A Self Organizing Map for Exploratory Analysis of PET Radiomic Features

Emad Alsyed, Rhodri Smith, Stephen Paisey, Christopher Marshall and Emiliano Spezi

***Abstract*–Texture analysis for quantification of intratumor uptake heterogeneity in PET/CT images has received increasing attention. This allows the extraction of a large number of 'radiomic' features to be correlated with end point information such as tumor type, therapy response, prognosis. The conventional complex workflow for calculation of texture features introduces numerous confounding variables. This non exhaustively includes, imaging time post administration of radiopharmaceutical and the method and extent of functional volume segmentation. A lack of understanding on the dependency of texture features with these variables serves as a detriment to the urgent need to standardize texture measurements to pool results from different imaging centers. The utilization of machine learning techniques for feature (and their combinations) selection serves as a promising method to alleviate redundancy in radiomics. To this avail, we introduce for the first time the application of a Kohonen self-organizing feature map to identify the emergent properties present when performing texture analysis. The application of the self-organizing map to radiomic analysis serves as a powerful general-purpose exploratory instrument to reveal the statistical indicators of texture distributions. For this purpose, texture features from PET-CT images of 8 pre-clinical mice with mammary carcinoma xenografts were analyzed with varying post injection imaging time and tumor segmentation contour size. This varying distribution of texture parameters were interpreted by the self-organizing map to reveal two distinct clusters of texture features which are dependent on contour size, providing additional evidence that contour size and hence segmentation method is a confounding variable when performing texture analysis. Furthermore, the self-organizing map can be utilized as a method to incorporate this revealed dependency in a prediction model in the presence of end point information, which will be an area of future work.**

***Index Terms*— PET, Artificial Intelligence, Self-Organizing Map, Texture Analysis, Radiomics, Machine Learning, Cancer.**

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I. Introduction

MEDICAL imaging forms an essential component in all phases of cancer management. Traditionally medical images are interpreted visually by radiologists and clinicians. The rapid development of artificial intelligence (AI) has revolutionized the ability to recognize complex patterns in imaging data and provide a depth of quantitative analysis previously unachievable. Positron Emission Tomography (PET) imaging contributes significantly in the staging, diagnosis and treatment for several types of cancer [1]. The extraction of texture features from PET defined metabolic tumors has received increasing research interest. In the field now described as "radiomics" texture features and their combinations have demonstrated correlation with dependent variables, such as classification of tumor type, therapy response, disease characteristics and prognosis. This demonstrated powerful ability of PET radiomics may serve as a linchpin to personalized cancer treatment with the associated promised improvements in survival [2] [3].

Before large scale clinical implementation of PET radiomics standardization of the entire workflow for feature extraction is required. Efforts towards the standardization of the texture metric calculation have proved promising [4]. Multiple confounding variables however may cause a variation on radiomic features. Several investigations have assessed the impact of image reconstruction type [5], respiratory motion [6] segmentation [7][8] and in our previous work contour size and post injection imaging time [9] on texture features.

To date only a limited number of studies have utilized advanced machine learning techniques to investigate the value of texture analysis in PET imaging [10][11]. A self-organizing map SOM is a type of artificial neural network (ANN) that is trained using unsupervised learning to produce a lower dimensional representation of the input data on an underlying manifold. Manifold learning has shown successful in other areas of image processing, such as respiratory motion correction [12] and image segmentation [13][14]. To the authors knowledge, no published research has implemented a self-organizing map (SOM) to explore, capture and cluster the statistical variability of PET texture parameters.

Kohonen's Self-Organizing map (SOM) takes a set of input data (with L texture parameters) and maps it onto a two dimensional grid of neurons (figure 1) [15][16]. Each neuron

in the grid is assigned a weight vector $W = (w_{j1}, w_{j2}, \dots, w_{jD})$ with the same dimensionality as that of the input data $j = (1,2,\dots L)$. The training utilizes competitive learning. Training examples are fed into the network at random, the Euclidean distance to all weight vectors is computed. The neuron weights are updated (eq 1); the neuron whose vector is most similar to the input is called the best matching unit.

$$w_{t+1}^{jd} = w_t^{jd} + \eta h(j,k)(x_d - w_{jd}^t), \quad for \quad 1 \le d \le D \qquad (1)$$

Where η is the learning rate parameter and $h(j,k)$ is the neighborhood function which has the value 1 at the winning neuron k and decreases as the distance between j and k increases. Each high dimensional data point is thus embedded onto a single neuron which most accurately reproduces its structure.

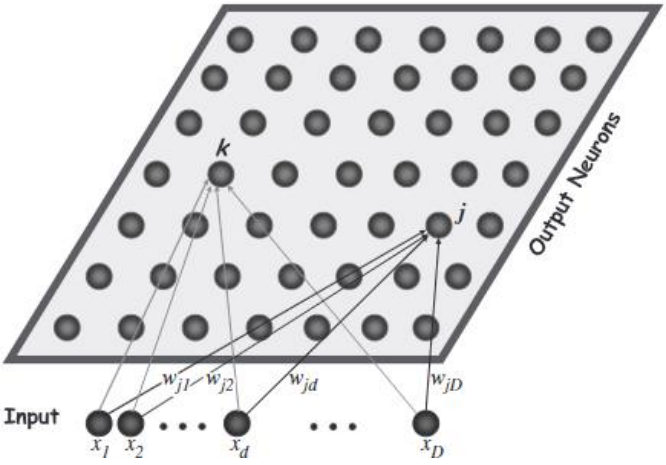

Fig. 1. Illustrative example of a self-Organizing Map [16].

II. Methods

Radiomic features were extracted from PET images of eight mice with 4T1 tumors (mammography carcinoma xenografts) utilizing SPAARC (an in-house developed tool built on Matlab [17]). Mice were injected with 10.0 ± 2.0 MBq of 18F-FDG and imaged 50 minutes post injection, dynamically for 20 minutes, 50 minutes with a Mediso Nanoscan PET/CT. Images were re-binned into 4 x 5 minutes PET scans (50-55, 55-60, 60-65 and 65-70 minutes post injection). Four different systematic 3D-Contour sizes (4, 4.5, 5, 5.5 mm) were segmented on the first time point (55 minutes) using Velocity 3.2.1 software (Varian Medical Systems, Palo Alto, CA). Contours obtained on the first time point were overlaid on all other images which were re-binned into subsequent time points. Figure 2 shows coronal and sagittal slices of lower right flank with four different contours for the first mouse. Texture features were extracted for each volume at each time points using SPAARC (Spaarc Pipeline for Automated Analysis and Radiomic Computing an in-house developed tool built on Matlab). Thus, each feature has 128 observable values that resulted from 8 mice, 4 different time points and 4 different contour sizes. For inter-comparison of different textures, the Zscore for each texture measurement was calculated (Z-omic). The mean Z-omic for 8 pre-defined groups of texture was calculated (morphology, statistical, intensity histogram, GLCM, GL3D, GLZ, GLD and NGT). The R software was used to learn the self-organizing map of the averaged Z-omic using 16 organizing neural networks, a learning rate of 0.05 and a Gaussian neighborhood function with standard deviation 1.

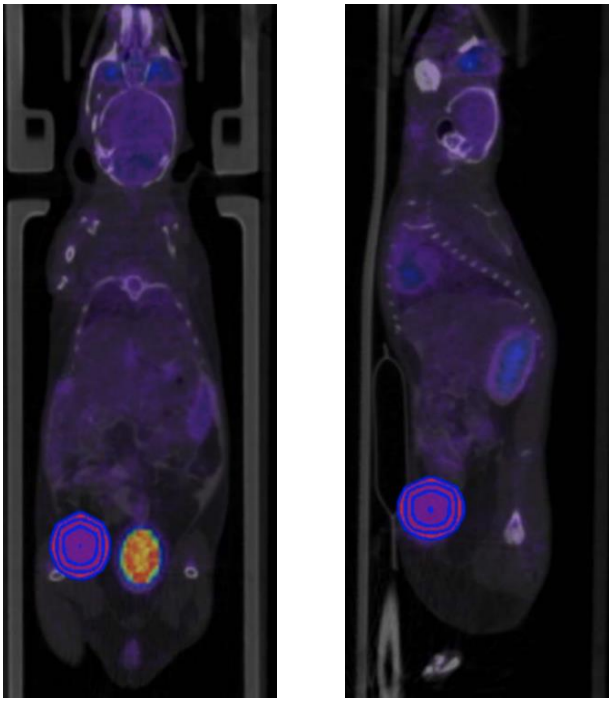

Fig. 2. Coronal (left) and sagittal (Right) slices of lower right flank (left of image) with four different contours for the first mouse.

III. Results

From the input dataset each instance of measured texture (Zomic) is assigned to a single node that best represents its distribution of variability. The classification of each node and the relative contribution of the grouped features is demonstrated in the codes plot (figure 3).

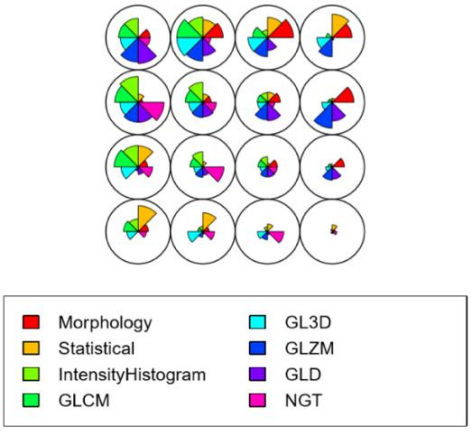

Fig. 3. Codes plots for the texture features.

To investigate the effect of confounding variables (Contour Size, Imaging Time) on the variability of texture parameters cluster analysis on the distribution of the contour sizes and imaging time points over the nodes of the SOM may be performed. In view that the SOM is blind to the confounding variables (i.e contour size and imaging time) it is evidenced that an emergent property of the statistical variability of the grouped textures is the extremes of contour size. Figure 4 and 5 present the distribution of the first and fourth contour size with respect to the self-organized features. No such relationship was observed with respect to the distribution of image time points over the nodes of the SOM. Taken together, these results suggest that the statistical distribution of the input texture has clear modes which are dependent on contour size.

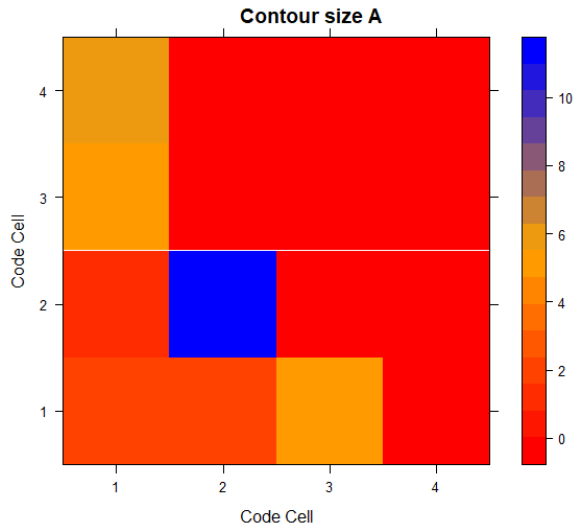

Fig. 4. The distribution of the first contour size with respect to the self-organized features.

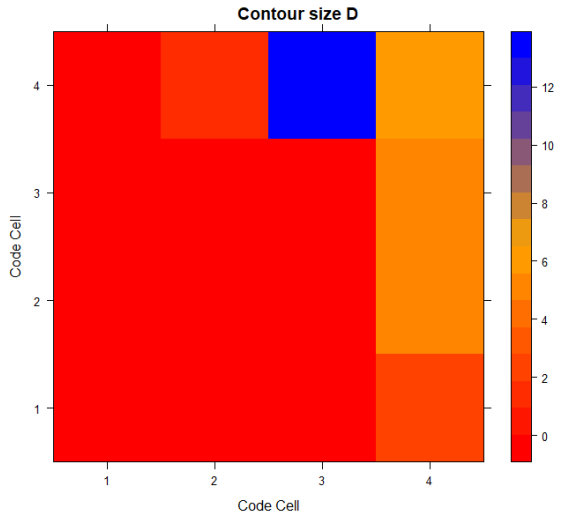

Fig. 5. The distribution of the fourth contour size with respect to the self-organized features.

IV. Conclusions

We introduce the novel application of a self-organizing map to texture feature analysis and demonstrate its ability for the first time in identifying emergent properties that effect Radiomics variability, in this case contour size. The SOM may also be utilized with outcome data to serve as a predictive tool for dependent variables (e.g prognosis, therapy response). In so doing the learnt representations of self-organized features serve as the attributes for prediction which will take into consideration the statistical variability in the underlying dataset. This serves as an area for future work.

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