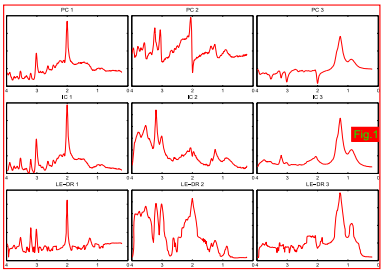
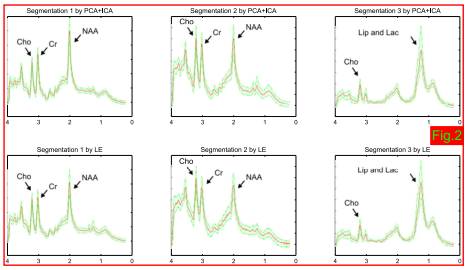
NONLINEAR LAPLACIAN EIGENMAPS DIMENSION REDUCTION OF IN-VIVO MAGNETIC RESONANCE SPECTROSCOPIC IMAGING ANALYSIS

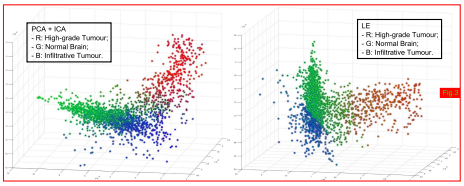
Guang Yang[1], Felix Raschke[1], Thomas Richard Barrick[1], and Franklyn A Howe[1]
[1]*Division of Clinical Sciences, St. George's University of London, London, United Kingdom*

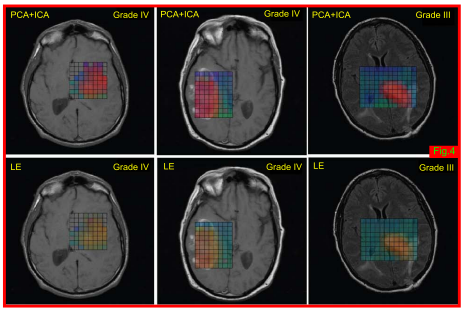
Introduction: The gold standard of histopathological characterisation of brain tumours is from a biopsy, an invasive surgical method with associated risks[1]. ^{1}H *magnetic resonance spectroscopy imaging* (MRSI) provides in vivo metabolic information with clinical potential to supplement standard MRI for non-invasive diagnosis of brain tumours. Manual interpretation and analysis of large multivoxel MRSI data sets is difficult and time-consuming. Therefore, pattern recognition (PR) techniques are used to assist MRSI based tumour identification and characterisation[2,3], and they can be applied to patient MRSI data with suspected gliomas with an aim to segment regions relating to tumour core, tumour infiltration and normal brain. Dimensionality reduction (DR) is an important prerequisite for PR to reveal compact and informative representations of the observed data. PCA and ICA are well-known DR techniques used in PR of ^{1}H MRS data[4], but the data must have certain characteristics to be best analysed by these methods, *e.g.*, PCA implicitly assumes Gaussian sources while ICA has linear independent assumption[5]. In contrast, nonlinear DR techniques do not rely on the linearity assumption for segmentation; therefore, high-dimensional data embedded in more complicated manifolds can be identified where linear methods often fail. In this work, we advocate the spectral manifold learning method of Laplacian eigenmaps (LE)[6] as a DR technique suitable for MRSI data sets, with correlation to standard MRI to aid confirmation of our results. Compared to the previous PCA and ICA approach, the LE method gives promising results with respect to separation of brain and tumour tissue.





Materials and Methods: Data was acquired from 29 glioma patients who had given written informed consent in accordance with local ethics procedures, and tumour diagnosis was confirmed from histology. MR data were acquired at 1.5T using 2D MRSI (TR/TE=2000/30ms with outer volume suppression) of a 15mm thick axial slice through the centre of the observable mass. MRSI data were pre-processed by zero-filling prior to Fourier transform in 2D to produce a 32x32 matrix of voxels with in-plane spatial resolution of 7mm. Spectra were limited to 4ppm to 0.2ppm (M=498 data points) aligned to Cho at 3.21ppm, and the phased real part of the spectra used for PR analysis of N=1965 voxels in total. We developed an in-house program to analyse the MR spectra using the LE method. The aim of the LE method is to compute a low-dimensional representation of the data that preserves the local neighbourhood information. In so doing, a solution is obtained that reflects the geometric structure of the manifold. We constructed a weighted adjacency graph G with N nodes, in which each node represents a particular spectrum. To achieve this *k*-nearest neighbours method was applied to determine connectivity between the nodes according to the Euclidean distance in $\Re^N$. The smoothness assumption of the manifold justifies the use of Euclidean distance, so that the manifold geodesics are locally approximated by Euclidean distances in the space where the manifold is embedded. Then a heat kernel was used to define the weights of connected edges, $W_{ij} = \exp(-||s_i - s_j||/\sigma^2)$ if s_i and s_j are connected; otherwise, $W_{ij} = 0$. Next the Laplacian matrix $L = D - W$, was constructed in which W is the adjacency matrix and the corresponding degree matrix is $D_{ii} = \sum_j W_{ij}$. Based on standard spectral graph theory, a reasonable mapping is given by a matrix $Y \in \Re^{MxN}$, that is $Y = (y_1, y_2, \ldots y_n)$, which maps the weighted adjacent graph G to a low-dimensional space, where the connected nodes remain close together and is given by $\arg\min_y \sum_{ij} ||y_i - y_j||^2 W_{ij} \equiv \arg\min_y \mathrm{tr}(Y^T L Y)$, which is equivalent to solving the generalised eigenvalue problem $Ly = \lambda Dy$. Three corresponding eigenvalues from LE DR were assigned to an 8-bit colour channel respectively allowing 24-bit RGB MRSI colour maps to be overlaid on standard MRI images to visualise normal tissue (Green), tumour infiltration (Blue) and tumour core (Red).





Results: Fig.1 shows the results of data reduction represented as spectra, *i.e.*, eigenvectors, for the three methods: (a) PCA alone, (b) PCA followed by ICA, and (c) nonlinear LE. Comparison of ICA and nonlinear LE analysis, suggests that the three DR components represent normal brain (IC 1 and Reduced Data Dimension 1, *i.e.*, LE-DR1), infiltrative glioma (IC 2 and LE-DR2), and high-grade necrotic glioma (IC 3 and LE-DR3). However, PCs have a large out-of-phase metabolite signals so do not represent definitive tissue classes. The eigenvalues from the ICA and LE were used as an index to classify individual voxels as one of the three different tissue classes: (a) normal brain, (b) infiltrative tumour and (c) high-grade/necrotic tissue (Fig.2 shows the median spectrum for each of the three classes (solid red curves) with 25% and 75% quartiles above and below the median (dashed green curves) respectively. The median spectrum for tissue class (a) were similar across methods (IC 1 and LE-DR1) and can be considered as representing a segmentation of normal brain. Similarly, the median spectrum for tissue class (b) across methods showed higher Cho to Cr ratio than normal but with reduced NAA. This is suggestive of voxels with a mixture of both tumour and normal tissue and can be considered a segmentation of tumour infiltration. Furthermore, both techniques provide spectra representative of high-grade glioma in the median spectrum for tissue class (c). Scatter plots of the three tissue segmentation classes using PCA followed by ICA and nonlinear LE (Fig.3) suggests that the proposed nonlinear LE method may provide a more defined segmentation of normal brain and tumour infiltration. These findings are supported using RGB colour mapping overlaid on conventional MRI. RGB colours are mapped according to the three segmentations of the MRSI data sets (Fig.4). Three of the 30 cases are presented. The results found by using PCA followed by ICA generated more regions with both normal brain and tumour infiltration classes (cyan voxels); however, the LE method provided a more discrete segmentation (either blue or green voxels) as also indicated by the scatter plots (Fig.3).

Conclusions: We have developed a new metric to characterise brain tissue of glioma patients into normal, tumour infiltration, and tumour core segmentations. We advocated a nonlinear LE analysis for our MRSI data sets that is rationalised by the fact that the source components before DR have a nonlinear component due to the acquisition method and tissue structure. We have demonstrated that our proposed application using nonlinear LE method offers robust DR results in one step. This is in contrast to previous studies, which used a two-step process where ICA relied on pre-processing using PCA. Brain tissue segmentations with scatter plots and colour map overlays support the results of using nonlinear LE.

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