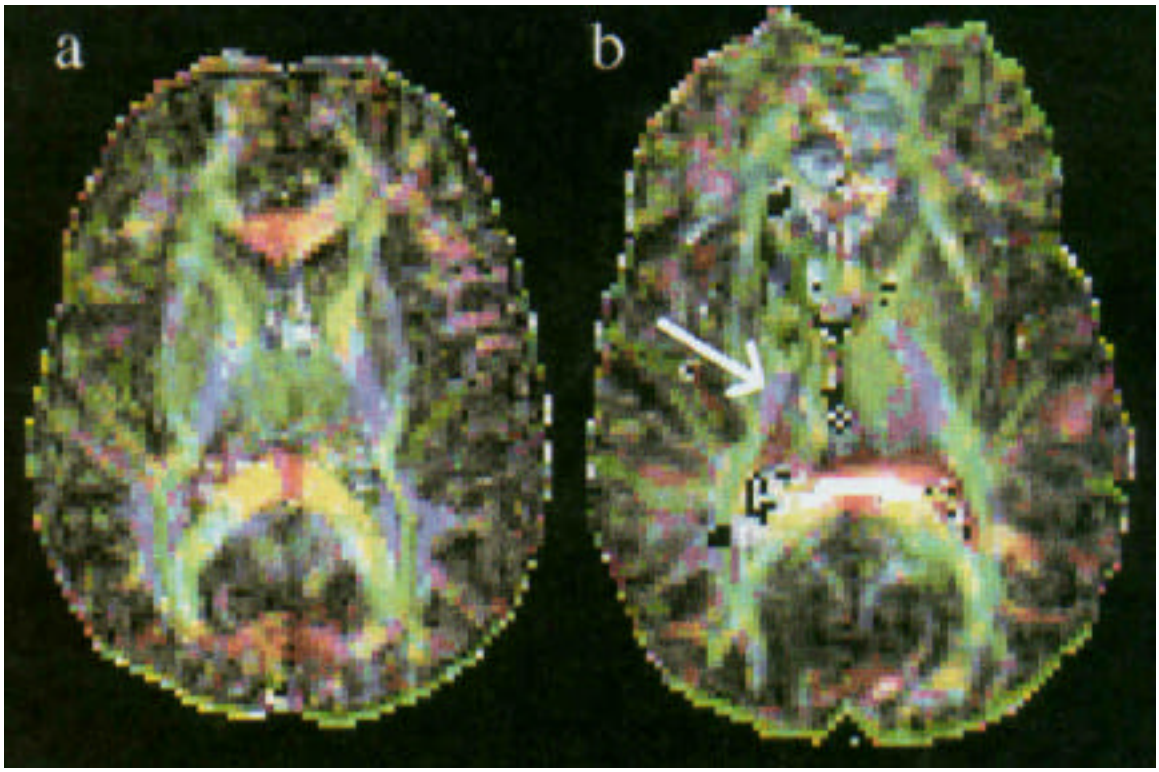
Fundamental Principles of Diffusion-Weighted Imaging

(the abridged, watered down version)



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Medical Imaging

The adoption of nuclear magnetic resonance imaging (NMR) by the medical community in the seventies has revolutionized the scientific visualization of the human body. Though other high-resolution techniques such as computerized tomography (CT) and positron emission tomography (PET) also have their niche in the modern imaging world, only MRI is based on principles that do not use ionizing radiation [1, 2]. Both with its relatively high spatial resolution (higher than CAT, PET, ultrasound, and external EEG/ERP [1]) and its ability to detect differences in soft tissues, MRI is particularly useful in helping to understand the complex neuroanatomic structure of the brain. Even laypeople understand the importance of this new imaging tool. Indeed, along with the development of the polio vaccine and antibiotics, the American populace has cited medical imaging, and specifically MRI, as one of the greatest scientific advances of the century[3].

However, perhaps the most impressive feature of NMR is its versatility. The principles of magnetic resonance have applications in medicine, materials science, chemistry, and physics. In the fields of medical imaging and neuroscience, NMR has recently diversified into new arenas. Functional imaging, for example, enables the detection of brain regions involved in performing specific tasks by measuring the rate of oxygen flow [4]. Newer functional techniques are actually using the nuclear properties of sodium to image neural responses directly [5]

But despite the advances in functional neuroimaging, structural MR has changed relatively little since its inception. Though technological advances have enabled images

of increased resolution in less time, a standard neuroanatomic picture is still the result. T1, T2, and T2* weighting, though effective at producing important clinical and research data, all are unable to detect the directional properties of the matter that they image [6]. In effect, each voxel is measured independently of all others in the image.

However, a relatively new technique known as diffusion-weighted imaging (DWI) enables visualization of the intrinsic directionality within the brain by detecting small movements in water molecules. DWI gives promise as a new way of further understanding the anatomy of the brain, as well as a tool for diagnosing several common pathological conditions. This paper is an attempt to briefly describe the principles of DWI, as well as its clinical and research applications.

Theory

DWI is based on the physical nature of diffusion, the random motion of molecules caused by their intrinsic kinetic energy dissipation [7]. Each molecule experiences a "random walk," known as Brownian motion, as it moves through the substrate. Thus, if two molecules begin at the same location in space, it is probable that they will be located in two very different places after some time. Though the motions of individual molecules are random and thus unpredictable, the position of the molecules on average can be modeled according to Einstein's Law [8] which determines the radius of the smallest sphere that contains all possible locations of a molecule after time, t:

$$R = \sqrt{6Dt}$$

where

D = diffusion coefficient
t = time allowed for diffusion

According to Einstein's Law, for a substance with a given diffusion coefficient, D, a molecule's distance from its point of origin is dependent only on the time allowed to diffuse (on average). However, there is a catch. In order for Einstein's Law to properly model diffusion, molecules must be unimpeded in their walk (Figure 1), resulting in isotropic diffusion. If molecules are impeded in one or one or more directions, the diffusion is said to be anisotropic. Anisotropic media are abundant in the human body, and the detection of this anisotropy provides the foundation for DWI. For example, one of the most anisotropic structures in the body is the axon. Because of the tubular hydrophobic structure of axons, water diffuses much more rapidly along the axon than across the its membrane.

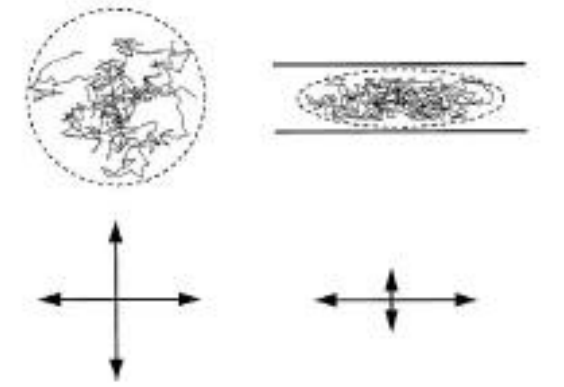
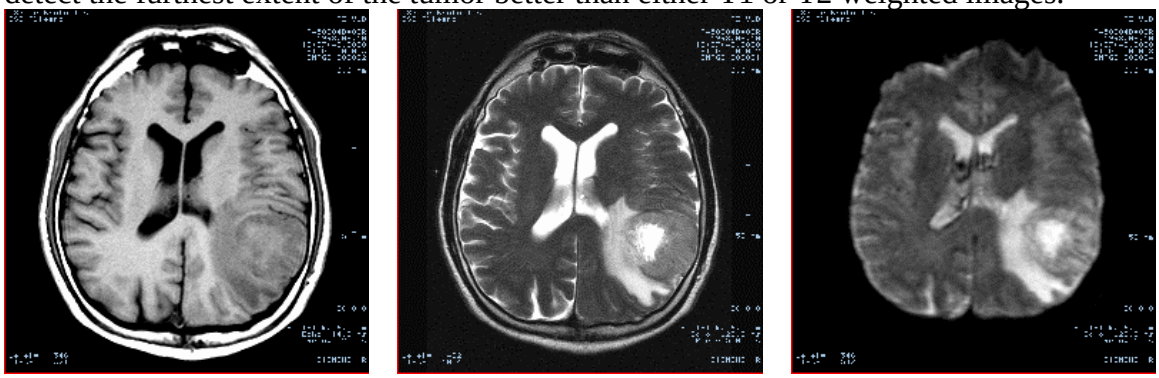


Figure 1: Brownian motion as generated by a computer simulation (From Lim et al.) [9]. On the left, the "random walk" is illustrated through an isotropic medium. The right demonstrates the result of motion in an anisotropic medium. The vectors representing net molecular motion are larger in one axis when compared to the other.

Imaging

Imaging the small diffusions of water molecules creates new challenges for MRI technology [7]. In addition to the usual magnetic field gradient pulses associated with a spin-echo sequence [2], two additional magnetic pulses must be applied [10]. The first of these pulses results in a dephasing of the nuclear spins of the molecules affected by the B gradient (similar to the effect of T2 relaxation). The strength of this magnetic field on the hydrogen nuclei in water is partially based on their position in space. After the 180˚ echo pulse occurs, the second magnetic pulse gradient is applied [7]. This matching pulse acts to rephase the nuclear spins, preserving the signal of the echo. However, if the nuclei in question have moved since the dephasing pulse, the rephasing process will be incomplete, resulting in signal loss. Differences in signal intensity due to incomplete spin rephasing form the basis of the DWI image (Figure 2).

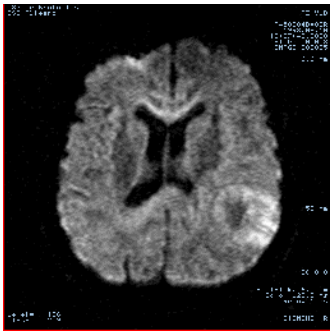
Figure 2: Two traditional structural MR images and a diffusion-weighted image in a subject with glioblastoma [8]. The diffusion-weighted image has a b-value of 300 sec/mm, a medium sensitivity to anisotropy. Note that the diffusion-weighted image is able to detect the furthest extent of the tumor better than either T1 or T2 weighted images.



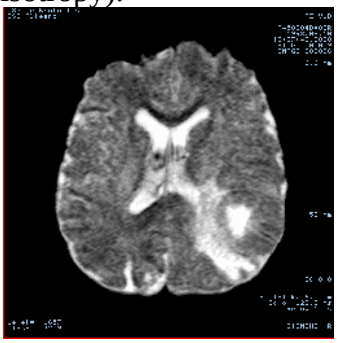
T1-Weighted T2-Weighted Diffusion-weighted

Though the many complexities and variations in diffusion imaging are far beyond the scope of this paper, their resultant images are of interest. In addition to the raw image, known simply as a diffusion-weighted image (shown above), post-acquisition processing is often applied to construct a diffusion image. Since diffusion-weighted imaging takes advantage of the same nuclear phenomenon as T2 weighting (nuclear spins/precessing motion [6]), T2 intensities can influence the DWI. By performing a simple image subtraction (creating a difference image of the two stacks), the "T2 shine through" can be eliminated (Figure 3)[8]. This corrected image can be further processed to produce apparent diffusion coeffficient (ADC) maps which give measures of anisotropy that are not dependent on experimental parameters, plane of acquisition, or scanner [7].

Figure 3: Diffusion image and ADC maps of a subject with edema. [8]. Note that the diffusion image no longer contains hyperintensities caused by T2 relaxation. The ADC map, independent of experimental parameters, gives a true scalar measure of anisotropy (though no information on the exact direction of the anisotropy).



Diffusion Image



ADC map

By measuring the diffusion of water from several (usually 6) different planes, one can reconstruct the directionality of structures, particularly large white mater fiber bundles, by using a tensor (3 x 3 matrix); this process is known as diffusion tensor imaging (DTI). The addition of other scan pulses sensitized to different direction of

diffusion enables the calculation of a vector for each voxel that describes the primary direction of water movement in that area [7]. Color mapping of this data produces brilliant images detailing white matter pathway trajectories (Cover).

Though the use of diffusion-weighted-imaging and all of its derivations have significant drawbacks (including longer computation times and ambiguities regarding the true nature of some anisotropy in the brain), they also provide a new perspective on the structure of the brain. Clinically, DWI is particularly useful in detecting ischemia and edema well before other techniques can visualize any anomalies [7]. In a research setting, DWI can display the orientation of white matter tracts in both normal and affected groups [11](such as schizophrenics), as well as even tracking the course of axonal development in newborns and children [12, 13].

Bibliography:

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Cover:

The picture on the first page is a color map of the anisotropy found in a normal brain (left) and a brain after head trauma to the internal capsule. Different colors indicate diffusion along different axis: red medio-lateral, green in the anterior-posterior, and blue superio-inferior. The author notes the reduced anisotropy (and increased isotropy) in the case of head trauma (arrow), possibly indicating an edema (From Werring, 1998[4]).