Stepwise heterogeneity analysis of breast tumors in perfusion DCE-MRI datasets

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Abstract

The signal curves in perfusion dynamic contrast enhanced MRI (DCE-MRI) of cancerous breast tissue reveal valuable information about tumor angiogenesis. Pathological studies have illustrated that breast tumors consist of different sub-regions, especially with more homogeneous properties during their growth. Differences should be identifiable in DCE-MRI signal curves if the characteristics of these sub-regions are related to the perfusion and angiogenesis. We introduce a stepwise clustering method which in a first step uses a new similarity measure. The new similarity measure (SM) compares how parallel washout phases of two curves are. To distinguish the starting point of the washout phase, a linear regression method is partially fitted to the curves. In the next step, the minimum signal value of the washout phase is normalized to zero. Finally, SM is calculated according to maximal variation among the point wise differences during washout phases. In the second step of clustering the groups of signal curves with parallel washout are clustered using Euclidean distance. The introduced method is evaluated on 15 DCE-MRI breast datasets with different types of breast tumors. For evaluation purposes, we compared SM similarity measure with three widely used similarity measures: Euclidean distance, correlation coefficient and cosine measure. The evaluation shows a significantly improved performance of our new similarity measure compared to the widely used measurements. The use of our new heterogeneity analysis is feasible in single patient examination and improves breast MR diagnostics.

Purpose of the study

The signal curves in perfusion dynamic contrast enhanced MRI (DCE-MRI) of breast tumors give us valuable information about tumor angiogenesis and their characteristics. Pathological studies show that breast tumors consist of different sub regions with more homogeneous properties during their growth. Differences should be identifiable in DCE-MRI signal curves if the characteristics of these sub-regions are related to the perfusion and angiogenesis. We introduce a stepwise clustering method which in a first step uses a new similarity measure. The new similarity measure (SM) compares how parallel washout phases of two curves are. In the second step of clustering the groups of signal curves with parallel washout are clustered using Euclidean distance.

Method

A new similarity measure (SM) is defined and used in our cluster analysis of breast tumors in 15 female patients. SM measures the amount of parallelism of two signal curves in the washout phase. To distinguish the starting point of the washout phase, a linear regression method is partially fitted to the curves. In the next step, the minimum signal value of the washout phase is set to zero. Finally,

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the SM is determined as follows: the distance at each time point of the min-zero washout curves are calculated. For a washout part with n time points, we obtain n distances. In the next step the n distances are sorted in decreasing order. The similarity measure is then calculated from following formula:

$$sm_{ii'} = \sqrt{\sum_{j=1}^{n/2} (d_j^{ii'} - d_{(n-j)}^{ii'})}$$

where $d^{ii'}$ is the sorted list of the distances at time points of washout curve i and curve i'. The calculation process of the similarity measure is depicted schematically in figure 1. The voxels of tumor regions in DCE-MRI datasets are clustered using hierarchical clustering in combination with the complete linkage method. The number of clusters is given by an estimated maximal dissimilarity according to the noise in tumor signal curves. In the second step of clustering the groups of signal curves with parallel washout are clustered further using Euclidean distance (see Figures 3 and 4).

Results

The SM is compared to Euclidean or cosine measures and correlation coefficient. Two clustering results are compared by their sum of the standard deviations Si of the clusters. The Si is the standard deviation of the slopes of regression lines of washout part of the curves in the cluster i. Our clustering result has significantly a smaller sum of standard deviations for all datasets which means that the variety of curves inside a cluster is less than other methods. The numbers of sub regions in tumors with similar characteristics are also similar.

New work to be presented

A new method for clustering of DCE-MRI signal curves is introduced. The advantage of this method compared to other existing methods beside its simplicity is that it is not based on a fix number of clusters. The main idea behind the clustering is the introduced similarity measure SM and separation of clustering method in two steps using two different similarity measures. The SM takes the form of the pattern of washout phases of the signal curves into account. As a result, we have clusters with parallel washout curves.

Conclusions

The new similarity measure can successfully cluster the tumor in sub regions of similar enhancement patterns (see Figures 2 and 3). The main factor of a correct estimation of the number of sub regions in the tumor depends on the choice of a proper similarity measure. The new similarity method is not a metric so that the open question is how far the implementation of other clustering methods like mean shift or k-mean is affected by this issue. Finally, beside the introduced evaluation method, still a biological oriented evaluation of method is of significant importance. Two this end, the results of the clustering method will be compared with gross pathology cuts of the tumor in a further step.

Publication history

This work is not published in any journals or is not presented in any conferences.

Figures

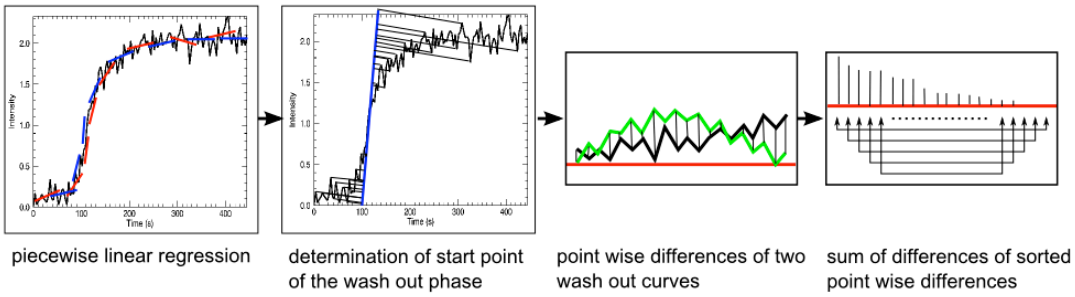

Fig. 1 Schematic illustration of the calculation of the new similarity measure (SM).

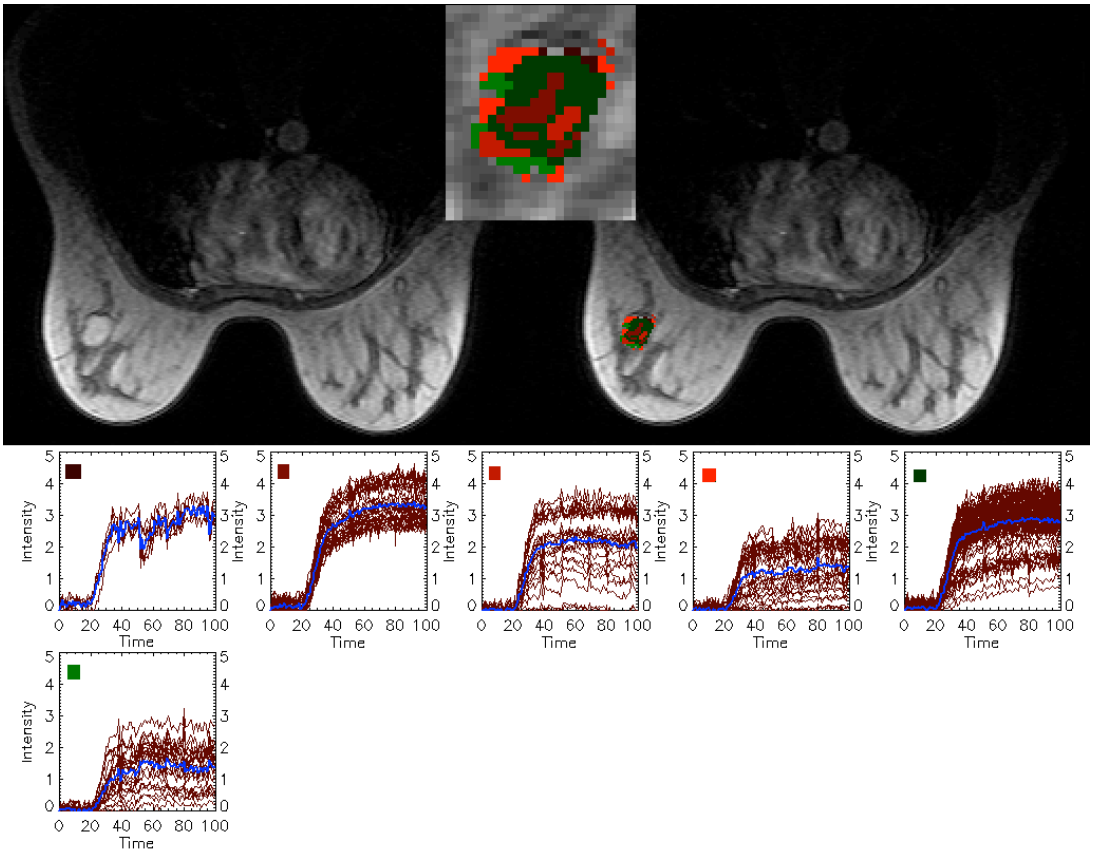

Fig. 2 Top: clustering result for a noisy dataset. The tumor region is divided in six sub regions. Bottom the curves inside these six clusters are depicted. The blue curve is the mean curve of the cluster.

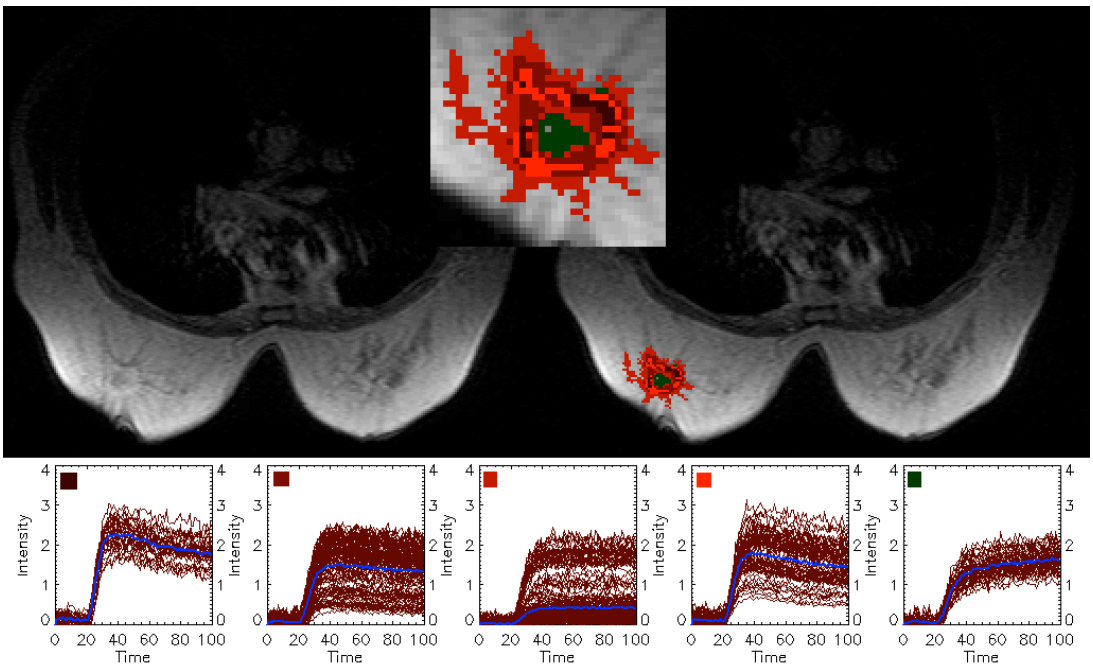

Fig. 3 Top: clustering result for a dataset with less noise. The tumor region is divided in five sub regions. Bottom: the curves inside these five clusters are depicted. The blue curve is the mean curve of the cluster.

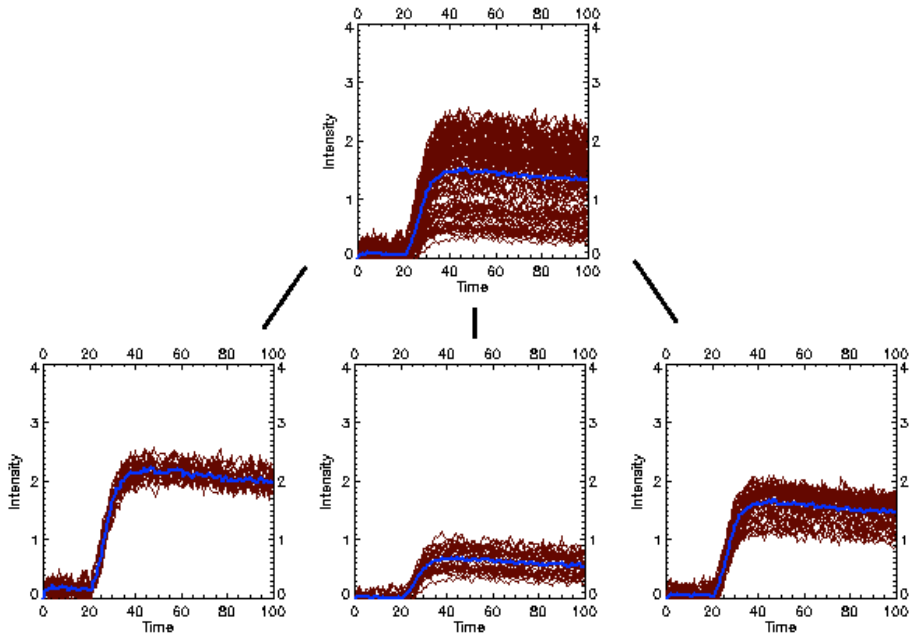

Fig. 4 The second step of clustering using Euclidean distance is depicted for the second cluster (from the left) of the tumor in figure 3. The second cluster is divided into three sub clusters.