Spatio-temporal topology of the post-contrast signal enhancement in normal-appearing white matter 1-3 months post-stroke

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Background: Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) has limitations in the assessment of subtle blood-brain barrier (BBB) permeability changes mainly due to noise levels comparable to true signal values. We evaluate the use of Graph-variate signal analysis (GVSA) in selecting regions of interest across the normal-appearing white matter, hypothesised to be reflective of true signal levels in this tissue, to ameliorate these problems.

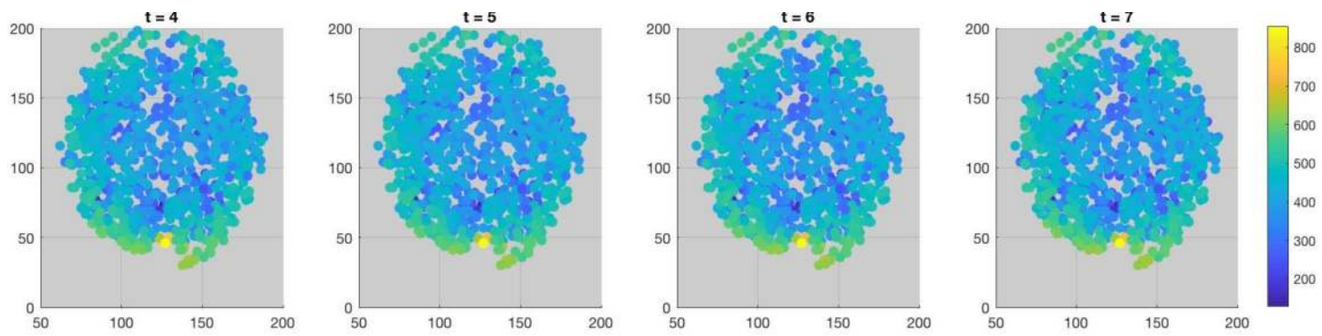
Materials and methods: We used data from 40 small vessel disease (SVD) patients who had a recent small subcortical infarct (RSSI), obtained at 1-3 months post-stroke. Images of normal-appearing white matter were sparsified into a coherent spatial graph representation by down-sampling via 3D skeletonisation. We then mapped skeletal voxel clusters and pathways into nodes and connecting edges, respectively. The post-contrast time-series at each node was the average of brain fluid flow over its 2-voxel-radius neighbourhood. We averaged the instantaneous correlations between signals connected through the graph to get one value for each node and time-point. Signal activations comprised the 5% highest values over the time-node array. We used the Kruskal-Wallis test to determine whether the Euclidean distances between the spatio-temporal activations and RSSI discriminated patients with different baseline vascular risk factors or SVD burden, and/or patterns of RSSI evolution.

Clinical parameter	p-value
Presence of brain microbleeds (y/n)	0.00049
Periventricular Fazekas scores (0-3)	< 0.0001
Deep Fazekas scores (0-3)	< 0.0001
Perivascular spaces scores in basal ganglia (0-3)	0.00029
Perivascular spaces scores in centrum semiovale (0-3)	0.00017
Any cavitation or lacune ay 1 year (y/n)	0.0214
Complete lacune at 1 year (y/n)	0.108
Typical FLAIR lacune at 1 year (y/n)	0.0098
Hypertension (y/n)	0.993
Hyperlipidaemia (y/n)	0.226
Recent or current smoker (y/n)	< 0.0001

Table. Comparison of the distribution of the median Euclidean distances (ED) between the activations at each time point and the centre of the RSSI, in patients grouped as per the clinical parameters evaluated. Tabulated are the p-values from the Kruskal-Wallis tests after weighting the ED at each time point by the number of activations at the given time point.

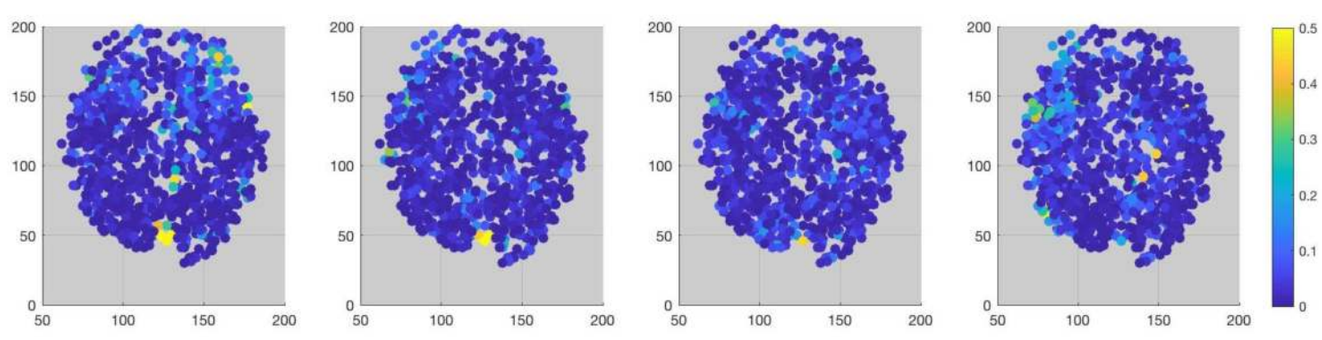
Conclusions: The DCE-MRI signal was clearer in locations spatially related to the RSSI with distinctive patterns related to the SVD markers, as expected. Thus, GVSA is promising for identifying regions of interest to study MRI signal dynamics when changes are subtle and signal levels are comparable to noise.

Signal looks identical across time



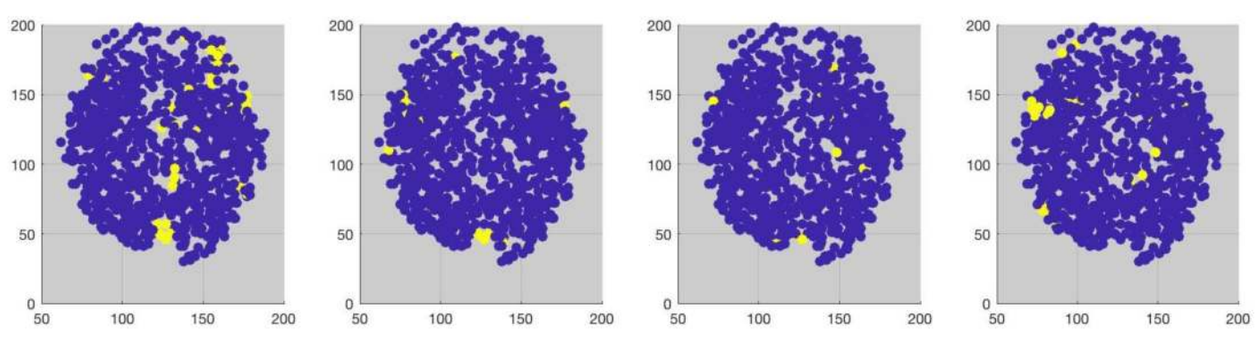
DCE-MRI signal averaged over neighbourhoods

GVSA teases out correlated signal variations



GVSA applied using instantaneous correlation

ROIs to use for further analysis



"Activations" taken as top 5% over node-time array

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