapid uptake of water intracellularly and can cause cellular swelling [19]. This cellular swelling in diffusion MRI is reflected as a reduction in the ADC parameter. The vasogenic edema that follows cytotoxic edema allows the penetration of fluid and proteins into the interstitial extracellular space; the extracellular volume increases and the ADC is subsequently increased [20].

There are two different approaches to the evaluation of diffusion MRI in epilepsy. The first category refers to peri-ictal and postictal studies, namely, immediately or shortly after a seizure, while the second category includes interictal studies conducted between seizures.

2.3 Peri-ictal and Postictal Studies

2.3.1 Status Epilepticus (SE)

One of the earliest studies of DWI in SE was that of Wieshmann and colleagues in 1997, which referred to a female patient with focal motor SE (jerking of the right leg). Their diffusion findings denoted a decrease of 27% in ADC in the left motor cortex and a 31% increase of ADC of the subcortical white matter compared to the contralateral hemisphere [21]. Two years later, Diehl and coworkers and Lansberg and associates came to similar results [22, 23]. More specifically, Diehl's group investigated the distribution of ADC in 35 patients with focal motor SE and noticed an ADC decrease of 23% in the frontal region of interest. Additionally, the region of maximal decrease coincided with the area of seizure activity according to the intraoperative EEG [22]. Lansberg and coworkers observed a cortical hyperintensity on T2 images, and their ADC measurements showed a decline of 36% in the affected hemisphere compared to the unaffected one [23]. Other studies associated ADC reduction with diffuse atrophy in both occipital lobes and revealed an osmotic connection between epileptogenic and surrounding areas [24, 25]. In 2004, the findings of Hong and colleagues included an increased signal in T2 images and also increased ADC in the left temporoparietal area, which indicated vasogenic edema. However, in many follow-up scans, "normal" ADC and no atrophy were detected as a result of successful treatment of the seizures [26, 27]. It is important to highlight the fact that the potential etiologic factors of epilepsy can vary widely, since a stroke, encephalitis, or an infection, for example, can provoke epileptic seizures. In that sense, all the aforementioned underlying pathologies can affect the diffusion MRIs, and it is significantly complex to search for diffusion changes that are not caused by epileptic seizures. Every different study implements appropriate protocols and analysis methods that are adjusted to the clinical characteristics of the patient groups.

2.3.2 Temporal Lobe Epilepsy (TLE)/ Drug-Resistant Epilepsy

To measure ADC in patients with TLE, Diehl and coworkers presumed that DWI may detect and delineate the epileptogenic region [28]. Nine patients with intractable epilepsy were scanned after EEG documented seizures (45–150 min). The etiology of TLE was hippocampal sclerosis (HS), left mesial temporal lobe tumor, SE, or unknown. As a consequence, only one of the six TLE patients showed estimable decreases in ADC. Two SE patients exhibited a reduction or no change in ADC, while the patient with an incompletely resected temporal lobe tumor exhibited ADC abnormalities.

Thus, Diehl's group came to the conclusion that only occasionally may postictal DWI help the delineation of epileptic areas in patients with TLE. Similar findings were also derived from the study of Hufnagel and associates, in which after diffusion analysis in a group of nine patients with refractory epilepsy, ADC changes during postictal DWI were complex [29]. DWI scans were acquired 2–210 min after a seizure, and postictal ADC values varied from a 25–31% decrease in the epileptogenic zone (two patients) to widespread bilateral increase after a seizure provoked by flumazenil (one patient). Three of the remaining patients had generalized ADC changes after generalized or prolonged seizures, and the last three revealed no significant changes after short-lived seizures or if the interval between the seizure and the first DWI scan was up to 15 min long. In some cases, estimable differences in ADCs were noticed only in patients with neocortical ictal onset zones or in the neocortical portion of the temporal lobe [30].

Konermann and coworkers [31] implemented a different method in order to cause epileptiform activity. They scanned 12 patients with intractable TLE or/and extratemporal lobe epilepsy interictally and 10 min after seizure after the injection of 1 mg of flumazenil. Their interictal result was a considerable ADC increment in the hippocampus of the epileptogenic area of all TLE patients. Postictal results showed significant ADC reduction in all patients compared to interictal scanning but altered corresponding to the different regions of interest (ROIs). A large decrease of 14.8% was observed in the hippocampus on the seizure-onset side, while this decrease became lower for both the parahippocampal gyrus on both sides and in the cortex on the non-ictogenic side.

More recent studies have investigated DTI measures such as FA and MD in intractable focal epilepsy and inquired into their utility in the preoperative assessment of patients with epilepsy. Diehl and coworkers [32] conducted a representative study and detected a postictal decrease in MD, which is probably associated with cellular swelling in areas of seizure focus and seizure spread; on the other hand, FA appeared less sensitive in changes. Interictal and postictal images were acquired from a group of 18 patients with intractable focal epilepsy. Their results were compared to those of 27 normal controls. Interictal findings revealed an appreciable increase of MD in 72% of patients, whereas 50% of the patients had significant relative decrease in MD (40% of patients had focal changes) postictally. No significant fluctuation in FA was noticed between postictal and interictal data [32]. According to another study performed by Salmenpera and colleagues [33], the evaluation of MD may indicate the networks involved in seizures but it is not an effective method for the accurate delineation of the seizure focus. Interictal scans and a scan after 23 seizures were performed in 21 patients with intractable focal epilepsy. The interval was about 53 min between seizure onset and scanning. The results after comparison with 20 normal controls showed that in 11 patients and in 12 of 23 seizures, increases and decreases of MD were observed. Five patients revealed both increases and decreases postictally, and in four patients the changes co-localized with postulated seizure focus. Taking into account all these postictal studies, it is evident that there are examples of discordance between their results. Different types of seizures, various etiologies, and the small sample size are all factors that complicate the reproducibility and the corroboration of the results.

2.3.3 Interictal Studies

Interictal studies include qualitative and quantitative analysis of diffusion MRIs acquired during the period between seizures. There is a list of interictal studies of DTI in epilepsy that chronologically start in 1999, when Krakow and colleagues [34] analyzed data from one patient with a malformation of cortical development (MCD) in the right hemisphere. They utilized DTI, functional MRI, and CSI to study partial and secondarily generalized seizures of the patient and came to the conclusion that DTI showed the heterogeneous microstructure of the MCD attended by reduced FA and elevated MD. This MR technique provides a wealth of microstructural, biochemical, and functional information regarding the epileptogenic tissue that cannot be obtained with other noninvasive means [34].

Both publications of Eriksson and associates [35] and Rugg-Gunn and coworkers [36] in 2001 investigated the combination of DTI and statistical parametric mapping (SPM) in a group of patients with partial seizures. Eriksson's group [35] compared 22 patients with partial seizures and MCD with 30 normal controls and found areas of reduced FA in 17 out of 22 patients, increased FA in 2 out of 22 patients, and increased MD in 10 out of 22 patients. Rugg-Gunn's group [36] calculated FAs and MDs of 40 patients (10 with partial seizures and acquired lesions and 30 with partial seizures and normal MRIs); they also discovered decreased FAs and elevated MDs in all of the patients. Moreover, there were nine patients in whom the abnormalities identified on conventional MRI concurred with the areas of decreased FA. Both studies indicated changes in tissue beyond the affected area that appeared normal on conventional MRIs.

There is an association between the epileptogenic hippocampal formation and abnormalities in DTI measurements in unilateral TLE [37]. Assaf and colleagues studied 12 patients with unilateral TLE, compared them with a group of 14 healthy controls, and found that FA was lower in contrast to values of the contralateral hippocampus. In addition, the MD of hippocampal formation was significantly greater ipsilateral to the epileptogenic focus. A study of 2005 showed that diffusion abnormalities were localized not only in the areas of the epileptogenic hippocampus but also that a larger network was involved [38]. It was Thivard and coworkers who scanned 35 well-defined medial TLE patients (caused by hippocampal sclerosis) and 36 normal controls in order to examine the impact of mesial TLE on the architecture of a wide cerebral network. Their findings showed decreased FA ipsilaterally in temporal lobe formations and in extratemporal regions and increased MD in the affected epileptic hippocampus. MD of the contralateral normal hippocampus, amygdala, and temporal pole displayed a reduction. Figure 2.6 depicts a T2-weighted image, the ADC and FA maps, and the tractogram of a patient with hippocampal sclerosis.

The expected reduction of FA and increment of MD was corroborated by two more studies: Gross and coworkers [39] and Dumas de la Roque and colleagues [40]. More specifically, Gross' group [40] evaluated five patients with refractory epilepsy and focal cortical dysplasia (FCD) and analyzed their DTI images producing FA maps and calculating MDs. The results revealed decreased FA, increased MD, and white matter hyperintensities on T2-weighted images in three patients and no abnormalities in the other two patients. Dumas de la Roche and coworkers [39], on the other hand, performed a dedicated investigation of FA. They measured FA in the internal capsule, in normal white matter, close to the area affected by the lesion and away from it in 15 patients with a cortical lesion identified on structural MRI. An up to 10% reduction in FA was detected in 12 patients away from the lesion and in 13 patients close to the lesion. Furthermore, FA in the internal capsule was normal, and a lower but significant decrease of FA was observed in the WM adjacent to and away from the lesion. Thus, they came to the same conclusion as did Eriksson and Rugg-Gunn; DTI changes can reveal WM abnormalities that appear normal on conventional MRI [35, 36, 39]. A subsequent study of Salmenpera and associates analyzed high resolution DTI data of 7 patients with unilateral TLE and 13 healthy controls and detected abnormal FA values compared to the control group [41]. High-resolution DTI recognizes lateralizing MD and FA abnormalities in patients with TLE. According to Focke and coworkers (2008), DTI detects extensive alterations in mesial TLE with hippocampal sclerosis [42]. In this study, the affected networks in patients that underwent presurgical evaluation were localized mainly in the limbic system and the ipsilateral temporal lobe.

The utility of ADC interictal measurement as a complementary tool in lateralizing the epileptogenic lesion was investigated in a series of studies [43–47]. Increased ADCs of the affected hippocampi were observed in patients with TLE, mTLE, HS, and in cases of temporal lobe resection. This increase may reflect neuronal loss in the epileptogenic area, gliosis, loss of structural organization, and an expansion of extracellular space (an indicator of HS).

In contrast to postictal studies, the majority of interictal studies corroborate the increase of MD and decrease of FA in the epileptogenic regions. However, the small sample size both of the patients and control group in interictal studies cannot provide experimental results with adequate statistical significance to define their contribution to the presurgical planning.

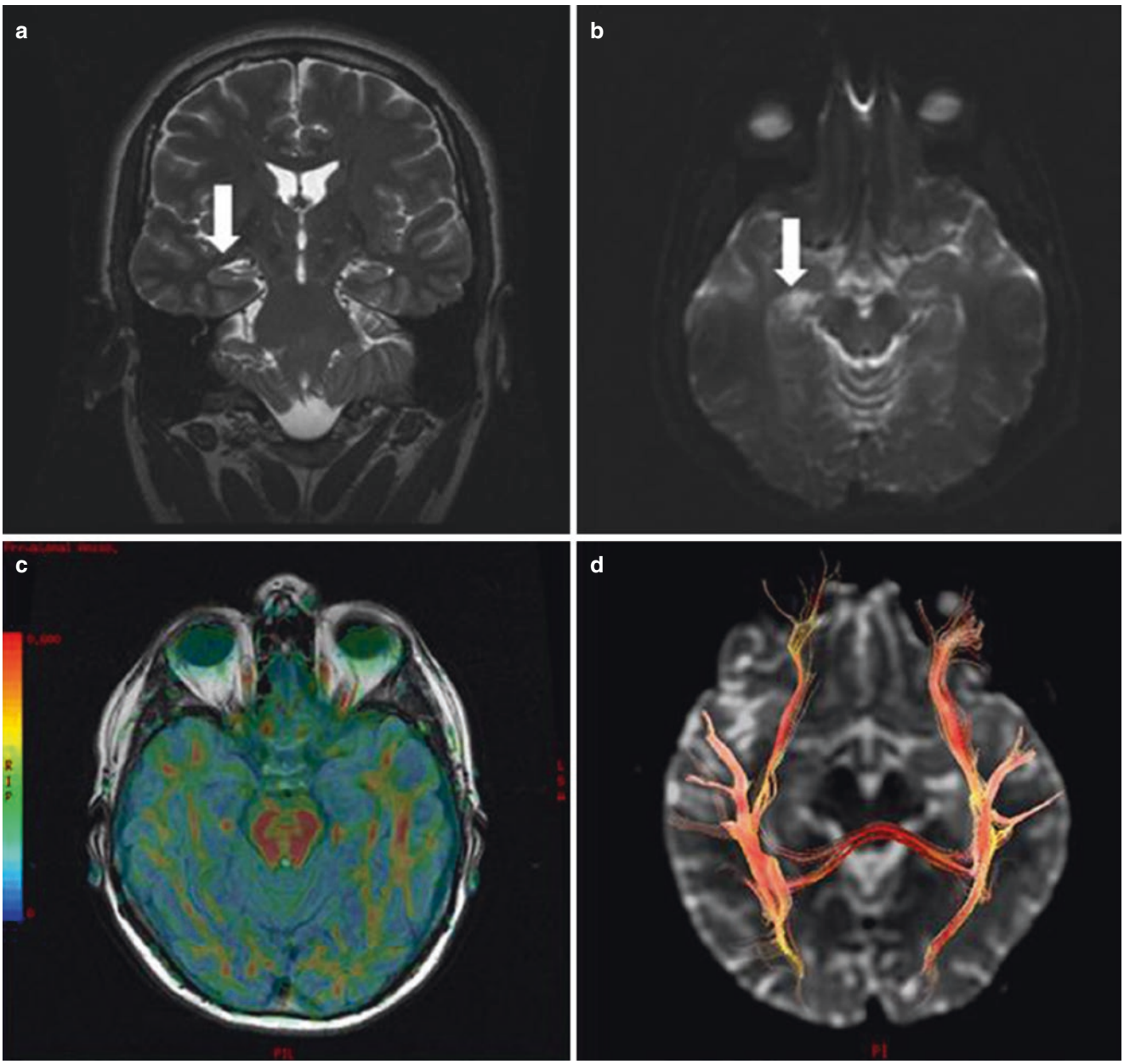

Fig. 2.6 (**a**) High resolution T2-weighted image; (**b**) Apparent diffusion coefficient map; (**c**) FA map; (**d**) Tractography in a patient with hippocampal sclerosis

2.4 Tractography

White matter comprises a highly coherent structure full of neuronal fibers and facilitates the anisotropic diffusion of water. As a result, calculation of fiber orientation can be derived from the combination of FA values with directionality. This concept is the theoretical basis of fiber tractography, which enables a three-dimensional visualization of the white matter networks noninvasively [48].

Fiber tractography algorithms are based on the fact that monitoring the tensor's orientation makes the detection of intravoxel connections more feasible. There are a variety of algorithms; however, all of them concluded on a line propagation approach (Fig. 2.7), which can yield colored maps of fiber tracks. Various tractography techniques have been reported [49–52].

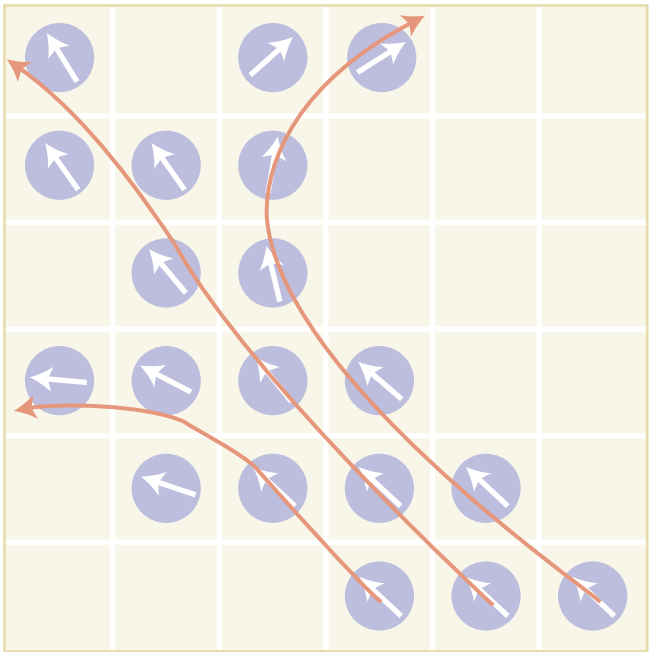

Fig. 2.7 Schematic diagram of the interpolation approach (nonlinear line propagation)

There is also a series of studies that employ DTI and tractography and created atlases of the human brain [53, 54]. Thus, a damage to a given fiber tract (such as disruption or displacement) could be a valuable diagnostic parameter, as it could be evaluated by three-dimensional tractograms [55, 56].

The definition of a "seed" region of interest (ROI) on the color orientation map is required in order to reconstruct and visualize white matter tracts. Most software applications have the option of a "structural view." Placement of a seed ROI leads to a white matter track oriented through the ROI. If the user desires the representation of the fiber pathway that connects one ROI to another one, the placement of a second ROI determined as the "target" ROI on the image should take place. This procedure is pictorially depicted in Fig. 2.8.

Tractography techniques also provide useful information in relation to presurgical planning; nonetheless, they present limitations such as in cases of crossing and kissing fiber tracts, which should be taken into consideration when these methods are used for preoperative guidance.

Diffusion gradients are applied in multiple directions in DTI; therefore the amount of noncollinear gradients applied may range from 6 to 55. Nevertheless, the optimal range is still debatable in the literature, and an optimal number has not yet been defined [57–59]. A principal disadvantage associated with an increase in the number of DTI gradients is scan time. Increasing the number of directions simultaneously increases scan time and may easily exceed the limits of clinical practice [60]. Therefore there is a constant cost-benefit analysis debate between the imaging time and the number of gradients applied in order to acquire adequate diffusion information.

Nevertheless, the wider use of higher field scanners (3T or more) and the further development of acquisition and post-processing techniques should result in the increased role of this promising advanced technique in both research and clinical practice.

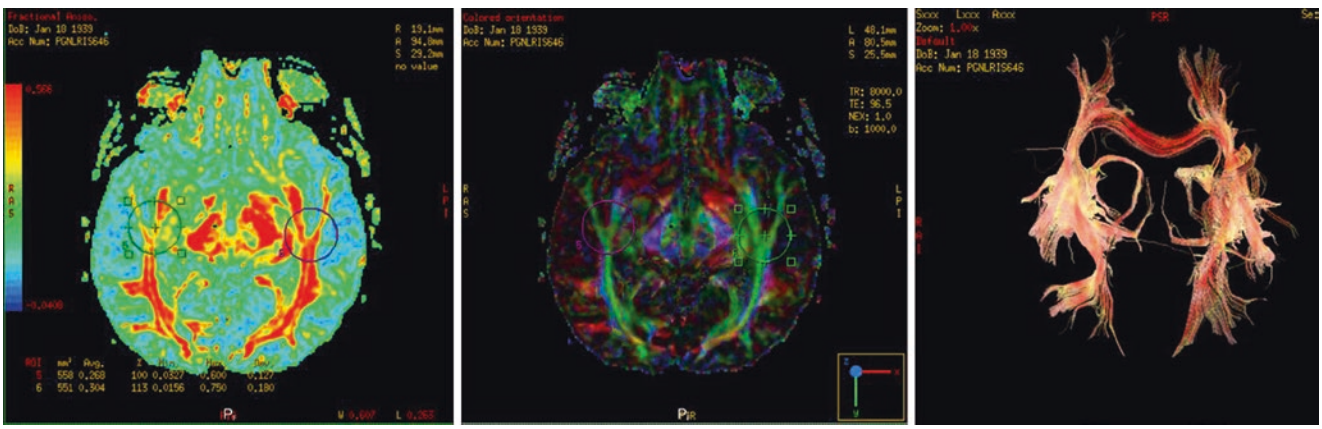

Fig. 2.8 ROI placement on colored orientation map (*left*) fiber tracts (*right*)

2.4.1 Tractography in Epilepsy

The noninvasive technique of fiber tractography deploys data collected by DTI and visualizes a map of white matter tracts after a three-dimensional reconstruction. This neural network determines anatomic connections between different cortical areas, including the epileptogenic zone, and assists the decoding of brain structure and function. Additionally, functional areas of language, memory, and vision, for example, can be delineated and aid the presurgical evaluation of an intracranial mass resection.

The parahippocampal gyrus (PHG) is the link between the hippocampus and neocortical areas; their connections may constitute the plinth of "memory and visual processing" theoretical framework [61]. Powell and associates came to this conclusion after searching the connectivity of the parahippocampal gyrus using DTI and fast marching tractography in a group of ten healthy controls. They found that lingual and fusiform gyri are the link between the parahippocampal gyrus and the orbitofrontal areas, the extra striate occipital lobe and the anterior/posterior temporal lobe. Moreover, their results bore testament of a direct hippocampus and PHG connection for the first time. In 2005 Concha and coworkers [62] studied eight patients with TLE and unilateral mesial temporal sclerosis and related their disorder to the bilateral pathologic limbic system. The results concerning TLE patients demonstrated a bilateral decrease of FA in the fornix, while patients with unilateral mesial temporal sclerosis showed bilateral abnormalities in the fornix and cingulum. In a longitudinal study 2 years later the same authors reported that the eight aforementioned patients underwent an anterior temporal lobe resection [63]. However, their follow-up scan (1 year later) continued to show DTI abnormalities in the genu of the corpus callosum and the contralateral tracts of the fornix, cingulum, and external capsules. The interpretation of this outcome was the presence of an underlying structural impairment in the affected areas.

Despite the fact that tractography appears to have very positive perspectives, it also has limitations. Anatomic structures attended by crossing and kissing fibers can lead to erroneous calculation of fiber orientation. Additionally, the size variation between an actual nerve fiber (μm) and the spatial resolution of DTI (mm) can often be responsible for the wrong estimation of a tract direction [64]. A three-dimensional visualization of a brain network is the outcome of complex data processing; therefore it is difficult to know whether a reconstructed fiber represents an actual one localized in the same place.

2.5 Memory and Language Networks

In 2008 Yoharajah and coworkers [65] evaluated the correlation between FA, volume, and memory performance in 18 patients with TLE before they underwent a surgical intervention. Significantly decreased FA and volume were detected in areas connected ipsilateral to the epileptogenic region in patients with left TLE, while patients with right TLE revealed correlations between verbal and nonverbal memory and left and right FA. In chronic temporal lobe epilepsy, extensive information regarding the integrity of the aforementioned connections may prospectively evaluate lessening of memory [65]. The correlation of memory performance and the uncinate fasciculus can also be evaluated. Memory scores were marked in 28 patients with TLE, and it was established that an increase in radial diffusivity and a reduction in FA were associated with visual delayed memory [66].

Functional lateralization refers to the distinction of a human brain function and can occur both in the right and left hemispheres. Powell and coworkers [67] studied the lateralization of language processes utilizing fMRI and diffusion MR tractography in ten right-handed normal controls. Volume and FA measurements showed that both of them were higher on the left compared to the right brain. This asymmetry is associated with the lateralization of the language function [67]. The same authors published a new study 1 year later in which they observed structural reorganization of WM tracts in patients with left TLE [68]. This was an indicator of change in the lateralization of language, and as a result they concluded that fMRI and tractography are a successful combination for studying the function of language.

A recent study of 2015 investigated the utility of diffusion MR tractography in the detection of fiber tracts linked to language cortices and concerned children with intractable epilepsy [69]. In the presurgical planning they constructed maps of the language network using fMRI and tractography in order to accomplish a more precise resection. In 12 healthy children who were examined, the localization of language activation regions was 77% accurate, and in children with epilepsy the accuracy was up to 82%. This kind of fMRI-tractography analysis could assist the presurgical work-up of pediatric interventions as a useful diagnostic tool [69].

2.6 Visual Networks

A severe lesion of the Meyer loop (disruption) leads to superior vision loss. A superior homonymous quadrantanopia is a complication of anterior temporal lobe resection [70] and is interpreted as the loss of vision in a quarter of the visual field [71]. Diffusion MR tractography was used to evaluate the optic radiation pre- and postsurgically via a three-dimensional reconstruction in one patient with quadrantanopia [70]. It was concluded that imaging of the optic radiation can play a significant role in the prediction of postoperative visual field deficits [70]. Another study investigated the correlation of optic radiation integrity and visual loss in patients with cerebral arteriovenous malformation (AVM) using tractography, and it was demonstrated that this method could constitute a useful tool in the assessment of surgical risk [72].

One in ten patients who undergo an anterior temporal lobe resection (ATLR) suffer a visual fields deficit (VFD) postoperatively. Twenty patients were scanned presurgically 3–12 months after surgery and fiber tractography was used to visualize the optic radiation. The result was that 60% of the patients suffered a VFD. Hence, tractography can provide an accurate delineation of optic radiation in order to potentially reduce the VDF probability [73].

Conclusions

It is evident that the most important aspect of epilepsy surgery is the ability to accurately identify the epileptogenic zone. Structural MRI and clinical, electrophysiologic, and neurophysiologic data have an established role in the localization of the epileptogenic foci. Nevertheless, about 30% of epilepsy patients may have unclear MRI evidence, and the presurgical assessment may remain controversial. It should also be mentioned that even a detailed structural MRI may not reveal the true extent and functional status of the abnormality.

The introduction of DWI, DTI, and diffusion MR tractography has provided an insight into the underlying pathophysiology of epileptogenesis and offers the potential to discover meaningful details of the microarchitecture of the affected tissue. In conclusion, advanced MRI techniques are increasingly becoming an essential part of both the diagnostics and presurgical guidance of epilepsy by accomplishing successful identification of the epileptogenic focus when this area is undetectable on structural MRI or when structural MRI and clinical and electrophysiologic findings are not in agreement.

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