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Determination of intra-axial brain tumors cellularity through the analysis of T2 Relaxation time of brain tumors before surgery using MATLAB software

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Abstract

Introduction: Timely diagnosis of brain tumors could considerably affect the process of patient treatment. To do so, para-clinical methods, particularly MRI, cannot be ignored. MRI has so far answered significant questions regarding tumor characteristics, as well as helping neurosurgeons. In order to detect the tumor cellularity, neuro-surgeons currently have to sample specimens by biopsy and then send them to the pathology unit. The aim of this study is to determine the tumor cellularity in the brain.

Methods: In this cross-sectional study, 32 patients (18 males and 14 females from 18-77 y/o) were admitted to the neurosurgery department of Shohada-E Tajrish Hospital in Tehran, Iran from April 2012 to February 2014. In addition to routine pulse sequences, T2W Multi echo pulse sequences were taken and the images were analyzed using the MATLAB software to determine the brain tumor cellularity, compared with the biopsy

Results: These findings illustrate the need for more T2 relaxation time decreases, the higher classes of tumors will stand out in the designed table. In this study, the results show T2 relaxation time with a 85% diagnostic weight, compared with the biopsy, to determine the brain tumor cellularity ($p<0.05$).

Conclusion: Our results indicate that the T2 relaxation time feature is the best method to distinguish and present the degree of intra-axial brain tumors cellularity (85% accuracy compared to biopsy). The use of more data is recommended in order to increase the percent accuracy of this techniques.

Keywords: MATLAB software, T2 relaxation time, Intra-axial tumor, MRI

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1. Introduction

Tumors are masses of cells that replicate in an increasingly uncontrollable way (1). They are able break out in different tissues and organs of the body and fall into two categories: benign and malignant (2, 3). Brain tumors that are rooted in the brain Parenchyma are referred to as intra-axial. If the origin of the tumor is outside of the brain (or it is due to metastasis), it is called extra-axial (4, 5). Since the brain is completely covered by skull, it is possible to make a timely diagnosis if only para-clinical equipment and appropriate diagnostic tools are available to identify the state of the brain (6, 7). However, brain tumor diagnosis is usually made when unexplainable patient symptoms are reported (8-10). The extent of tumor threats depend upon a set of factors, including the type of the tumor, size of the tumor, its origin, cellularity of the tumor, and the way it develops (11, 12). However, brain tumor diagnosis is usually made when unexplainable symptoms in the patient are brought about by the tumor (13, 14). In addition, surgery plans and designs play a contributing role in the extent and intensity of post-surgery side effects (15). Therefore, if the surgeon can acquire exhaustive information regarding tumor characteristics via para-clinical equipment (MRI in particular), neurosurgeons may be able to modify their surgery plan to minimize the side effects of the operation (16). Making timely diagnosis of a brain tumor has a considerable impact on the process of the affected patient's treatment. To accomplish this, para-clinical methods, MRI in particular, play a significant role (17, 18). MRI is able to answer many significant questions regarding tumors characteristics, as well as aid neurosurgeons. Yet there are some mysterious and unknown aspects in MRI, including cellularity of tumor. In order to detect the tumor cellularity, the current methods require specimens taken through biopsy and then send them to the pathology unit, after they directly encounter the unknown cellularity of the tumor during the operation (19-21). The aim of the present study is to identify important information regarding tumor cellularity by using specific MRI protocols before the surgery.

2. Material and Methods

A group of 32 patients (18 males and 14 females from 18-77 y/o) were randomly selected from patients suffering intra-axial brain tumors were admitted to the neuro surgery department of Shohada-E-Tajrish Hospital in Tehran (Iran) and gave permission to undergo an operation from April 2012 to February 2014. To ensure the accurate functioning of the software, a different group of 8 patients was sampled in the same way at the final stages of the study. MRI pulse sequences were performed using a Siemens Avanto MRI 1.5 T. It was used on a quadrature coil of brain and particular holding pads to perform MRI pulse sequences of the brain. We conducted the initial analysis of the images with the aid of MRI Syngo b17 software and final analysis was completed using MATLAB software. The MATLAB analysis program (below program) was written to extract T2 relaxation times:

```
function w = Jamil weight (f_mat)
[m n d] = size (f_mat);
var = zeros (m,d);
var_t = zeros (m,1);
w = zeros (m,1);
% calculate inter class VAR
for k =1:d
for I = 1:m
av = sum (f_mat (i,:,k))/n;
var (i,k) = (sum ((abs (f_mat (i,:,k)-av)).^2))^0.5;
end
end
% calculate between class VAR
for i=1:m
av_t=sum (sum (f_mat (i,:,:))) / (n*d);
var_t(i,1) = (sum(sum(((f_mat(i,:,:)-av_t).^2))))^0.5;
end
w=1- (((sum(var')') /d)./var_t);
w (find(var_t==0)) = 0;
Main function of program
%vec=zeros (16,2);
%F=zeros (3,1);
train_file_dir='C:\Users\ebtekar\Desktop\Jamil\excel_ file\';
f_mat=train_Jamil (train_file_dir)
```

```
w=weight_Jamil (f_mat)
Feature function of program
% F(1) = T2
function F= feature_Jamil (vec)
TE=vec (:,1);
SI=vec (:,2);
% calculate F1= T2
SI60=0.37*SI (1);
k=find (SI<SI60);
k=k(1);
T2=TE (k)- (SI60-SI(k))*((TE(k)-TE(k-1))/(SI(k-1)-SI(k)));
F (1) = T2;
train function of program
function F_mat = train_Jamil (train_file_dir)
for j = 1:3 % number of various cellularity
folder=sprint ('%d.xlsx',j);
ff =[train_file_dir folder]
tab = xlsread (ff);
po = find (tab==22);
size_po = size (po);
for I = 1:size_po (1% number of samples per cellularity
vec (:,1) = tab (po(i):po (i)+15,1);
vec (:,2) = tab (po (i):po (i)+15,2);
F= feature_Jamil (vec);
F_mat (:,i,j) = F;
end
end
```

The patients initially underwent MRI which comprised of a routine sequence, as well as the intended sequence of the study, specifically T2 Multi echoes (16 echo) (Table 1). Images are then processed. They were initially processed by using the MRI scanner and the final process and analysis of the images were conducted using MATLAB software. Finally, MATLAB outputs were registered next to the tumor cellularity identified by the surgeon during the surgery. The patient entered the MRI scanner head first and supine on the bed.

Table 1. Parameters of routine brain pulse sequences that were performed in this study

Parameters	Plane	TR (ms)	Matrix size	FOV (cm)	Slice thickness (mm)	ETL
T2W-FSE	Axial	113	320×256	26	5	17
T1W-FSE	Axial	9	320×256	24	5	2
FLAIR	Axial	90	320×256	24	5	11
T2W-FSE	Coronal	113	320×256	23	4	17
T1W-FSE	Sagittal	9	320×256	24	4	2
T2W SE-Multi echo	Axial	22-44-352	320×256	24	4	1

After setting up a quadrature coil to taking image of the brain and holding pads, the patient was sent into the magnet and the scanning processes began. Using parameters already optimized and saved (Table 1), brain routine pulse sequences, including FLAIR, T1W, T2W in the axial plane, T2W in the coronal plane, T1W in the sagittal plane, and T2W Multi echo pulse sequence in the axial plane (Figure 1) were provided. Parallel Imaging techniques, Generalized Auto calibrating Partially Parallel Acquisition (GRAPPA) with a speed factor of 2 was used in all sequences for time reduction. To begin the final analysis, data from the MRI, along with the results of tumor cellularity were sorted into three individual files until retrieved by MATLAB. Files 1 through 3 concerned information about the patients whose tumor cellularity degrees were between 1 to 3. For each file the related table illustrates the mean signal intensity per echo, ranging from 22 to 352 milliseconds with echo intervals of 22 milliseconds. The surgeon, who is one of the main project assistants, assesses the cellularity of tumor during surgery by dividing it into three classes:

1) A tumor that can't be suctioned, razor sharp tools are required to cut them.
2) Tumors that can be crushed and suctioned.

3) Tumors that can be suctioned, but they are not liquid or necrotic in structure.

The intended MATLAB software program consists of four functions, which include Main, Feature, Train, and Weight. The functions take the features and vectors from the file of images and extracts the features. The features include T2 relaxation time, the slope of the graph for T2 relaxation time, and the maximum slope of the for graph T2 relaxation time.

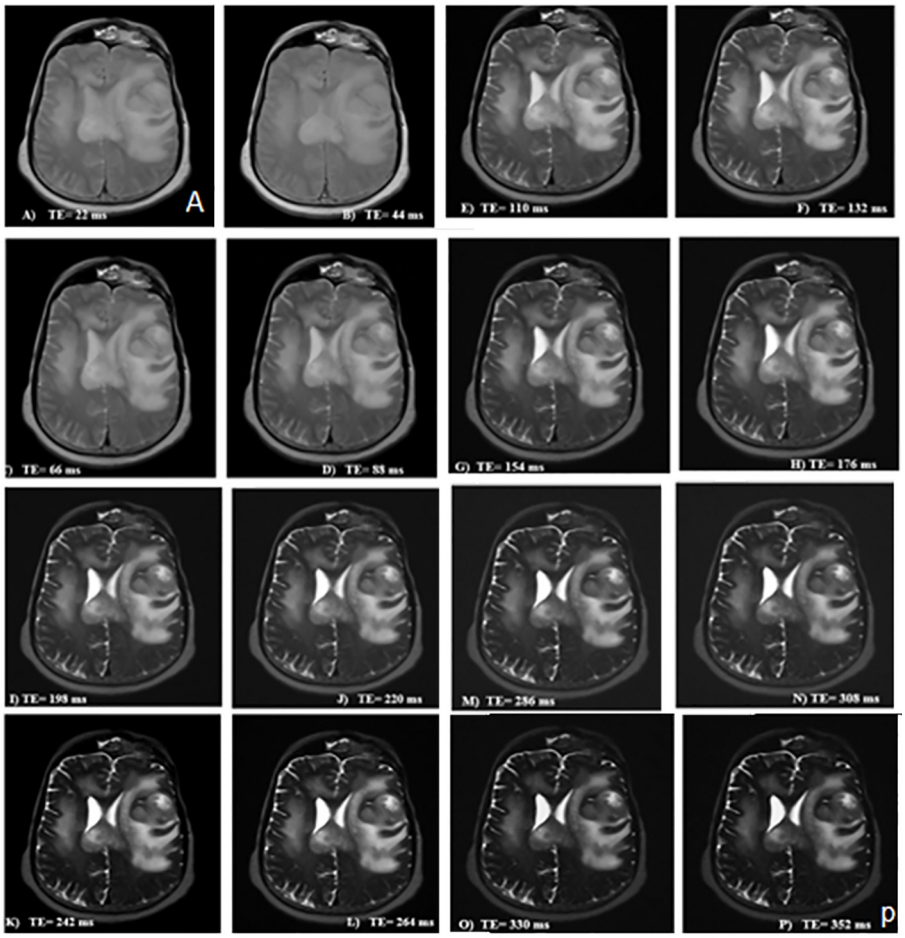

Figure 1. Images provided in sequence (T2 SE Multi echo -16) from a patient who suffers from a tumor GBM by TR equal to 3000 ms and a TE of 22 ms (Figure A) to 352 ms (Figure P). The interval between the echoes was 22 ms for images A to P. By increasing echo time, the T2 contrast of the image may be heavily biased.

3. Results

In this study, the extracted feature of MATLAB software indicated that the best feature, compared with biopsy results, to separate the extent of cellularity from among the features above is T2 relaxation time. Another effective extracted feature is the slope of the T2 relaxation time, which exhibits a 81% diagnostic accuracy compared to biopsy. Finally, the maximum slope of the T2 relaxation time feature had a 79% diagnostic accuracy compared to biopsy. As mentioned earlier, the greater the weight of a feature, the higher capability it possesses to distinguish between classes of tumor cellularity ($p<0.05$). As is shown in the ROI in Figure 2 and the signal intensity in the ROI in Figure 3, T2 relaxation time has a direct relationship between the structures and inter-molecule bond type of each substance and tissue. It is evident that an increase in the tissue intensity, as well as in the strength of inter-molecule relations, brings about a reduction in T2 relaxation times. This occurs because of the increasing inter-actions among the spins or hydrogen of that tissue, and the tissue diffuses quicker and appears to be darker on images with T2 weighted contrast.

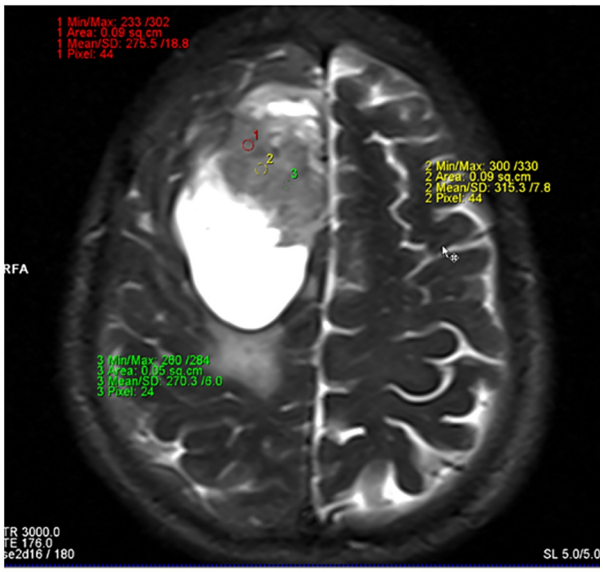

Figure 2. The oligo astrocytoma tumor in a patient with a cystic mass that has a cellularity of grade 3. This image was taken at the initial analysis; three ROIs are drawn on the solid part of tumor.

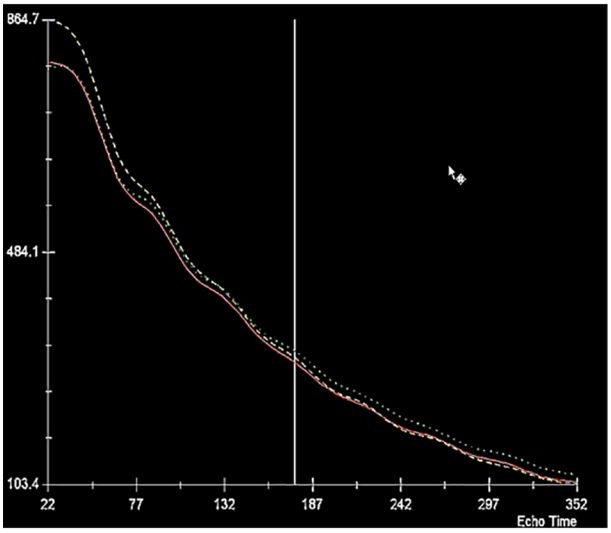

Figure 3. Diagram of T2 relaxation time related to drawing ROI by MRI scanner, where the horizontal axis is TE and the vertical axis is signal intensity.

4. Discussion

The main focus of this research was finding the relationship between the effective criteria for tissue cellularity and MRI images. Therefore, SE multi echo sequences and MATLAB software were used in order to find the T2 relaxation time of tumoral tissue and discover the relationship between cellularity and T2 relaxation times. The features extracted using MATLAB software during this study showed that T2 relaxation has the highest diagnostic accuracy of all features, due to a direct relation to tissue cellularity, compared with biopsy results. To separate the extent of cellularity among the features above, T2 relaxation time was extracted from optimized sequences, such as SE-Multi echo, and is capable of correlating with molecular cellularity. Advanced analysis software can help achieve beneficial results by defining tumor cellularity. It appears that when the extent of cellularity for a tissue or lesion is higher, the T2 relaxation time curve of the tissue or lesion shows a steeper slope (22). It should be noted that similar studies in other works that are quantitative and observation base confirm this result (17, 20, 23). In some similar studies, tumor cellularity was evaluated based on quantitative results and, according to the signal intensity of tumors in PDw and T2w, the diagnostic accuracy result has been low (24, 25). Signal intensity with T2 contrast

directly relates to the molecule structure of each substance and/or tumoral tissues. With regards to the T2 relaxation time, it can be said that the cellularity of a tissue or lesion correlates directly with the steepness of the slope of the T2 relaxation time curve of the tissue or lesion. The main problem in this study was the relatively small number of patients, though the number of patients for this clinical trial is sufficient.

5. Conclusions

The results of this research demonstrated that, of the features or characteristics defined for the software, T2 relaxation time feature is the best indicator to distinguish and present the degree of intra-axial brain tumors cellularity (85% accuracy compared to biopsy). It is because this feature, as opposed to other features, has the highest weight. In other words, the higher the weight of the feature, the higher the capability and certainty it has in distinguishing the classes of tumor cellularity. These findings showed that if the T2 relaxation time of highly consistent tumors is less and the T2 relaxation time curve has a steeper slope, with a maximum peak, and can be based on the tumor cellularity classification, the tumor falls into a low class. In contrast, an increase in T2 relaxation time is accompanied by a reduction in tumor cellularity. The most clinical application of this study involves reducing the number of biopsy of brain tumors to determine tumor cellularity. This study can be continued in some other area, including the pituitary gland and liver lesions.

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Conflict of Interest:

There is no conflict of interest to be declared.

Authors' contributions:

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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