FUZZY COGNITIVE MAP-BASED METHODOLOGY FOR GRADING BRAIN TUMORS

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Abstract: This research work presents a novel modeling method for grading brain tumors. The accurate determination of brain tumor malignancy (grade) is crucial because it determines and specifies patient's treatment planning and management. The novelty of the method is based on the use of the Soft Computing of Fuzzy Cognitive Maps (FCMs) to represent and model experts' knowledge (experience, expertise, heuristic), and on the use of a computational intelligent method the efficient AHL algorithm for enhancing the FCM's classification ability.

The proposed method was tested and validated for clinical material, comprising 100 cases. FCM grading model achieved a diagnostic output of accuracy of 92.68% (38/41) and 93.22% (55/59) for brain tumours of low grade and high grade, respectively. The results of the proposed grading model present reasonably high accuracy in comparison to other methods. The proposed approach present sufficient interpretability and transparency in decision process, which make it a convenient consulting tool in characterizing tumor aggressiveness in clinical practice.

Introduction

Brain tumors are considered as one of the most lethal and difficult to treat forms of cancer [1]. Pathologists evaluate the aggressiveness of brain tumors by visually examining tissue section (biopsies) based on guidelines determined by the WHO (World Health Organization) [2]. According to the WHO grading system, the appearance of certain histopathological features, such as cellularity, pleomorphism, mitosis, necrosis, vascular proliferation, and apoptosis, classify tumors on the basis of their aggressiveness as low or high-grade tumors. Low-grade tumors are less insistent and are associated generally with good prognosis. High-grade tumors are more aggressive, and are characterized by rapid growth and tendency to invade to nearby tissues [3]. The determination of the degree of tumor grade is the most critical step when diagnosing brain tumors because it specifies treatment planning and patient management [4].

Although the WHO grading scheme provides accurate definitions for tumour grade determination, the relative importance given by different pathologists to each of the grading criteria may vary significantly promoting inter and intra observer variability that has been shown to significantly influence the quality of diagnosis [5].

Computer based techniques, have been extensively examined for improving grade diagnosis. Decaestecker *et al.* have analyzed histological variables from Feulgen stained biopsies; employing the Nearest Neighbor classifier, they discriminated different grade tumors with an accuracy of 55% [6]. Sallinen *et al.* have developed a decision tree model evaluating histological features derived from different staining procedures (Feulgen, ki-67, Hematoxylin-Eosin) enhancing the prognostic efficiency of the WHO scheme [7]. Belacel et al have presented a fuzzy-logic based system analyzing quantitative nuclear features extracted by Feulgen stained slides. Their system exhibited an accuracy of 66% in discriminating tumor grades [8]. Moreover, Reinhold et al have evaluated quantitative nuclear features by analyzing ki-67 stained images, discriminating low from high grade tumors with an accuracy of 88% [9].

In a resent study published by our research group, an automatic grading system compatible with clinical routine has been proposed. The system based on support vector machines and quantitative nuclear features extracted from Hematoxylin-Eosin stained slides, yielded an overall accuracy of 89.7% [10].

In this study, we introduce a new methodology based on Fuzzy Cognitive Maps (FCMs) to model the process of grading brain tumors.

The FCMs technique constitutes an attractive knowledge-based method, combining the robust properties of fuzzy logic and neural networks. It represents causal knowledge as a signed directed graph with feedback and provides an intuitive framework to incorporate the experts' knowledge and experience [11].

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Our purpose was not only to automate the diagnostic process of tumor grading, but also to build a human-friendly assisting tool, exhibiting interpretability, and providing some insight as to how it derives its outputs. The latter might be beneficial for the pathologists for better evaluation and understanding, of the diagnostic criteria for brain tumors characterization.

Material and Methods

The clinical material comprised 100 Hematoxylin-Eosin stained biopsies of brain tumors collected from the Department of Pathology of the University Hospital of Patras, Greece. Tumors were classified by experienced staff as low (41/100) or high (59/100) according the WHO grading system.

To design the FCM model for astrocytomas tumour grading, three experienced histopathologists played the role of experts and they designed the FCM model for grading following the FCM developing methodology [12]. Histopathologists were asked to describe the conceptual methodology that they use in every day clinical practice to assign the grade of a tumour and they stated that they usually utilize eight concepts to judge for the tumour grading; (see Table 1). The first eight concepts are the main histopathological features and key characteristics, which encode the degree of tumor malignancy and are well documented in bibliography. Thus the FCM model is consisted of these 8 concepts: the concept C_1 represents the cellularity, C_2 the mitoses, C_3 the apoptosis, C_4 the multinucleated cells, C_5 the giant cells, C_6 the vascular proliferation, C_7 the necrosis, C_8 the pleomorphism, and a ninth concept representing the tumour grade.

Then, histopathologists were asked to describe the degree of influence among the concepts and they present their interrelationship using the following IF-THEN rule to infer a linguistic weight representing the cause and effect relationship between every pair of concepts:

*IF value of concept C_i is **A** THEN value of concept C_j is **B** and thus the linguistic weight w_{ij} is **C***

Where ***A, B, C*** are linguistic variables taking values in the range [-1,1].

The linguistic variables ***C*** proposed by the three experts for each interconnection are aggregated using the SUM method and so an overall linguistic weight is produced which is defuzzified with the Centre of Gravity method and finally a numerical weight for w_{ij} is calculated. Using this method all the weights of FCM model are inferred and the FCM shown in fig.1 is developed.

The advantage of this methodology is that it is not required for experts to accurately determine the causality weights using numerical values, but rather to describe qualitatively the degree of causality among concepts.

The feature values correspond to the values that histopathologists assign in every day practice when they examine brain tumour on the microscope. They usually use either two discrete values (0 or 1), or three discrete values (0 or 0.5 or 1), or fuzzy values (low, medium, high) as they described by the qualitative characteristics shown in Table 1.

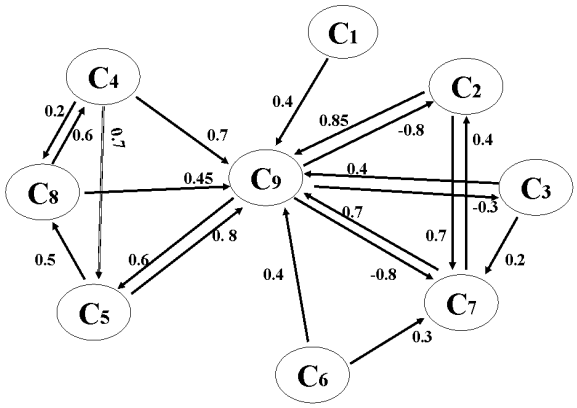

Figure 1: The FCM model for grading brain tumors

The value A_i of the concept C_i expresses the degree of its corresponding physical value. At each simulation step, the value A_i of a concept C_i is calculated by computing the influence of other concepts C_j's on the specific concept C_i following the calculation rule:

$$A_i^{(k+1)} = f(A_i^{(k)} + \sum_{\substack{j=1 \\ j \neq i}}^{N} A_j^{(k)} \cdot w_{ji}) \qquad (1)$$

where $A_i^{(k+1)}$ is the value of concept C_i at simulation step $k+1$, $A_j^{(k)}$ is the value of concept C_j at simulation step k, w_{ji} is the weight of the interconnection from concept C_j to concept C_i and f is a sigmoid threshold function.

Table 1: Main histopathological features of tumour grading

ID	Features (Concepts)	Qualitative Description
C1	Cellularity	mildly, moderate, intense
C2	Mitoses	present, absent
C3	Apoptosis	present, absent
C4	Multinucleated cells	present, absent, numerous
C5	Giant cells	present, absent, numerous
C6	Vascular proliferation	present, absent, intense
C7	Necrosis	present, absent, intense
C8	Pleomorphism	mildly, moderate, intense
C9	Tumour grade	low, high

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To increase the classification ability of the FCM model, the Active Hebbian Leraning (AHL) algorithm is applied to adjust the weights of the FCM [13]. The AHL algorithm adapts all the weights of the FCM model using an acyclic fragment approach for concepts (asynchronous activation and interaction among concepts based on the initial experts' knowledge). Main advantage of the AHL algorithm is that is based on an asynchronous decision making process exactly the same as human does and it takes into consideration the input values of concepts so that to strength and weaken the FCM causal links between concepts increasing the classification capabilities of the FCM. In this way the AHL algorithm enhances the FCMs' effectiveness, flexibility and robustness, and creates an advanced FCM with dynamic behaviour and modelling abilities [11].

After the FCM model development and the determination of the necessary specifications for the implementation of the AHL algorithm, the proposed FCM model was used to evaluate one hundred cases (tissue biopsies) of brain cancer. For every case, the qualitative linguistic values for each concept was transformed in the interval [0,1] where FCM concepts take values. For every case, FCM tool for brain tumor grading start to interact, new weighted interconnections among concepts are calculated implementing the AHL algorithm and new updated values for concepts are calculated. After a limited number of interactions the FCM tool converge and the value of concept C9 representing the classification grade for every case is calculated.

Results

The proposed FCM grading tool achieved a classification accuracy of 92.68% (38/41) and 93.22% (55/59) for brain tumours of low grade and highgrade, respectively. Fig. 2, illustrates the final values of concept C_9 at converge region (we refer to this value as "Grade") for each of the one hundred brain tumor cases. The horizontal axis (X) gives the calculated values of "Grade" after implementing the AHL algorithm and the vertical axis (Y) represents the number of cases used for each grade category.

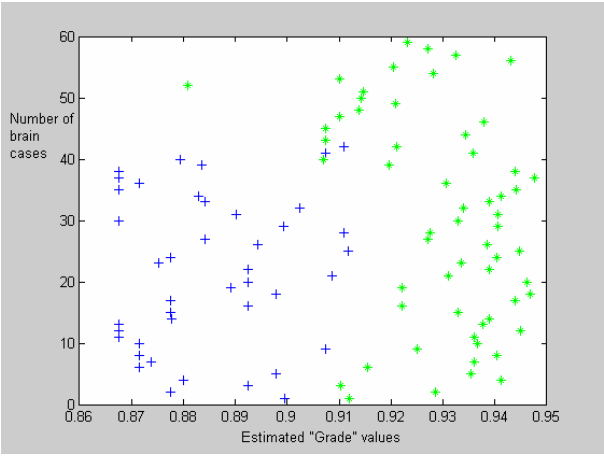

Figure 2: Grade value for 100 cases

For low grade cases the estimated "Grade" values are represented by '+', and for high grade cases the estimated "Grade" values are represented by '*'. It is clear that the proposed approach was able to give distinct different values for the most of low grade and high grade cases.

The classification task requires the determination of a decision or a threshold line. The minimum distance method was employed to determine the decision line defining each grade category. More specifically, using this method the mean values m1 and m2, for low-grade and high-grade categories, were estimated. The decision line is determined as the perpendicular bisector of the line joining m1 and m2. Thus, the value of 0.9085 determined as the threshold value for low grade and high grade categories (regions).

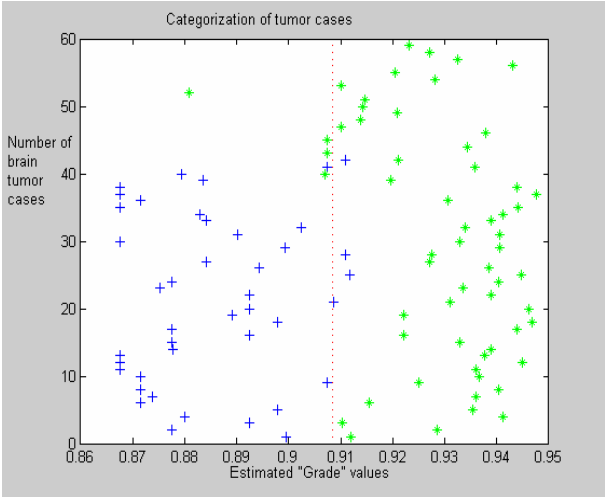

Figure 3: Categorization of astrocytomas based on decision line

Figure 3 illustrates the decision line, which separates the calculated "Grade" into two categories, low grade and high grade respectively. "Grade" values greater than 0.9085 represent high grade cases whereas values lower than 0.9085 represent low grade cases.

Discussion

Brain tumour characterization into low or high-grade defines groups of patients that are significantly different in regard to aggressiveness of disease, and is particularly crucial for the subsequent treatment course. High-grade tumours are frequently treated with radiation therapy whereas many low-grade not. Consequently, the accurate diagnosis is of vital importance since misdiagnosis may lead to inadequate therapy of high-grade or to aggressive therapy of low-grade tumours [14].

Tumour grading in clinical routine is performed by visual observation and recognition of structural tissue parameters during microscopic inspection. However, pathologist's subjective interpretation has been shown to influence diagnostic accuracy [5].

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Computer assistant grading has been extensively examined and currently remains an active research area [6-10]. Previous efforts to standardize classification of tumors have been focused on the analysis of quantitative parameters by means of pattern recognition techniques. In this paper, our aim was to evaluate the contribution of a soft computing approach to improve the uncertainty level in diagnostic decision, utilizing traditional diagnostic concepts and exploiting human specialized knowledge. The novelty of the method was based on the use of FCMs to represent and model experts' knowledge (experience, expertise, heuristic), and on the use of the efficient AHL algorithm for enhancing the classification ability of the FCM.

The proposed FCM-based grading model was able to give diagnostic output with reasonably high accuracy. More specifically, a classification accuracy of 92.68% (38/41) and 93.22% (55/59) was achieved for brain tumours of low and high-grade, respectively. These primary results are comparable with those reported in bibliography [9-10]. Moreover, FCMs fulfil the physicians' requirements for transparency and explicability. Pathologists are now able to understand the model and to evaluate its results. The latter is of particular interest since provides means for better understanding of the diagnostic criteria for tumour grading, reducing the uncertainty level and improving the inter-intra observer agreement.

Furthermore, the ability of the FCMs to model and structure accumulated knowledge and expertise might be useful in practicing pathologists who initially might find difficulty in interpreting the various histological characteristics in degrees of tumour aggressiveness.

Concluding the proposed method possesses three main characteristics: High accuracy, interpretability and transparency. These features render the FCM-based grading model an attractive alternative solution for assisting brain tumor grading, in clinical practice.

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