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Recognition of Brain Metastases and Detection of Origin of Cancer using Region Growth Algorithm

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Abstract: Approximately 60% of patients with brain metastases have subacute symptoms. Symptoms are usually related to the location of the tumor. About 85% of the lesions are in the cerebrum, 15% are in the cerebellum, and 5% are in the brainstem. Morning headache with nausea and vomiting together with papilledema are suggestive of intracranial hypertension. Features such as headache, nuchal rigidity and photophobia indicate meninges involvement. The timing of the onset of these symptoms is subacute rather than acute. Detection of brain metastases in patients with undiagnosed primary cancer is unusual but still an existing phenomenon. In these cases, identifying the cancer site of origin is non-feasible by visual examination of magnetic resonance (MR) images. Recently, radiomics has been proposed to analyze differences among classes of visually imperceptible imaging characteristics.
Keywords: brain metastases, meninges, radiomics.

I. INTRODUCTION

Detection of brain metastases in patients with undiagnosed primary cancer is unusual but still an existing phenomenon. In these cases identifying the cancer site of origin is non-feasible by visual examination of magnetic resonance (MR) images. Recently radiomics has been proposed to analyze differences among classes of visually imperceptible imaging characteristics. The brain is that the commonest organ for distant metastases of Lung and breast. Prognosis for patients with brain metastases remains extraordinarily poor. For these patients, it is important to incorporate intracranial treatment at the side of treatment of the first tumor as a result of the treatments for different microscopic anatomy varieties of lung or breast aren't the same, it might be useful if the management of those brain metastases was additionally in line with the pathological types of breast and lung. However, it's not continually possible to determine the pathological varieties of the first tumor by usually used diagnostic test or surgical respiratory organ surgical procedure. Additionally, the designation of those brain metastases is typically created via imaging strategies. Thus, it would be useful if pathological varieties of breast or lung might be inferred through the imaging findings of the brain metastases. Image-based brain metastasis characteristics embrace lesion size, imaging signal intensity, degree and technique of image sweetening, and para-tumor puffiness. The value of MRI within the diagnostic work-up of brain metastases for carcinoma is proscribed. One attainable remedy for this limitation is to use texture analysis (TA) of the MRI data set.

In general, textures area unit advanced spatial pattern with characteristic options together with brightness, color, slope, and size. Texture could carry substantial data concerning the development of a organic structure and may be wont to interpret and analyze the photographs. Although it's simple for humans to acknowledge texture, it may be troublesome for a pc to interpret the feel. TA may be wont to facilitate interpret these texture parts and mathematically quantify the advanced patterns. TA studies are employed in many fields (eg, geographical science, meteorology, pc vision, and medical imaging) since it absolutely was 1st planned in 1973. The medical applications of tantalum give a quantitative means that of analyzing and characterizing the properties of tissues as well as physiological and pathological data. Preliminary proof has steered that tantalum will aid clinicians in cancer designation as a result of the usually used visual scrutiny of pictures could also be unable to recognize delicate variations in textural data such as coarseness or regularity, the applying of tantalumon MRI could enhance the worth of MRI examinations and provide data to differentiate pathological varieties of brain metastases from carcinoma noninvasively.

A. Brain Metastases

Brain metastases are cancer cells that have spread to the brain from primary tumors in other organs in the body (see the image below). Metastatic tumors are among the most common mass lesions in the brain. An estimated 24-45% of all cancer patients in the world have brain metastases.

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B. Signs and Symptoms

Approximately 60% of patients with brain metastases have subacute symptoms. Symptoms are usually related to the location of the tumor and may include the following:

1) Headache
2) Seizure
3) Nausea
4) Vomiting
5) Nuchal rigidity
6) Photophobia
7) Cognitive dysfunction
8) Motor dysfunction

C. Diagnosis

1) *Lab studies:* Laboratory investigations include blood work, such as CBC, electrolyte panel, coagulation screen, and liver function panel.
2) *Imaging studies:* Images provide information on tumor burden in the brain and associated structures, in addition to the rest of the body, and are integral part in formulating the optimal treatment plan. Imaging studies include the following:

a) Chest radiography
b) Computerized tomography (CT)
c) Positron emission tomography (PET)
d) Magnetic Resonance Imaging (MRI)

D. Background of Brain Metastases

Metastatic tumors are among the most common mass lesions in the brain. In the world, an estimated 98,000-170,000 cases occur each year. This is about 24-45% of all cancer patients. The prevalence of brain metastasis is thought to be 120,000-140,000 per year. This disease accounts for 20% of cancer deaths annually, a rate that can be traced to an increase in the median survival of patients with cancer because of modern therapies, increased availability of advanced imaging techniques for early detection, and vigilant surveillance protocols for monitoring recurrence. In addition, most systemic treatments (eg, the use of chemotherapeutic agents, which may penetrate the brain poorly) can transiently weaken the blood-brain barrier (BBB) and allow systemic disease to be seeded in the CNS, leaving the brain a safe haven for tumor growth.

Metastases from systemic cancer can affect the brain parenchyma, its covering, and the skull. This discussion is restricted to the incidence, patho physiology, and management of metastases to the brain parenchyma.

E. Patho physiology

To metastasize, tumor cells have to gain access to the circulation, survive while circulating, pass through the microvasculature of the adopted organs, extravasate into the organ parenchyma, and reestablish themselves at the secondary site. This process requires the tumor cells to penetrate the basement membrane and cross the sub endothelial membrane. Tumor cells achieve this by producing proteolytic enzymes, particularly metalloproteinases and cathepsins to help them to break down the basal matrix and enhance their invasiveness. Tumor cells modulate the expression of fibronectin, collagen, or laminin, and change the type of integrin receptor on their surface and on the surface of the surrounding stromal cells, resulting in desegregation of the stromal cells and creating a permissive environment for them to expand and invade. Invading cells detach from the tumor mass, disperse, and traverse the epithelial/endothelial boundary; they will use the vascular conduit to colonize distant organs. Furthermore, they have to survive intravascular circulation and avoid immune surveillance during this journey. They accomplish that by coating themselves with a shield made out of the coagulating elements such as fibrin and platelets in the blood. These metastatic emboli also produce adherens to slow themselves down to a halt in the blood stream. These adheren molecules allow the circulating cancer cells to reattach onto the vascular wall and gain entry to the host tissue by disruption of the endothelial barrier. This leads to re-establishment of distant micrometastasis.

Tumor cells can survive in environments of low oxygen tension. When a tumor increases in volume by more than 2-3 times, the tumor expresses angiogenic factors such as angiopoietin-2 and vascular endothelial growth factors. These angiogenic modulators promote sprouting of surrounding blood vessels, which results in tumor angiogenesis. Additionally, these paracrine factors influence

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the readiness of target organs to accept tumor growth to prepare a favorable microenvironment for the tumor to undergo exponential growth and become a macrometastasis.

Different tumors metastasize preferentially to different organs. Cells with similar embryologic origins are generally believed to have similar growth constraints and express similar sets of adhesion molecules, such as addressins. An example is melanoma; the cells are closely related to CNS cells (they are derived from the neural crest cells), and melanoma commonly metastasizes to the brain. Certain cell-surface markers in cancer are indicators and/or predictors of distant metastasis, eg, nm23 and CD44 in breast cancer. Similarly, breast cancer cells that are HER positive are more likely to metastasis to the brain. Renal, gastrointestinal, and pelvic cancer tend to metastasize to the cerebellum, whereas breast cancer is more commonly found in the posterior pituitary. Thus, the trafficking of cancer cells to their final destination is not entirely random and may be guided by factors produced by stromal cells of their host organ.

Recently, it has been shown that metastases may have originated from cancer initiating cells, which are more resistant to therapy by virtue of their stemlike properties. Additionally, cancer cells recruit bone marrow–derived cells to modify the microenvironment of distant recipient sites, forming a premetastatic niche by alternating the level of fibronectin and making the site more favorable for the colonization of metastatic tumor.

Cancer cells have been shown to recruit bone marrow—derived cells to modify the microenvironment of distant recipient site; the formation of a premetastatic niche by alternating the level of fibronectin and making the site more favorable for the colonization of metastatic tumor.

F. Mortality/Morbidity

The most common origins of brain metastasis are systemic cancer of the lung, breast, skin, or GI tract. In 2700 cases from the Memorial Sloan-Kettering Cancer Center in New York, the distribution of primary cancers was as follows: 48% lung, 15% breast, 9% melanoma, 1% lymphoma (mainly non-Hodgkin), 3% GI (3% colon and 2% pancreatic), 11% genitourinary (21% kidney, 46% testes, 5% cervix, 5% ovary),10% osteosarcoma, 5% neuroblastoma, and 6% head and neck tumor. Of note, renal, GI, and pelvic cancers tend to metastasize to the cerebellum, whereas breast cancer most commonly affects the posterior pituitary. Cancer-cell trafficking may not be entirely random, and factors produced by stromal cells may guide their final destination in the brain.

Table 1 shows other data for sources of brain metastases and Sources of Primary Tumor in Brain Metastases

Primary Tumor Site	Percentage (%)
Lung	21
Breast	9
Melanoma	40
Lymphoma, mainly non-Hodgkin	1
GI tract	3
Genitourinary tract	11
Osteosarcoma	10
Head and neck	6

Primary lung tumors account for 50% of all metastatic brain tumors. Lung cancer is the most common origin of metastatic disease. Of lung cancer patients who survive for more than 2 years, 80% will have brain metastases.

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The average time interval between the diagnosis of primary lung cancer and brain metastases is 4 months. Interestingly, small cell carcinomas, which are only 20% of all lung cancers, account for 50% of brain metastases from lung cancer. In a retrospective study, 6.8% of the first cancer recurrence was in the brain.

Breast tumor is the main source of metastatic disease in women, followed by melanoma, renal, and colorectal tumors. Breast cancer is a heterogeneous disease demonstrating genotypic and phenotypic diversity. The interval between the diagnosis of primary breast cancer and brain metastasis can be up to 3 years. The first site of distant failure is the brain, alone or as a component of metastatic disease, and a proportionately high number are ER- or HER2 negative. Yet HER positive cancer is twice as common to metastasize to the brain. Additionally, it has been shown that nm23 and CD44 in breast cancer are indicators for distant metastasis.

Melanoma commonly metastasizes to the brain. Melanoma has an increased
incidence among other systemic cancers in terms of metastasizing to the brain. About 40-60% of patients with melanoma will have brain metastasis. Melanoma cells are closely related to CNS cells due to their embryonic origin and neural crest cells, and they share common antigens such as MAG-1 and MAG-2. After melanoma is detected in the brain, median survival is 3 months. These metastases are poorly responsive to all treatments. Approximately 14% of cases have no identifiable primary tumor. Melanomagenic tumors also involve the pial/arachnoid. In CT imaging, they are marginally enhanced with contrast compared with bronchogenic cancer. They are distinctive in MRI because of the melanin or due to hemorrhage. Others metastatic tumors that commonly bleed are thyroid and renal cell carcinoma. Unfortunately, patients with brain metastasis from melanoma are known to do poorly despite therapy.

Metastatic disease from the breast, thyroid, renal cells, and colon are more commonly found as a single metastatic lesion, whereas metastatic disease from lung cancer and melanoma are more commonly found to be multiple lesions. Testicular tumor is a uncommon cancer and yet it more frequently metastasizes to the brain as compared with lung cancer.

Patients with brain metastasis at the same time of having systemic cancer (synchronous metastasis) tend to do worse as compared with patients with metachronous metastatic disease.

G. Gender

Although melanoma spreads to the brain more commonly in males than in females, gender does not affect the overall incidence of brain metastases.

H. Age

About 60% of patients are aged 50-70 years.

CNS metastasis is not common in children; it accounts for only 6% of CNS tumors in children.

Leukemia accounts for most metastatic CNS lesions in young patients, followed by lymphoma, osteogenic sarcoma, and rhabdomyosarcoma.

Germ-cell tumors are common in adolescents and young adults aged 15-21 years.

II. LITERATURE SURVEY

Texture analysis methods quantify the spatial variations in gray level values within an image and thus can provide useful information on the structures observed. However, they are sensitive to acquisition conditions due to the use of different protocols and to intra- andinter scanner variations in the case of MRI. The influence was studied of two protocols and four different conditions of normalization of graylevels on the discrimination power of texture analysis methods applied to soft cheeses. Thirty-two samples of soft cheese were chosen at two different ripening periods (16 young and 16 old samples) in order to obtain two different microscopic structures of the protein gel. Proton density and T2-weighted MR images were acquired using a spin echo sequence on a 0.2 T scanner. Gray levels were normalized according to four methods: original gray levels, same maximum for all images, same mean for all images, and dynamics limited to 3. Regions of interest were automatically defined, and texture descriptors were then computed for the co-occurrence matrix, run length matrix, gradient matrix, autoregressive model, and wavelet transform. The features with the lowest probability of error and average correlation coefficient were selected and used for classification with 1-nearest neighbor (1-NN) classifier. The best results were obtained when using the limitation of dynamics to, which enhanced the differences between the two classes. The results demonstrated the influence of the normalization method and of the acquisition protocol on the effectiveness of the classification and also on the parameter selected for classification.

Texture analysis was applied to high-resolution, contrast-enhanced(CE) images of the breast to provide a method of lesion discrimination. Significant differences were seen between benign and malignant lesions for a number of textural features, including

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entropy and sum entropy. Using logistic regression analysis (LRA), a diagnostic accuracy of Az=0.80+- 0.07 was obtained with a model requiring only three parameters. By initially dividing the patient data into training and test datasets, reasonable model robustness was also established. The goal was to investigate the feasibility of differentiating brain metastases from different types of lung cancers using texture analysis (TA) of T1 post contrast MR images. Methods: TA was performed, and four subset textures were extracted and calculated separately. The capability of each texture to classify the different types of lung carcinoma was investigated using the Kruskal-Wallis test and receiver. Operating characteristic analysis. K-nearest neighbor (KNN) classifier model and back-propagation artificial neural network (BPANN) classifier model were used to build models and improve the predictive ability of TA. An efficient textural feature extraction algorithm (TFEA) based on higher order statistical cumulant namely Kurtosis for a class of brain MR imaging applications was proposed. Using a model that represents the wavelet coefficient energies of the sub-bands of multi-level decomposition of the image as a basis, a feature set involving three parameters for each band corresponding to probability density function (PDF)of generalized Gaussian type is derived. The logical correctness and working of the proposed TFEA are first verified based on MATLAB ver.2010a tool. The algorithm is applied in conjunction with one of the popularly used canny edge detection algorithm for segmenting a class of real and synthetic magnetic resonance(MR) images to detect the region of a tumor if present. The use of the proposed approach results in reduced feature set size thus obviating the need for employing specialized feature selection/reduction algorithms. A detailed look at the experimental results clearly show an improvement in the segmentation quality compared with conventional method.

Early detection of brain metastases increases survival in patients with cancer, since image-guided radio surgery treatment was discussed. As support for the qualitative diagnosis made by radiologists, Computer Assisted Diagnosis provides a quantitative and reproducible analysis. This article reviews the methods for an automatic detection of brain metastases in contrast-enhanced T1-weighted magnetic resonance imaging. Model-based methods detect metastases due to their high degree of similarity with models representing their morphology, mainly templates. On the other hand, methods based on brain symmetry and intensity search intensity differences between both brain hemispheres with respect to the symmetry axis. Model-based methods are more commonly used because they allow the detection of metastases of a wider range of measures.

In paper**,** aims at developing a joint FDG-PET and MRI texture-based model for the early evaluation of lung metastasis risk in soft-tissue sarcomas (STSs). We investigate if the creation of new composite textures from the combination of FDG-PET and MR imaging aggressive tumors. Towards this goal, a cohort of 51 patients with histologically proven STSs of the extremities was retrospectively evaluated. All patients had pre-treatment FDG-PET and MRI scans comprised of T1-weighted andT2-weighted fat-suppression sequences (T2FS). Nine non-texture features (SUV metrics and shape features) and forty-one texture features were extracted from the tumor region of separate (FDG-PET, T1 and T2FS) and fused(FDG-PET/T1 and FDG-PET/T2FS) scans. Volume fusion of the FDG-PET and MRI scans was implemented using the wavelet transform. The influence of six different extraction parameters on the predictive value of textures was investigated. The incorporation of features into multivariable models was performed using logistic regression. The multivariable modeling strategy involved imbalance-adjusted bootstrap resampling in the following four steps leading to final prediction model construction: (1) feature set reduction; (2) feature selection; (3) prediction performance estimation; and (4) computation of model coefficients. Uni variate analysis showed that the isotropic voxel size at which texture features were extracted had the most impact on predictive value. In multivariable analysis, texture features extracted from fused scans significantly outperformed those from separate scans in terms of lung metastases prediction estimates.

The objective of this study is to investigate the use of pattern classification methods for distinguishing different types of brain tumors, such as primary gliomas from metastases, and also for grading of gliomas. A computer assisted classification method combining conventional magnetic resonance imaging (MRI) and perfusion MRI is developed and used for differential diagnosis. The proposed scheme consists of several steps including ROI definition, feature extraction, feature selection and classification. The extracted features include tumor shape and intensity characteristics as well as rotation invariant texture features. Features subset selection is performed using Support Vector machines (SVMs) with recursive feature elimination. The binary SVM classification accuracy, sensitivity, and specificity, assessed by leave-one-out cross-validation on102 brain tumors, are respectively 87%, 89%, and 79% for discrimination of metastases from gliomas, and 87%, 83%, and 96% for discrimination of high grade from low gradeneoplasms. Multi-class classification is also performed via aone-versus-all voting scheme.

III. PROPOSED SYSTEM

We propose a method using contrast-enhanced magnetic resonance(MR) images of brain metastases from lung and breast cancer to establish a model able to differentiate both classes by means of Texture analysis and classification techniques. In proposed method using MR images of brain metastases from lung and breast cancer are detected using edge detection, where detected region

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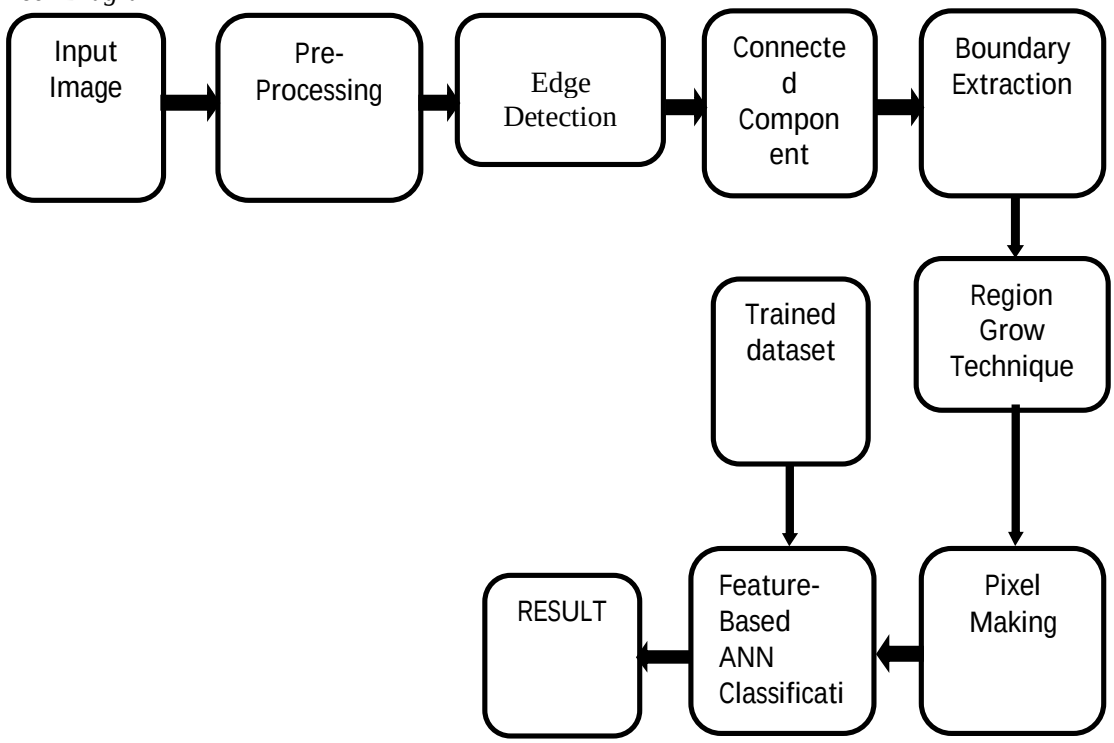
boundaries are extracted using Boundary extraction technique. Region grow technique and pixel masking is used to extract the features. Based on the features obtained, using Artificial Neural Network Classifier region properties of metastases.

A. Block Diagram



B. Pre-processing

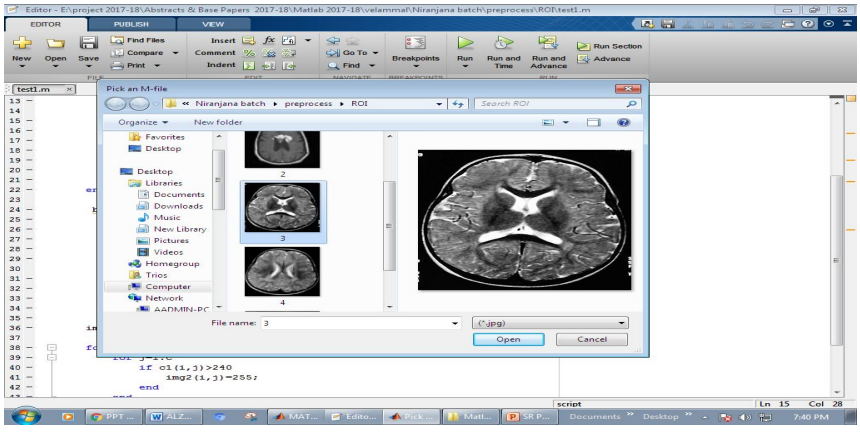
1) Conversion of Image to grayscale image
2) Process of removing noises from input image
3) Enhanced quality of input image

C. Edge Detection

1) Edge Detection is the process of dividing an image into multiple parts based on its boundaries. This is typically used to identify objects or other relevant information in digital images.
2) Skull detection: By taking the assumption that brain is the largest connected structure inside the head we select the component whose area is the biggest.

IV. RESULT

A. The screen shots of the output done using matlab 2016R is shown.



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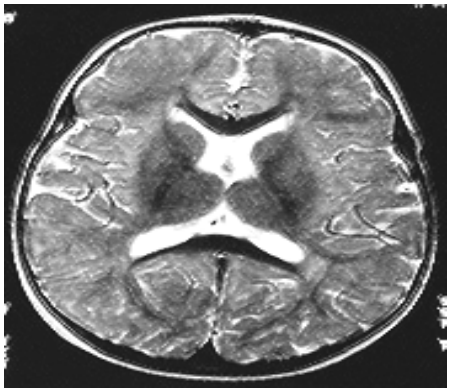
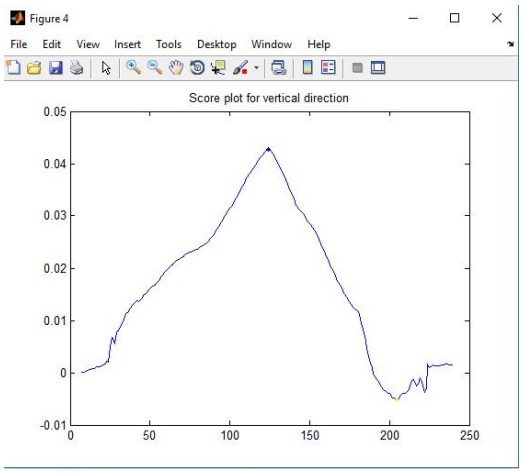
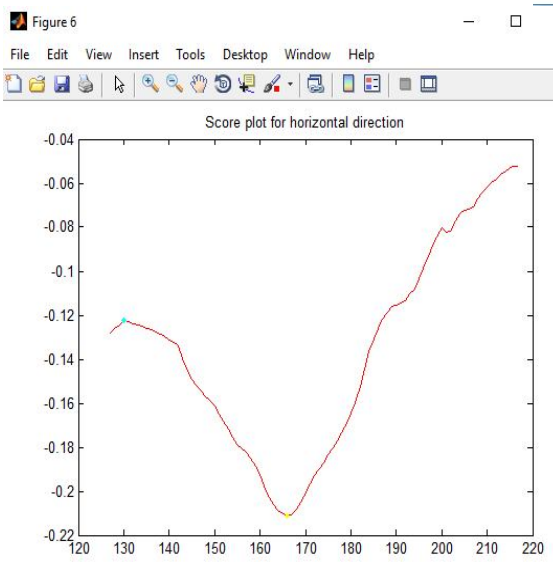
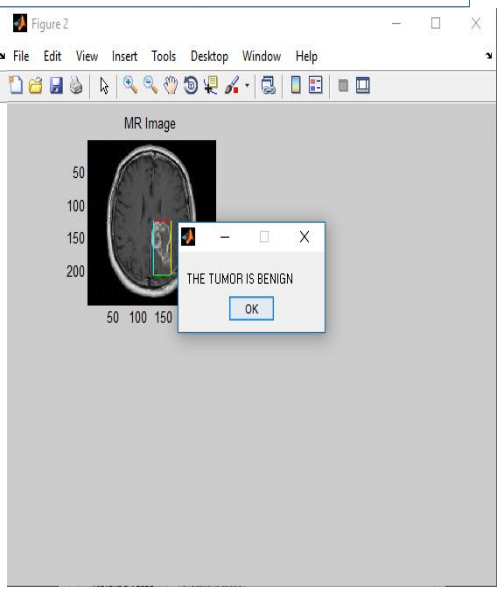
Filterd Image

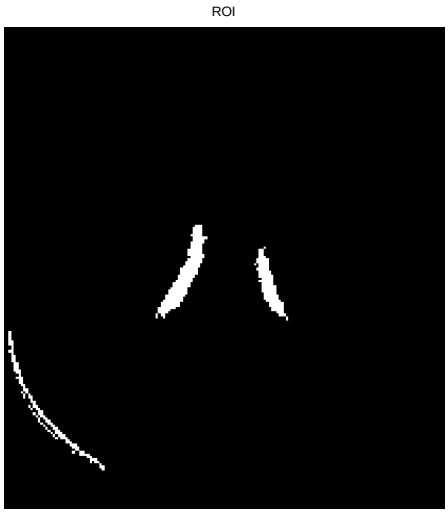








BINARY IMAGE



V. CONCLUSION

The project will promise to identify the brain metastases growth using the brain MR images from which the origin of the primary site of cancer can be determined. The stages of cancer is accurately detected using the region growth technique based on the statistical properties and feature extraction with improved accuracy.

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