Diffusion MRI at large *b* values: what's the limit?

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Introduction: In a free medium diffusion is a gaussian process resulting in an attenuation, S/So, of the NMR signal according to $S = S_0 e^{-bD}$ (where D is the diffusion coefficient and b the diffusion weighting) In biological tissues, however, diffusion becomes a much more complex phenomenon due to effects of restriction, compartmentation, active and passive transport, flow, tortuosity, ... and the above relationship is only a coarse approximation[1]: Using large *b* values the NMR signal deviates from a mono-exponential description. Although more complex models have been proposed such as bi-compartimentation[2], with[3] or without exchange, restriction[4] or a continuum of different diffusion pools [5], the origin of the diffusion signal remains elusive. Information encoded at high *b* values is expected to allow a better description of the signal decay[6] and to refine the proposed models. For instance, enhanced fiber anisotropy seen with higher diffusion sensitizing may improve tracking capabilities, up to the cortex[7]. Unfortunately signal acquired at high b values is usually very low due to the limited gradient hardware performances of MRI systems. Therefore, inventive ways must be sought to gain this information with exploitable quality and statistical significance; How high in *b* value can we go in experimental conditions and still get relevant information?

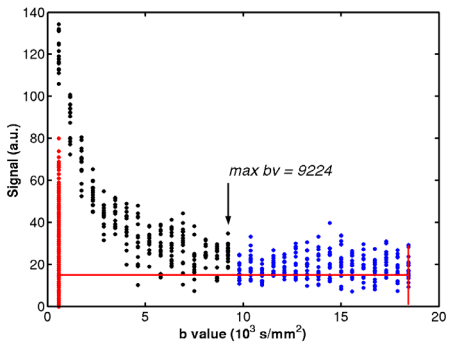

Figure 1: Significant (black) and non significant (blue) signal. Noise distribution (left), median (line) and standard deviation (right) are shown in red.

To answer this question we propose a criterion for definitive signal loss. This criterion should be: (i) model independent, (ii) defined in a statistically significant manner, (iii) compatible with different diffusion experiments. Using such a criteria we find relevant signal information even at very high *b* values (18000 s/mm^2), far higher from commonly called "high *b*" values[6] (~3000 s/mm^2)

Material and Methods: Standard diffusion EPI images were acquired with linearly increasing 32 values. 16 repetitions were made at each *b* (0 to 18500 s/mm^2) and six diffusion directions. For each *b* value, noise and pixel by pixel signal distribution and were compared. A non-parametric Wilcoxon test was used (α = 0.1%), taking as null hypothesis that both the noise distribution of a ROI outside the brain and the pixel distribution for the *b* value are identical. We define max*bv* as the last *b* value that negates the null hypothesis, that is, the last *b* value where signal distribution is statistically different from noise (as illustrated in figure 1). This analysis was made, voxel by voxel, for each diffusion direction and max*bv* maps were computed.

Studies were carried out on a Signa 1.5T (GEMS, USA). EPI parameters were: TE/TR 157/1000 ms (Δ/δ = 62.6/56.1 ms) in plane resolution 1.875 x 1.875 x 5 mm^3. Diffusion experiments were made in six non-collinear directions (xz, -xz, yz, y-z, xy, -xy). Standard DTI EPI acquisition with 55 directions and b = 1000 s/mm^2 (TE 71.8 ms), and T1 IR 3D scan were made for anatomical reference.

Results and Discussion: Maps of max*bv* on a voxel-by-voxel basis are shown in figure 2. A relevant point is that there is still significant signal at very high *b* values (up to 18000 s/mm^2) in highly organized fiber tracks perpendicular to the gradient direction. As expected *maxbv* in WM varies greatly with the diffusion direction. It also should be emphasized that this value for max*bv* is obtained *without* averaging and with very low α. This implies that there is indeed much information to recollect at higher diffusion weighting level for these areas. Another point is that all relevant information for gray matter is lost at *b* around 2500 s/mm^2, it is therefore useless to go higher on diffusion weighting if the cortex is the region of interest. However optimized max*bv* analysis for this *b* range should be made.

It is important to emphasize that max*bv*, by construction, depends on experimental parameters, namely max*bv* depends on initial SNR, especially TE and B_0. Yet, it is possible to infer its value for different conditions using coarse approximations or numerical methods.

Conclusion: We propose a method to estimate the highest b value which can be used to acquired diffusion images with exploitable quality. This value depends on SNR and acquisition parameters, as well as tissue diffusion figures. The results emphasize that it is possible to still acquire significant signal at very high b values, and gain valuable information at this level of diffusion weighting. The max*bv* calculation has been successfully applied: (i) to choose the pertinent b value to be used accordingly to the specific tissue under study[8] (white matter parallel or perpendicular to diffusion direction, grey matter); (ii) to determine the highest usable diffusion values in q-space studies to completely describe the signal decay[9]; (iii) to define a noise cut-off criteria for fitting analysis[8], on a pixel by pixel basis. Other possible applications are optimization of *b* values span for each diffusion direction independently or to monitor, in real time, diffusion MRI experiments allowing extra flexibility and quality in data acquisition.

References: *1.Le Bihan NMR Biomed 8:375, 1995 2. Clark et al., MRM 44:852, 2000. 3. Stanisz et al., MRM 37:103, 1997. 4. Sehy et al, MRM 48: 765, 2002..5. Yablonskiy et al, MRM, 50: 664, 2003. 6. Zaman A: et al. 20th ESMRMB, p7 , 2004. 8. Meca C. et al, submitted 12th ISMRM meeting 9. Chabert S. et al, submitted 12th ISMRM meeting*

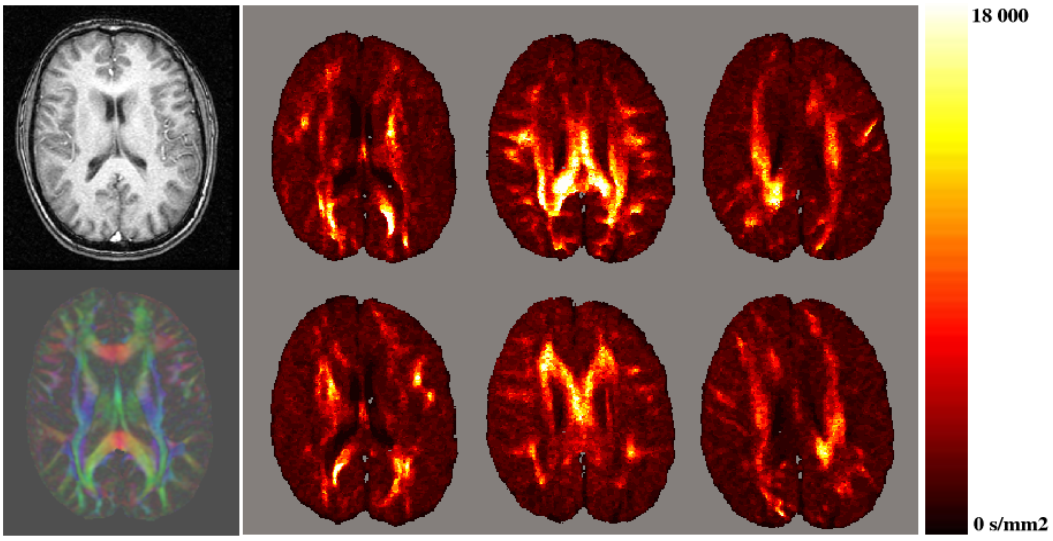

Figure 2: Max*bv* maps for six different gradients directions. Paired directions are vertically aligned (xz, -xz, yz, y-z,, xy, -xy). Anatomical and FA-RGB coded images are shown as anatomical references.