Time-of-Flight MRA at 7 Tesla

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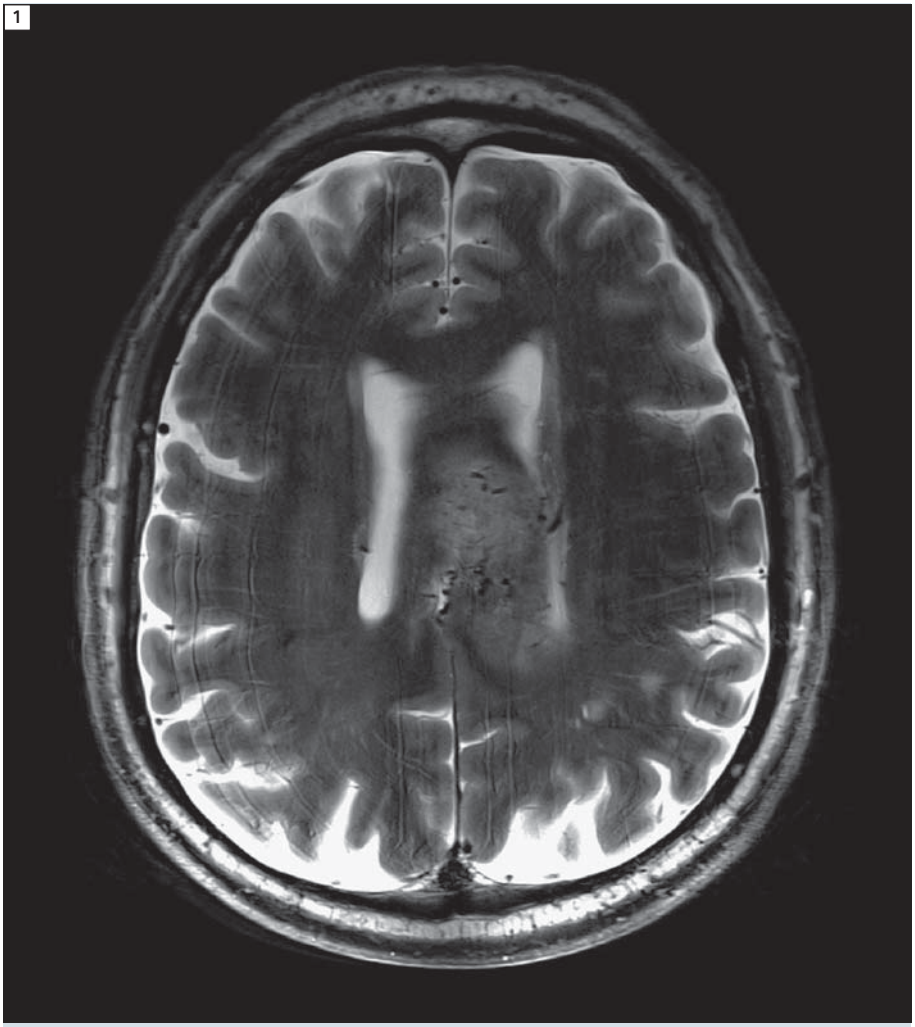


1 T2w TSE image with 300 µm in-plane resolution of a 70-year-old patient with a glioblastoma. The central lesion is visualized with excellent detail, in particular the internal venous vascular network.

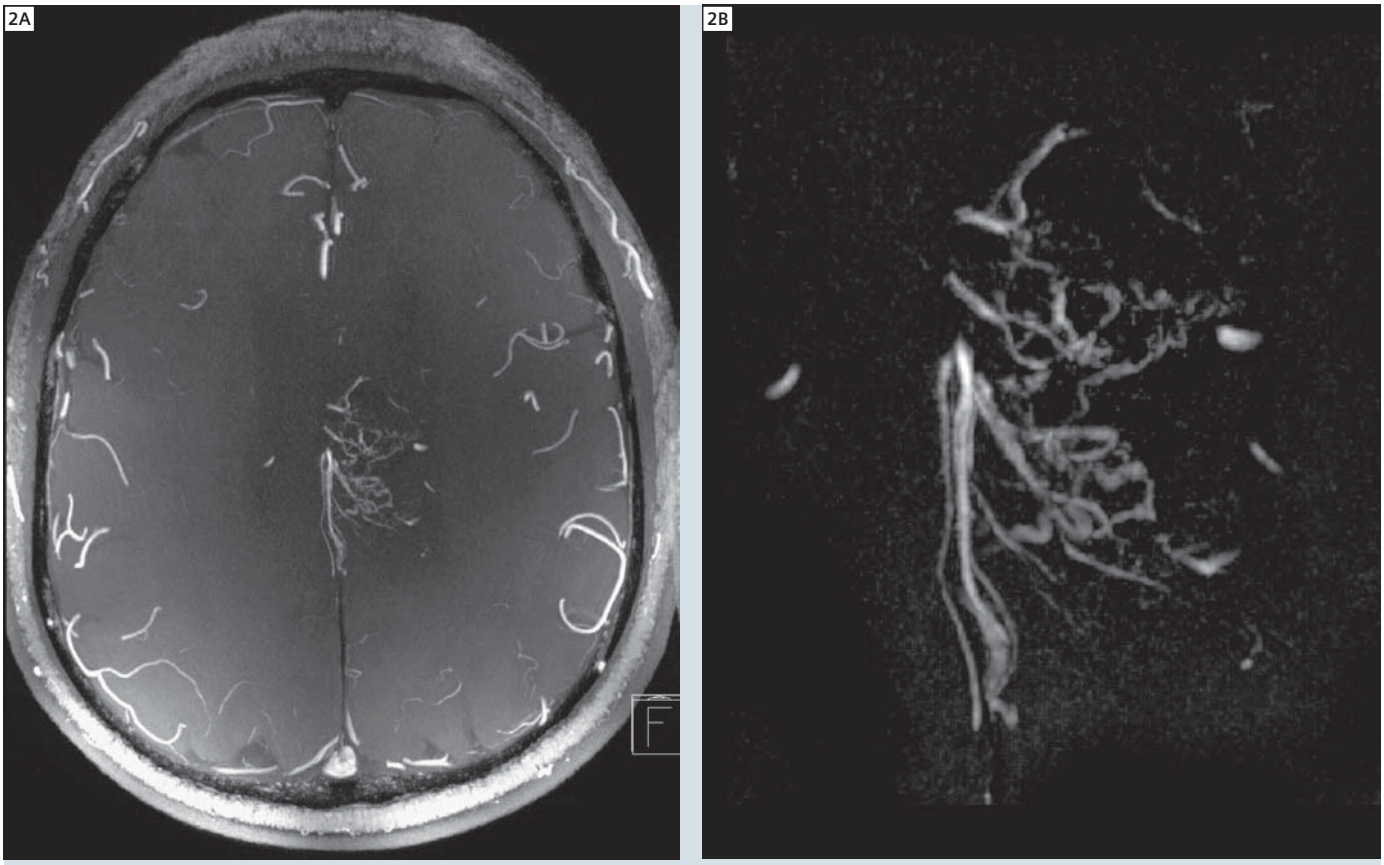
Introduction

Over the recent 10 years more than 20 whole-body high field MR systems with field strengths exceeding 4 Tesla have been installed worldwide. The majority of these systems operate at a B_0 of 7 Tesla; however, already four 9.4 Tesla systems are in operation, and an 11.7 Tesla installation in Paris is expected to be finished soon.

The increased signal and the specific new contrasts available at higher magnetic field strengths have been used in various applications. The higher signal strength has been utilized to acquire high-resolution morphologic MR images with 200 µm in-plane voxel size. The enhanced susceptibility difference between oxygenated and de-oxygenated blood, which increases the BOLD contrast nearly linearly with field strength, has been exploited in neuro-functional MRI studies. The prolonged longitudinal relaxation time of blood has been used in arterial spin labeling perfusion studies to visualize the tagged blood for a longer time during the passage through the tissue. Finally, high field MR systems have allowed acquiring spectroscopic data sets with a better spectral differentiation of the individual metabolites.

Time-of-Flight MR Angiography (TOF-MRA)

One particular application that has been shown to profit from higher field strengths is time-of-flight (TOF) MR angiography [5, 16, 10, 7]. In TOF-MRA

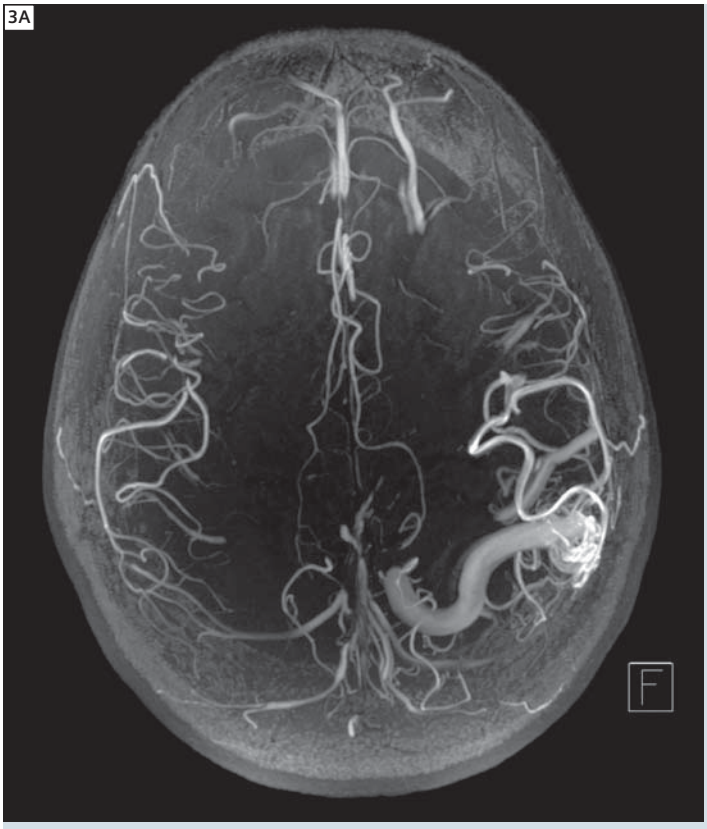


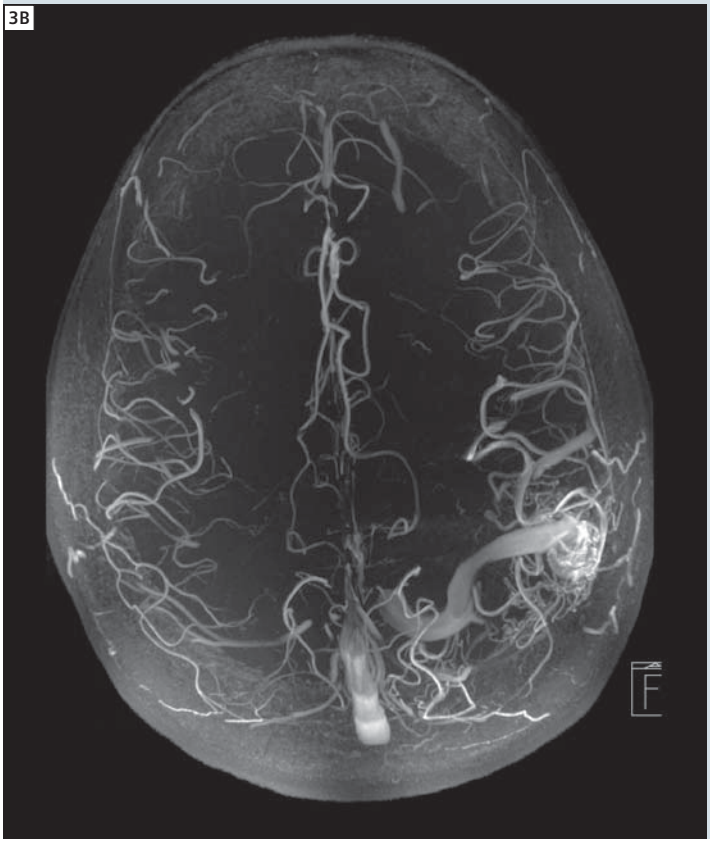
2 Targeted MIP image of a 3D TOF-MRA data set from the same patient as in Fig 1. The irregular tumor-supplying vessels are clearly visualized in the high-resolution MRA data.

use is made of the signal difference between the unsaturated blood flowing into an imaging slab and the partially or fully saturated signal of the static tissue surrounding the blood vessels. The 3D TOF-MRA data sets show the vessels against a dark background, and for data post-processing and visualization typically maximum intensity projections (MIP) are calculated. TOF-MRA is preferably used in the delineation of the arterial intracranial vessels, because the direction of the flow from the arteries in the neck into the skull is clearly defined. Furthermore, in the brain long image acquisition times of 5 to 10 min are possible due to the lack of patient motion. To acquire the TOF-MRA data sets 3D spoiled gradient echo (FLASH) pulse sequences are applied with flow compensation in all three directions to minimize flow-related signal voids in the vessels. In TOF-MRA not a single thick 3D imaging slab is used as in morphologic 3D imaging, but multiple overlapping thin slabs (MOTSA) are sequentially acquired to reduce the progressive saturation that the blood experiences during its passage through the imaging slab. To further reduce this saturation effect, the flip angle is often increased over the slab (Tilted Optimized Nonsaturating Excitation, TONE) which leads to a nearly constant signal for those blood spins that traverse the slab at a predefined velocity. Furthermore, magnetization transfer contrast (MTC) pulses are applied to selectively saturate the static tissue and thus to increase the vessel-to-background contrast.

Theoretically, TOF-MRA profits twofold from higher field strengths. First, the increased MR signal allows reducing the voxel size so that smaller vessels can be delineated. Unfortunately, the SNR increase is scaling only linearly with field strength, whereas the increase in spatial resolution – if isotropic – reduces the signal by the third power of the linear voxel dimensions (Δx). Thus, to maintain the SNR, with an increase of the field strength by a factor of 2.3 (e.g. from 3T to 7T) Δx can theoretically only be reduced by a factor of $\sqrt[3]{2.3}$=1.3. Fortunately, this argument is only valid if the signal within the voxel is homogeneously distributed – in TOF-MRA, small blood vessels can occupy only a fraction of the voxel volume (partial volume effect), and thus a reduction of Δx does not necessarily reduce the amount of signal-emitting spins from blood. In practice, the linear voxel dimensions are therefore often reduced further than the theoretical limits given above.

A second advantage of higher field





3 Comparison of a 3D TOF-MRA of a 33-year-old AVM patient acquired at 3T and at 7T. In the 3T data the arterial feeders of the AVM appear with a stronger signal, but they are also clearly seen at 7T. Smaller vessels in the AVM nidus are better delineated at 7T demonstrating the complexity of the vascular network. Note that at 7T no venous suppression was applied due to SAR constraints and, thus, the sagittal sinus remains visible.

strengths is the increase of the longitudinal relaxation time T1 with B_0. For the same imaging parameters, longer T1 values lead to a lower FLASH steady state signal of static tissue, and tissue background suppression is becoming more effective. At 3 Tesla, the T1 of white brain matter is 840 ms [17], which increases to 1130 ms at 7 Tesla. For typical TOF-MRA imaging parameters of TR = 15 ms and $\alpha = 20°$ the FLASH signal of white brain matter is then reduced by 22%. At 7 Tesla the background signal constitutes only 18% of the blood signal, so that it often becomes indistinguishable from noise. Note, that this estimate is only valid near the entry of the vessel into the imaging slab where the blood signal has not experienced any RF excitations. The longer the blood remains in the slab the more it gets saturated. Since the blood T1 is also prolonged at higher field strengths this saturation significantly reduces the contrast-to-noise ratio along the path of the blood vessel [3].

Challenges of TOF-MRA at high magnetic fields

The implementation of TOF-MRA protocols at high magnetic fields is challenging due to a number of different problems. At tissue boundaries the static gradients caused by the susceptibility differences have to be compensated by the imaging gradients to avoid local image distortions. In TOF-MRA of the brain this effect is noticeable near the nasal cavities where tissue-air interfaces are present, but it is less pronounced in the brain itself, which has a relatively homogeneous susceptibility.

A more severe limitation is given by the increased energy deposition of the RF system – to achieve the same flip angle as at 3 Tesla the amount of RF energy at 7 Tesla needs to be increased by a factor of $(7/3)^2 = 5.3$. Thus, energy-intensive RF pulses such as MTC pulses cannot be applied due to regulatory constraints (i.e., specific absorption rate or SAR limits). Since background suppression is

already very effective at higher fields, the omission of the MTC pulses is no fundamental problem. Another sort of RF pulse, however, is also difficult to integrate due to the SAR limitations: parallel saturation slab pulses, which suppress the signal from venous blood to avoid venous signal overlay in the MIP reconstructions.

Fortunately, there are several options to integrate saturation pulses into TOF-MRA sequences that lead only to a limited increase of the time-averaged SAR. The saturation pulses can be applied less often than the normal excitation pulses – if e.g. the saturation pulse is inserted only after every 10th k-space line, this significantly reduces the total SAR of the pulse sequence. One drawback of this implementation is the reduced saturation efficiency which can lead to non-vanishing signal in veins with a moderate to high blood flow velocity.

Another method to reduce the RF energy of a pulse is given by the variable rate selective excitation (VERSE) technique [2]: here, use is made of the fact that only a certain fraction of the pulse (typically, the so-called main lobe) is contributing most to the SAR of the RF pulse. By selectively reducing the RF amplitude in combination with the gradient amplitude the duration of the RF pulse is only moderately increased, but a substantial reduction in RF power is achieved. In principle, VERSE can be used with every slice-selective RF pulse, and so a SAR reduction can be achieved both for the normal slab-selective excitation pulse as well as for the 90° saturation pulses [6]. VERSE requires a very good synchronization of the gradient activity with the RF pulse modulation, it increases the sound pressure levels [13] and it makes the RF pulse more susceptible to off-resonance effects due to the lower gradient amplitudes [12]. Thus, in practice a compromise between SAR reduction, off-resonance susceptibility and gradient noise needs to be found.

Clinical applications of TOF-MRA at 7 Tesla

In the following two clinical applications of TOF-MRA of the brain are presented, that profit especially from the increased spatial resolution provided by the higher field strength: imaging of tumor blood vessels and of arterio-venous malformations.

Tumor vasculature

The growth of highly malignant brain tumors is facilitated by the ability to induce neoangiogenesis to maintain the supply with nutrients. This is mainly achieved by expression of several growth factors, the most important being vascular endothelial growth factor (VEGF) [8]. Neoangiogenesis leads to a higher microvascular density inside the tumor. Modern therapies target the factor mediated signaling cascade to inhibit neoangiogenesis. One of the most recent agents is Bevacixumab (Avastin), a monoclonal antibody against VEGF [15]. Alternatively, radiotherapy and radiosurgery target the neovasculature of the tumor.

High-grade brain tumors often show a diffuse network of blood vessels, which are less organized [1], more tortuous and of more irregular diameter than normal brain vessels. During tumor growth, the vascular pattern changes from regularly shaped vessels as found in normal tissue to more dilate and higher caliber vessels as well as glomeruloid vessels in glioblastoma [1]. This reorganization leads to a decrease in microvascular density, i.e. the number of vessel cross sections in a given area, but an increase in the mean area occupied by vessels. As the size of the induced microvessels is usually below the detection limit of MRI at 1.5 or 3T, perfusion MRI markers like relative cerebral blood volume (rCBV) or relative cerebral blood flow (rCBF) have been investigated. Whereas a differentiation of lower and higher grade tumors according to their rCBV and rCBF levels is usually possible in large patient groups, due to the limited reproducibility of perfusion MRI it is difficult to use them for follow-up examinations in clinical routine. In addition, VEGF also increases vascular permeability, leading to an extravasation of contrast agent into the tissue, which is not accounted for in most perfusion models. With conventional MRI at 1.5T or 3T the small 100 µm to 300 µm vasculature is not directly visible due to limitations in both spatial resolution and SNR. At 7 Tesla TOF-MRA can be applied with a spatial resolution of 300 µm and better. In combination with an excellent background suppression of the signal from static tissue this higher resolution is capable of visualizing the neovasculature of malignant brain tumors. In Figure 1, a T2w 7 Tesla image of a 70-year-old patient with an astrocytoma WHO grade IV (glioblastoma) is shown. The lesion is visualized with very good contrast in both T1 and T2-weighted images, and the heterogeneous interior is clearly resolved in susceptibility-weighted images that particularly highlight the venous vasculature [4].

In the TOF-MRA data of the same patient the arterial vasculature is highlighted (Fig. 2), and the highly anomalous vessels are seen - this vascular network can clearly be identified as neo-vasculature because of its irregular shape and surplus vessels not found in normal brain parenchyma. The following imaging parameters were used: TR 15 ms, TE 4.8 ms, flip angle 19°, TONE setting 70%, parallel imaging GRAPPA 2x, bandwidth 165 Hz/pixel, matrix 516 x 704, FOV 14 x 200 mm², 4 slabs, partition thickness 410 µm, TA 4x 2:34 min. At a lower field strength this vessel network could not be visualized. Thus, there is first evidence that therapies targeting neo-angiogenesis might be better assessed with high-resolution TOF-MRA providing comparable results than the different perfusion imaging techniques.

Arteriovenous malformations (AVM)

Arteriovenous malformations are congenital vascular lesions that arise during the embryonic stage from capillary dismorphogenesis. As a consequence, AVMs manifest as one or more arteries that feed a nidus of abnormal vessels instead of the normal capillary bed, and

which are then drained by one or more veins. AVMs are the cause of 1–2% of all strokes, and have a 2–3% risk of hemorrhage [9]. TOF-MRA can provide an overview of the architecture of the AVM, and it helps to identify abnormally dilated feeding and draining vessels. At present, X-ray digital subtraction angiography is still considered the gold standard for AVM imaging due to the higher spatial resolution that allows identifying very small feeding vessels.

With TOF MRA at 7 Tesla the feeding arteries, the nidus and the draining veins are excellently visualized (Fig. 3). Compared to TOF-MRA data acquired at 3T, at first glance no significant difference between the 3T and the 7T data is visible. However, the more detailed visualization of the small sub-millimeter vasculature of the nidus at 7 Tesla becomes apparent. If not operable, AVMs are treated either by embolisation to occlude the feeding arteries, or with radiation therapy to initiate an endothelial reaction which will gradually reduce the free vessel lumen and thus increase the vascular resistance. With the high spatial resolution provided with TOF-MRA, which is delineating the free vessel lumen, the slow lumen reduction of the feeding arteries might be visualized directly, so that treatment-related changes in the angioarchitecture can be identified at an earlier stage.

A quantitative comparison between the 3T and the 7T data is difficult, because different RF coils were used for data acquisition. At 3T, the MAGNETOM Tim Trio system's 32-channel receive-only head coil was used, whereas at 7T a 24-channel transmit receive coil was applied. Due to the intrinsic transmit inhomogeneity at 7 Tesla, a spatially varying contrast is seen in the 7T TOF data, because the flip angle decreases from the center of the coil (where flip angle calibration was performed) to the periphery.

Conclusion

Time-of-flight MRA benefits from the increased SNR and the different contrasts available at higher field strengths. The increase in spatial resolution is particularly beneficial for the assessment of intracranial lesions such as AVMs and high-grade gliomas.

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