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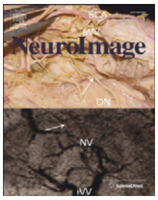

A generalised framework for super-resolution track-weighted imaging

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ABSTRACT

Track-density imaging (TDI) was recently introduced as a method to achieve super-resolution imaging using whole-brain fibre-tracking data (the so called tractogram). A similar approach to achieve super-resolution was later applied for average pathlength mapping (APM). These two methods have in common that the tractogram information is used to create an image with novel contrast and super-resolution properties. In this study, we present a generalised framework for creating *super-resolution track-weighted imaging* (TWI), where the intensity of the map can be made dependent on *any specific property* of the streamlines or their set of spatial coordinates. Furthermore, each contrast can be determined by a number of characteristics that are under user control. It is shown that TDI and APM represent specific cases of this generalised framework, and that this framework opens up the possibility of generating a large range of images with novel image contrasts. Finally, it is shown that the same super-resolution principles as those introduced in the original TDI method are also applicable to any of these new images.

Introduction

Whole-brain fibre-tracking, also referred to as tractography, is a powerful application of diffusion MRI that allows the non-invasive study of the white matter connections in the brain. Recently, a new method to achieve super-resolution using the information contained in the whole-brain fibre-tracking results (the so called 'tractogram') was described (Calamante et al., 2010). In this method, known as track-density imaging (TDI), the intensity of the image is proportional to the number of streamlines traversing each voxel. Sub-voxel information is provided by the long-range continuity information contained in the fibre tracks (or streamlines), such that super-resolution TDI maps can be generated with higher spatial resolution than that of the acquired diffusion MRI data (Calamante et al., 2010). The super-resolution properties of this new methodology have recently been validated using in vivo and in silico data (Calamante et al., 2011a), and the anatomical contrast of the TDI maps compared to myelin and Nissl histology using ex vivo mouse data (Calamante et al., 2011b).

A similar approach to achieve super-resolution was later applied to mapping the average pathlength of a tractogram (Pannek et al., 2011). In this technique, known as average pathlength mapping (APM), a map of the mean length of all streamlines going through a voxel is calculated. In the same manner as for the TDI technique, the resolution of the APM method is not limited to that of the acquired diffusion MRI data, such that super-resolution can be achieved.

These two methodologies have in common that an image with higher spatial resolution and a novel contrast mechanism is created from the results of whole-brain fibre-tracking. In this study, we present a generalised framework for performing *super-resolution track-weighted imaging* (TWI), where the intensity of the map can be made dependent on *any specific property* of the streamlines or their set of spatial coordinates. It will be shown that the two above-mentioned techniques (TDI and APM) represent specific cases of this generalised framework, and that this framework opens up the possibility of generating a large range of images with novel image contrasts. Furthermore, it will be shown that the same super-resolution principles as those introduced in the original TDI method are also applicable to these new images. To avoid any misunderstandings, we emphasise that the new TWI maps represent *track*-weighted images as opposed to *tract*-weighted images, i.e. they are images weighted by the streamlines generated through whole-brain fibre-tracking as opposed to by the actual physical white matter bundles.

Abbreviations: APM, average pathlength map; b, diffusion-weighting b-value; $b0$, image without diffusion weighting (i.e. $b=0$); CSD, constrained spherical deconvolution; D_{av}, average diffusivity; DEC, directionally-encoded colour; FA, fractional anisotropy; FOD, fibre orientation distributions; FWHM, full-width at half maximum; iFOD2, 2nd order integration over fibre orientation distributions; K, number of streamlines; ε, coordinate along the streamline; λ, length of the streamline; λ_{max}, maximum length constraint for the streamlines; l_{max}, maximum harmonic order; *ls*TDI, length-scaled TDI; M_P, mean value of the property P for the streamlines traversing a given voxel; MT, magnetisation transfer; P, property of the streamline or its set of spatial coordinates; RGB, red–green–blue; S_P, sum of the property P for the streamlines traversing a given voxel; T_2, transverse relaxation time; TDI, track density imaging; TOI, track-of-interest; TWI, track-weighted imaging; TW-MP, track-weighted mean P; TW-TP, track-weighted total P; TW-TT$_2$, TW-TP map for the case of the property $P=T_2$; $W(\varepsilon)$, neighbourhood weighting function.

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The use of fibre-tracking for quantification of diffusion MRI properties has been the subject of considerable previous work (e.g. Ciccarelli et al., 2003; Correia et al., 2008; Hagmann et al., 2010; Zhu et al., 2011). Many of these studies use fibre-tracking to define a track-of-interest (TOI), where some diffusion property (e.g. the fractional anisotropy (FA)) is assessed. More recently, an elegant alternative approach was proposed (Rose et al., 2010), where a diffusion property (e.g. FA) is combined with a whole-brain connectivity matrix to generate a connectome (e.g. the FA connectome) to study neurological disease processes. The formalism presented in the current work is fundamentally different because the whole-brain fibre-tracks and the associated property are used to generate a super-resolution image with a novel contrast, i.e. the proposed method is used as a mapping strategy to generate a new image with higher spatial resolution. Furthermore, previous studies on quantification along tracks commonly required some level of user interaction to select the track(s) of interest; the use of whole-brain tracking in TWI avoids this potential source of subjectivity.

Materials and methods

Super-resolution track-weighted imaging

Let us assume we have a whole-brain fibre-tracking dataset. This tractogram consists of *N* streamlines, each constrained to a maximum length λ_{max}, which have been created from a diffusion MRI dataset with an acquired resolution of $X_{acq} \times Y_{acq} \times Z_{acq}$ mm^3. We can assign to each streamline in the tractogram a number of *properties* of the curve, such as its length, its mean curvature, torsion, etc. (NB. In cases where the property of interest varies along the spatial extent of the curve, statistics other than the mean of this parameter, such as median, minimum, maximum, sum, etc., can be also considered). Alternatively, we can assign to each streamline in the tractogram a property of an associated map over the *set of coordinates* of the curve, such as the mean (or the sum, median, maximum, minimum, etc.) of a tensor property (Basser, 1995) along the track (e.g. the mean fractional anisotropy (FA), the median average diffusivity (D_{av}), etc., along the track), or the mean value of another diffusion map (e.g. the mean kurtosis along the track), or even the value of a non-diffusion related map (e.g. the standard deviation of the T_2 values along the track, the mean magnetisation transfer constant, the maximum fMRI activation, etc.). We refer to this particular selection (which is under user control) as the *track-wise* statistic, because it is the statistic chosen to assign a property to each streamline (or track) in the grid element. In this way, each streamline in the tractogram can have a number of associated 'properties' linked to them. For simplicity, we will consider only one of these properties, which we will refer to as *P* for the remainder of the description.

In a similar way as that described for the TDI methodology (Calamante et al., 2010), let us now overlay on the diffusion MRI field-of-view a grid with elements of size $X_{rec} \times Y_{rec} \times Z_{rec}$ mm^3, where the subscript *rec* stands for 'reconstructed'. Note that the dimension of the grid elements can be smaller than the acquired voxel resolution, which will lead to the super-resolution nature of the track-weighted imaging technique (Calamante et al., 2010).

For each element of the grid (at position *r*), we can now calculate the *sum* of the property *P*, S_P, over all of the streamlines traversing the grid element:

$$S_P(r) = \sum_{i=1}^{K(r)} P_i \tag{1}$$

where the index *i* indicates the *i*-th streamline traversing that grid element, whose total number is given by *K*(*r*). A map can then be calculated, by assigning to each grid element the relevant value S_P. We will refer to this map as the *track-weighted total P* (TW-TP). (NB. Note that when the property $P_i = 1$, then $S_P(r) = K(r)$, and the TWI map reduces to the TDI method (Calamante et al., 2010)). Fig. 1 shows a schematic illustration of the methodology: the figure shows a couple of elements of the grid (see small blue and yellow pixels in Fig. 1a — note that these grid elements are smaller than the acquired diffusion MRI voxel size, as is shown here by the voxel size of the background FA map). In the illustrative example of Fig. 1b, there are $K = 18$ streamlines traversing the grid element (located in the corpus callosum). For each of the streamlines, a given property is calculated (e.g. the mean T_2 along the streamline), and the 18 resulting values (one for each of the streamlines in the grid element) are added up. The resulting sum of the mean T_2 values is assigned as the intensity of that grid element in the super-resolution TW-TT_2 map. The procedure is repeated for each element of the grid, until the super-resolution TW-TT_2 map is completed. If a grid element has more than one fibre population (e.g. see yellow pixel in Fig. 1c, where there are $K = 20$ streamlines traversing the grid element, corresponding to 3 fibre bundles), then the intensity of that grid element will represent a combined property of all those multiple fibres.

We can also consider, instead of the sum of the property *P*, the *mean* value of the property for each streamline traversing the grid element:

$$M_P(r) = \frac{S_P(r)}{K(r)} \tag{2}$$

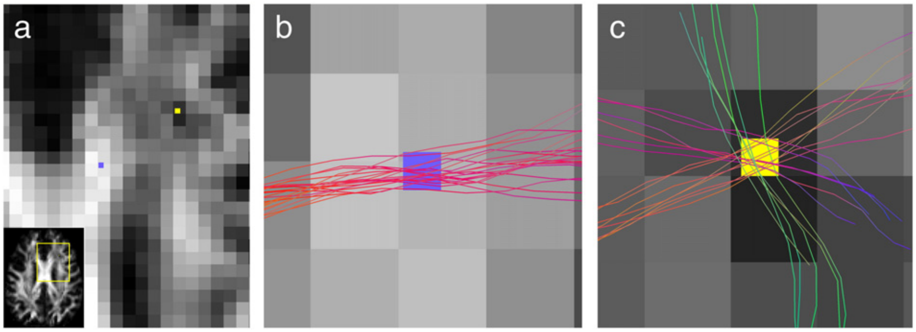

Fig. 1. Illustrative example to the track-weighted imaging method. (a) Zoomed region in an axial FA map (see inset for location); two elements of the super-resolution grid are highlighted by the blue and yellow pixels. (b) Zoomed area in the neighbourhood of the blue grid element, with the streamlines traversing the grid element overlaid; this location corresponds to an area with a single fibre population (corpus callosum). (c) Zoomed area in the neighbourhood of the yellow grid element, with the streamlines traversing the grid element overlaid; this location corresponds to an area with three fibre populations. The colour-coding of the streamlines is the standard RGB convention (red: left–right, green: anterior–posterior, blue: inferior–superior).