**Use of contrast agents in functional imaging techniques: Perfusion or Dynamic contrast-enhanced MRI vs non-enhanced techniques**

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**Introduction**

There are two basic techniques for measuring brain perfusion using MRI. The most widely used technique is by far Dynamic Susceptibility Contrast (DSC) enhanced perfusion, in which a bolus of a chelated paramagnetic contrast agent (usually Gadolinium) is rapidly injected through a large catheter and flowed using a rapid imaging sequence, usually a gradient-echo or spin-echo EPI technique. In this technique, the contrast agent is thought to stay within the vasculature, and as such, can be referred to as an intravascular perfusion technique (for reviews, see (1,2)).

Arterial Spin Labeling (ASL) on the other hand uses magnetically labeled water protons as an endogenous tracer. The basic scheme in ASL is very simple, and consists in two subsequent acquisition: a labeling one, during which the arterial water spins are labeled proximally to the region of interest; and a so-called control acquisition, during which the arterial water magnetization is left untouched (for reviews, see (2,3)). Since the endogenous labeling tracer used in ASL is water, it can be considered as a free diffusible agent, and will almost instantaneously leave the intravascular space when the labeled bolus reaches the tissue.

**Perfusion parameters**

Now, both methods provide different estimates of perfusion, and different parameters linked to this concept. Generally, Gadolinium is thought to provide estimates of cerebral blood volume (CBV), blood flow (CBF), mean transit time (MTT=CBV/CBF), as well as vascular parameters such as time to peak of the bolus (TTP) for example. On the other hand, ASL is generally considered to be providing mainly (if not only) CBF. Indeed, as it uses a free diffusible tracer, there is no way to get an estimate of CBV, as the tracer cannot differentiate between the intra- and extra-vascular spaces. As such, it is also impossible to get an estimate of the “mean transit time” as defined earlier. However, by being slightly more inventive in the sequence used, one can also gather some other parameters, such as territorial (or selective) labeling of various vessels independently (4). Furthermore, by using similar techniques as those used in DSC, that is by following the bolus of labeled arterial water, one further get related vascular parameters, such as arterial transit time (ATT – time taken by the blood to reach the tissue from the time of labeling), or even arterial blood volume (aBV), by looking at the difference between the ASL signal with and without crushing of all arterial signal (5). So, in summary, both techniques can
actually provide quite some information on the amount of blood reaching a particular tissue and its timing characteristics.

Advantages and Drawbacks

DSC has some advantages over ASL. First, it is a much higher SNR method, and therefore, can provide whole organ perfusion in usually around one minute. ASL has made great progresses in the last couple of years, but it is still a SNR-limited technique, and therefore requires longer scan times (typically ~8-10min at 1.5T and 4-5min at 3.0T), at the cost of potential motion artifacts.

But ASL has some benefits over DSC in that it is a truly non-invasive quantitative method, capable of providing absolute CBF measurement, while DSC is by definition invasive, requiring the injection of an exogenous contrast agent through a high gauge catheter, and is still struggling with the issue of quantification, mainly due to the lack of direct linear relationship between contrast concentration and signal changes, especially in the presence of partial volume effects (6). As such, ASL can be repeated over time, for measuring signal changes due to functional or pharmacological challenges for example, and can be used in patients where the use of gadolinium chelates might be restricted, such as in children, in patients undergoing chemotherapy or with kidney insufficiency (because of the risks of nephrogenic systemic fibrosis or NSF).

ASL can also be made insensitive to transit time delays (2,3), but will still show artificially reduced CBF in case of very late arrival time of the bolus as in the presence of collateral perfusion, and this is not a problem for DSC by its very nature. Another typical artifact found in both methods is related to the presence of intravascular tracer concentration. In that respect, ASL can deal with this artificial signal slightly better than DSC, as many implementations have been made using vascular crusher gradients, inefficient in DSC, or depending on the technique, simply by waiting long enough for the arterial blood signal to disappear before acquiring the ASL signal (2,3). Finally, ASL ash the possibility to provide estimates of the perfusion territories of individual arteries, which is not the case for DSC (4).

Conclusion

In summary, non contrast-enhanced based methods provide an interesting alternative to DSC for the measurement of perfusion, and can be actually implemented in a rather easy way into any clinical protocol, only requiring an additional few minutes, as has been done for example at Wake Forest (7-9). Generally, it is expected that specific applications will still require the use of Gadolinium contrast agents, such as super-acute stroke imaging, where both SNR and speed are of paramount importance, but for many other cases, alternative techniques such as ASL might fulfill the bill just as well, with less hassle, requiring less preparation and being ultimately also cheaper.

References