Diffusion-weighted Imaging of the Liver: A Pictorial Review

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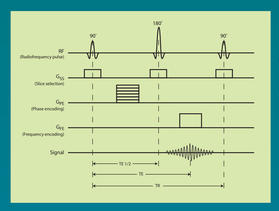
PRINCIPLES OF DWI

- Diffusion Weighted Imaging (DWI) provides tissue contrast by the measurement of the diffusion properties of water molecules within tissues. Molecules move in Brownian motion, or molecular diffusion, which is the concept that any molecule in a fluid will be randomly displaced due to agitation by thermal energy.
- Diffusion of water molecules can occur via random diffusion due to concentration differences (Fick's law of diffusion) or in response to factors such as temperature or ion-ion interaction, as well as a combination of other factors.
- In biological tissues diffusion is also affected by the biophysical properties of tissue cell organization (cell membranes, fibers and macromolecules), density, microstructure and microcirculation.
- Pathological processes which change the volume ratio or physical nature of intra- and extracellular spaces affect the diffusion of water molecules; restricted or impeded diffusion is seen in tissues with high cellularity, (e.g. tumors, abscesses, fibrosis and cytotoxic edema), and relative free or unimpeded diffusion is encountered in tissues with low cellularity or tissues with disrupted cell membranes, (for example in cysts and necrotic tissues).
- DWI imaging provides information that reflects tissue cellularity and the integrity of cellular membranes.

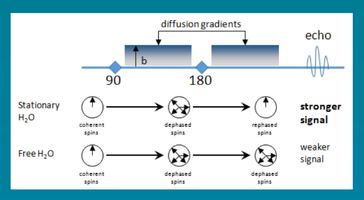
Drawing depicts the Brownian motion of water molecule, which manifesting as random motion due to agitation by thermal energy

PROPERTIES OF DWI SEQUENCE

- Two bipolar magnetic field gradient pulses are added to a conventional pulse sequence with multiple b-values.
- Conventional sequences may include spin echo (SE), fast spin echo (FSE) or gradient echo (GE). Echo-planar imaging (EPI) is the gold standard pulse sequence used in abdominal DWI
- Two bipolar gradient pulses must be equal in magnitude and timing before and after the 180 degree refocusing pulse of the pulse sequence.
  - First pulse dephases the magnetization of moving and static spins.
  - Second pulse rephases static spins but not moving spins, eliciting a strong signal from stationary or "restricted" water molecules, while diminishing the signal of moving water molecules.
- The b-value represents the diffusion factor (measured in s/mm2) and represents the strength of the diffusion weighting. The sensitivity of the imaging sequence to water diffusion can be altered by changing the b-value. The higher the b-value, the more sensitive the sequence is to diffusion effects.



Basic timing diagram of spin echo sequence. The first 90-degree RF pulse flips the spins into a transverse plane and the second 180-degree RF pulse at time TE/2 to rephrase the spins. The signal read out is performed at time TE



Basic timing diagram of a diffusion sequence. Two bipolar gradient pulses of equal magnitude and duration are added to a spin echo sequence before and after the 180-degree RF pulse. The signals generated by the "restricted" water molecules are additive and become stronger than the free water molecules

ADC MAPPING

- The amount of diffusion is quantitatively defined using the apparent diffusion coefficient (ADC), apparent because factors including capillary perfusion, temperature, magnetic sensitivity of the tissue, and motion all affect the actual diffusion.
- The ADC is calculated by performing a mono-exponential fit to the relationship between the measured signal intensity (in logarithmic scale) and the b-values as follows:

  ADC = ln (Si/S0) / (bi-b0)

  S0 is signal intensity for b0, and Si is signal intensity for bi
- The slope of the line that describes this relationship for each voxel represents the ADC. The calculated ADC values for all voxels are usually displayed as a parametric map (automated on most clinical MR systems), and by drawing a region of interest onto this map, the mean or median ADC value in the region of interest that reflects water diffusivity can be recorded
- Low ADC values mean restricted diffusion (i.e. tissues which are highly cellular), and high ADC values are seen in areas with relative free diffusion (i.e. tissues with low cellularity). Performing DWI measurements by using two or more b-values (tumor detection and characterization are possible based on differences in water diffusivity by observing the relative attenuation of signal intensity on images obtained at different b-values. As the b-value increases, a structure of lower ADC loses signal faster than structures of higher ADC, and tissue contrast increases.
- Additional b-values (greater than at least 2) can be considered when the primary goal is to obtain an accurate ADC measurement (i.e., to assess tumor response or liver fibrosis), because increasing the number of data points can reduce error in the ADC estimation. However this increases the acquisition time.

LIVER DWI UTILITY/ADVANTAGES

Diffusion weighted imaging (DWI) has demonstrated promise in application to liver lesions particularly those related to tumor detection, characterization, and response to treatment.

Tumor Detection

- Background signal suppression in diffusion-weighted images results in increased conspicuity of focal lesions and high lesion-to-background contrast.
- DWI has a higher sensitivity and specificity and positive predictive value (PPV) for detection of HCC < 20mm in comparison to conventional contrast enhanced MRI
- DWI is demonstrated to have higher sensitivity, better image quality and fewer artifacts at a b-value of 50 as compared to fat suppressed T2 sequences in the assessment of metastatic disease

Tumor Characterization

- Reduced ADC values have been reported in most malignant lesions, likely related to cellular membrane impeding the mobility of water molecules.
- However, there are solid lesions exhibit decreased ADC due to high cellularity, i.e. abscess
- ADC values cannot discriminate between solid benign and malignant lesion, since there are considerable overlap
- ADC values may allow for inferences as the characterization of liver lesions. In general, benign lesions such as cysts and hemangiomas have higher ADC values than malignant lesions. Further characterization of lesions may be achieved by comparing b-values, for example, cystic components have been shown to demonstrate suppression at higher b-values.

Treatment response

- Cell death and reduced tumor cellularity are expected in response to treatment on theoretical ground. Increase in tumor ADC have been observed in several studies with liver metastasis and HCC.
- ADC change is observed earlier than morphologic alteration and may be as earlier as 24-48 hours after treatment.
- An increase in ADC has been observed in in responders to both systemic treatment and local regional therapies ((RF ablation and chemoembolization)
- Exact evolution of ADC cannot be described accurately because of concurrent processes such as cellular swelling, fibrosis and perfusion changes

PITFALLS/LIMITATIONS OF DWI

IMAGE QUALITY

- Single shot echo planar DWI (SS EP DWI) is the gold standard in abdominal DWI technique. It has limited image quality arising from poor signal-to-noise ratio (SNR) limited spatial resolution, and echo-planar imaging-related artifacts
- Inherent to the technique and EPI sequence is low spatial resolution and low SNR due to hardware limitations and high bandwidth. Because the EPI sequence is comprised of an incomplete spin echo formation, SNR is decreased; SNR can be increased, but only at the sacrifice of spatial resolution in the process.
- Optimization of EP DW imaging can be achieved by combining parallel imaging, decreased frequency encoding points, and small diffusion gradients to achieve image quality and SNR similar to those of T2 weighted imaging.

ADC REPRODUCIBILITY

- ADC measurement reproducibility and inter-imager variability are critical issues to consider to ensure consistent and widespread application of quantitative ADC measurements for disease characterization and tumor response assessment.
- Techniques applied to acquire DW images, including the choice of b-values, vary considerably consequently resulting in considerable differences in the ADC values of benign and malignant lesions that have been reported in various summary statistics.
- Lack of standardization of protocols for both data acquisition and analysis is an obstacle to widespread adoption of DWI of the liver for lesion characterization and tumor assessment.
- ADC overlap exists among cellular benign hepatic lesions (e.g. FNH and Adenoma). As such, benign solid lesions (FNH, adenomas) may sometimes display restricted diffusion (low ADC). While necrotic malignant lesions can demonstrate free diffusion (high ADC values).

DWI ARTIFACTS

Motion artifacts

Single shot echo-planar sequences are inherently sensitized to the motion of diffusion and therefore highly sensitive to other kinds of motion that may produce artifacts, including bulk motion, motion secondary to cardiac motion (mostly affecting the left hepatic lobe) and respiration. Regarding respiratory movement artifacts, abdominal DWI can be conducted using breath hold scans or free breathing with respiratory triggering, with varying advantages/disadvantages to both.

1. Breath-hold single-shot echo planar imaging of the liver can quickly evaluate the whole liver, generally in one or two breath holds of 20-30 seconds each, decreasing the chances of bulk movement of the patient within the scanner, but this is with the accompanying disadvantages of decreased SNR, lower spatial resolution and a limitation on the number of b-values that can be included in data acquisition.
2. Respiratory triggering can substantially improve signal and spatial resolution secondary to the use of multiple signal acquisitions that results in thinner image sections, and the ability to accommodate multiple b-values which can reduce errors in ADC calculations. The disadvantage to respiratory triggering is the overall increase in acquisition times, which can result in increased chance of bulk movement of the patient in the scanner.
3. Cardiac movements are primarily perceived problematic in DWI evaluation of the left hepatic lobe, making ADC measurements of this region unreliable. It has been shown that motion artifacts caused by spin dephasing secondary to cardiac motion are worse at higher b-values causing high ADC values over the left hepatic lobe. Artifacts secondary to cardiac movements can be overcome by using pulse or cardiac triggering during image acquisition, but it has been shown that cardiac gating is not always reliable and it inherently increases acquisition times significantly which can again result in additional artifacts secondary to bulk motion of the patient within the scanner.

DWI ARTIFACTS (cont)

Susceptibility artifacts

- Susceptibility artifacts can be seen as bright spots, spatial distortion or signal drop out and are primarily caused by metal artifacts or magnetic field inhomogeneity, the latter of which can be overcome by shimming techniques. Susceptibility effects resulting from air in the stomach or colon may specifically obscure or diminish visualization of the left hepatic lobe.

Chemical shift artifacts

Chemical shift artifacts can be caused by air-tissue interfaces or fat-water interfaces and may appear as geometrical distortion and image shearing artifacts.

Eddy currents

Eddy currents may appear as geometrical distortion and image shearing artifacts and are typically caused by the rapid on and off switching of the gradients.1 Eddy current correction algorithms can be used to reduce these distortion artifacts.

CASE 1: Giant Cavernous Hemangioma

Hepatic haemangiomas (also known as hepatic venous malformations) are benign non-neoplastic hypervascular liver lesions. They are mesenchymal in origin and usually are solitary but can be multiple. Histologically, the lesions are composed of multiple vascular channels lined by endothelial cells supported by thin fibrous stroma. They are frequently diagnosed as an incidental finding on imaging and most patients are asymptomatic. Giant cavernous hemangiomas are a minor subset of hepatic hemangiomas. The term giant hemangioma is reserved for lesions larger than 5 cm. Giant cavernous hemangioma may contains areas of central necrosis/liquefaction, hemorrhage, peripheral calcification, fibrosis and thrombosis, resulting in heterogeneous appearance and incomplete opacification, even on very delayed imaging

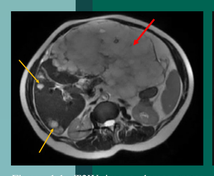


Figure 1.1: T2W image demonstrates a large hyperintense lesion (red arrow) involving nearly the entire left lobe of the liver. There are additional smaller lesions of similar signal characteristics in the right lobe (yellow arrow)

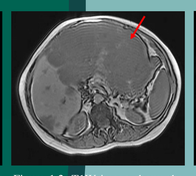


Figure 1.2: T1W image shows the mass appearing mildly hypointense to the liver parenchyma (red arrow)

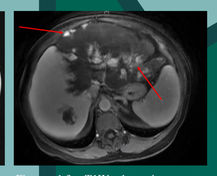


Figure 1.3: T1W dynamic contrast imaging demonstrates predominantly peripheral nodular discontinuous with gradual filling (red arrow)

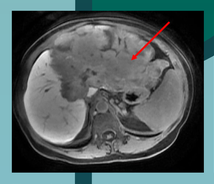


Figure 1.4: Slow filling of contrast is identified well into hepatobiliary phase (red arrow)

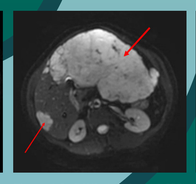


Figure 1.5: DWI (b-value of 500) demonstrates increased signal through the large lesion and smaller additional lesion (red arrow)

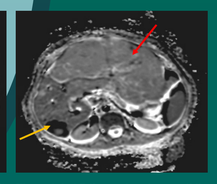


Figure 1.6: ADC mapping shows mildly hyperintense signal intensity within the large lesion (red arrow). Note that the smaller lesion demonstrates a large area of restriction (yellow arrow)

Case 2: Hepatic Cyst

Simple hepatic cysts may be isolated or multiple and may vary from a few millimeters to several centimeters in diameter. Simple hepatic cysts are benign developmental lesions that do not communicate with the biliary tree. The current theory regarding the origin of true hepatic cysts is that they originate from hamartomatous tissue. On histopathological analysis, true hepatic cysts contain serous fluid and are lined by a nearly imperceptible wall consisting of cuboidal epithelium, identical to that of bile ducts, and a thin underlying rim of fibrous stroma. In general, cystic lesions of the liver in the adult can be classified as developmental, neoplastic, inflammatory, or miscellaneous lesions. Because the clinical implications of and therapeutic strategies for cystic focal liver lesions vary tremendously according to their causes, the ability to differentiate noninvasively all types of cystic tumors is extremely important.

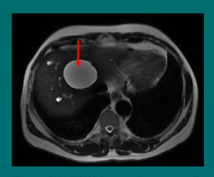


Figure 2.1: T2W image shows a well-defined homogeneous hyperintense cyst (red arrow)

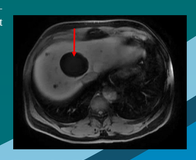


Figure 2.3: T1W dynamic contrast phase shows absence enhancement of the cyst (red arrow)

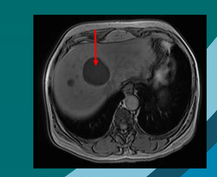


Figure 2.2: T1W image shows the cyst with hypointense signal intensity (red arrow)

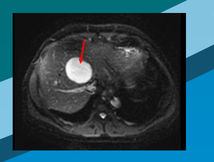


Figure 2.4: DWI (b-value of 500) shows increased signal intensity of the cyst (red arrow)

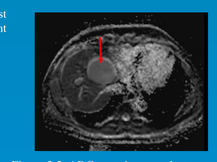


Figure 2.5: ADC mapping reveals non-restricted feature of the cyst with signal intensity remaining hyperintense (red arrow)

CASE 3: Carcinoid Tumor with Liver Metastasis

Neuroendocrine tumors arise from various neuroendocrine cells whose normal function is to serve at the neuroendocrine interface. Neuroendocrine cells are present not only in endocrine glands throughout the body that produce hormones, but are found in all body tissues Carcinoid cancer and related neuroendocrine tumors (NETs) are small, slow growing tumors found mostly in the gastrointestinal system. When carcinoid tumors occur in the digestive tract or pancreas, the substances they produce are released into a blood vessel that flows directly to the liver (portal vein), where enzymes destroy them. Therefore, carcinoid tumors that originate in the digestive tract generally do not produce symptoms unless the tumors have spread to the liver. Carcinoid tumors can produce an excess of hormonelike substances, such as serotonin, bradykinin, histamine, and prostaglandins. Excess levels of these substances can sometimes result in a diverse set of symptoms called carcinoid syndrome.

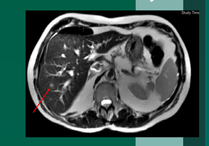


Figure 3.1: T2w image shows a small hyperintense lesion in the posterior right hepatic lobe (red arrow)

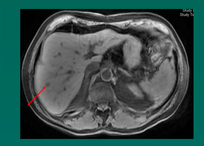


Figure 3.2: T1W sequence shows the lesion with hypointense signal intensity (red arrow)

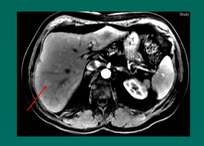


Figure 3.3: T1W dynamic contrast sequence shows mild diffuse enhancement of the lesion (red arrow)

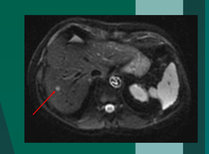


Figure 3.4: Diffusion imaging sequence (b-value of 500) shows increased signal intensity of the lesion (red arrow)

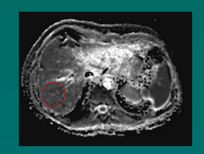


Figure 3.5: ADC mapping show fairly homogeneous signal throughout the liver. No hypointense or hyperintense signal intensity is seen in the expected location of the lesion (region enclosed by red circle)

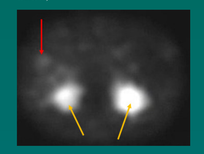


Figure 3.6: Octreotide scan shows a vague area of increased uptake in the right hepatic lobe (red arrow), corresponding to the enhancing lesion in the liver. Bilateral intense activity posteriorly represent kidney uptake (yellow arrows)

CASE 4: Focal Nodular Hyperplasia

Focal nodular hyperplasia is the second most common form of benign liver tumor after hemangiomas. The tumor more commonly occurs in young women. It is usually asymptomatic and generally discovered during imaging tests for other conditions. Focal nodular hyperplasia is well-circumscribed tumor-like hypervascular solid mass histologically characterized by a proliferation of hepatocytes, bile ductules, Kupffer's cells, and blood vessels arranged in an abnormal pattern. The multiple nodules of hyperplastic hepatocytes are divided by fibrous septa that may or may not radiate from a central fibrous scar. Focal nodular hyperplasia is believed to originate in utero as an arteriovenous malformation in the liver. The localized enriched blood supply stimulates the growth of normal hepatic elements. Bile ductules and abnormally enlarged arterial vessels are prominent throughout the scar and septa that extend from the central portion of the lesion to the periphery.

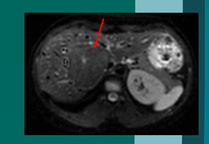


Figure 4.1: T2W sequence shows a large mass (red arrow) appearing nearly isointense to the liver with a hyperintense central scar (yellow arrow)

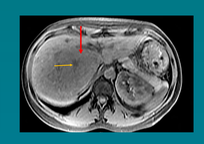


Figure 4.2: TW1 sequence shows isointense signal intensity of the mass (red arrow) with a hypointense central scar (yellow arrow)

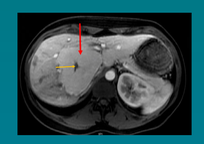


Figure 4.3: The mass shows avid contrast enhancement on arterial phase (red arrow) with the central scar remains hypointense (yellow arrow)

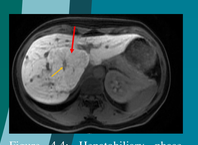


Figure 4.4: Hepatobiliary phase shows homogeneous uptake of contrast (red arrow) indicating presence of functioning hepatocytes. The scar appears hypointense (yellow arrow) due to lack of normal hepatocytes

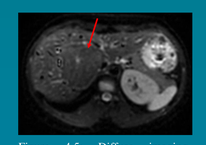


Figure 4.5: Diffuse imaging (b-value of 500) shows hypointense signal intensity of the focal nodular hyperplasia (red arrow)

TAKE HOME POINTS

- Diffusion images should always be interpreted in conjunction with all available conventional sequences including post-contrast imaging and clinical history.
- DWI has a higher sensitivity, specificity and PPV for small HCC in cirrhotic liver than conventional contrast enhanced MRI
- DWI offers better lesion to liver contrast and background suppression of signals arising from bile ducts and vessels
- DWI sequences are acquired without IV contrast reducing the risk the contrast induced nephropathy and nephrogenic systemic sclerosis in patients with low GFR's.
- DWI is very sensitive to artifacts rendering the interpretation more difficult
- ADC values should not solely used to discriminate between solid benign and malignant lesion, since there are considerable overlap
- An increase in ADC has been observed in responders to both systemic treatment and local regional therapies (RF ablation and chemoembolization)

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