fMRI in Presurgical Planning at 7T

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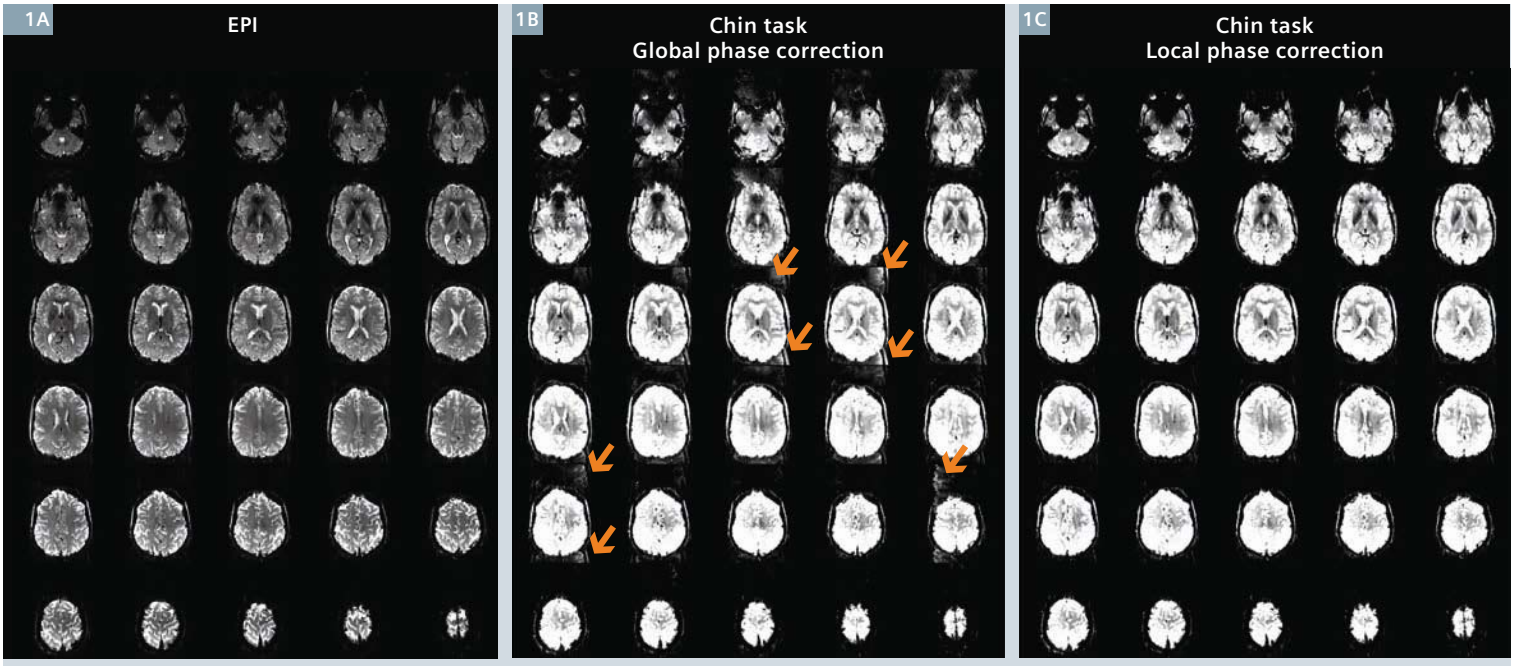
Functional Magnetic Resonance Imaging (fMRI) can be used to define brain regions which must be left intact when patients undergo surgery. Critical function is mapped with fMRI using a relevant task [1], generally presented in a simple block design and repeated a number of times. The localization of essential function needs to be reliable and accurate; some literature indicates that a shift of resection margins by only 1 mm close to eloquent brain areas may determine whether postoperative deficits are reversible or permanent [2].

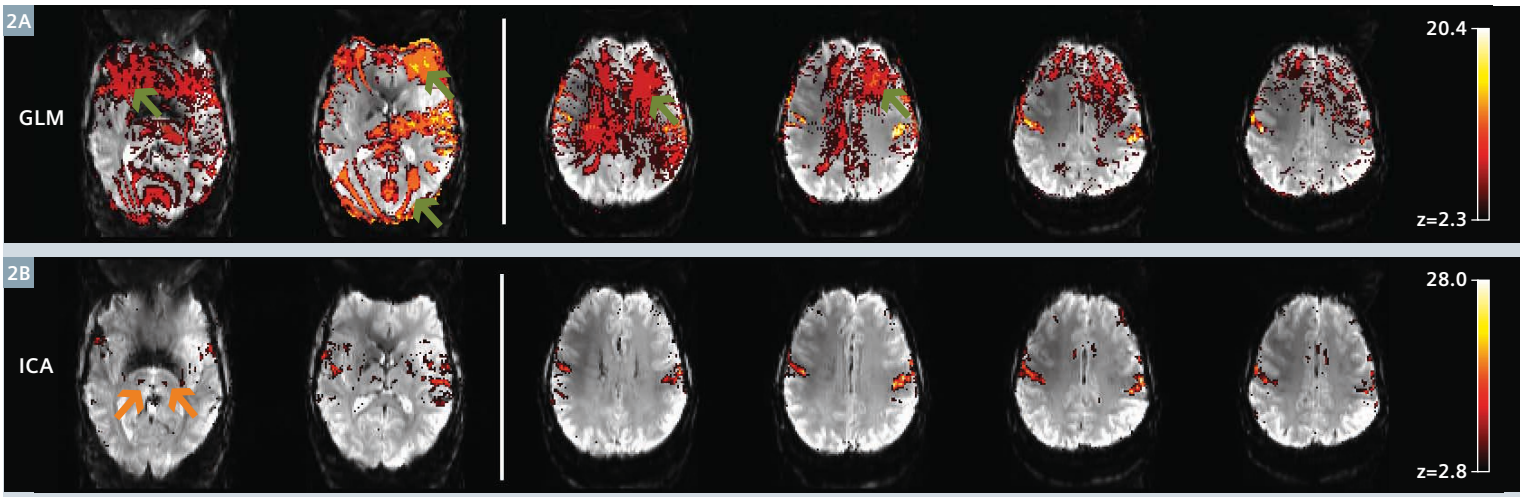
High signal-to-noise ratio (SNR) at ultra-high field provides elevated sensitivity to BOLD signal changes as has been demonstrated both in healthy subjects [3, 4] and, more recently, patients [5]. Increased BOLD sensitivity allows resolution to be increased and very weak activation to be detected in previously undiagnosable patients with large and rapidly evolving tumors and complex pathologies. Improving the reliability of clinical fMRI through the use of ultra-high field and new acquisition methods offers the possibility to increasingly supplant invasive diagnostic procedures such as intraoperative cortical stimulation.

As in the high field (3-4T) regime, signal dropout in 7T* EPI can be reduced by increasing resolution [6, 7] and using parallel imaging acceleration [8, 9]. Parallel imaging reconstruction artifacts arising from motion and respiration either during the acquisition of GRAPPA reference lines (or Auto-Calibration Scans – ACS) or between acquisition of the ACS lines and the EPI time series can lead to serious reconstruction artifacts, particularly at very high field. Many clinical fMRI tasks are prone to generate motion, particularly motor foot and chin tasks, and language paradigms

*MAGNETOM 7T is ongoing research. All data shown are acquired using a non-commercial system under institutional review board permission. MAGNETOM 7T is still under development and not commercially available yet. Its future availability cannot be ensured.



1 Nyquist ghost reduction by robust phase correction. **(1A)** A single EPI time point acquired with parameters commonly used in presurgical planning [5]. **(1B)** The mean of the fMRI time series in which the subject performed a chin task (scaled to show Nyquist ghosts, indicated by arrows). **(1C)** The mean of the same fMRI time series reconstructed with an improved 'local' phase correction (scaling same as centre panel). Virtually no residual Nyquist ghost is visible.



2 General linear model (GLM) results for a patient with a right frontal tumor are contaminated by motion artifacts (green arrows). The independent component analysis (ICA) component for this task networks shows no motion contamination, bilateral activation throughout primary motor areas and basal ganglia activation not apparent in GLM results.

involving overt speech [5, 10]. These parallel imaging artifacts can be reduced by acquiring the ACS lines with FLASH [11] or by acquiring all the segments required for each slice in rapid succession, with low flip angle – 'FLEET' [12].

Nyquist ghost artifacts are also more pronounced at higher field. The mean of an fMRI time series acquired during a chin task (which generates similar artifacts to those observed in clinical language paradigms involving overt speech) shows serious ghosting using a phase correction method which was standard in the product EPI sequence in earlier versions of *syngo* (Fig. 1B). We found ICA a useful means to isolate activation from stimulus-correlated artifacts in such data [10], as can be seen in Fig. 2.

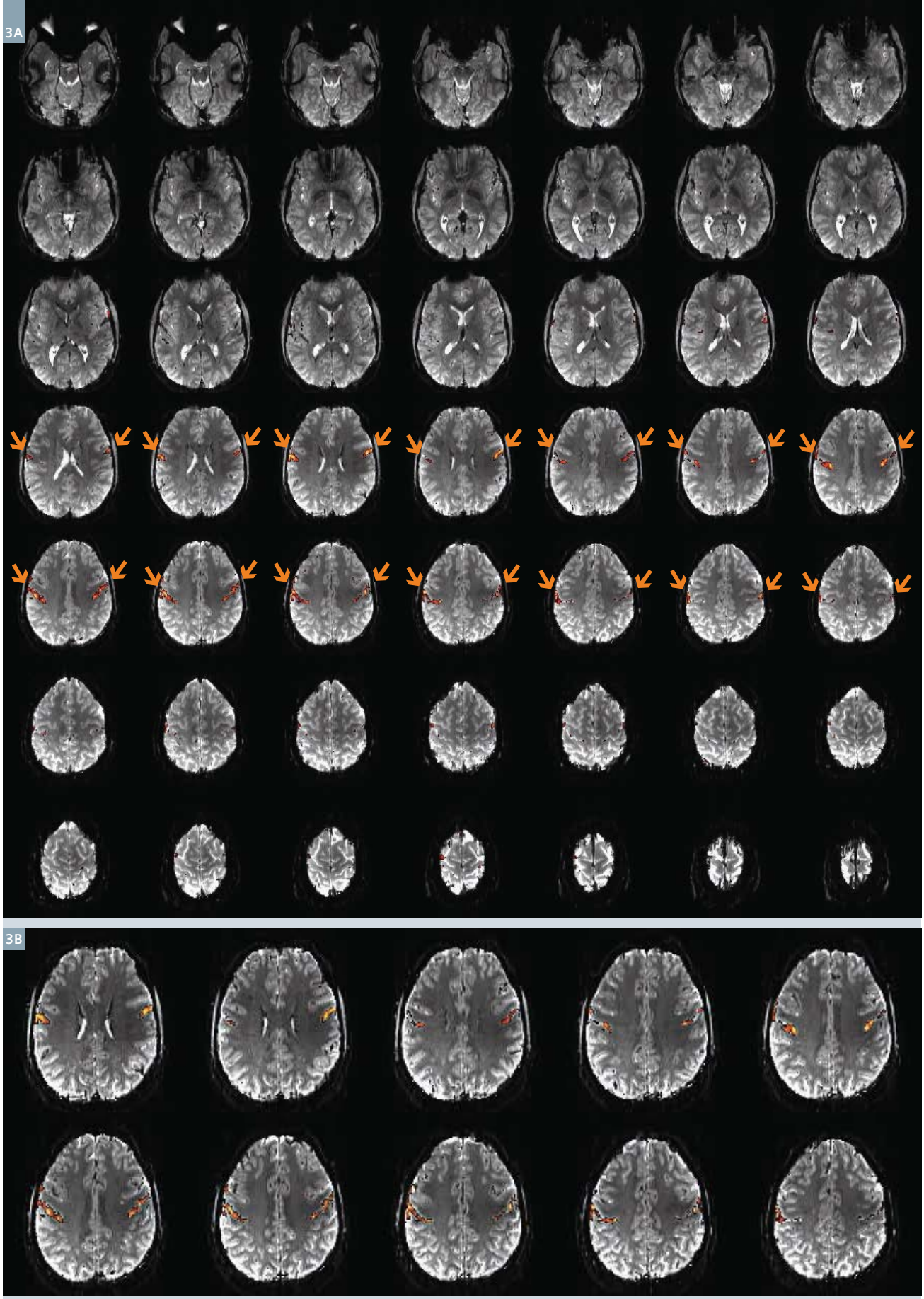
It is far better to remedy the problem at source, however, and the development and implementation of a local phase correction (now as default in the product EPI), hugely reduces Nyquist ghosts (Fig. 1C).

A useful alternative approach to the problem of Nyquist ghosting is offered by the IDEA EPI sequence [13], in which every readout line is sampled twice; once with positive and once with negative readout gradient. The data from positive readouts and negative readouts are assigned to two separate (usually undersampled) *k*-spaces. Avoiding the need to reverse alternate *k*-space line, this method yields images which are virtually ghost-free.

A recent development in EPI with enormous clinical potential due to the high temporal SNR per unit time is the 'simultaneous multislice' (SMS, a.k.a. 'multiband') approach, in which a number of slices are excited and read out simultaneously. Slice-dependent shifts in the image position in the blipped CAIPIRINHA approach make it possible to cleanly reallocate the overlapping signal in images to the correct slices, allowing the TR to be reduced by the SMS factor with very low g-factor penalty [14]. This approach was used in the results shown in Fig. 3.

Geometric distortions of EPI scale proportionately with field strength. The clinical implications of image distortion depend on how analysis is performed. There is great divergence in analysis approaches in clinical fMRI, as there is in the neurosciences in general. For clinical reports, the local standard is to apply as little preprocessing as possible and perform all analysis in the native EPI space. If functional data is coregistered to individual anatomy, however, clinically relevant shifts in activation occur [15]. Even at 7T these can be effectively corrected with multichannel field mapping [16]. A residual confound occurs, however, when there is motion between the field map and the functional data. This motivates the development of dynamic approaches to distortion correction in which the field map is derived, or updated, from the fMRI data themselves [17].

We end this description of methods of particular usefulness for ultra-high field clinical fMRI with an example of the quality of 7T fMRI data that is currently achievable with the approaches described. Five minutes of resting state EPI data was acquired from a single subject with a 7 Tesla MAGNETOM scanner using a 32-channel head coil (Nova Medical, Wilmington, MA, USA), with 50 slices of 1.5 mm isotropic resolution, using in-plane GRAPPA factor 2 and SMS factor 2, TE 22 ms, TR 1500 ms. Distortions were corrected using a multichannel field map [16]. ICA [18] reveals a component reflecting the motor resting state network [19] illustrated in Fig. 3, showing that reliable, high resolution mapping of primary motor regions is possible in just a few minutes, even in patients who are not able to perform a task [20, 21].

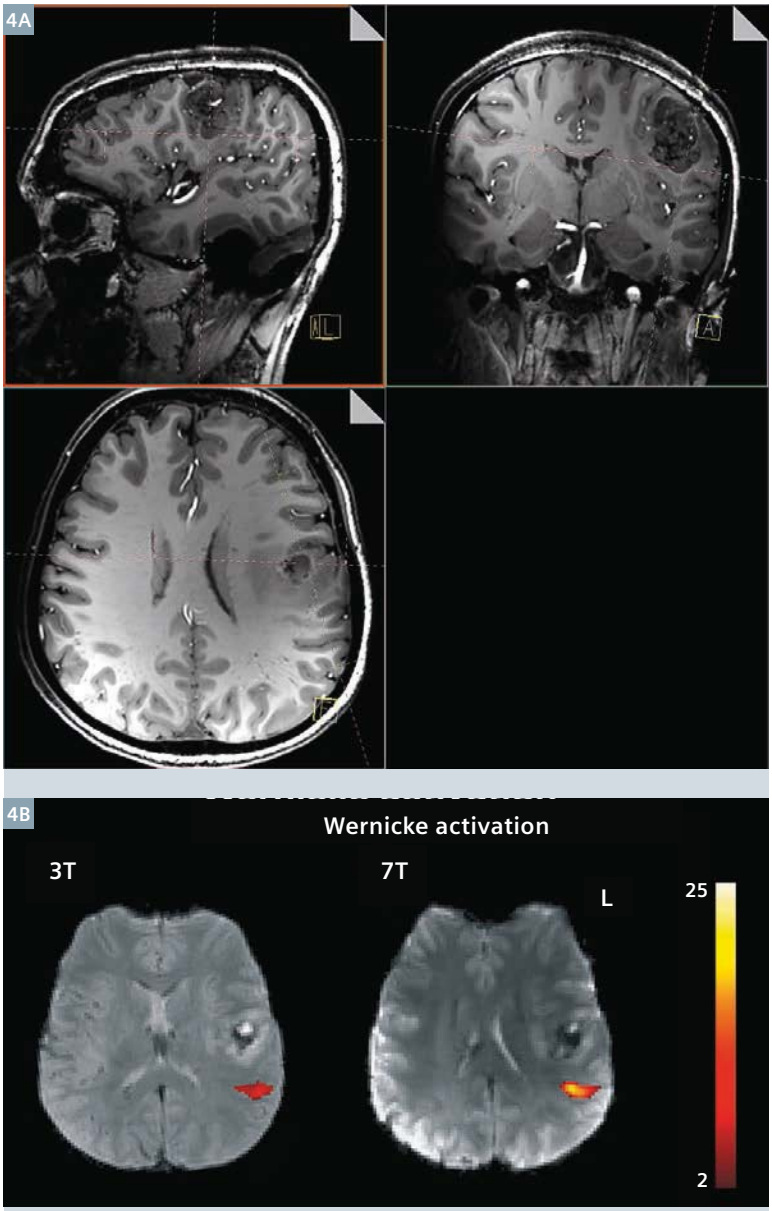


3 Fast, high-resolution mapping of primary motor areas using resting state functional connectivity (1.5 mm isotropic resolution, a single 5 minute run). Primary motor activation is highlighted on all slices (upper panel, at arrows) and selected slices are shown in the lower panel.

Clinical application of 7T fMRI: An example from presurgical planning

We compared BOLD response at 3T and 7T during a simple motor task in 17 patients referred for presurgical diagnosis in the first ultra-high clinical fMRI study [5]. There was increased activation within the primary motor hand area at 7T compared to 3T despite increased ghosting and motion artifacts.

While motor tasks typically elicit robust activations in well-defined cortical regions, cognitive tasks such as language evoke more complex activation patterns which often involve more problematic inferior frontal regions. There is significantly improved functional sensitivity in Wernicke's area at 7T compared to 3T as in the example in Fig. 4 of a 28-year-old patient with a left temporo-parietal tumor (the clinical language localization indicated left dominance in Wernicke and Broca). Contrary to the situation in Wernicke's area, there was no improvement in signal or activation statistics in Broca area at 7T because of increased signal loss [22].



4 MPRAGE of a patient with a tumor of unknown origin **(4A)** and activation in Wernicke's at 3T and 7T **(4B)**, showing the improvement in functional statistics at ultra-high field.

We anticipate improvements in 7T results in such problematic regions with developments in coils and shimming, as well as more robust GRAPPA reconstruction and physiological noise correction methods.

Clinical application of 7T fMRI: Outlook

Ultra-high field fMRI with high spatial and temporal resolution is particularly useful when investigating pathological alterations of neuronal tissue – tumors, lesions and neurodegeneration may weaken activation strengths as the vascular response is reduced [23]. This encourages the clinical use of 7T fMRI in presurgical functional localization, in assessing and monitoring neuroplasticity in various neuropathologies and in identifying non-invasive biomarkers for brain diseases. Moreover, higher sensitivity improves the detection of subtle differences between normal and pathological conditions, which is important for classification and prognosis in various neurological diseases (e.g. Alzheimer's disease).

The clinical importance of high sensitivity for weak functional activations also applies to the assessment and monitoring of neuroplastic changes in the cortex (e.g. tumor, stroke) as well as subcortical regions (e.g. Parkinson's disease, brainstem or cerebellar lesions) or peripheral nerve damage. The latter was investigated in patients suffering from a complete brachial plexus lesion who underwent a nerve reconstruction of the lesioned musculocutaneous nerve (innervating the biceps) via new inputs from the intact phrenic nerve (end to side connection) [24]. The healthy diaphragm area was able to add a new – phylogenetically not designed – function (moving the arm) to its already existing dedication (moving the diaphragm for breathing). Detecting such new types of neuroplasticity depends on the ability to monitor small brain activation changes. Ultra-high field fMRI was able to provide improved and earlier detection of neuronal reorganization.

Ultra-high field fMRI is opening up the possibility to study more subtle disruption and reorganization of function in an increasingly wide range of pathologies. The partnership between physicists and neurologists is essential to continue to realize the potential of ultra-high field fMRI and see it applied in the clinic.

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