Brain arteriovenous malformations: The long way ahead in physics, chemistry and MR-Angiography practice before fully replacing digital subtraction angiography.

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Publication type: Invited Editorial

Cite this article

Sarkar S. Brain arteriovenous malformations: the long way ahead in physics, chemistry, and MR angiography practice before fully replacing digital subtraction angiography. Eur Radiol. 2023 Oct;33(10):7136-7138. doi: 10.1007/s00330-023-10063-x. Epub 2023 Aug 15. PMID: 37581665.

Brain arteriovenous malformations: The long way ahead in physics, chemistry and MR-Angiography practice before fully replacing digital subtraction angiography.

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Abstract

Typically, only high field systems are equipped with stronger gradients and short RF pulse designs, a must for high temporal resolution that are also responsible for high SAR, high susceptibility as well as neurostimulation. Gradient induced image noise tends to be high at 3T. Often vendors try to ameliorate such increased image noise with multi-channel head arrays and aggressive filter designs allowing an appearance of high SNR and CNR quality; however, the achievable SNR and CNR in the AVM remain limited as the analyzed articles by Zhuo et al seem to have in common. A short term solution to harvest advantages of high fields with acceptable T2 loss may be to use fast 3D shimming to generate a high degree of homogeneity in the operator selected AVM tissue. In addition, to avoid susceptibility increase at high fields by the contrast pooled into neovasculature, not only for AVM but also for other vascular imaging applications, improved CM design need to accompany any such robust shimming routines. Until that and more are achieved, DSA may retain its superiority in the follow-ups of treated AVMs.*

Zhuo et al have compared the 3D and 4D contrast enhanced magnetic resonance angiography (CE-MRA) from carefully screened seven prior works [1]. Their summary and conclusions are in favor of 3D CE-MRA and show higher sensitivity from 3D than from 4D datasets that should raise reader concern as well as their interest. The articles that Zhuo et al have analyzed also did not find any significant advantage of high field compared to 1.5T other than a slightly better time resolution. The MR vendors and clinicians may need to confirm or confront such analysis. Zhuo et al have correctly listed probable causes of such a pattern. In this editorial, plausible explanations with a focus on transmetallation of contrast media (CM) and the susceptibility challenges from high fields in imaging technique development are pointed out.

This editorial mostly agrees with the work of Zhuo et al as a valuable summary of where 3D MRA stands but finds it necessary to project what to expect from MRA going forward in near future. There are two excellent AVM works from AJNR [2, 3] that point out to an encouraging development, albeit, both have some drawbacks as will be noted here. Those had demonstrated the utility of non-contrast arterial spin labeling MRA (ASL-MRA) as a strong and complementary tool to increase the reliability of 4D time-resolved CE-MRA. While the MRA developments have pursued sparse scanning of k-space and potentially higher signal from higher magnetic fields for speed, the geometry of the AVM vessels and the nature of contrast media within such geometries have not been adequately explored. A key ingredient to ensure accuracy using any of the data skipping tools like parallel

imaging and echo-sharing to treated AVM geometries, is some kind of a priori knowledge about changes in AVM geometry (vessel morphology), but also importantly, the tissue chemistry with time and treatments. Morphology prediction may be possible with AI algorithms to iterate a user-supplied a priori input to both CE-and-ASL MRA. One may note that contrast chemistry in a radiated tissue is inadequately understood today and the quality loss in terms of magnetic susceptibility increases as we bring in high and ultra-high fields and paramagnetic particles at high density to produce MRA. In simple terms, the goal of CE-MRA is to use Gd-CM to create large and reproducible differences in spin-lattice relaxation times (T_1) among arteries, veins and other tissues without losing signal due to transverse spin-spin relaxation in presence of inhomogeneities (T_2* induced) that may lead to wrong conclusion about AVM recurrence.

However, abnormal, entangled vessels and dilated draining veins within AVMs pose both structural and flow imaging bias for any CM. The vessel size distribution, flow directions and artery vs vein fractions are not known a priori. A high-quality CE-or-ASL MRA protocol (3D or 4D) requires standardization that is not biased to a particular tissue geometry nor vary from patient to patient for the same indication. Unfortunately, it is hard to find such a CM that is equally sensitive to straight and entangled geometries. Contrast-filled vessels with turbulent flow are paramagnetic tubes that respond to static and pulsing magnetic fields differently when placed at different angles. So non-contrast ASL-MRA has a unique advantage but ASL solutions also depend on a priori knowledge of vessel geometry in order to place ASL prep slab and optimize ASL parameters.

It is also important to pay attention to radiosurgery induced MRI signal changes observed by multiple workers. One explanation could be that both signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) in and around the AVM depend on the presence of (A) native or endogenous metal ions as explored in an in-vitro contrast work [4], (B) residual prior CM (iodinated or Gd) and (C) excess reactive species generated post-radiosurgery [5]. It is natural for most of the CM to extract biometals over time from the target AVM tissue and from nutrients available in vascular architecture affecting local T_1 and T_2^* relaxation times. Morales et al [6] have identified that iodinated CM (for example, from prior CT or DSA) can shorten T_1 and T_2^* relaxation times at both 1.5T and 3T and a mechanism via chelation reaction of endogenous paramagnetic biometals has been suggested for ligands in X-ray CM that explains work of Morales et al [4]. To minimize the role of residual Gd from prior CE-MRAs one may explore better strategies to deliver Gd. Note that transmetallation with endogenous Calcium as well as with Fe^{3+} or Mn(II-IV) remains a valid concern [4]. It has been suggested that the size of Gd^{3+}, being exactly the same as that of Ca^{2+}, is the key reason for Gd toxicity for Calcium binding proteins [7]. On the other hand Gd-CMs, although vastly improved in macrocyclic geometries, are still unstable and seem to transmetallate with available metal ions (Fe^{3+} or Mn(II-IV), Ca^{2+}) in acidic or hypoxic environments [4]. Increased expression of membrane-bound enzymes such as Carbonic Anhydrase (CA) catalyzing hydrated carbon

dioxide (CO_2) to protons (H^+) and bicarbonate (HCO_3^-) ions in the irradiated tissue have been suggested [5]. Shortened T_1 and T_2 relaxation times (and hence also T_2*) often show MR signal changes after radiosurgery and most likely cause the overestimation of the diagnostic sensitivity of 3D-MRA at 1.5T (that is less sensitive to those relaxation time changes) with more severe SNR and CNR loss at 3T [8]. Abnormal contrast enhancement has been observed even after 2 years in 70% of radiation treated AVM regions [9]. Hence chemistry of CM and physics of morphological changes together may explain the poor high field performance conclusions in the work of Zhuo et al.

The advancements in high field (3T and 7T) along with sensitive RF coils and performance gradient designs can offer higher spatial and temporal resolution but the loss of CNR even for simple phantoms is evident when low flip angle radiofrequency (RF) pulses are used [10]. This is partially due to a common specific absorption rate (SAR) mitigating trend in the industry practiced by all vendors for the past decade that may need to be more carefully implemented with further research at high fields as shown by Sarkar et al [11]. Zhuo et al have reached to a similar conclusion for the loss of CNR in the high field CM appearance in AVM environment but have not tried to explain in terms of magnetic susceptibility or contrast chemistry. The Gadolinium-based contrast media (Gd-CM) assume that T_1 relaxation benefits for SNR and CNR will outweigh the susceptibility induced signal loss due to the exponent TE/T_2*, where TE is the echo time. If the MRA no longer remains a T_1-weighted sequence and the condition T_2*>>TE is no longer fulfilled at high fields then one may have to reconsider using lower fields.

Typically, only high field systems are equipped with stronger gradients and short RF pulse designs, a must for high temporal resolution that are also responsible for high SAR, high susceptibility as well as neurostimulation. Gradient induced image noise tends to be high at 3T. Often vendors try to ameliorate such increased image noise with multi-channel head arrays and aggressive filter designs allowing an appearance of high SNR and CNR quality; however, the achievable SNR and CNR in the AVM remain limited as the analyzed articles by Zhuo et al seem to have in common. A short term solution to harvest advantages of high fields with acceptable T_2* loss may be to use fast 3D shimming to generate a high degree of homogeneity in the operator selected AVM tissue. In addition, to avoid susceptibility increase at high fields by the contrast pooled into neovasculature, not only for AVM but also for other vascular imaging applications, improved CM design need to accompany any such robust shimming routines. Until that and more are achieved, DSA may retain its superiority in the follow-ups of treated AVMs.

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