High resolution imaging of the human brain at 1.5T with co-registration and complex averaging

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Introduction

The current trend in clinical MRI is towards the use of increasingly higher magnetic fields. In a few years the standard clinical field strength, currently 1.5T, is likely to become 3T. Correspondingly, the trend in anatomical imaging of the human brain is towards achieving higher spatial resolution. However, among the few studies which have demonstrated that myelination patterns within the living human cortex are detectable by MRI, results were obtained at 1.5T [1,2] as well as at 3T [3]. The laminar structure of the cortex was exemplified in these studies by the *in vivo* visualization of the stria of Gennari; an in-plane resolution of at least 300 µm was needed, and was achieved by greatly sacrificing the slice resolution (>1.5mm) and orienting the slices such that partial volume effects were kept to a minimum. It is crucial for the understanding of the human brain to establish the correspondence between the functional organization of the neocortex and its cytoarchitectonic fields. The latter are most reliably delineated by objective cytometry on stained histological brain sections [4]. High resolution MRI is indispensable to the quest for the mapping of structure-function, both by providing an intermediate step between the microscopic (~µm) resolution of the histological cuts and the crude resolution (>1mm) of functional MRI studies, and by supplementing histological studies with high resolution images of the entire post mortem brain before it possibly deforms during paraffin embedding and cutting.

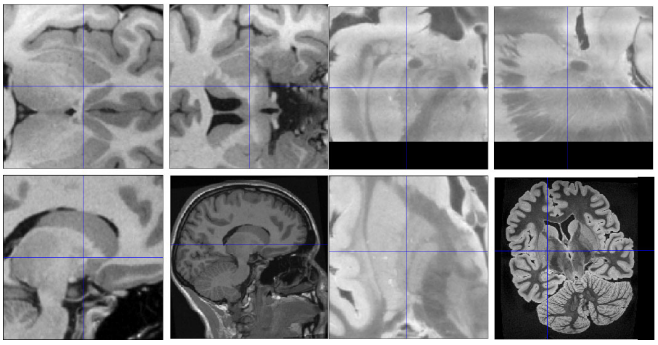
We report in the following on two examples of high resolution imaging obtainable on a clinical 1.5T scanner, and the method used to acquire them. One example demonstrates *in vivo* imaging with 0.61mm isotropic resolution. The other illustrates 0.35mm isotropic imaging of the post mortem brain.

Methods

We aimed at obtaining *in vivo* and post mortem brain images with the highest possible resolution attainable under the following set of constraints: (i) whole brain coverage; (ii) isotropic resolution; (iii) reasonable measurement time for an SNR of ~15 (similar to that from a standard 1x1x1mm MP-RAGE anatomical scan at 1.5T). Conditions (i) and (ii) are necessary for good white matter-grey matter segmentation, volumetry, and identification of anatomical structures. The latter (arbitrary) condition was found to be for our experimental setup 2 ½ hrs (two sessions) for *in vivo* measurements and one day up to one weekend (36-60 hrs) for post mortem brain imaging. All the measurements were performed on a 1.5T scanner (Siemens Sonata), equipped with a 40mT/m gradient coil and a standard volume RF coil for head imaging. A single volunteer (female, age 24) was chosen for the *in vivo* high resolution scan. For the post mortem study, a formalin fixed brain (male, fixation time 2 years, obtained through the University of Düsseldorf brain donor program) was imaged in a cylindrical container filled with formalin, to ensure proper coil loading. The Siemens 3D MP-RAGE (magnetization-prepared, rapid acquisition gradient echo) was chosen for the *in vivo* scans and TSE (turbo spin echo) for the post mortem brain, each with optimized parameters for their respective subjects. Both original sequences were modified to output phase images in addition to the standard magnitude images.The MP-RAGE measurement parameters were: TR=2320ms, TE=3.88ms, TI=1240ms, flip=20, FOV=195x195x0.61 mm, matrix size 320x320, 208 slices/slab, total acquisition time 14:32 min; 2 sessions of 5 acquisitions each, performed on two different days. The TSE measurement parameters were: TR=950 ms, TE=13ms, flip=180, turbo factor=5, FOV=148x160x0.36 mm, matrix size 414x448, 40 slices/slab, 5 slabs (4 slabs, respectively). NEX=4 was required such that the SNR in the scans allows for a good coregistration; total acquisition time was 6:12 hrs. For whole brain coverage, 9 slabs of 40 slices each were needed; the 9 slabs were acquired in two separate scans (5+4 slabs, interleaved) in order to avoid large intensity variations in slices were the intensity profiles from adjacent slabs overlap. The total acquisition time for the whole brain (5 + 4 slabs) was thus 12:24 hrs; 5 whole brain scans were performed over the course of a weekend.. Each saved scan consisted of a magnitude and a phase image in DICOM format. 3D volumes, both magnitude and phase, were reconstructed and saved in Analyze format; the magnitude images were coregistered with the first scan of the series, and the phase and magnitude 3D data sets were resliced; all these operations were performed using MATLAB, based on functions from theSPM2 software package [5]. In contrast to the averaging method which is commonly used, where only magnitude images are summed up, we use the resliced complex matrices for averaging. This ensures incoherent summation of the random noise and maximizes the gain in SNR.

Results and discussion

Coregistration of successive scans is obviously needed for *in vivo* imaging over longer periods of time where subject motion is important. However, the method also proved particularly useful for the post mortem scans. This is most probably due to the fact that the imaging gradients warm up, and therefore heat the passive shims, during continuous use over a period of 60 hrs, and the resulting shift in the spatial encoding frequencies is equivalent to a translation of the object in the direction of the applied gradient. The effect is especially clear in the case of the readout gradient. Coregistration of scans acquired at an interval of 48 hrs resulted in a shift of 0.29mm in the read-out direction (z), of 0.1mm in the second phase encode direction (y, encoding within the slab) and 0.02mm in the third direction (x, in-plane phase encoding). These are very significant corrections for the required resolution of 0.35mm, and summing of uncorrected images clearly leads to blurring. Using complex averaging, the SNR achieved *in vivo* after 10 averages was ~15, compared to ~6 for the individual scans. For the post mortem brain, an SNR of ~27 was achieved by averaging 5 scans of NEX=4 each (of individual SNR ~13). Fig. 1 shows slices containing the nuclei in the basal ganglia, as an example of the level of detail which can be observed: left, *in vivo*, at 0.61mm resolution, magnified region of 8x8x8cm; and right, post mortem, at 0.35mm resolution, magnified region of 4x4x4cm. The structure of the hippocampus can also be observed very well *in vivo* at this resolution, and the laminary structure of the cortex, including the stria of Gennari, can be seen well in the post mortem brain scans (details not shown).



Conclusions

We show optimized high resolution MRI results obtained on a 1.5T scanner, with 0.61 isotropic resolution *in vivo* and 0.35 isotropic resolution for the post mortem brain. Coregistration and reslicing of the images also turns out to be very important in high resolution imaging of the post mortem brain when imaging is performed over a long period of time. Using complex averaging instead of summing only magnitude images results in the expected increase in SNR of the square root of the number of averages.

References

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