# Imaging microstructure: Application of oscillating gradient diffusion sequences on a 3T clinical MRI scanner

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**Target Audience:** Clinicians/physicists interested in microstructure imaging.

**Purpose:** To estimate and distinguish between various diameters of microfibres in (microcapillary and asparagus) phantoms and also, of axons in the corpus callosum (CC) of healthy volunteers using trapezoidal oscillating gradient spin-echo (tOGSE) diffusion sequences on a standard 3T clinical MRI scanner.

**Method:**

tOGSE sequence implementation: tOGSEs were implemented onto a 3T Philips Achieva MRI clinical scanner with all the relevant checks for gradient heating and peripheral nerve stimulation. They are controlled with the following parameters: number of half periods of the oscillations (N), frequency of the oscillations (*f*), b-value (b), diffusion sensitizing gradient duration time pre/post 180° RF pulse (δ) and diffusion time (Δ).

*Table 1: The table shows the tOGSE sequences and its parameters that were used to carry out phantom and volunteer scanning.*

| Subj | tOGSE sequence parameters ( *N, f, b,* δ, Δ) | Gradient diffusion direction and measurement no. |
|---|---|---|
| Microcapillaries | 3, 32.6Hz, 2525s/mm$^2$, 45.9ms, 58.7ms | Perpendicular to fibre direction (measurement 1) |
| Asparagus | 3, 30.8Hz, 2799s/mm$^2$, 48.6ms, 58.8ms | |
| In-vivo CC | 3, 32.9Hz, 2524s/mm$^2$, 45.6ms, 59.2ms | |
| Microcapillaries | 6, 65.3Hz, 404s/mm$^2$, 45.9ms, 58.7ms | Perpendicular to fibre direction (measurement 2) |
| Asparagus | 6, 61.7Hz, 486s/mm$^2$, 48.6ms, 58.8ms | |
| In-vivo CC | 6, 65.8Hz, 396s/mm$^2$, 45.6ms, 59.2ms | |
| Microcapillaries | 12 ,130Hz, 79s/mm$^2$, 45.9ms, 58.7ms | Perpendicular to fibre direction (measurement 3) |
| Asparagus | 12, 123Hz, 97s/mm$^2$, 48.6ms, 58.8ms | |
| In-vivo CC | 12, 131Hz, 77s/mm$^2$, 45.6ms, 59.2ms | |
| Microcapillaries | 1, 32.6Hz, 1483s/mm$^2$, 8.5ms, 95.9ms | Perpendicular and parallel to fibre direction (measurement 4 & 5) |
| Asparagus | 1, 30.8Hz, 1973s/mm$^2$, 9.6ms, 97.7ms | |
| In-vivo CC | 1, 32.9Hz, 1913s/mm$^2$, 9.6ms, 94.8ms | |

Imaging protocol: For all subjects: TE = 120ms, TR = 3s, gradient strength = 62mT/m. The imaging plane was perpendicular to the expected diffusion direction. The imaging resolutions were: 0.40mm*1.60mm*10mm (Microcapillaries), 2mm*2mm*5mm (Asparagus) and 1.5mm*1.5mm*4mm (volunteers). The number of signal averages were 10, 10 and 3, respectively. The combination of oscillation frequencies and diffusion sensitising gradient directions in Table 1 were chosen to probe the expected diffusivities and fibre diameters based on previous research[1]. Different b-values were used for each set of measurements, since there is a different maximum achievable b-value for each oscillation frequency.

Phantoms and volunteers: *Phantom 1:* An array of parallel microcapillaries (inner diameter of 10μm and length of 1mm) within a thin plate of 1mm thickness. *Phantom 2:* A hydrated asparagus stem with symmetrically distributed cylinder fibres[2]. *Volunteers:* Mid-sagittal slices of the CC of 2 healthy human volunteers were chosen because, histologically, CC (mainly at the genu) is composed of the most coherent set of parallel axons in the human brain[3]. Imaging time for each volunteer was 3 minutes

Model fitting to estimate diameter estimation: A three stage fitting model procedure[4] (grid search, gradient descent and MCMC 10000 iterations, 1000 burn-in) was used to fit the parameters of each subject to the measured signal. The final estimated diameter was the mean over all MCMC estimates. The tissue models[5] used for our phantoms/volunteers were: (a) ZeppelinCylinder with fixed fractional volume to represent signal from the microcapillaries, (b) ZeppelinCylinderDot for asparagus ('Dot' signifies trapped water within fibre walls) and (c) ZeppelinCylinderCSF for CC ('CSF' denotes signal contamination from the CSF surrounding the CC). In all models, zeppelin and the parallel cylinders of single radius represent the extra-fibre and intra-fibre compartment, respectively, with no signal exchange between the two compartments.

**Results and discussion:**

Microcapillaries: Estimates of the microcapillaries diameters are shown in Fig.1, where each pixel contains 100s of microcapillaries. The mean diameter is 9.63μm, however, deviations at the edges of the microcapillaries plate do occur and may be due to partial volume effects.

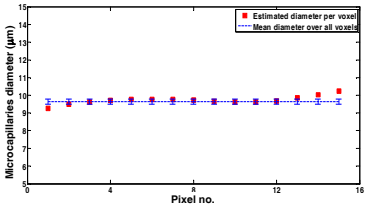


*Figure 1: Graph of diameters along a segmentation of the micro-capillaries phantom (mean diameter = 9.63±0.14μm)*

Asparagus: Literature[2] reports vascular bundles, with a mean diameter of 19μm, which surround symmetrically distributed larger fibres (mean diameter of 96μm) known as pith regions. The grey arrows in Fig.2a suggest appearances of the pith regions with diameters between 75-100μm, which occur next to regions of ~150μm. The histogram plot (Fig.2b) shows the predominance of potential vascular bundle structures with diameters of 30-40μm. Even with this deviation from literature values, there are still significant differences between the possible pith regions and vascular bundles, which is consistent with literature[2].

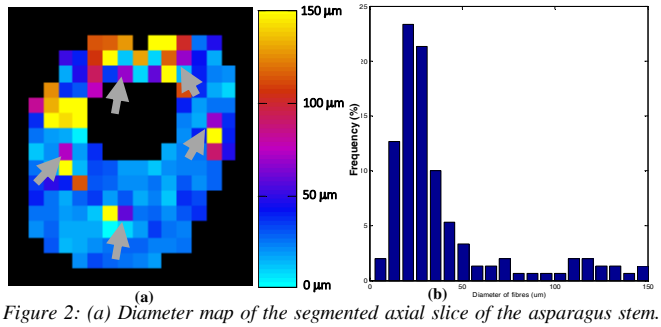


*Figure 2: (a) Diameter map of the segmented axial slice of the asparagus stem. The grey arrows point to the symmetrical occurrences of possible pith regions within the asparagus, where diameters between 75-100μm tend to occur next to diameters of ~150μm. (b) Histogram of the fibre diameters occurring in (a).*

Corpus Callosum: Published histology[6] suggests axon diameters ranging from 0.5μm to 14μm across the CC, with the mid-body regions consisting of the larger axons (>7μm). Fig.3a and 3b of the axon diameter maps show inhomogeneity in the most homogenous regions (genu) of the CC. SNR calculation of the segmented CC show SNR < 10 at the genu (pink arrow) for both subjects, which may explain the deviation from the published values. The large number of low diameter estimations (<1μm), occurring at the posterior end (green arrow) in Fig.3b may also be caused by the low SNR values in those regions. The white arrow in Fig.3a show possible partial volume effects across the posterior body which suggest further discrepancy with the expected results. However, the diameter estimations, although not following the patterns in [4] and [6], are mainly in the range between 0-10μm, which is similar to the values reported in literature[6].

**Conclusion:** To our knowledge, this is the first demonstration of microfibre diameter estimations using tOGSEs on a 3T clinical MRI scanner. This extends the work of previous studies that have applied OGSE sequences in human subjects, which showed changes in the ADC and DTI parameters[7, 8]. Successful validation of this technique is evident in its application to estimating diameters of microcapillaries and asparagus fibres using only 5 measurements. Future work will focus on resolving partial volume effects, applying eddy current corrections and improving sequences using optimisation techniques as in [1].

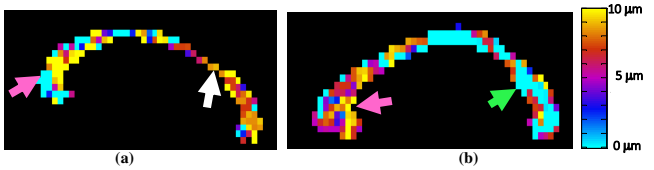


*Figure 3: Segmented CC, of (a) subject 1 (b) subject 2, showing the map of axon diameters. All values occur in the range of 0-10μm and is consistent with literature[6, 7].*

**References:**

**[1]** Drobnjak et al 2013 *Microporous and Mesoporous Materials* 178(0) 11-14; **[2]** Boujraf et al 2001 *MAGMA* 13 82-90; **[3]** S. G. Waxman 1995 Oxford University Press **[4]** Alexander et al 2010 *NeuroImage* 52(4) 1374-1389; **[5]** Panagiotaki et al 2012 *Neuroimage* 59(3) 2241-2254; **[6]** Aboitiz et al 1992 *Brain Research* 598 143-1 53; **[7]** Kershaw et al 2013 *NeuroImage,* 70 (10-20) **[8]** Baron and Beaulieu 2013 *MRM*;