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# Application of Diffusion- and Perfusion- Weighted Imaging in Acute Ischemic Stroke

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Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/30857>

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## 1. Introduction

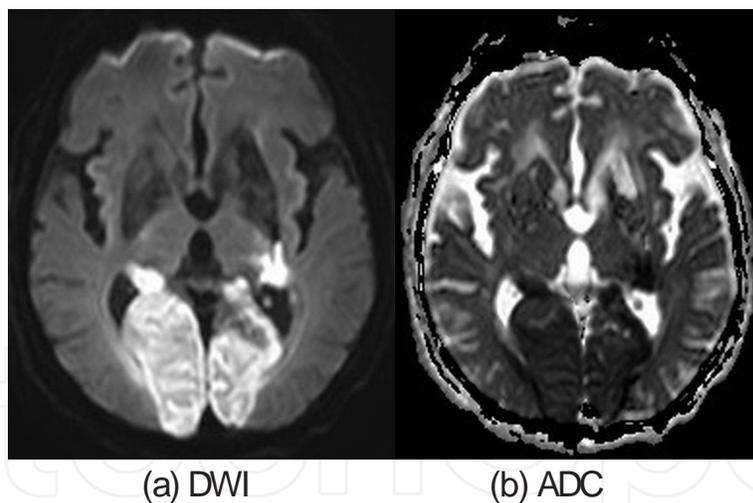
Stroke is one leading cause of morbidity and mortality worldwide, with acute ischemia constituting approximately 80% of all cases (Srinivasan et al. 2006). In the past imaging was primarily used to exclude hemorrhage and other causes. Yet diagnostic classification and clinical prognosis are major challenges in acute stroke. This is of particular importance since the approval of intravenous tissue plasminogen activator therapy for acute ischemic stroke within a narrow therapeutic window of 4.5 hours (Hacke et al. 2008; Wahlgren et al. 2008). It then becomes clear that advance imaging techniques would be much needed to identify this subgroup of patient who could be beneficial for thrombolytic therapy.

Computed tomography (CT) scan has been the traditional method for acute stroke imaging with excellent sensitivity for acute intracerebral hemorrhage, but demonstrates limited sensitivity for detection of ischemic infarction, with a reported sensitivity of 40-60% only within 6 hours of onset, and a negative predictive value of 17% (von Kummer et al. 2001). Magnetic resonance (MR) imaging has no doubt superior spatial and contrast resolution as compared with CT, achieving higher sensitivity and accuracy. It has even emerged over last few years to become as sensitive as CT in depiction of acute intracranial hemorrhage (Fiebach et al. 2004; Kidwell et al. 2004). Perfusion-weighted imaging (PWI) and diffusion-weighted imaging (DWI) had played an influencing role since their introduction in late 1980s. Application DWI and PWI offer complex information regarding infarction and perfusion deficits, significantly improving the diagnostic yield. In a recent meta-analysis, Schellinger et al. (2010) found that the ability to correctly diagnose acute ischemic stroke on MR was significantly higher than CT, demonstrating an odds ratio of 25 ( $p < 0.0001$ ; confidence interval: 8-79). It also brings forward the concept of salvageable brain tissue as indicated by penumbra which is a rather dynamic entity that exists within a narrow range of perfusion pressures, carrying

significant implication on therapy selection and prediction of clinical outcome. The goal is to salvage the ischemic but viable penumbral tissue from progression into infarction.

## 2. Diffusion-weighted imaging

In DWI, the random motion or diffusion pulse of water molecules in a tissue compartment through a magnetic field gradient causes phase shifting leading to intravoxel dephasing and hence loss of signal intensity (Poustchi-Amin et al. 2001). In region of acute infarct or irreversible ischemia, the decreased diffusion of water molecules due to presence of cytotoxic edema (neuronal and glial cell swelling) from intracellular water accumulation and disruption of membrane ionic homeostasis will manifest as an increase in signal intensity, reflecting a decrease in apparent diffusion coefficient (ADC). ADC is “apparent” only because the actual measurement cannot be obtained by DWI due to presence of unmeasured variables that influence the rate of diffusion, such as temperature of the tissue and actual route of the diffusing molecule. Images are acquired sequentially with the axis of diffusion sensitization in three orthogonal planes, with their average yielding an image with minimal anisotropy-related hyperintensity. As a result, infarcted tissue appears bright in comparison with normal brain tissue. This has significant impact in helping to identify area of acute ischemia from chronic ischemic, and hence stratify treatment plan.



**Figure 1.** a) DWI shows hyperintense signal along bilateral posterior cerebral arterial territories. b) corresponding ADC map demonstrates hypointense signal.

In human, restricted diffusion showing increased DWI signal with reduced ADC value (Figure 1) have been observed as early as 30 minutes after onset of ischemia (Srinivasan et al. 2006). ADC continues to decrease for 3-5 days, reaching its minimum value of about 50% between 24-48 hours after symptoms onset before returning to baseline at approximately 1-4 weeks, so called pseudonormalization. At this stage, mildly hyperintense DWI signal with normalized ADC value will be seen. ADC increases afterwards with value higher than

normal value associated with variable DWI signal (from T2 effect) for upto months, presumably related to increased quantity of extracellular water. It is important to note that DWI signal can remain hyperintense for a long period (initially due to restricted diffusion but latter due to T2 shine-through effect) and cannot reliably estimate infarct age alone, while reduced ADC value almost always point to acute infarction. Yet, tissue with very low ADC value may recover and no single threshold can distinguish salvageable from unsalvageable tissue (Fiehler et al. 2002). Therefore we must interpret DWI with ADC maps together cautiously.

DWI-ADC carries high sensitivity (88-100%) and specificity (86-100%) in depiction of acute ischemia (Beaulieu et al. 1999; Gonzalez et al. 1999; Lövblad et al. 1997, 1998). However, with increasing cases of DWI-negative stroke reported and bearing in mind the existence of patient selection bias in the reported series, the true sensitivity probably lies between 80%-90% in general (Schellinger et al. 2010). In a prospective randomized study comparing between DWI and CT scan in evaluation of acute ischemic stroke, Fiebach et al. (2002) reported that the sensitivity of infarct detection was significantly better based on DWI (91%) than on CT (61%), achieving good interrater homogeneity and better accuracy even for readers with limited experience. This is due to relative insensitivity of CT for ischemia beyond 10ml per 100/min. as compared with DWI (Barber et al. 1999). False negative is unusual but is generally more common in posterior fossa stroke (Oppenheim et al. 2000) due to the presence of susceptibility artifacts from basal skull. Risk of hemorrhagic transformation is one feared complication and frequently asked question, especially when thrombolysis is contemplated. It had been postulated that a DWI lesion volume  $> 100\text{cm}^3$  was highly associated with hemorrhagic transformation, in particular when there was no associated DWI-PWI mismatch, hence contraindication to thrombolysis. However this would require further study for confirmation. Mixed results had been shown regarding the accuracy of baseline DWI in determination of final infarct volume. While it was widely thought that it would underestimate the final size of infarction (Yamada et al. 2002), Warach et al. (2000) in his double-blinded placebo-controlled study involving patients suffering from anterior-circulation stroke syndromes, found that baseline DWI lesion volume significantly correlated with baseline National Institute of Health Stroke Scale (NIHSS) scores and follow-up lesion volume at 12 weeks. Therefore, it is well established that DWI is accurate and superior to CT for diagnosis of acute ischemic stroke and can probably predict baseline clinical stroke severity as well as final lesion volume.

### **3. Perfusion-weighted imaging**

PWI provides information on hypoperfused area and momentary hemodynamic state of the brain tissue before structural brain tissue damage, therefore to identify areas of reversible ischemia early before it progresses to permanent infarction. It can be performed by exogenous method (dynamic or steady state susceptibility contrast-enhanced MR imaging by injection of MR contrast) or by endogenous method (arterial spin labeling by magnetically tagging water protons in arterial blood).

### 3.1. Mechanism

Dynamic susceptibility contrast-enhanced MR perfusion imaging involves rapid imaging with gradient echo or spin echo echo-planar imaging during the first passage of a paramagnetic contrast agent through the entire brain. 10 to 20 brain slices are usually repeatedly imaged immediately before and for 70 to 80 seconds after contrast injection, with 20 to 40 images per slice obtained. It makes use of the tissue signal changes caused by susceptibility ( $T2^*$ ) effects to generate signal drop (shortening of  $T2$  and  $T2^*$ ) and creates a hemodynamic time-signal intensity curve for each voxel, which in turns depends on cerebral blood volume and cerebral blood flow (Seevinck et al. 2010). It is through the dynamic monitoring of these signal changes in perfused tissue that hemodynamic parameters can be estimated. In contrary, steady state susceptibility contrast-enhanced MR perfusion allows estimation of blood volume, microvessel density and vessel size from the contrast-induced signal changes. Spin echo and gradient echo transverse relaxation rates are measured before and after contrast injection, typically with use of ultrasmall superparamagnetic iron oxide particles (longer half-life and higher susceptibility difference) from which parameters are derived (Wu EX et al. 2004). This method however is mainly of use in research level only.

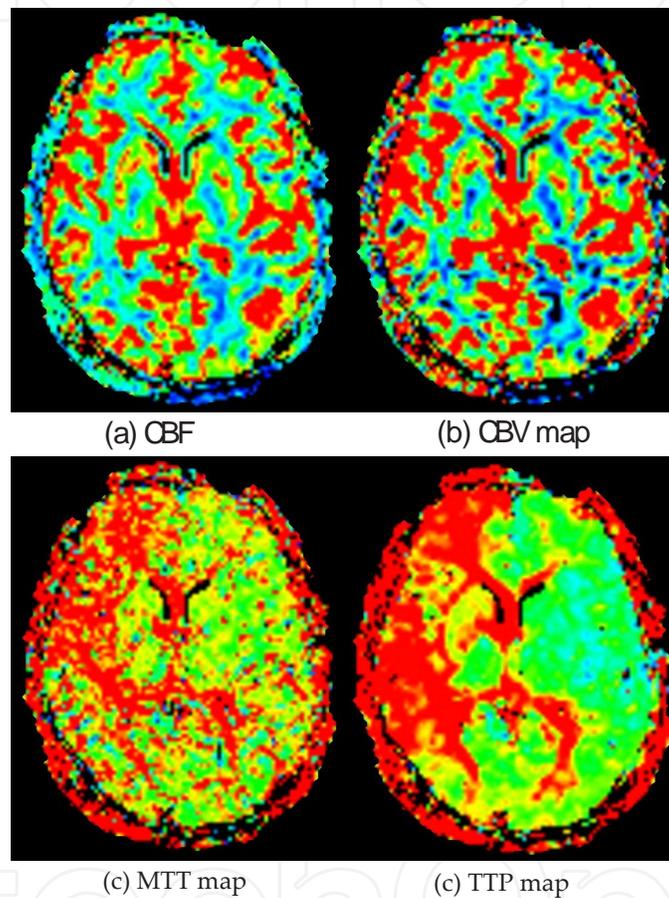
Quantification depends on measuring the signal intensity change within tissues which itself is the susceptibility effect of the contrast agent. The ram images are processed on a pixel-by-pixel basis to generate perfusion maps of different parameters. Time-to-peak (TTP) can be readily obtained by simple data processing from the tissue response curve. Cerebral blood flow (CBF), cerebral blood volume (CBV) and mean transit time (MTT) are time dependent parameters requiring utilization of computational deconvolution methods (such as singular value decomposition, circular value decomposition, Fourier transformation) with knowledge of arterial input function for quantification. The arterial input function is defined under visual control by drawing 5-10 intravascular voxels within the proximal & distal segments of the concerned artery of the unaffected hemisphere (Zaro-Weber et al. 2010a). Point to note is that these are relative values only due to variable confounding factors which will be discussed in later section.

Arterial spin labeling is a non-invasive method exploiting the spins of endogenous water protons to measure perfusion without the need of gadolinium. An inversion radiofrequency pulse is used to tag & invert the spin polarity of the flowing arterial protons with respect to stationary arterial proton, at a level proximal to the imaging slab (Deibler et al. 2008). The tagged spins then enter the imaging plane and exchange with tissue, allowing pair-wise subtraction to yield the perfusion map after acquisition of multiple runs for signal intensity averaging. The detected MR signals would be analyzed and perfusion parameters can be obtained. However, it has a low signal-to-noise ratio requiring longer imaging time.

### 3.2. Image analysis

Perfusion imaging is the method of choice for demonstrating ischemic brain tissue in hyperacute stage of stroke. The central portion with maximal perfusion abnormality will progress irreversibly to infarction while the outer area with only slight perfusion abnormality may recover (Hossmann 1994; Rohl et al. 2001). No single threshold has thus far been able to reliably

discriminate salvageable from unsalvageable tissue definitely (Wu O et al. 2006) since absolute quantification of cerebral perfusion is not really possible and perfusion thresholds change with time (Butcher et al. 2003). Interpretation is based on the concept that as CBF falls, CBV is initially unchanged or increased (from vasodilatation due to autoregulation) in conjunction with prolonged MTT and TTP. If such autoregulatory mechanism is exhausted, CBV will then decrease and CBF continues to fall to a level of irreversible ischemia with eventual infarction. Therefore a mismatch between MTT/TTP and CBV or CBF map indicates presence of potentially salvageable tissue (Figure 2).



**Figure 2.** Patient with right internal carotid artery (ICA) occlusion shows mild reduced a) CBF & b) CBV; but marked elevated c) MTT & d) TTP along right ICA territory.

### 3.3. Parameters threshold

Depending on different processing methods, differing results regarding the reliability and threshold of each parameter resulted. MTT or TTP delay relative to the contralateral hemisphere has been used in preference to CBF & CBV because of the more conspicuous changes and better correlation with initial stroke severity and change in infarct size, hence final functional outcomes in individual patient (Kane et al. 2007; Muir et al. 2006). In the contrary, pre-treatment lesions on DWI and ADC maps were non-discriminative.

### 3.3.1. Time-to-peak (TTP)

Restrepo et al. (2004) found that TTP map was most useful in demonstrating perfusion changes, showing good signal-to-noise ratio facilitating identification of lesion boundary, rendering it a parametric surrogate marker for efficacy of acute stroke treatment. A perfusion delay of 6 seconds relative to the non-affected hemisphere on TTP maps acquired before the initiation of stroke treatment helped predict the lesion size on T2-weighted images on day 8 irrespective of the treatment regimen (Kidwell et al. 2002; Nighoghossian et al. 2003; Seitz et al. 2005). Neumann-Haefelin et al. (1999) reported a TTP delay of >6 seconds best predicted final infarct volume while a TTP delay >4 seconds correlated best with acute stage neurologic deficit, signifying the true penumbra lies between 4 to 6 seconds. Kajimoto et al. (2003) depicted same result with a TTP delay of >4 seconds (sensitivity 79%, specificity 96%) in his study evaluating patients with chronic stroke. Sobesky et al. (2004 & 2005) validated these threshold values in patients with acute stroke, and demonstrated matched results when comparing with PET-derived data, also showing a TTP delay threshold of >4 seconds with sensitivity of 84% & specificity of 77%, and a penumbral volume threshold of >6 seconds. Takasawa et al. (2008) later reported a TTP delay threshold of >4.8 seconds which is also similar, as supported more recently, by Zaro-Weber et al. (2010a) showing a TTP delay threshold of >4.2 seconds best predicted penumbral flow, with a sensitivity of 91% and specificity of 82%. These consistent findings strengthen the TTP delay threshold to lie between >4-5 seconds.

### 3.3.2. Mean transit time (MTT)

Grandin et al. (2001 & 2003) reported a MTT delay of 8.1 seconds best predicted infarct growth whereas a MTT delay of 5.3 seconds defined the hypoperfused area that did not progress to infarction, to indicate oligemic tissue. Yamada et al (2002) supported the accuracy of MTT maps showing a sensitivity of 85-94% and positive predictive value of 54-61% for final infarct volume. Such results were in coherent with other studies, with Parsons et al. (2002) depicting a >6 seconds threshold, Bristow et al. (2005) depicting a >7seconds threshold, Takasawa et al. (2008) depicting a > 6-7 seconds threshold, and more recently, Zaro-Weber (2010a) demonstrating a >5.3 seconds threshold with a sensitivity of 88% & specificity of 78%. Therefore, we can conclude that a MTT delay between 5.3 -8.1 seconds denotes the true penumbra.

### 3.3.3. Cerebral blood flow (CBF)

CBF has found to be a good indicator of penumbral flow. Early study by Liu et al. (2000) revealed a cut off value of 48% of the unaffected hemisphere for depiction of penumbral flow. From positron emission tomography (PET) scan, it was found that neurological dysfunction occurred after CBF dropped below 20mL/100g of brain tissue per minute while infarction occurred shortly after CBF dropped below 10mL/100g of brain tissue per minute (Latchaw et al. 2003). Zaro-Weber et al. confirmed in two of his recent trials (2009 & 2010a) that threshold values of <20mL/100g/min (sensitivity 76%, specificity 96%) and <21.7mL/100g/min (sensitivity 89%, specificity 87%) respectively were of best estimate of penumbral flow, adding to its consistency and strength in validation. Therefore, a CBF between 10 -20mL/100g of brain tissue per minute becomes the intermediate zone and represents penumbral flow.

#### 3.3.4. Cerebral blood volume (CBV)

CBV shows the least correlation with penumbral flow with limited studies validating its penumbral threshold level in past literatures, especially in comparison with PET. Liu et al. (2000) depicted the threshold level to be 87% of the unaffected hemisphere while Hatazawa et al. (1999) found the threshold level to be 85% in their studies comparing with single photon emission CT (SPECT). Zaro-Weber et al. (2010a) recently, in the only study comparing with PET, found the penumbral threshold flow at  $<1.5\text{mL}/100\text{g}$  with a sensitivity of 82% and specificity of 79%.

### 4. Diffusion-weighted – Perfusion-weighted imaging

Ischemia is a complex and multifactorial process. Its clinical severity on initial presentation is a major determinant of clinical outcome, correlating strongly with the extent of the lesion. Proportion of patients with diffusion/perfusion mismatch and its size will depend on the severity of stroke and time delay to imaging. Based on the heterogeneity of the ADC and PWI values in depiction of ischemic lesion (Bandera et al. 2006), as well as occasional recovery of DWI-abnormal tissue (Davis & Donnan 2005), it becomes clear that it is unlikely any single DWI or PWI parameters or threshold values will reliably predict the degree of ischemia or infarct. Combination of diffusion- and perfusion-weighted imaging has revolutionized acute stroke imaging, allowing early & accurate delineation of the actual ischemic lesion or penumbra. Diffusion-perfusion mismatch is a quantitative and reliable measure with important pathophysiologic & therapeutic implications, becoming the surrogate of ischemic penumbra that provides valuable information for neurointervention planning, especially within the crucial therapeutic window. The Desmoteplase for Acute Ischemic Stroke and Dose Escalation of Desmoteplase for Acute Ischemic Stroke studies demonstrated that patients with PWI-DWI mismatches who were treated with desmoteplase experienced higher rate of reperfusion and better clinical outcome (Furlan et al. 2006; Hacke et al. 2005). Earlier studies by Parsons et al. (2001 & 2002) demonstrated greater recanalization, reperfusion and penumbral salvage in a group of patients with DWI-PWI mismatch compared with the control group in acute stroke patients treated with intravenous tissue plasminogen activator. Luby & Warach (2007) also found that mismatch volumes can provide highly reliable and consistent results with improved sensitivity. Early PWI lesions are typically larger than early DWI lesions. Finding of normal diffusion-weighted images and altered perfusion parameters (mismatch) is a simple and practical mean to define the tissue at risk, which correlates with poor clinical outcome (Derex et al. 2004; Parsons et al. 2002). If untreated or reperfusion does not occur, progressive enlargement of the DWI lesion over time is expected, signifying progressive infarction of the initial PWI lesion. This can be rapid in patient with poor collateral circulation. Conversely, a pattern of DWI lesion equaling the volume of PWI lesion indicates absence of penumbra or no salvageable tissue.

## 5. Reliability and pitfalls

The reliability of mismatch volume and percentage of measurements had been discussed though not extensively investigated. Obtaining precise parameters is one major problem as only the “relative” but not absolute perfusion changes can be measured due to presence of significant confounding factors, hence nowadays we mostly rely on the relative maps of perfusion. So, exactly how precise can the penumbral threshold be quantitatively estimated by CBF, CBV, TTP and MTT? What are the overall accuracy, reproducibility and reliability?

Firstly, perfusion imaging is sensitive to vascular delays (tracer arrival delay and tissue transit time) and dispersion effects (Calamante et al. 2002), especially in the derivation of the nondeconvoluted TTP map. Any minor physiologic change such as heart rate and cardiac output can potentially change the mismatch zone. Lack of standardization between MR machines, measurement technique or associated errors from pulse sequence parameters, image processing and analytic software are other major concerns. Measurement of arterial input function is particularly problematic with lack of standardized protocol in measurement of signal intensity around the artery. Besides, the tissue signal intensity does not demonstrate a linear relationship to tissue contrast concentration (Latchaw et al. 2003). Past studies attempted to optimize perfusion maps by venous output function (Knutsson et al. 2007), separated measurement of CBV (Newman et al. 2003), advanced mathematical correction (van Osch et al. 2003), partial volume artifact correction, and bulk-blood correction (Zaharchuk et al. 2009) but were found technically difficult requiring further validation.

We have to understand that considerable individual variation regarding the penumbral flow exists and absolute quantification of the perfusion maps is difficult. So far, perfusion maps had been mainly validated with respect to infarct delineation on follow-up MR imaging but with uncertainty of perfusion changes during the time interval in between (Zaro-Weber et al. 2010a). Improved validation had been made by direct comparison with PET for in vivo perfusion measurement in normal subjects and chronic cerebrovascular disease, but with only few in acute stroke setting (Grandin et al. 2005; Ibaraki et al. 2007; Lin et al. 2001; Ostergaard et al. 1998; Tanaka et al. 2006), raising uncertainty that such values may not precisely demonstrate the exact tissue at greatest risk of infarction, hence leading to misleading & unreliable interpretation (Keir & Wardlaw 2000). Despite so, PET-based calibration of perfusion imaging demonstrated superior result with best correction of the absolute perfusion values. Nevertheless, different post-processing algorithms differ, producing variations in lesion size and measured parameters. Indeed, ideal technique of perfusion imaging and its post-processing have not yet established. Zaro-Weber et al. (2010b) found that the variation of penumbral flow for each patient was high and hence with great error, emphasizing the need for an individual correction procedure or calibration with independent cohort. In a later study, he also found that the mean flow rate on contralateral hemisphere well explained the variability of individual perfusion thresholds such that it could be used to yield the best estimate of penumbral threshold. Based on these, a PET-validated look-up table was derived to calibrate the best individual penumbral threshold from the values of the contralateral hemispheric reference, allowing a much improved volumetric congruence. Linear regression analysis demonstrated

best agreement for TTP and good agreement for CBF and MMT while that for CBV was less pronounced. Despite this seemingly advantage, further validation (especially in an independent cohort) will be needed before its implementation in clinical use. In the meantime, standardization in both the data processing methods and software is also much needed. A consensus on which parameter is best to be used for prediction should also be made.

Arterial spin labeling has additional limitation regarding its own method, in that assumptions on tagging efficiency, delay time to imaging and flow quantification are based on normal population. Whether the same setting can be translated to various disease states has yet to be tested properly (Deibler et al. 2008). Besides, it has a relatively low signal-to-noise ratio, further adding to uncertainty in its accuracy. Therefore dynamic contrast enhanced susceptibility MR imaging technique is still the preferred method for quantitative perfusion imaging.

## 6. Transient ischemic attack

Transient ischemic attack should not be taken lightly as it carries a subsequent risk of ischemic stroke of 10% within 7 days and 30% within 90 days of symptoms onset, in particularly during the first 48 hours (Johnston et al. 2000; Mlynash et al. 2009). Subsequent risk of myocardial infarction, arrhythmia and congestive heart failure are increased. Hence appropriate prevention strategy is important in reducing the risk.

Establishment of the diagnosis of transient ischemic attack has been a major challenge since most patient present normal neurologically with resolution of the clinical deficit at the time of consultation and imaging, resulting in negative finding on conventional MR brain imaging. DWI & PWI can provide objective measurement of brain ischemia, even better than angiography as lesions are mostly small and may reflect occlusion of distal intracranial vessels that is angiographically occulted. Past studies demonstrated variable lesion depiction rate from 16 to 67% on DWI in patients with TIA (Crisostomo et al. 2003; Kastrup et al. 2002; Kidwell et al. 1999; Krol et al. 2005; Redgrave et al. 2007; Restrepo et al. 2004; Rovira et al. 2002) but it had been argued that these patients should be labeled as ischemic stroke with infarction rather, regardless of the duration of symptoms with a clinical implication of potential poorer clinical outcome. This was still much debatable as report had described complete resolution of both DWI and PWI abnormalities on follow-up images (Kidwell et al. 1999; Neumann-Haefelin et al. 2000; Rovira et al. 2002). Initial studies had also found that approximately one-thirds of the DWI lesions would normalized to a certain degree if they were imaged within a 3 hour time window (Fiehler et al. 2002; Kidwell et al. 2000). PWI should substantiate the yield given its ability to reveal hypoperfusion accompanying or preceding development of DWI abnormalities. Nevertheless, the occurrence of patients with positive PWI and negative DWI was variable, reported to be 3 to 33% (Krol et al. 2005; Mlynash et al. 2009; Restrepo et al. 2004). Ma et al. (2009) explained in his study model that the classical mismatch pattern would fragment with time due to a number of more random events such as variable ages & composition of the clots, random locations of vessel occlusion with consequent differences in vulnerability of tissue, and variable degree of collateralization from neighboring vessels.

Therefore, the yield is expected to be >50% if such patients are scanned urgently after symptom onset. It is useful in helping to identify a subset of patients with diffusion-perfusion mismatch who would require close observation, and possible further investigation such as angiography assessment which would then have a high yield (>50%) for detection of potentially relevant lesion, hence to assist in subsequent management. It helps to differentiate those that who are likely to improve or reverse spontaneously from those who are likely to progress.

## 7. Clinical impact

There is no true imaging gold standard in acute stroke. DWI has a well established role in depiction of acute infarction while it is also clear that perfusion imaging can provide information that cannot be depicted in other techniques, thus seemingly superior. After all, is there a role for perfusion imaging in affecting clinical decision making and hence, influencing patient outcomes? Previously, we have already discussed that perfusion-diffusion mismatch correlates with poor clinical outcome and that treatment of large perfusion-diffusion mismatch can result in improved clinical outcome. Such can lead to the attracting prospect of expanding the narrow therapeutic time window by selecting eligible patients via DWI-PWI mismatch, as demonstrated in various series & trials (Albers et al. 2006; Davis et al. 2008; Furlan et al. 2006; Hacke et al. 2005 & 2009; Parsons et al. 2002; Schellinger et al. 2007), but with lack of proper prospective study or strong evidence-based validation so far to support its role in alteration of patient outcomes. Beside, the exact role of perfusion imaging was often vague and its benefits in decision making were usually under-evaluated or retrospectively compared with clinical parameters only (Provenzale et al. 2008). Further, it is not yet established that patients without mismatch will be unresponsive to thrombolysis, since DWI lesions can potentially resolve as discussed previously. More importantly, nowadays in most stroke centers, decisions for administration of thrombolytic agents in patients suffering from acute ischemic stroke are often made without prior perfusion imaging, nor even diffusion imaging. Decisions are routinely made on clinical ground in particular for those presenting at <4.5 hours, raising doubts over its added value. This is perhaps the main reason for lack of literature addressing the influencing role of perfusion imaging in decision making of thrombolysis. In addition, the feasibility and practicality of MR imaging in acute stroke assessment are always in doubt. Clearly, time is an important factor. The whole process of perfusion imaging together with subsequent data analysis can be time-consuming especially in less experience hands. After all, routine use of PWI to assess acute ischemic stroke is open to dispute. Until we have a compelling randomized prospective blinded study assessing the efficacy of perfusion imaging in decision making in assessment of acute ischemic stroke, perhaps the most convincing role at present is prediction of final infarct volume which demonstrates strong correlation, and hence helping to predict the clinical outcome in individual patient. On the other hand, it can also be of great use in monitoring of evolution of ischemia and subsequent therapeutic response. Despite these seemingly limitations and arguments on methodical issues, many believe that the accumulated evidence of the importance of DWI-PWI mismatch is already good enough to establish a role in daily practice if allow.

## 8. Conclusion

With advances in imaging technology, there is substantial evidence and data to support the feasibility & superiority of MR imaging in acute ischemic stroke. PWI is complementary to DWI in acute stroke assessment. DWI-PWI mismatch provides a good, rapid & reliable estimation of the penumbra, helping to select suitable candidate for acute thrombolytic therapy, especially for patients presenting with unknown onset time or beyond the 4.5 hours therapeutic window. PWI lesion can resolve rapidly after successful thrombolysis or reperfusion, leading to improved clinical outcome. Only then will we know for every individual patient, at certain time after stroke, with particular clinical features and parameters on DWI/PWI, which will be the best clinical management.

## Author details

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