Investigation of the Resolution Dependence of White Matter Structure Analysis by Means of Variography

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Introduction: Investigation of human cerebral white matter (WM) structure plays an important role in neuroscientific research [1] and in monitoring of neurodegenerative diseases [2]. The methods employed range from complex techniques such as diffusion tensor imaging to simpler greyscale value analyses, such as variography, a method originally introduced in geosciences for the investigation of correlations in spatial data. In [3] it was demonstrated that variography applied to MR images is a useful tool to investigate age-related WM alterations in healthy subjects. By means of the variogram, tissue heterogeneity and typical correlation distances of the WM structure can be quantified. However, the variogram changes with the support of the data, that is with the shape and size of the measured volumes. This change is called regularisation. In MRI, regularisation is determined by the experimental details which are summarised in the point-spread-function (PSF). In this work, the influence of image resolution on the variogram is investigated. A digitised, high-resolution photograph of a human brain slice is successively reduced in resolution by cutting off the high *k*-space frequencies. The low-resolution variograms are corrected by including the regularisation in the parameter estimation and are compared to the original image parameters. It is demonstrated that the consideration of regularisation facilitates a reasonable estimation of the correlation parameters, even if the resolution is reduced up to a factor of 3.

Materials and Methods: A photograph of a human brain slice of 0.1mm thickness digitised with an isotropic in-plane resolution of 0.1mm (Fig.1a) was used as a data source. This image forms an ideal reference since it is virtually free from noise and artefacts. The WM was manually segmented (Fig.1b) and the variogram of the image intensities, $I(\mathbf{x})$, was calculated using the classical estimator (Eq.1) for 150 distance intervals, d_i, equally distributed from 0mm to 15mm. To simulate the process of MR imaging, the original image was transformed into frequency space using a fast Fourier transform (FFT). The high frequencies were successively cut off to decrease image resolution and the resulting truncated *k*-spaces were transformed back to the spatial domain using an inverse FFT. Thus, 5 low-resolution images with isotropic in-plane pixel sizes of 0.2mm, 0.3mm, 0.6mm, 0.8mm and 1.0mm were generated. The variograms were estimated in a manner similar to that for the high-resolution image using adapted numbers of distance intervals (75, 50, 25, 18, 15) to maintain statistical properties comparable to those of the original image. In order to obtain quantitative correlation parameters, the variograms were fitted with the sum of 2 exponential models (Eq.2) leading to three independent parameters, namely the heterogeneity ratio σ_l^2/σ_s^2 and the individual correlation distances of each model, $d_{c,s}$ and $d_{c,l}$. Consideration of regularisation is based on the general equation of regularisation for a measured volume, v (Eq.3, [4]). Here, v_d is the volume, v, displaced by d. The integrals can be approximated by a discrete sum (Eqs.4/5). With knowledge of the *k*-space size, and therefore knowledge of the PSF, the weighting function, $w(d',d)$, can be calculated (a detailed derivation of $w(d',d)$ is omitted). The low-resolution variograms were fitted again with the exponential models, this time including the regularisation according to Eq. 5.

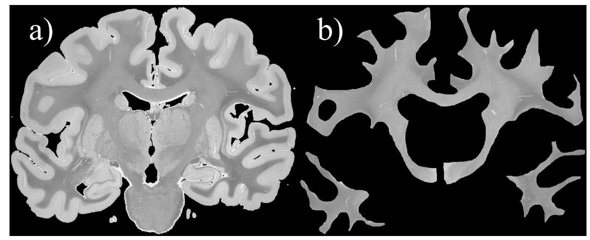

***Fig.1**: high resolution photograph (left), segmented WM (right)*

(1) $\gamma(d) = \dfrac{1}{2N(d_i)}(I(x_k) - I(x_l))^2, \quad |x_k - x_l| \in d_i$

(2) $\gamma_{\text{mod}}(d) = \sigma_s^2(1-\exp(-d/3d_{c,s})) + \sigma_l^2(1-\exp(-d/3d_{c,l}))$

(3) $\gamma_{reg}(d) = \bar{\gamma}(v_d, v) - \bar{\gamma}(v, v), \quad \bar{\gamma}(v_1, v_2) = \iint_{v_1, v_2} \gamma(|x_1 - x_2|) dx_1 dx_2$

(4) $\bar{\gamma}(v_d, v) = \iint_{v_d, v} \gamma(|x_1 - x_2|) dx_1 dx_2 \approx \sum_i w(\tilde{d}_i, d)\gamma(\tilde{d}_i)$

(5) $\Rightarrow \gamma_{reg}(d) = \sum_i (w(\tilde{d}_i, d) - w(\tilde{d}_i, 0))\gamma(\tilde{d}_i)$

Results: Figure 2 illustrates the error introduced by reduced resolution as a function of the new voxel size divided by the original voxel size, i.e. the resolution reduction factor. In Fig. 2a the mean squared deviations between high- and low-resolution variograms for the corrected and uncorrected data are illustrated. In both cases the deviations increase with voxel size but the corrected variograms show a better agreement with the high-resolution reference than the uncorrected ones (factor 2 to 10). Figures 2b-2d show the difference of the estimated correlation parameters between high- and low-resolution images with and without consideration of regularisation. The heterogeneity ratio (Fig. 2b) is overestimated. However, for the corrected variograms the errors are significantly lower and particularly for a voxel size below 0.8mm, the error remains almost constant at about 15%. In the case of short correlation distance, the situation is more complex. Below voxel sizes of 0.6mm, the corrected data show a rather good agreement (below 15%) to the original parameters, for larger voxels the estimation fails (error up to 140%). The uncorrected parameters show an underestimation ranging from 20% to 90%. For the long correlation distance there is hardly any difference between the parameters estimated from the corrected and the uncorrected variogram. In both cases the error stays below 15% for voxels smaller than 0.6mm.

Conclusions and Outlook: The results demonstrate that the voxel size has a major influence on the shape of the variogram and therefore also on the estimation of the correlation parameters. Under consideration of regularisation, the deviation between original and low resolution variogram can be significantly reduced up to a factor of 10. However, the estimation of the correlation parameters for larger voxels is still highly biased (up to 140%). In particular, the estimation of the short correlation distance is not reliable if the voxel size is several times larger than the size of the correlation structure. The results presented indicate that a resolution reduction of a factor of 3 can be well compensated by a correct consideration of regularisation with errors below 15%. The knowledge of these errors plays an important role in the evaluation of correlation parameters obtained from images acquired with typical MR resolutions of 1mm. In the next step these results will be included in the analysis of MR images. Furthermore, more general effects of the PSF, such as an intrinsic *k*-space weighting as present in many MR sequences, will be considered.

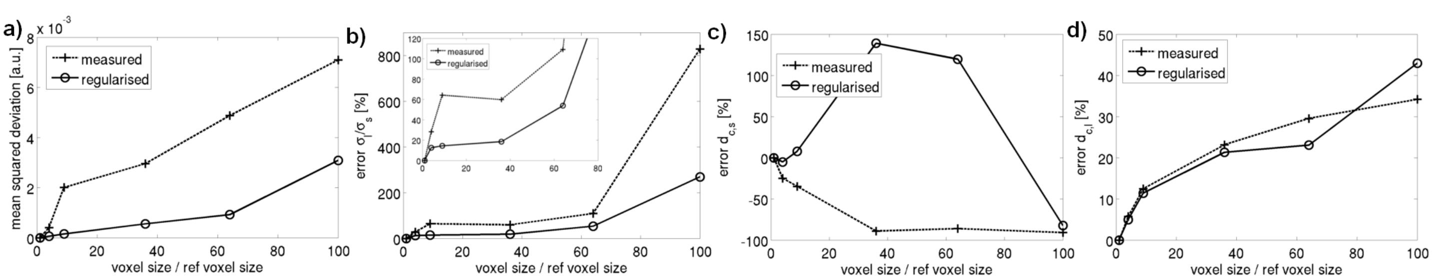

***Fig.2:** Deviations of variograms and the estimated correlation parameters with respect to the voxel size with and without regularisation.*

References: **[1]** Evans et al. Neuroimage 2006; 30:184-202 **[2]** Polman et al. Ann Neurol 2005;58:840-846 **[3]** Keil et al., Proc. Intl. Soc. Mag. Reson. Med. 19 (2011) **[4]** Journel & Huijbregts, Mining Geostatistics, 1991