A Major Project Report
On

A NOVEL DENOISING AND SEGMENTATION OF BRAIN TUMOR IN MRI IMAGES

Submitted for partial fulfillment of the requirements for the award of the degree
of
BACHELOR OF TECHNOLOGY
IN
ELECTRONICS AND COMMUNICATION ENGINEERING

BY

Mr. Preetham Ganesh Kamisetty (15641A0496)

Under the Guidance of
Ms. G. Radhika
(Assistant Professor)

DEPARTMENT OF ELECTRONICS AND COMMUNICATION ENGINEERING
VAAGDEVI COLLEGE OF ENGINEERING
(Autonomous, Affiliated to JNTUH, Accredited By NBA)
BOLLIKUNTA, WARANGAL - 506 005

2015-2019

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CERTIFICATE

This is to certify that the project work entitled "**A NOVEL DENOISING AND SEGMENTATION OF BRAIN TUMOR IN MRI IMAGES"** is a bonafide work carried out by **Mr. Preetham Ganesh Kamisetty (15641A0496)** in partial fulfillment of the requirements for the award of degree of **Bachelor of Technology** in ***Electronics and Communication Engineering*** from Vaagdevi College of Engineering, (Autonomous) during the academic year 2018-2019.

Ms. G. Radhika **Mr.M.Shashidhar** **Assistant Professor** **Head of the Department**

ACKNOWLEDGEMENT

The development of the project though it was an arduous task, it has been made by the help of many people. We are pleased to express our thanks to the people whose suggestions, comments, criticisms greatly encouraged us in betterment of the project.

We would like to express our sincere gratitude and indebtedness to our project Guide **Mrs.B.Sreedevi, Associate Professor,** for her valuable suggestions and interest throughout the course of this project.

We would like to express our sincere thanks and profound gratitude to **Dr. K. Prakash**, principal of **Vaagdevi College of Engineering,** for his support, guidance and encouragement in the course of our project.

We are also thankful to Head of the Department **Mr. M.Shashidhar**, **Associate Professor** for providing excellent infrastructure and a nice atmosphere for completing this project successfully.

We are also thankful to **Project Coordinators,** for their valuable suggestions, encouragement and motivations for completing this project successfully.

We are thankful to all other faculty members for their encouragement

We convey our heartfelt thanks to the lab staff for allowing us to use the required equipment whenever needed.

Finally,We would like to take this opportunity to thank our family for their support through the work. We sincerely acknowledge and thank all those who gave directly or indirectly their support in completion of this work.

Mr. Preetham Ganesh Kamisetty (15641A0496)

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ABSTRACT

Objectives: The objective of this work is to study denoising and segmentation methods to extract brain tumor area from the MRI image, implemented using MATLAB 2013b and to examine its performance metrics.

Methods/Statistical Analysis: As preprocessing stage is essential for better segmentation as it removes noise that makes images having similar qualities so that tumor area can be shown and extracted with great accuracy. An anisotropic diffusion filter with 8-connected neighborhood is employed for noise removal and Fast Bounding Box (FBB) for exactly showing tumor area on MRI images. Finally Support vector machine classifies the boundary and extracts the tumor from the MRI image.

Findings: Brain tumor is the major cause of cancer deaths in human which is due to uncontrollable cells growth in brain portion. Prior detection, diagnosis and accurate healing of brain tumor are the primary work to prevent human death. Image segmentation can also be done in several approaches like thresholding, region growing, watersheds and contours. Specialists with their basic knowledge do manual segmentation, which is time consuming process, where this limitation can be overcome by our fully automatic proposed method. Employing of an isotropic diffusion filter with 8-connected neighborhood compare to 4-connected neighborhood results in considerable improvements in terms of lower identical error rates. Our proposed Fast Bounding Box (FBB) method is applied that exactly shows tumor area on MRI images and its central region is selected judiciously to have sample points required for functionality of one class SVM classifier training. To achieve optimal classification level there is necessity of SVM with optimum efficiency, so that we adapted Support vector machine that immediately stops its operation once all the points are separated.

Application/Improvements: Segmented tumor obtained with precision are very useful for radiologists and specialists to had good idea of estimating tumor position and size with great dealt with ease and without any prior information.

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CHAPTER 1

PROJECT OVERVIEW

1.1 INTRODUCTION

Brain has a very difficult structure and is viewed as a kernel section in the body. Nature has tightly preserved the brain within a skull that hinders the study of its function as well as makes the analysis of its diseases more complex. Brain tumors either include in the significant spinal canal or throughout the skull. Computerized defect detection in MRI is really priceless in several diagnostic and therapeutic usages like CT images, MRI images, are two imaging modalities that assist researchers and medical practitioners to gain knowledge about the brain through watching noninvasively. Noise elimination or denoising is an essential task in image processing applications. As per image enhancement we define it as a gathering of events that emphasize the acceptable study for the specified image which makes targeted elements of the image less complicated to peer or lowering the noise. Regularly, noise removal is having resilient influence on the major elements of the image processing system.

In present days major constraint in biomedical field is noise, which is termed as a random signal produced by electronic instruments. But today's electronic equipment is designed to reduce the noise certain extent. Regularly in order to study the noise we require prior knowledge for judging the characteristics of a desired signal and undesired noise present in the MRI images.

Recent MRI imaging technique can provide complete information about human body internal view. It is completely secured and free from any kind of injury due to radiation, since there is no drug injecting into the human body. Likewise Positron Emission Tomography (PET), Computer Tomography (CT) is the other techniques available for medical imaging applications. In traditional methods even experienced doctors also taking more time to identify the diseases. So for this reason inevitability of clear-cut and fully automatic process that can make available detailed evidence to the doctor is imperative.

Similar works previously undertaken by authors mainly rely on the manual and automatic natured segmentation on MRI brain tumors, that are broadly categorized into two types non-intelligent and intelligent based. We presented image denoising using Haar and Daubechies Transforms. It is found to be

Daubechies3 (db3) wavelet seems to be more efficient than Haar wavelet for reducing a certain level of speckle noise in the medical images and also it

enhances the visual quality of the medical image a lot. We state that there are numerous noise reduction techniques had been developed for removing noise and conserving edge details in images. Each technique has its own suppositions, benefits and restrictions. Finally the idea behind these techniques is to acquire better results in terms of quality and in removal of different type of noises.

In this project we presented a technique to improve the image quality with the help of denoising and resolution enhancement. Here the paper concentrates on the average**,** median type of filter and Wiener type filtering for image denoising purpose and an interpolation based Discrete Wavelet Transform (DWT) method for resolution enhancement. In the author presented work where it improves Signal to Noise Ratio (SNR) of CT images utilizing wavelet transforms. It analyzed signals and the entire set of wavelet share some common properties but each wavelet has a certain unique properties of Image decomposition, denoising and reconstruction which provide difference in PSNR. In the author proposed Symlets wavelet technique using 2-D DWT in image processing. The scope of the effort comprises compression and denoising, image clarity and being in quench of the decomposition and phases of threshold and to discover energy retained (image recovery) and misplaced.

In spite having major constraints and challenges in case brain tumor segmentation in terms of irregular shape and location, among those one severe challenge is how to inspect the real data nonlinear distribution. Likewise the main job of one class classification in is to pick the data that belongs to target class or not. Additionally one-class Support Vector Machines (SVMs) is employed in such cases of brain tumor segmentation in that have learning nonlinear distribution of real data is considered without prior knowledge.

As we summarized the rest of this paper as follows: Section 2 describes the methods and materials used in the algorithms. Section 3 elucidates the simulation results and its discussion. Finally, conclusions are in the last section.

CHAPTER 2

PROPOSED METHOD AND MATERIALS

2.1 Block diagram

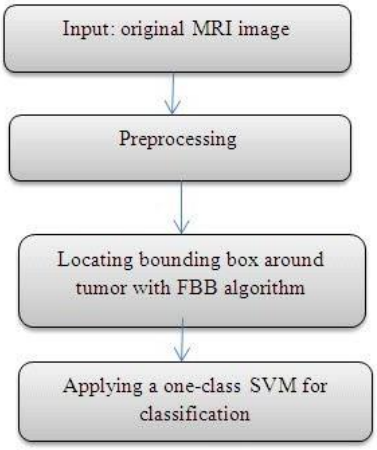


Fig 2.1: Block diagram of the proposed approach.

2.2 Components Required:

- Isotropic diffusion filter
- Fast Bounding Box (FBB)
- Support vector machine
- MATLAB2013b

2.3 Proposed Method

Our main intension in current work is brain image denoising and segmentation algorithms using FBB and SVM for improved performance. Brain tumor segmentation on brain MRI images which is unconditionally automatic and thus no requirement of human involvement. Figure 1 shows the block diagram of the proposed approach explained as follows below.

2.3.1 Pre-Processing:

The pre-processing phase has two folds:

- During the first step useless parts of skull present outside are to be eliminated, for doing this boundary of skull is identified with the aid of automatic global thresholding technique, which can generate binary mask image thus it is becomes very easy to eliminate the useless parts of the skull that present outside to it. Therefore by following likewise required

Calculations in further steps and segmentation computation can greatly reduce.

- In this step noise in brain MRI images are removed where these noises are present in random nature in image to be eliminated before segmentation process without disturbing the edges and reduce the image clarity. So therefore an anisotropic diffusion filter with 8-connceted neighborhood is used in order to eliminate the noise with ease.

$$I(x,y,t) = I_0(x,y) * G(x,y,t) \quad \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

$I(x,y,t)$ is filtered image

$I_0(x,y)$ is original image

$G(x,y,t)$ is Gaussian kernel with different scale parameter t

- In this filtering technique treated to be iterative process of heat diffusion and equalization method where $I(x,y,t)^{(x=y)}$ is the initial condition, and it is alike to time 't'. Here we presented a determination for the prior indicated problem that documents space variant (anisotropic) obscuring appropriate to trace edges with more accuracy. We employed the 4-connected neighborhood for calculation purpose where here we used for calculations 8-connected neighborhood.

2.3.2 FBB Procedure

Basically presence of tumor in brain contains right and left symmetry which is in dissimilar symmetry. Here FBB technique is applied to know the similarity of gray scale intensity histograms, then by using Bhattacharya coefficient calculation the tumor portion is marked by rectangle bounding box automatically.

2.3.3 SVM Classification

In one class SVM classifier the tumor pixels are considered as training set. When we detect tumor of different shapes in MRI image those parts are extracted with bounding box without affecting healthy part in brain image and to overcome this type of catastrophe, only the central part is considered as sample points. Moreover to simplify the job kernel RBF with SVM is taken into consideration thus feature extraction process also completes during training step of SVM only, thus results in elimination of feature extraction process in this technique.

As extension work our proposed technique embedded with the algorithm having capability of finding the tumor at different locations of the brain, by this means the output comprises of oblong pack around the brain tumors. Further symmetrical axis line isolates brain into two equilibrium regions one being test image and other being reference.

The output for the input image it takes the input as MRI image then finds the boundary of the brain and axis of symmetry In order to detect the tumor precisely horizontal and vertical score values must plotted contrary to the number of days and growth rate, when the plots shows dissimilar it indicates presence of tumor. The similarity among two normalized intensity histograms can be obtained by coefficient of Bhattacharya by considering horizontal and vertical score function. By using the centroids of the border marker method the unsupervised mean shift clustering is instigated to catch the prevalent cluster successive in MR slices. MR images are taken as input for the simulation.

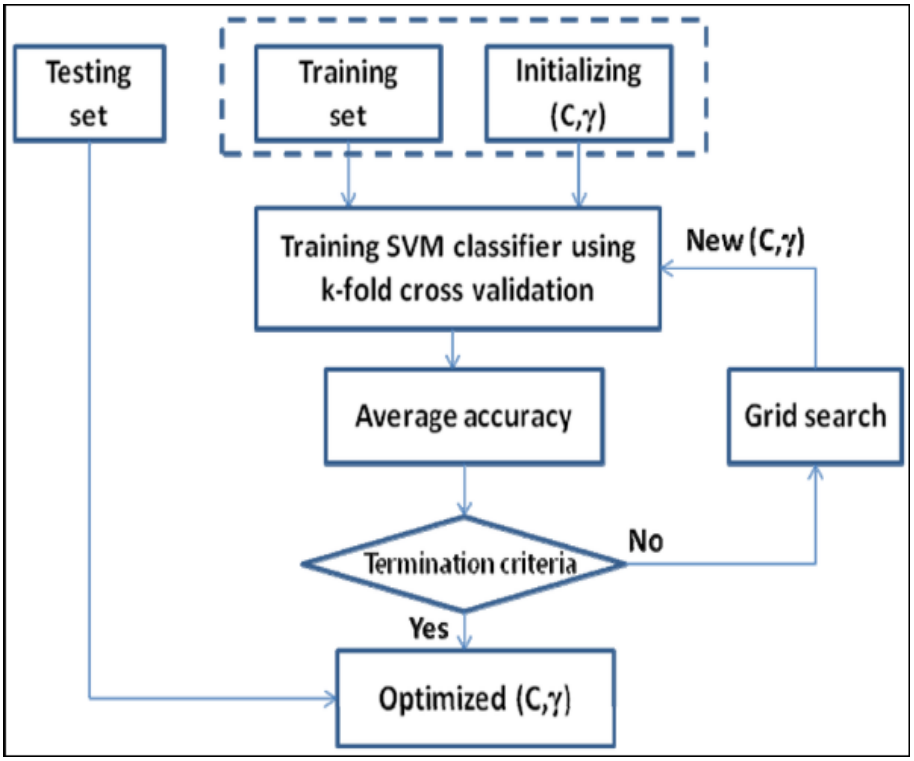


Fig 2.2: SVM working process Flow chart

Above figure shows the flow chart Support Vector Machine Working process

2.4 Magnetic resonance imaging

Magnetic resonance imaging is a medical imaging technique used in radiology to form pictures of the anatomy and the physiological processes of the body in both health and disease. MRI scanners use strong magnetic fields, electric field gradients, and radio waves to generate images of the organs in the body. MRI does not involve X-rays and the use of ionizing radiation, which distinguishes it from CT or CAT scans. Magnetic resonance imaging is a medical application of nuclear magnetic resonance (NMR). NMR can also be used for imaging in other NMR applications such as NMR spectroscopy.

While the hazards of X-rays are now well-controlled in most medical contexts, MRI may still be seen as a better choice than CT. MRI is widely used in hospitals and clinics for medical diagnosis, staging of disease and follow-up without exposing the body to radiation. However, MRI may often yield different diagnostic information compared with CT. There may be risks and discomfort associated with MRI scans. Compared with CT scans, MRI scans typically take longer and are louder, and they usually need the subject to enter a narrow, confining tube. In addition, people with some medical implants or other non-removable metal inside the body may be unable to undergo an MRI examination safely.

MRI was originally called 'NMRI' (nuclear magnetic resonance imaging) and is a form of NMR, though the use of 'nuclear' in the acronym was dropped to avoid negative associations with the word. Certain atomic nuclei are able to absorb and emit radio frequency energy when placed in an external magnetic field. In clinical and research MRI, hydrogen atoms are most often used to generate a detectable radio-frequency signal that is received by antennas in close proximity to the anatomy being examined. Hydrogen atoms exist naturally in people and other biological organisms in abundance, particularly in water and fat. For this reason, most MRI scans essentially map the location of water and fat in the body. Pulses of radio waves excite the nuclear spin energy transition, and magnetic field gradients localize the signal in space. By varying the parameters of the pulse sequence, different contrasts may be generated between tissues based on the relaxation properties of the hydrogen atoms therein.

Since its development in the 1970s and 1980s, MRI has proven to be a highly versatile imaging technique. While MRI is most prominently used in diagnostic medicine and biomedical research, it also may be used to form images of non-living objects. MRI scans are capable of producing a variety of chemical and physical data, in addition to detailed spatial images. The sustained increase in demand for MRI within health systems has led to concerns about cost effectiveness and over diagnosis.

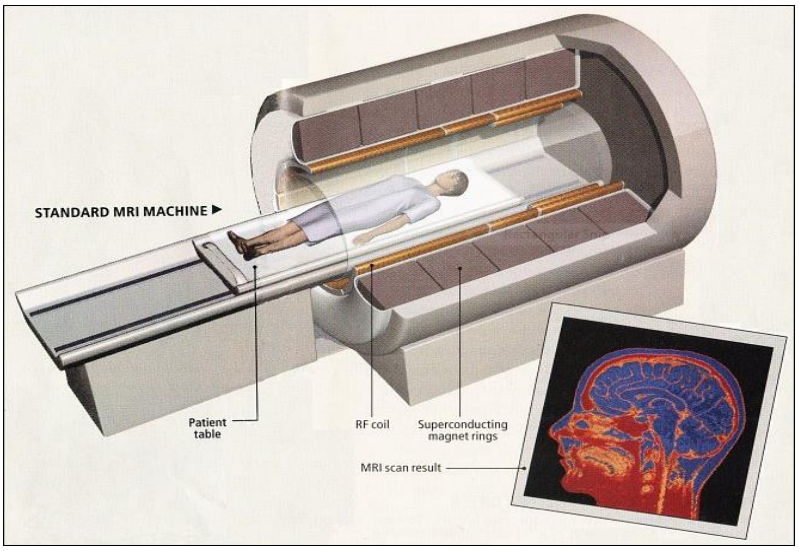


Fig 2.3: Magnetic resonance imaging

2.5 MATLAB

MATLAB (**mat**rix **lab**oratory) is a multi-paradigm numerical computing A proprietary programming language developed by MathWorks, MATLAB allows matrix manipulations, plotting of functions and data, implementation of algorithms, creation of user interfaces, and interfacing with programs written in other languages, including C, C++, C#, Java, Fortran and Python.

Although MATLAB is intended primarily for numerical computing, an optional toolbox uses the MuPAD symbolic engine, allowing access to symbolic computing abilities. An additional package, Simulink, adds graphical multi-domain simulation and model-based design for dynamic and embedded systems.As of 2017, MATLAB has roughly 1 million users across industry and academia. MATLAB users come from various backgrounds of engineering, science, and economics.

CHAPTER 3

TUMOR

3.1 Definition of Tumor

A tumor, also known as a neoplasm, is an abnormal mass of tissue that may be solid or fluid-filled.

It is not the same as a cancer, although some can develop into cancers. A tumor is a kind of lump or swelling and does not necessarily pose a health threat.

Fast facts on tumors.

Here are some key points about tumors. More detail and supporting information is in the main article.

- Tumors are not necessarily cancerous.
- Benign tumors cannot spread.
- A premalignant tumor is one that is not yet cancerous but is about to be.
- An excisional biopsy involves removing an entire lump or surrounding area.

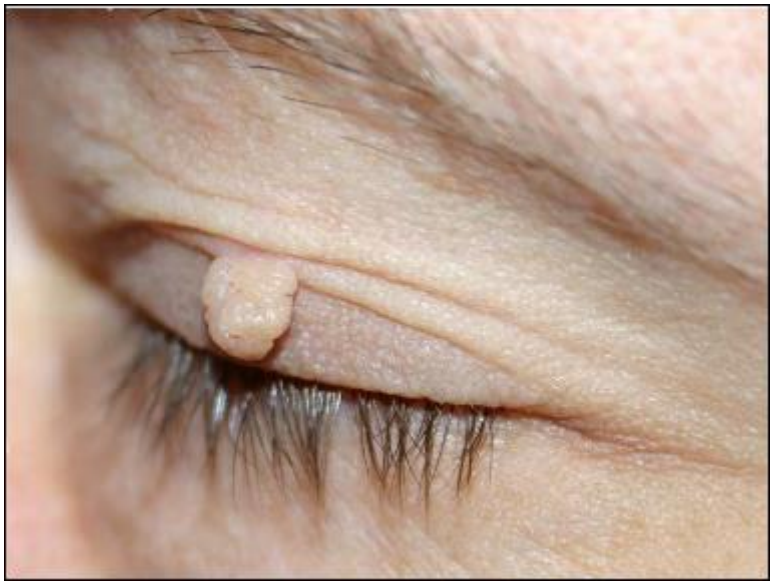


Fig 3.1: A soft fibroma of the eyelid is just one type of tumor.

- When doctors use the term tumor, they are talking generically and not about the size of the lesion.
- Tumor sizes may vary enormously.

- They may be referred to as masses, which are larger, or nodules, which refer to smaller lumps.
- Almost any type of cell or tissue can develop into a type of tumor.

3.2 Types of Tumors

There are many different types of tumors and a variety of names for them. Their names usually reflect their shape, the origin of the cell, and the type of tissue they appear in.

In general, tumors are divided into three groups:

- **Benign:** These are not cancerous and cannot spread. A benign tumor will remain in its current form. They do not generally return after being removed.

- **Premalignant:** A premalignant tumor is not yet cancerous but appears to be developing the properties of cancer.

- **Malignant:** Malignant tumors are cancerous. They can grow, spread, and get worse.

  There is sometimes no clear dividing line between cancerous, precancerous and non-cancerous tumors. In some cases, putting a tumor in a category can be an estimation, especially if the tumor is in the middle of the spectrum or changing rapidly. Some benign tumors can eventually become premalignant, and then malignant.

3.2.1 Benign

- Most benign tumors are not harmful to human health.
- However, even though they are not cancerous, some may press against nerves or blood vessels and cause pain or other negative effects. Benign tumors of endocrine tissues may result in the excessive production of some hormones.

3.2.1.1 Examples of benign tumors include:

3.2.1.1.1 Adenomas

Adenomas are tumors that arise from glandular epithelial tissue, the thin membrane that covers glands, organs, and other structures in the body.

A polyp in the colon is a type of adenoma.

Other examples:

- parathyroid adenoma
- eosinophilia adenoma
- basophilic adenoma
- bile duct adenoma
- chromophobe adenoma
- fibro adenoma
- hepatic adenoma

Adenomas do not start as cancers. However, they can change and become cancerous, taking the form of adenocarcinomas.

3.2.1.1.2 Fibroids or fibromas

- Fibroids are benign tumors that can grow on the fibrous or connective tissue of any organ. Uterine fibroids are common and can cause vaginal bleeding, pelvic pain or discomfort, and urinary incontinence. They can be "soft" or "hard" depending on the proportion of fibers to cells.
- There are many types of fibroma, including angiofibroma, dermatofibroma, and ossifying and non-ossifying fibroma.
- Some fibromas can cause symptoms and may require surgical removal. In rare cases, fibroids can change and eventually become cancerous. They are then called fibrosarcomas

3.2.1.1.3 Hemangiomas

- A hemangioma on the scalp of a child
- Hemangiomas are benign tumors that consist of excessive blood cells.
- They can sometimes be seen on the surface of the skin and are known as strawberry marks. The majorities of hemangiomas appears at birth and gradually go away after some months or years.
- Hemangiomas do not usually require any treatment. If they affect the ability of an individual to eat, hear, or see, the doctor may recommend treatment with corticosteroids.
- If the patient is over 10 years of age, they are more commonly removed using laser surgery.

3.2.1.1.4 Lipomas

- Lipomas are the most common form of soft-tissue tumor.
- They consist of fat cells. Most of them are very small, painless, soft to the touch, and generally movable. They are more common among people aged over 40 years. Experts disagree on whether lipomas can change and become cancerous.
- There is a range of lipomas, including:
  - angiolipoma
  - myelolipoma
  - fibrolipoma
  - spindle cell lipoma
  - hibernoma
  - atypical lipoma

3.2.2 Premalignant

- This type of tumor requires close monitoring
- Examples of premalignant growths include:

3.2.2.1 Actinic keratosis

- Also known as senile keratosis or solar keratosis, this is a premalignant growth consisting of patches of skin that turn crusty, scaly, and thick.
- Fair-skinned people are more at risk of developing these types of growths, especially those who are overexposed to sunlight.
- Actinic keratoses are seen as potentially premalignant, because around 20 percent of them progress to squamous cell carcinoma. Doctors usually recommend treating them because of this. Continuous exposure to the sun increases the risk of malignancy.

3.2.2.2 Cervical dysplasia

- This is a change in the normal cells lining the cervix.
- The growth can be premalignant and is at risk of developing into cervical cancer.
  - Cervical dysplasia is diagnosed with a PAP smear. It is most common in women aged 25 to 35 years and may be removed with freezing techniques or

- By removing the cone of tissue from the cervix.

3.2.2.3 Metaplasia of the lung

- These growths occur in the tubes that carry air from the windpipe into the lung, or the bronchi.
- The bronchi are lined with glandular cells, which can change and become squamous cells. Metaplasia of the lung is most commonly caused by smoking.

3.2.2.4 Leukoplakia

- Thick, white patches can form on the gums, the bottom of the mouth, the insides of the cheeks, and, less commonly, on the tongue. They cannot be scraped off easily.
- Experts believe smoking or chewing tobacco is the main cause. Although Leukoplakia is rarely dangerous, a small percentage can eventually become cancerous. Many mouth cancers occur near areas of leukoplakia.
- The condition usually clears up when people quit smoking. Quitting both alcohol and tobacco together has better results. The patches can be removed using a laser, a scalpel, or a cold probe that freezes the cancer cells.

3.2.3 Malignant

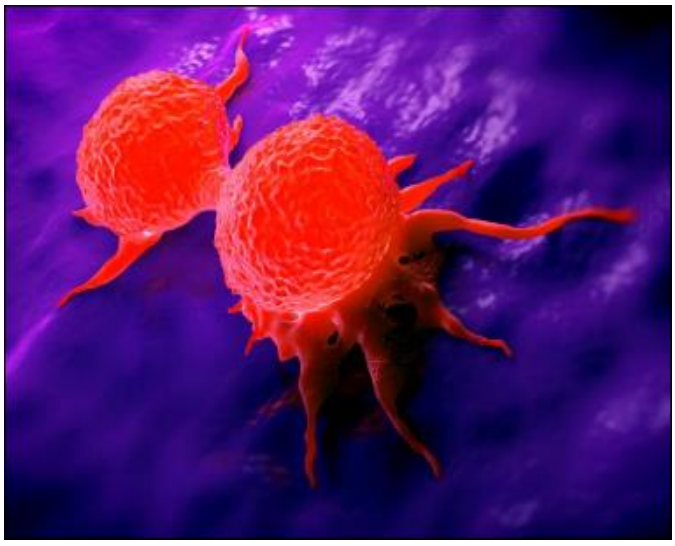


Fig 3.2: Malignant Tumor

- Malignant tumors divide and spread rapidly, colonizing new areas.
- Malignant tumors are cancerous tumors that can potentially result in death.

- Unlike benign tumors, malignant ones grow quickly, and can spread to new territory in a process known as metastasis.
- The abnormal cells that form a malignant tumor multiply at a faster rate.
- The cancer cells that metastasize are the same as the original ones. If a lung cancer spreads to the liver, the cancer cells now growing in the liver are still lung cancer cells. They have, however, acquired the ability to invade other organs.

3.2.3.1 Types of Malignant Tumor

Different types of malignant tumor are made up of specific types of cancer cells, including:

- **Carcinoma:** These tumors are formed from epithelial cells. For example, carcinomas can occur in the stomach, prostate, pancreas, lung, liver, colon, or breast. Many of the most common tumors are carcinomas, especially among older adults.
- **Sarcoma:** These tumors start in connective tissue, such as cartilage, bones, fat, and nerves. They originate in the cells outside the bone marrow. The majority of sarcomas are malignant.
- **Germ cell tumor:** These are tumors made from the cells that give life, sperm and egg cells. Germ cell tumors most commonly occur in the ovaries or testicles. The majority of testicular tumors start from germ cells. Less commonly, germ cell tumors may also appear in the brain, abdomen or chest.
- **Blastoma:** Tumors formed from embryonic tissue or developing cells are known as blastomas and are more common in children than adults. Examples include medulloblastoma and glioblastoma, types of brain tumor, retinoblastoma, a tumor in the retina of the eye, osteoblastoma, a type of bone tumor, and neuroblastoma, a tumor of the nervous system found in children.

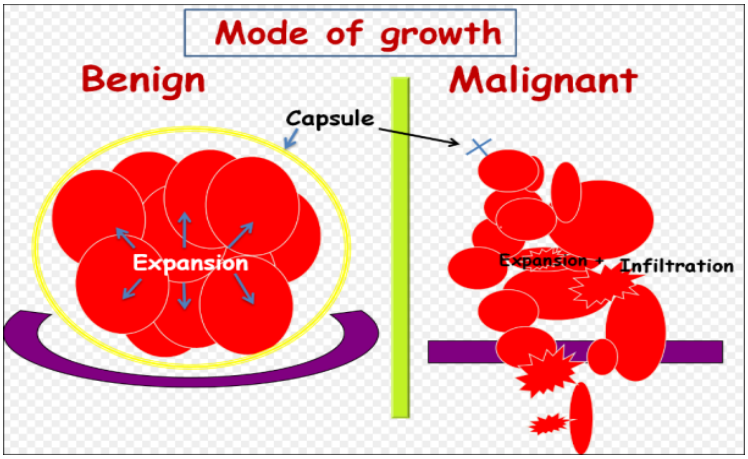


Fig 3.3: Malignant Tumor Mode of Growth

3.3 Diagnosis

To diagnose a tumor and decide whether a tumor is malignant or not, a sample must be taken by a surgeon or an interventional radiologist, sent to a laboratory, and examined under a microscope by a pathologist.

This sample is called a biopsy.

3.3.1 Biopsy

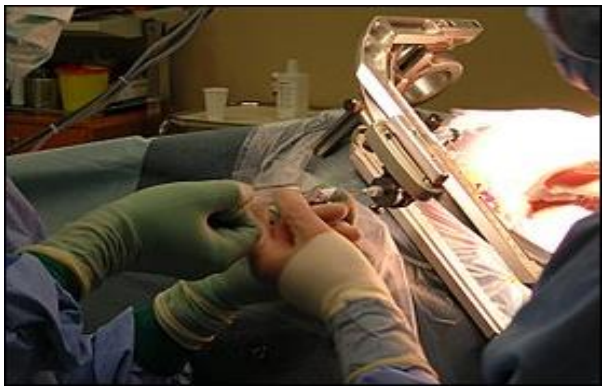


Fig 3.4: Brain biopsy

A **biopsy** is a medical test commonly performed by a surgeon, interventional radiologist, or an interventional cardiologist involving extraction of sample cells or tissues for examination to determine the presence or extent of a disease. The tissue is generally examined under a microscope by a pathologist, and can also be analyzed chemically. When an entire lump or suspicious area is removed, the procedure is called an **excisional biopsy**.

An **incisional biopsy** or **core biopsy** samples a portion of the abnormal tissue without attempting to remove the entire lesion or tumor. When a sample of tissue or fluid is removed with a needle in such a way that cells are removed without preserving the histological architecture of the tissue cells, the procedure is called a needle aspiration biopsy. Biopsies are most commonly performed for insight into possible cancerous and inflammatory conditions.

3.3.2 Types of Biopsy

There are three different types of biopsy:

3.3.2.1 Excisional biopsy

This involves the surgical removal of the entire lump or suspicious area.

- During an excisional biopsy, the doctor removes an entire lump or an entire area of abnormal skin, including a portion of normal skin. You'll likely receive stitches to close the biopsy site after this procedure.

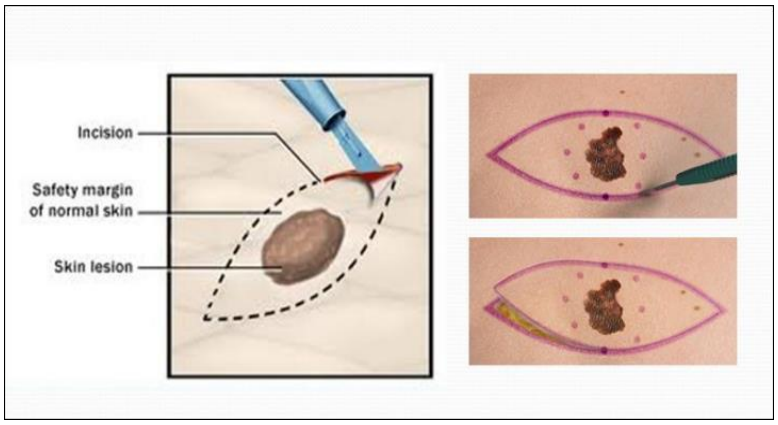


Fig 3.5: Excisional biopsy

3.3.2.1.1 Advantages of excisional biopsy

Excisional biopsy is accurate and gives few false negative results.

A pathologist's exam of the biopsy tissue gives information that helps plan your treatment, including:

- Tumor size
- Tumor type
- Tumor grade
- Hormone receptor status

- In some cases, excisional biopsy is the only surgery needed to remove the tumor.

3.3.2.1.2 Drawbacks of excisional biopsy

⇒ Compared to a needle biopsy, a surgical biopsy:

- Is more invasive
- Has a longer, more uncomfortable recovery time
- Has a higher risk of infection and bruising
- The amount of tissue removed during an excisional biopsy can also change the look and feel of the breast.

- If the biopsy results are benign (not cancer), more surgery may have been done than was needed.

3.3.2.2 Incisional or core biopsy

In this type of biopsy, a sample is surgically removed from the tumor.

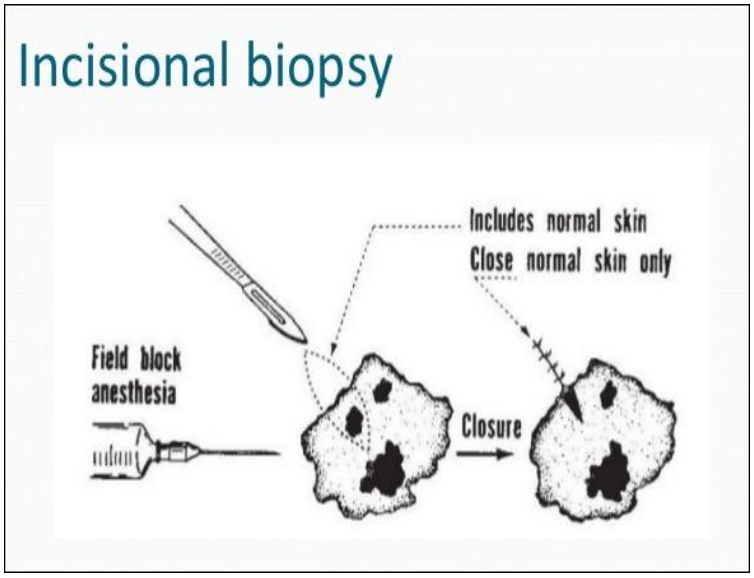


Fig3.6 Incisional or core biopsy

3.3.2.3 Needle aspiration biopsy

- Fluid or a sample of tissue is removed with a needle.
- Samples are often taken from different parts of the tumor for the most accurate results.
- Core needle biopsy uses a hollow needle to remove samples of tissue from the breast. It's the standard way to diagnose (or rule out) breast cancer.

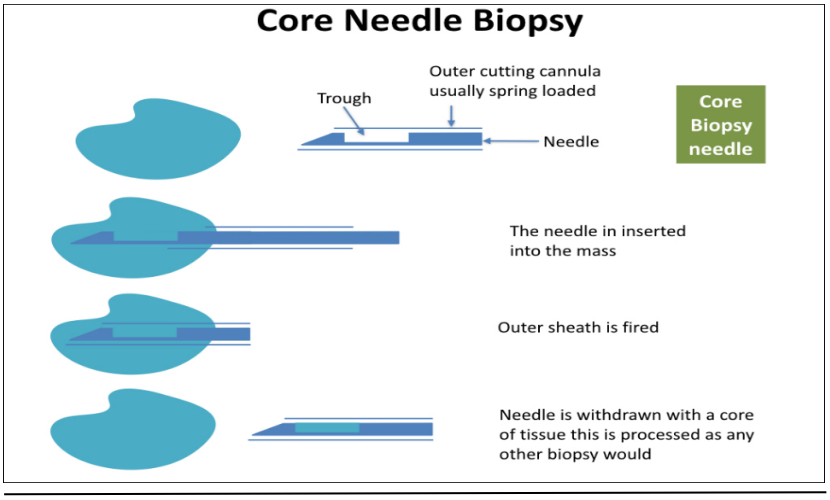


Fig 3.7: Core needle Biopsy

A pathologist studies these samples under a microscope to see if they contain cancer. If they do, more tests will be done to help plan your treatment.

3.3.2.3.1 Uses of core needle biopsy

Core needle biopsy can be used for a:

- Lump that can be felt (palpable mass)
- Suspicious area that can only be seen on a mammogram or other imaging test (nonpalpable abnormal finding)

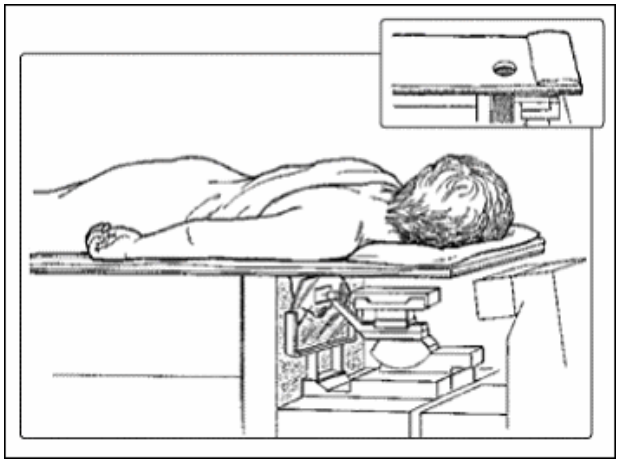


Fig 3.8: Needle Biopsy using stereotactic mammography

3.3.2.3.2 Advantages of core needle biopsy

Core needle biopsy is accurate when done by an experienced radiologist. It’s quick and doesn't involve surgery. There’s only a small chance of infection or bruising.

If breast cancer is found, the tissue removed during a core needle biopsy gives important information including:

- Tumor type
- Tumor grade
- Hormone receptor status
- If the tissue sample is benign (not cancer), surgery may be avoided. (In some cases, however, even if the tissue sample is benign, a surgical biopsy may be needed to confirm the diagnosis.)

3.3.2.3.3 Drawbacks of core needle biopsy

- One drawback of core needle biopsy is the needle can miss a tumor and take a sample of normal tissue instead. This is most likely to occur when the biopsy is done without the help of breast ultrasound, breast MRI or stereotactic mammography.

- If a tumor is missed, the biopsy will show cancer doesn't exist when in fact, it does. This is called a false negative result and delays diagnosis.
- For nonpalpable abnormal findings, false negative results occur in up to 4 percent of image-guided core needle biopsies.
- For palpable masses, false negative results occur less often than with nonpalpable abnormal findings.

- Another drawback of core needle biopsy is that it may not give full information about the tumor.

- For example, it can't tell the size of a tumor and sometimes, it can't tell whether a tumor is non-invasive breast cancer (ductal carcinoma in situ) or invasive breast cancer. Taking multiple tissue samples can help limit this problem.

However, in some cases, a surgical biopsy is needed to get complete information on the tumor.

3.4 Outlook

The outlook of a tumor will depend entirely on its type.

- A benign tumor may pose no health problems at all. A malignant tumor, however, can be fatal and difficult to treat. The severity of a malignant tumor also depends on the location of the tumor and how quickly it can metastasize.
- If you find a lump on your body that you suspect could be a tumor, have it checked by a doctor.
- The earlier a tumor can be identified, the quicker it can be treated if required.

CHAPTER 4

BRAIN TUMOR

4.1 Brain Tumor

A brain tumor occurs when abnormal cells from within the brain. There are two main types of tumors: malignant or cancerous tumors and benign tumors. Cancerous tumors can be divided into primary tumors that start within the brain, and secondary tumors that have spread from somewhere else, known as brain metastasis tumors. All types of brain tumors may produce symptoms that vary depending on the part of the brain involved. These symptoms may include headaches, seizures, problem with vision, vomiting, and mental changes. The headache is classically worse in the morning and goes away with vomiting. More specific problems may include difficulty in walking, speaking, and with sensation. As the disease progresses unconsciousness may occur.

The cause of most brain tumors is unknown. Uncommon risk factors include inherited neurofibromatosis, exposure to vinyl chloride, Epstein–Barr virus, and ionizing radiation. The evidence for mobile phones is not clear. The most common types of primary tumors in adults are meningiomas (usually benign), and astrocytomas such as glioblastomas. In children, the most common type is a malignant medulloblastoma. Diagnosis is usually by medical examination along with computed tomography or magnetic resonance imaging. This is then often confirmed by a biopsy. Based on the findings, the tumors are divided into different grades of severity.

Treatment may include some combination of surgery, radiation therapy, and chemotherapy. Anticonvulsant medication may be needed if seizures occur. Dexamethasone and furosemide may be used to decrease swelling around the tumor. Some tumors grow gradually, requiring only monitoring and possibly needing no further intervention. Treatments that use a person's immune system are being studied. Outcome varies considerably depending on the type of tumor and how far it has spread at diagnosis. Glioblastomas usually have poor outcomes while meningiomas usually have good outcomes. The average five-year survival rate for brain cancer in the United States is 33%.

Secondary or metastatic brain tumors are more common than primary brain tumors, with about half of metastases coming from lung cancer.

Primary brain tumors occur in around 250,000 people a year globally, making up less than 2% of cancers. In children younger than 15, brain tumors are second only to acute lymphoblastic leukemia as the most common form of cancer. In Australia the average lifetime economic cost of a case of brain cancer is $1.9 million, the greatest of any type of cancer.

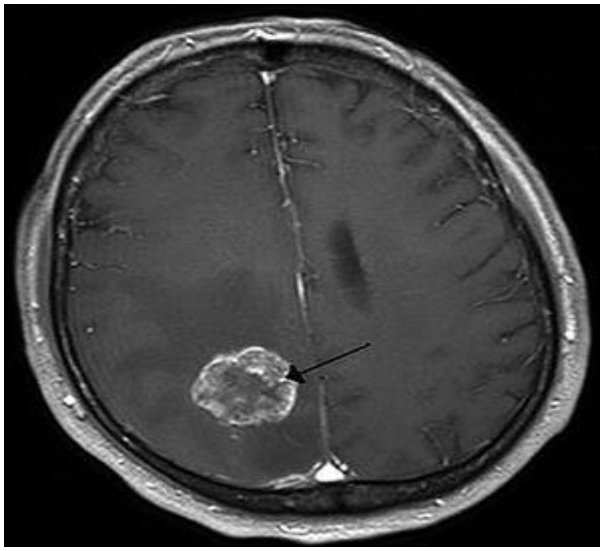


Fig 4.1: Intracranial neoplasm, brain tumour

4.2 Signs and symptoms

The signs and symptoms of brain tumors are broad. People with brain tumors will experience them no matter if the tumor is benign (not cancerous) or cancerous. Primary and secondary brain tumors present with similar symptoms, depending on the location, size, and rate of growth of the tumor. For example, larger tumors in the frontal lobe can cause changes in the ability to think. However, a smaller tumor in an area such as Wernicke's area (small area responsible for language comprehension) can result in a greater loss of function.

4.2.1 Headaches

Headaches as a result of raised intracranial pressure can be an early symptom of brain cancer. However, isolated headache without other symptoms is rarer, and other symptoms often occur before headaches become common. Certain warning signs for headache exist which make it more likely to be associated with brain cancer. These are as defined by the American Academy of Neurology: "abnormal neurological examination, headache worsened by Valsalva maneuver, headache causing awakening from sleep, new headache in the older population,

progressively worsening headache, atypical headache features, or patients who do not fulfill the strict definition of migraine".

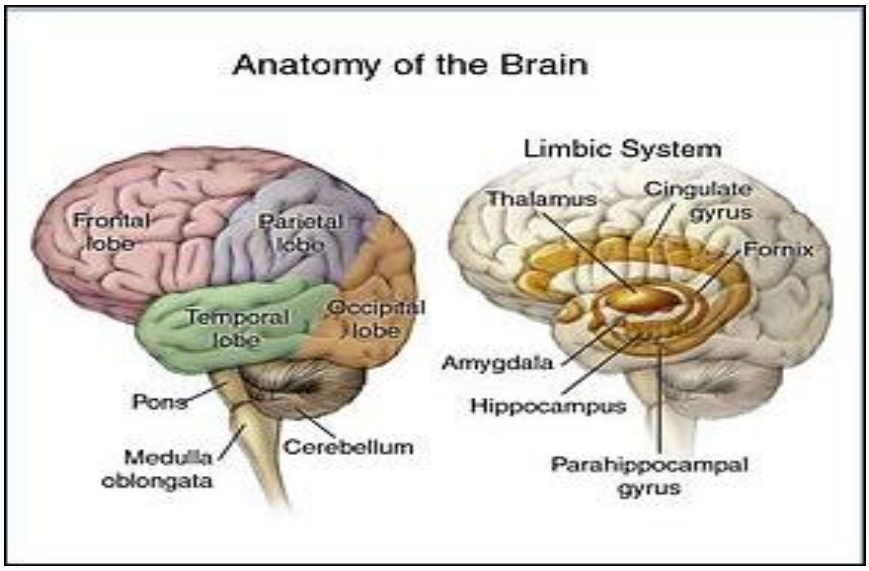


Fig 4.2: The main areas of the brain and limbic system.

4.2.2 Location specific symptoms

The brain is divided into 4 lobes and each lobe or area has its own function. A tumor in any of these lobes may affect the area's performance. The location of the tumor is often linked to the symptoms experienced but each person may experience something different.

- **Frontal lobe:** tumors may contribute to poor reasoning, inappropriate social behavior, personality changes, poor planning, lower inhibition, and decreased production of speech (Broca's area).
- **Temporal lobe:** Tumors in this lobe may contribute to poor memory, loss of hearing, difficulty in language comprehension (Wernicke's area).
- **Parietal lobe:** Tumors here may result in poor interpretation of languages, decreased sense of touch and pain, and poor spatial and visual perception.
- **Occipital lobe:** Damage to this lobe may result in poor or loss of vision.
- **Cerebellum:** Tumors in this area may cause poor balance, muscle movement, and posture
- **Brain stem:** Tumors on this can affect blood pressure, swallowing, and heartbeat.

4.2.3 Behavior changes

Despite the personality and behavior changes that occur in people with brain tumors, little research on such changes has been done. A person's personality may be altered due to the tumor damaging lobes of the brain. Since the frontal, temporal, and parietal lobes control inhibition, emotions, mood, judgment, reasoning, and behavior, a primary or secondary tumor in that region can cause inappropriate social behavior, temper tantrums, laughing at things which merit no laughter, and even psychological symptoms such as depression and anxiety. Personality changes can have damaging effects such as unemployment, unstable relationships, and a lack of control.

4.3 Cause

Epidemiological studies are required to determine risk factors. Aside from exposure to vinyl chloride or ionizing radiation, there are no known environmental factors associated with brain tumors. Mutations and deletions of so-called tumor suppressor genes, such as P53, are thought to be the cause of some forms of brain tumor. Inherited conditions, such as Von Hippel–Lindau disease, multiple endocrine neoplasia, and neurofibromatosis type 2 carry a high risk for the development of brain tumors. People with celiac disease have a slightly increased risk of developing brain tumors.

Although studies have not shown any link between cell phone or mobile phone radiation and the occurrence of brain tumors, the World Health Organization has classified mobile phone radiation on the IARC scale into Group 2B – possibly carcinogenic. Discounting claims that current cell phone usage may cause brain cancer, modern, third-generation (3G) phones emit, on average, about 1% of the energy emitted by the GSM (2G) phones that were in use when epidemiological studies that observed a slight increase in the risk for glioma – a malignant type of brain cancer – among heavy users of wireless and cordless telephones were conducted.

4.3.1 Pathophysiology

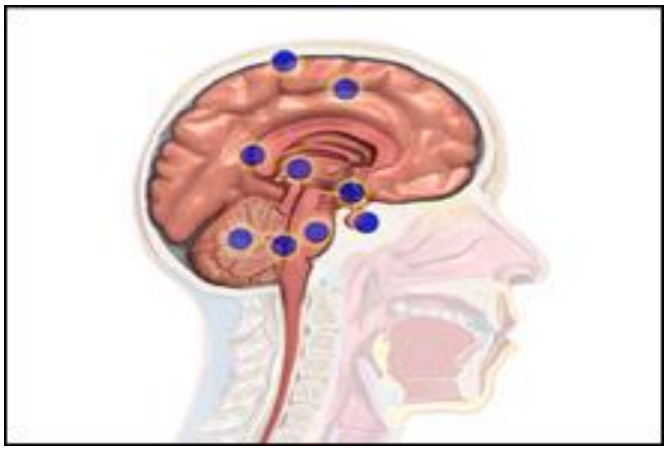


Fig 4.3: Brain cancer region

4.3.2 Meninges

Human brains are surrounded by a system of connective tissue membranes called meninges that separate the brain from the skull. This three-layered covering is composed of (from the outside in) the dura mater ("hard mother"), arachnoid mater ("spidery mother"), and pia mater ("tender mother"). The arachnoid and pia are physically connected and thus often considered as a single layer, the pia-arachnoid. Between the arachnoid mater and the pia mater is the subarachnoid space which contains cerebrospinal fluid (CSF). This fluid circulates in the narrow spaces between cells and through the cavities in the brain called ventricles, to nourish, support, and protect the brain tissue. Blood vessels enter the central nervous system through the perivascular space above the pia mater. The cells in the blood vessel walls are joined tightly, forming the blood–brain barrier which protects the brain from toxins that might enter through the blood. Tumors of the meninges are meningioma's and are often benign.

4.3.3 Brain matter

The brains of humans and other vertebrates are composed of very soft tissue and have a gelatin-like texture. Living brain tissue has a pink tint in color on the outside (gray matter), and nearly complete white on the inside (white matter), with subtle variations in color. Three separate brain areas make up most of the brain's volume:

- telencephalon (cerebral hemispheres or cerebrum)
- mesencephalon (midbrain)
- cerebellum

These areas are composed of two broad classes of cells: neurons and glia. These two types are equally numerous in the brain as a whole, although glial cells outnumber neurons roughly 4 to 1 in the cerebral cortex. Glias come in several types, which perform a number of critical functions, including structural support, metabolic support, insulation, and guidance of development. Primary tumors of the glial cells are called gliomas and often are malignant by the time they are diagnosed.

4.3.4 Spinal cord and other tissues

The pons in the brainstem is a specific region that consists of myelinated axons much like the spinal cord. The thalamus and hypothalamus of the diencephalon also consist of neuron and glial cell tissue with the hypophysis (pituitary gland) and pineal gland (which is glandular tissue) attached at the bottom; tumors of the pituitary and pineal gland are often benign. The medulla oblongata is at the start of the spinal cord and is composed mainly of neuron tissue enveloped in Schwann cells and meninges tissue. The spinal cord is made up of bundles of these axons. Glial cells such as Schwann cells in the periphery or, within the cord itself, oligodendrocytes, wrap themselves around the axon, thus promoting faster transmission of electrical signals and also providing for general maintenance of the environment surrounding the cord, in part by shuttling different compounds around in response to injury or other stimulus.

4.4 Diagnosis

Most of the brain is separated from the blood by the blood-brain barrier (BBB), which exerts a restrictive control as to which substances are allowed to pass. Therefore, many tracers that reach tumors in the body very easily would only reach brain tumors once there is a disruption of the BBB. Thus the disruption of the BBB, which can be detected by MRI and CT, is regarded as the main diagnostic indicator for malignant gliomas, meningiomas, and brain metastases.

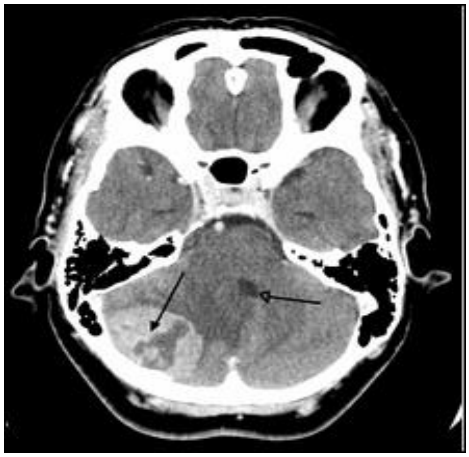


Fig 4.4: A posterior fossa tumor leading to mass effect and midline shift

Although there is no specific or singular clinical symptom or sign for any brain tumors, the presence of a combination of symptoms and the lack of corresponding clinical indications of infections or other causes can be an indicator to redirect diagnostic investigation towards the possibility of an intracranial neoplasm. Brain tumors have similar characteristics and obstacles when it comes to diagnosis and therapy with tumors located elsewhere in the body. However, they create specific issues that follow closely to the properties of the organ they are in.

The diagnosis will often start by taking a medical history noting medical antecedents, and current symptoms. Clinical and laboratory investigations will serve to exclude infections as the cause of the symptoms. Examinations in this stage may include the eyes, otolaryngological (or ENT) and electrophysiological exams. The use of electroencephalography (EEG) often plays a role in the diagnosis of brain tumors.

Swelling or obstruction of the passage of cerebrospinal fluid (CSF) from the brain may cause (early) signs of increased intracranial pressurewhich translates clinically into headaches, vomiting, or an altered state of consciousness, and in children changes to the diameter of the skulland bulging of the fontanelles. More complex symptoms such as endocrine dysfunctions should alarm doctors not to exclude brain tumors.

A bilateral temporal visual field defect (due to compression of the optic chiasm) or dilation of the pupil, and the occurrence of either slowly evolving or the sudden onset of focal neurologic symptoms, such as cognitive and behavioral impairment (including impaired judgment, memory loss, lack of

recognition, spatial orientation disorders), personality or emotional changes, hemiparesis, hypoesthesia, aphasia, ataxia, visual field impairment, impaired sense of smell, impaired hearing, facial paralysis, double vision, or more severe symptoms such as tremors, paralysis on one side of the body hemiplegia, or (epileptic) seizures in a patient with a negative history for epilepsy, should raise the possibility of a brain tumor.

4.5 Imaging

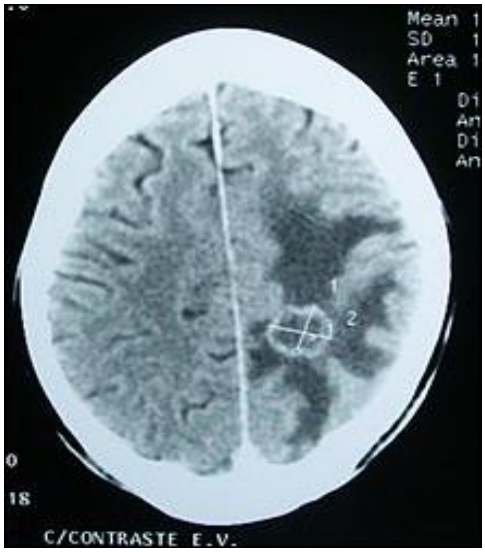


Fig 4.5: CT scan of a brain tumor, with its diameters marked as an X. There is hypo attenuating (dark) peritumoral edema in the surrounding white matter, with a "finger-like" spread.

- Medical imaging plays a central role in the diagnosis of brain tumors. Early imaging methods – invasive and sometimes dangerous – such as pneumoencephalography and cerebral angiography have been abandoned in favor of non-invasive, high-resolution techniques, especially magnetic resonance imaging (MRI) and computed tomography (CT) scans. Neoplasms will often show as differently colored masses (also referred to as processes) in CT or MRI results.
- Benign brain tumors often show up as hypodense (darker than brain tissue) mass lesions on CT scans. On MRI, they appear either hypodense or isointense (same intensity as brain tissue) on T1-weighted scans, or hyperintense (brighter than brain tissue) on T2-weighted MRI, although the appearance is variable.

- Contrast agent uptake, sometimes in characteristic patterns, can be demonstrated on either CT or MRI scans in most malignant primary and metastatic brain tumors.
- Pressure areas where the brain tissue has been compressed by a tumor also appear hyper intense on T2-weighted scans and might indicate the presence a diffuse neoplasm due to an unclear outline. Swelling around the tumor known as peritumoral edema can also show a similar result.

This is because these tumors disrupt the normal functioning of the BBB and lead to an increase in its permeability. However, it is not possible to diagnose high- versus low-grade gliomas based on enhancement pattern alone.

The definitive diagnosis of brain tumor can only be confirmed by histological examination of tumor tissue samples obtained either by means of brain biopsy or open surgery. The histological examination is essential for determining the appropriate treatment and the correct prognosis. This examination, performed by a pathologist, typically has three stages: interoperative examination of fresh tissue, preliminary microscopic examination of prepared tissues, and follow-up examination of prepared tissues after immunohistochemical staining or genetic analysis.

4.6 Pathology

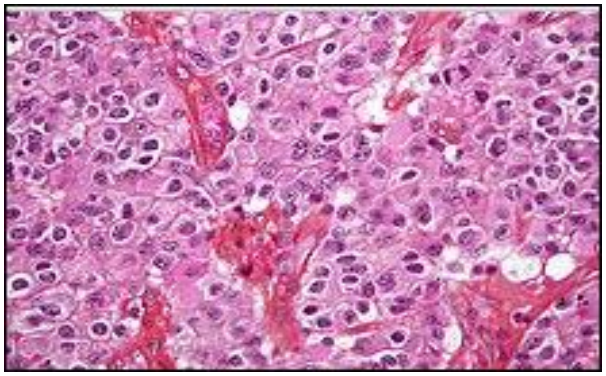


Fig 4.6: Micrograph of an oligodendroglioma, a type of brain cancer.
Brain biopsy. H&E stain.

Tumors have characteristics that allow determination of malignancy and how they will evolve, and determining these characteristics will allow the medical team to determine the management plan.

- **Anaplasia or dedifferentiation:** loss of differentiation of cells and of their orientation to one another and blood vessels, a characteristic of anaplastic tumor tissue. Anaplastic cells have lost total control of their normal functions and many have deteriorated cell structures. Anaplastic cells often have abnormally high nuclear-to-cytoplasmic ratios, and many are multinucleated. Additionally, the nuclei of anaplastic cells are usually unnaturally shaped or oversized. Cells can become anaplastic in two ways: neoplastic tumor cells can dedifferentiate to become anaplasias (the dedifferentiation causes the cells to lose all of their normal structure/function), or cancer stem cells can increase their capacity to multiply (i.e., uncontrollable growth due to failure of differentiation).
- **Atypia:** an indication of abnormality of a cell (which may be indicative for malignancy). Significance of the abnormality is highly dependent on context.
- **Neoplasia:** the (uncontrolled) division of cells. As such, neoplasia is not problematic but its consequences are: the uncontrolled division of cells means that the mass of a neoplasm increases in size, and in a confined space such as the intracranial cavity this quickly becomes problematic because the mass invades the space of the brain pushing it aside, leading to compression of the brain tissue and increased intracranial pressure and destruction of brain parenchyma. Increased intracranial pressure (ICP) may be attributable to the direct mass effect of the tumor, increased blood volume, or increased cerebrospinal fluid (CSF) volume, which may, in turn, have secondary symptoms.
- **Necrosis:** the (premature) death of cells, caused by external factors such as infection, toxin or trauma. Necrotic cells send the wrong chemical signals which prevent phagocytes from disposing of the dead cells, leading to a buildup of dead tissue, cell debris and toxins at or near the site of the necrotic cells
- **Arterial and venous hypoxia**, or the deprivation of adequate oxygen supply to certain areas of the brain, occurs when a tumor makes use of nearby blood vessels for its supply of blood and the neoplasm enters into competition for nutrients with the surrounding brain tissue.

More generally a neoplasm may cause release of metabolic end products (e.g., free radicals, altered electrolytes, neurotransmitters), and release and recruitment of cellular mediators (e.g., cytokines) that disrupt normal parenchymal function.

4.7 Classification

4.7.1 Secondary brain tumors

Secondary tumors of the brain are metastatic and have invaded the brain from cancers originating in other organs. This means that a cancerous neoplasm has developed in another organ elsewhere in the body and that cancer cells have leaked from that primary tumor and then entered the lymphatic system and blood vessels. They then circulate through the bloodstream, and are deposited in the brain. There, these cells continue growing and dividing, becoming another invasive neoplasm of the primary cancer's tissue. Secondary tumors of the brain are very common in the terminal phases of patients with an incurable metastasized cancer; the most common types of cancers that bring about secondary tumors of the brain are lung cancer, breast cancer, malignant melanoma, kidney cancer, and colon cancer (in decreasing order of frequency). Secondary brain tumors are more common than primary ones; in the United States there are about 170,000 new cases every year. Secondary brain tumors are the most common cause of tumors in the intracranial cavity. The skull bone structure can also be subject to a neoplasm that by its very nature reduces the volume of the intracranial cavity, and can damage the brain.

4.7.2 By behavior

Brain tumors or intracranial neoplasms can be cancerous (malignant) or non-cancerous (benign). However, the definitions of malignant or benign neoplasms differ from those commonly used in other types of cancerous or non-cancerous neoplasms in the body. In cancers elsewhere in the body, three malignant properties differentiate benign tumors from malignant forms of cancer: benign tumors are self-limited and do not invade or metastasize. Characteristics of malignant tumors include:

- uncontrolled mitosis (growth by division beyond the normal limits)
- **anaplasia:** the cells in the neoplasm have an obviously different form (in size and shape). Anaplastic cells display marked pleomorphism. The cell nuclei are characteristically extremely hyperchromatic (darkly stained) and enlarged; the nucleus might have the same size as the cytoplasm of the cell (nuclear-

cytoplasmic ratio may approach 1:1, instead of the normal 1:4 or 1:6 ratio). Giant cells – considerably larger than their neighbors – may form and possess either one enormous nucleus or several nuclei (syncytia). Anaplastic nuclei are variable and bizarre in size and shape.

- invasion or infiltration (medical literature uses these terms as synonymous equivalents. However, for clarity, the articles that follow adhere to a convention that they mean slightly different things; this convention is not followed outside these articles)
- Invasion or invasiveness is the spatial expansion of the tumor through uncontrolled mitosis, in the sense that the neoplasm invades the space occupied by adjacent tissue, thereby pushing the other tissue aside and eventually compressing the tissue. Often these tumors are associated with clearly outlined tumors in imaging.
- Infiltration is the behavior of the tumor either to grow (microscopic) tentacles that push into the surrounding tissue (often making the outline of the tumor undefined or diffuse) or to have tumor cells "seeded" into the tissue beyond the circumference of the tumorous mass; this does not mean that an infiltrative tumor does not take up space or does not compress the surrounding tissue as it grows, but an infiltrating neoplasm makes it difficult to say where the tumor ends and the healthy tissue starts.
- metastasis (spread to other locations in the body via lymph or blood).Of the above malignant characteristics, some elements do not apply to primary neoplasms of the brain.
- Primary brain tumors rarely metastasize to other organs; some forms of primary brain tumors can metastasize but will not spread outside the intracranial cavity or the central spinal canal. Due to the BBB, cancerous cells of a primary neoplasm cannot enter the bloodstream and get carried to another location in the body. (Occasional isolated case reports suggest spread of certain brain tumors outside the central nervous system, e.g. bone metastasis of glioblastoma multiforme.)
- Primary brain tumors generally are invasive (i.e. they will expand spatially and intrude into the space occupied by other brain tissue and compress those brain tissues); however, some of the more malignant primary brain tumors will infiltrate the surrounding tissue. Of numerous grading systems in use for the classification

of tumor of the central nervous system, the World Health Organization (WHO) grading system is commonly used for astrocytoma. Established in 1993 in an effort to eliminate confusion regarding diagnoses, the WHO system established a four-tiered histologic grading guideline for astrocytomas that assigns a grade from 1 to 4, with 1 being the least aggressive and 4 being the most aggressive.

4.7.3 Types of Brain Tumor

Tumors can be benign or malignant, can occur in different parts of the brain, and may be primary or secondary. A primary tumor is one that has started in the brain, as opposed to a metastatic tumor, which is something that has spread to the brain from another part of the body. The incidence of metastatic tumors are more prevalent than primary tumors by 4:1. Tumors may or may not be symptomatic: some tumors are discovered because the patient has symptoms, others show up incidentally on an imaging scan, or at an autopsy.

The most common primary brain tumors are:

- Gliomas (50.4%)
- Meningiomas (20.8%)
- Pituitary adenomas (15%)
- Nerve sheath tumors (8%)

These common tumors can also be organized according to tissue of origin as shown below:

Table 1: Organisation of Tumors according to tissue of origin as shown below

Tissue of origin	**Children**	**Adults**
Astrocytes	Pilocytic Astrocytoma (PCA)	Glioblastoma Multiforme (GBM)
Oligodendrocytes		Oligodendroglioma
Ependyma	Ependymoma	
Neurons	Medulloblastoma	
Meninges		Meningioma

4.7.3.1 Specific types

Anaplastic astrocytoma, Astrocytoma, Central neurocytoma, Choroid plexus carcinoma, Choroid plexus papilloma, Choroid plexus tumor,

Dysembryoplastic neuroepithelial tumour, Ependymal tumor, Fibrillary astrocytoma, Giantcellglioblastoma, Glioblastomamultiforme, Gliomatosiscerebri, Gliosarcoma, Hemangiopericytoma, Medulloblastoma, Medulloepithelioma, Meningealcarcinomatosis, Neuroblastoma, Neurocytoma, Oligoastrocytoma, Oligodendroglioma, Optic nerve sheath meningioma, Pleomorphicanaplastic neuroblastoma, Plemorphic xanthoastrocytoma, Primary central nervous system lymphoma, Sphenoid wing meningioma, Subependymal giant cell astrocytoma, Subependymoma, Trilateral retinoblastoma.

When a brain tumor is diagnosed, a medical team will be formed to assess the treatment options presented by the leading surgeon to the patient and his/her family. Given the location of primary solid neoplasms of the brain in most cases a "do-nothing" option is usually not presented. Neurosurgeons take the time to observe the evolution of the neoplasm before proposing a management plan to the patient and his/her relatives. These various types of treatment are available depending on neoplasm type and location and may be combined to give the best chances of survival:

- **Surgery:** complete or partial resection of the tumor with the objective of removing as many tumor cells as possible.
- **Radiotherapy:** the most commonly used treatment for brain tumors; the tumor is irradiated with beta, x rays or gamma rays.
- **Chemotherapy:** is a treatment option for cancer, however, it is not always used to treat brain tumors as the blood-brain barrier can prevent some drugs from reaching the cancerous cells.
- A variety of experimental therapies are available through clinical trials.

Survival rates in primary brain tumors depend on the type of tumor, age, functional status of the patient, the extent of surgical tumor removal and other factors specific to each case.

4.7.4 Cure

4.7.4.1 Surgery

The primary and most desired course of action described in medical literature is surgical removal (resection) via craniotomy. Minimally invasive techniques are becoming the dominant trend in neurosurgical oncology. The prime remediating objective of surgery is to remove as many tumor cells as possible, with complete

removal being the best outcome and cytoreduction ("debulking") of the tumor otherwise. In some cases access to the tumor is impossible and impedes or prohibits surgery.

Many meningiomas, with the exception of some tumors located at the skull base, can be successfully removed surgically. Most pituitary adenomas can be removed surgically, often using a minimally invasive approach through the nasal cavity and skull base (trans-nasal, trans-sphenoidal approach). Large pituitary adenomas require a craniotomy (opening of the skull) for their removal. Radiotherapy, including stereotactic approaches, is reserved for inoperable cases.
Several current research studies aim to improve the surgical removal of brain tumors by labeling tumor cells with 5-aminolevulinic acid that causes them to fluoresce. Postoperative radiotherapy and chemotherapy are integral parts of the therapeutic standard for malignant tumors. Radiotherapy may also be administered in cases of "low-grade" gliomas when a significant tumor burden reduction could not be achieved surgically.

Multiple metastatic tumors are generally treated with radiotherapy and chemotherapy rather than surgery and the prognosis in such cases is determined by the primary tumor, and is generally poor.

4.7.4.2 Radiation therapy

The goal of radiation therapy is to kill tumor cells while leaving normal brain tissue unharmed. In standard external beam radiation therapy, multiple treatments of standard-dose "fractions" of radiation are applied to the brain. This process is repeated for a total of 10 to 30 treatments, depending on the type of tumor. This additional treatment provides some patients with improved outcomes and longer survival rates.

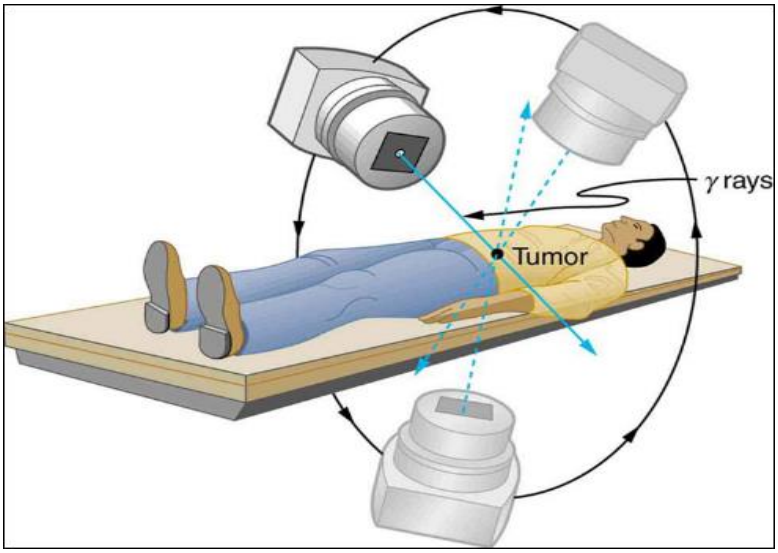


Fig 4.7: radiation therapy Treatment

Radiosurgery is a treatment method that uses computerized calculations to focus radiation at the site of the tumor while minimizing the radiation dose to the surrounding brain. Radiosurgery may be an adjunct to other treatments, or it may represent the primary treatment technique for some tumors. Forms used include stereotactic radiosurgery, such as Gamma knife, Cyberknife or Novalis Tx radiosurgery.

Radiotherapy may be used following, or in some cases in place of, resection of the tumor. Forms of radiotherapy used for brain cancer include external beam radiation therapy, the most common, and brachytherapy and proton therapy, the last especially used for children.

Radiotherapy is the most common treatment for secondary brain tumors. The amount of radiotherapy depends on the size of the area of the brain affected by cancer. Conventional external beam "whole-brain radiotherapy treatment" (WBRT) or "whole-brain irradiation" may be suggested if there is a risk that other secondary tumors will develop in the future. Stereotactic radiotherapy is usually recommended in cases involving fewer than three small secondary brain tumors.

People who receive stereotactic radiosurgery (SRS) and whole-brain radiation therapy (WBRT) for the treatment of metastatic brain tumors have more than twice the risk of developing learning and memory problems than those treated with SRS alone.

4.7.4.3 Chemotherapy

Patients undergoing chemotherapy are administered drugs designed to kill tumor cells. Although chemotherapy may improve overall survival in patients with the most malignant primary brain tumors, it does so in only about 20 percent of patients. Chemotherapy is often used in young children instead of radiation, as radiation may have negative effects on the developing brain. The decision to prescribe this treatment is based on a patient's overall health, type of tumor, and extent of the cancer. The toxicity and many side effects of the drugs, and the uncertain outcome of chemotherapy in brain tumors puts this treatment further down the line of treatment options with surgery and radiation therapy preferred.

Fig 4.8: Chemotherapy

UCLA Neuro-Oncology publishes real-time survival data for patients with a diagnosis of glioblastoma multiforme. They are the only institution in the United States that displays how brain tumor patients are performing on current therapies. They also show a listing of chemotherapy agents used to treat high-grade glioma tumors.

4.7.4.4 Other

A shunt may be used to relieve symptoms caused by intracranial pressure, by reducing the build-up of fluid (hydrocephalus) caused by the blockage of the free flow of cerebrospinal fluid.

4.7.4.5 Prognosis

The prognosis of brain cancer depends on the type of cancer d22iagnosed. Medulloblastoma has a good prognosis with chemotherapy, radiotherapy, and surgical resection while glioblastoma multiforme has a median survival of only 12 months even with aggressive chemoradiotherapy and surgery. Brainstem gliomas have the poorest prognosis of any form of brain cancer, with most patients dying within one year, even with therapy that typically consists of radiation to the tumor along with corticosteroids. However, one type, focal brainstem gliomas in children, seems open to exceptional prognosis and long-term survival has frequently been reported.

4.7.4.6 Glioblastoma multiforme

Glioblastoma multiforme (GBM) is the most aggressive (grade IV) and most common form of a malignant brain tumor. Even when aggressive multimodality therapy consisting of radiotherapy, chemotherapy, and surgical excision is used, median survival is only 12–17 months. Standard therapy for glioblastoma multiforme consists of maximal surgical resection of the tumor, followed by radiotherapy between two and four weeks after the surgical procedure to remove the cancer, then by chemotherapy, such as temozolomide. Most patients with glioblastoma take a corticosteroid, typically dexamethasone, during their illness to relieve symptoms. Experimental treatments include targeted therapy, gamma knife radiosurgery boron neutron capture therapy and gene therapy.

4.7.4.7 Oligodendrogliomas

Oligodendrogliomas are incurable but slowly progressive malignant brain tumors. They can be treated with surgical resection, chemotherapy, radiotherapy or a combination. For some suspected low-grade (grade II) tumors, only a course of watchful waiting and symptomatic therapy is opted for. These tumors show a high frequency of co-deletions of the p and q arms of chromosome 1 and chromosome 19 respectively (1p19q co-deletion) and have been found to be especially chemosensitive with one report claiming them to be one of the most chemosensitive tumors. A median survival of up to 16.7 years has been reported for grade II oligodendrogliomas.

4.7.4.8 Epidemiology

Figures for incidences of cancers of the brain show a significant difference between more- and less-developed countries (the less-developed countries have lower incidences of tumors of the brain). This could be explained by undiagnosed tumor-related deaths (patients in extremely poor situations do not get diagnosed, simply because they do not have access to the modern diagnostic facilities required to diagnose a brain tumor) and by deaths caused by other poverty-related causes that preempt a patient's life before tumors develop or tumors become life-threatening. Nevertheless, studies suggest that certain forms of primary brain tumors are more prevalent among certain groups of the population.

The incidence of low-grade astrocytoma has not been shown to vary significantly with nationality. However, studies examining the incidence of malignant central nervous system (CNS) tumors have shown some variation with national origin. Since some high-grade lesions arise from low-grade tumors, these trends are worth mentioning. Specifically, the incidence of CNS tumors in the United States, Israel, and the Nordic countries is relatively high, while Japan and Asian countries have a lower incidence. These differences probably reflect some biological differences as well as differences in pathologic diagnosis and reporting. Worldwide data on incidence of cancer can be found at the WHO (World Health Organisation) and is handled by the IARC (International Agency for Research on Cancer) located in France.

4.7.5 Research

4.7.5.1 Immunotherapy

Cancer immunotherapy is being actively studied. For malignant gliomas no therapy has been shown to improve life expectancy as of 2015.

4.7.5.2 Vesicular stomatitis virus

In 2000, researchers used the vesicular stomatitis virus, or VSV, to infect and kill cancer cells without affecting healthy cells.

4.7.5.3 Retroviral replicating vectors

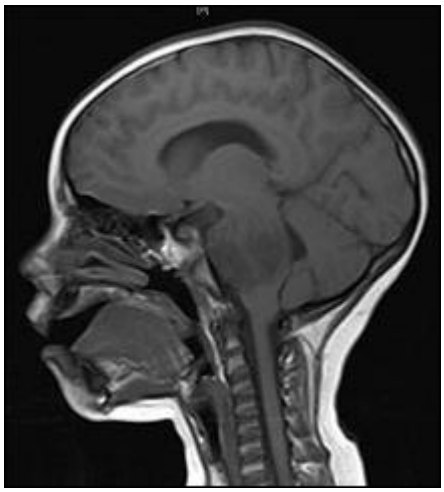


Fig 4.9: A brainstem glioma in four-year-old. MRI, sagittal, without contrast

Led by Prof. Nori Kasahara, researchers from USC, who are now at UCLA, reported in 2001 the first successful example of applying the use of retroviral replicating vectors towards transducing cell lines derived from solid tumors. Building on this initial work, the researchers applied the technology to *in vivo* models of cancer and in 2005 reported a long-term survival benefit in an experimental brain tumor animal model. Subsequently, in preparation for human clinical trials, this technology was further developed by Tocagen (a pharmaceutical company primarily focused on brain cancer treatments) as a combination treatment (Toca 511 & Toca FC). This has been under investigation since 2010 in a Phase I/II clinical trial for the potential treatment of recurrent high-grade glioma including glioblastoma multiforme (GBM) and anaplastic astrocytoma. No results have yet been published.

CHAPTER 5

WORKING

5.1 Pre-processing

By reducing noise and enhances some of the image features for further processing stages. It is evident that every MRI images contains noise and must be removed without affecting the useful portion like weak edges of image. It is the initial stage of every image processing application where its main job is to improve the image data and diminishes the quality of MRI images. For reducing this type of noise several methods are employed like Gaussian filtering technique, thresholding technique, medial filtering, wavelet transforms and also anisotropic diffusion filtering.

As mentioned earlier an anisotropic diffusion filtering technique that greatly removes noise present in MRI images by smoothing out images without affecting valuable date in edges and structures of image. Here to regulate level of smoothing in particular areas on edge structure in local is to be motivated. Finally enormously smoothing on homogenous areas and barely smoothing on strong edge areas to hold the structure in MRI images.

5.2 Fast Bounding Box Algorithm

Here the input brain MRI slice (axial view) have axis of symmetry that segments brain in to two halves one half treated as test image and other as reference image. Now in order to know the dissimilarity that is necessary for locating the tumor region, novel score function is employed that can search rapidly in two directions of brain region one along horizontal and other in vertical direction. This novel score function Bhattacharya Coefficient (BC) which is similarity measurement to detect rectangle between two normal histograms of grey scale intensity. It is evident that two grey scale intensity normalized histograms seems to be same the BC between them is 1and if not BC value is 0.

5.3 Support Vector Machine based Algorithm

As SVM is widely used technique in several fields of image processing like classification, segmentation to yield optimized results. Since it is capable of treating linear and nonlinear separation it is well-intentioned to apply for classification in the confined space. So the separation operation field f(x) is formulated as

$$f(x) = \sum_{x_j \in S} a_j y_j K(x_j, x) + b \qquad \text{---------- (2)}$$

Where, x_i designates the $y_j \in$ trainings, {+1,–1} embodies class label with S as a set of support vectors.

The dual formulation of the above is formulation (2) is prearranged as;

$$\min_{0 \le a_i \le C} W = \frac{1}{2} \sum_{i,j} a_i Q_{ij} a_j - \sum_i a_i + b \sum_i y_i a_i \qquad \text{……. (3)}$$

where the term a_i are supposed to be the coefficients of vector and whereas b treated to be offset value.

$y_i y_j Q_{ij} =$ K (x_j, x): Designates symmetric kernel matrix and C embodies parameters of error points.

As well-known Karush-Kuhn-Tucker (KKT) is employed to achieve an optimal point in this work as it possesses to solve constrained problems with great ease which is formulated as:

$$g_i = \frac{\delta W}{\delta_{a_i}} = \sum_i Q_{ij} a_j + y_j b - 1 = y_i f(x_i) - 1 \qquad \text{……(4)}$$

$$\frac{\delta W}{\delta_b} \quad \sum_j y_j a_j = 0$$

As stated above to there is necessity of speed up the processing , so revised kernel function with SVM converges rapidly as it having great ability of storing complete vector sets at once also starts initialization from reverse classes . In addition this method having the iterative style of summing up all the given candidates by means of feature violation either misclassified or else left unclassified and immediately stops its operation once all the points are separated. The further support vectors are delivered to C for the present or initialized help vector S. If no present SV block is incorporated in C to S, then all of the S vectors are support vectors. If the value of α_p is not up to zero, then the classification of C to S is just not needed. The violator is the pixel which is categorized incorrectly or not regarded as part of segment the place it's supposed to be**.** To achieve optimal classification level there is necessity of SVM with optimum efficiency.

5.4 Performance Metrics

Peak Signal to Noise Ratio (PSNR) is generally utilized for the quality measure of recovery of image. The signal in this case is the original data, and the noise is the error introduced by segmentation. When comparing segmentation, PSNR is an approximation to human perception of reconstruction quality. By having higher PSNR values shows higher quality reconstruction. Also PSNR in most cases defined via the MSE (Mean Squared Error).

$$MSE = \frac{1}{mn}\sum_{i=0}^{m-1}\sum_{j=0}^{n-1}[I(i,j) - K(i,j)]^2 \quad \ldots\ldots\ldots\ldots (5)$$

5.4.1 Mean square error

$$PSNR = 10.log_{10}\left(\frac{MAX_I^2}{MSE}\right) \quad \ldots\ldots\ldots\ldots (6)$$

Here, MAX_I is the maximum possible pixel value of the image. Generally as image pixels are denoted with 8 bits per sample, this is 255 and if it were denoted with linear PCM with B bits per sample, MAX_I is $2^B - 1$.

5.4.2 Structural content

It is coined to be correlation based measures. It means the closeness between two images which can be quantified in terms of correlation function.

$$SC = \frac{\sum_{i=0}^{m-1}\sum_{j=0}^{n-1}(K(i,j))^2}{\sum_{i=0}^{m-1}\sum_{j=0}^{n-1}(I(i,j))^2} \quad \ldots\ldots\ldots\ldots..(7)$$

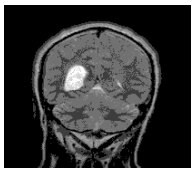
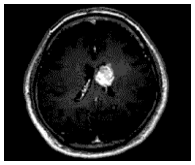
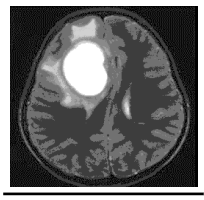
CHAPTER 6

RESULT

6.1 Simulation Results

In order to examine the proposed work of denoising and segmentation algorithms, we use the MRI database that contains images with different noise factors are performed and results corresponding to techniques are shown in Figures 2, 3 and 4. Also to quantitatively evaluate the denoising algorithm**,** the performance metrics like Peak Signal to Noise Ratio (PSNR), Mean Square Error (MSE) and Structural Content (SC) are used. Table 2 delineates the simulation results for the proposed algorithm.

Table 2: Performance metrics of proposed algorithm on the MRI database

IMAGE	PSNR In (dB)	MSE In (dB)	SC
	12.42	3.71	0.58
	11.50	4.59	0.94
	11.35	4.75	0.96

1

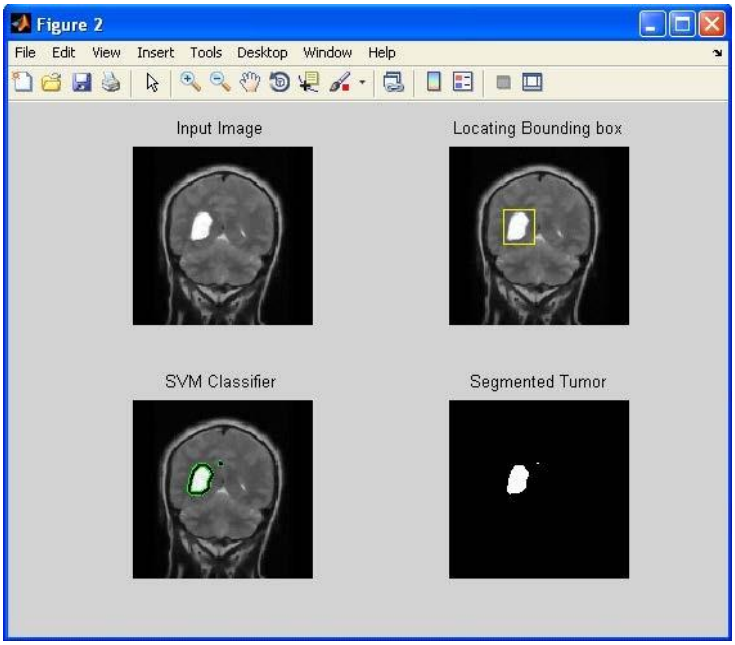


Fig 6.1: Pre-processing, Fast Bounding Box (FBB) and proposed one class SVM classification of the first MRI image.

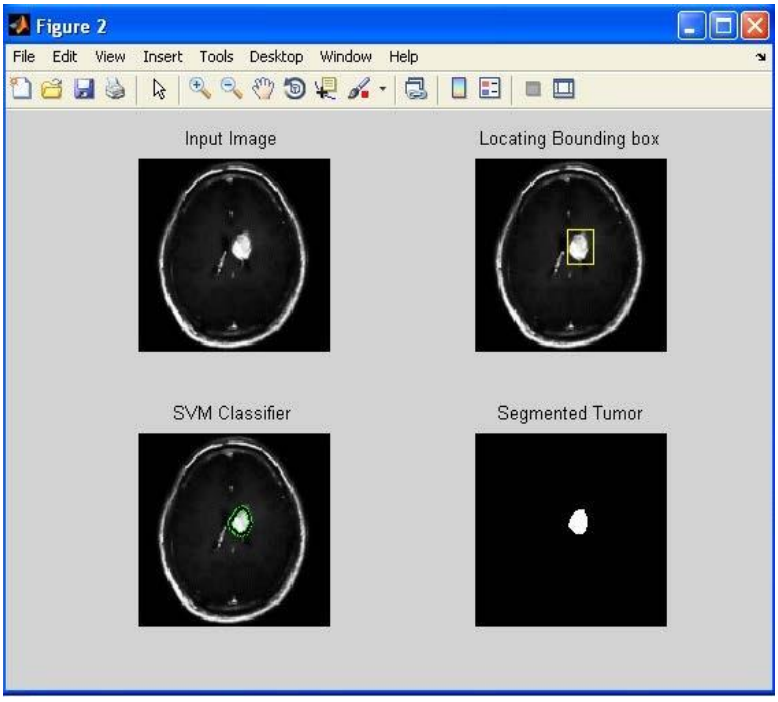


Fig 6.2: Pre-processing stage, Fast Bounding Box (FBB) and one class SVM classifier of second image.

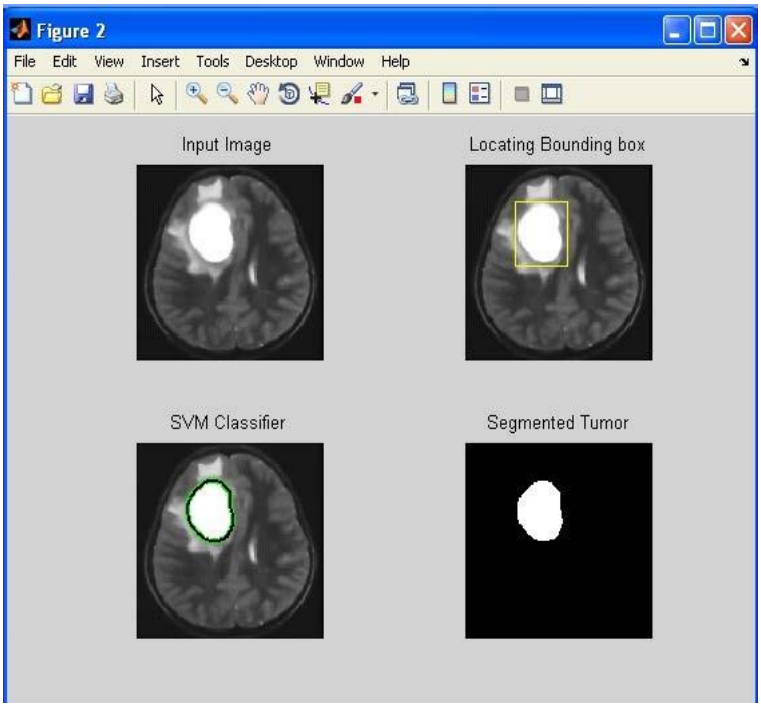


Fig 6.3: Pre-processing, Fast Bounding Box (FBB) and one class SVM classification of third image.

Since the brain skull mask image shown in Figure 6.4 (a), (b) is divided into two regions one is left and other is right considered to be test image and reference in order to examine Approximate Line Of Symmetry (ALOS).

Figure 6.5(a) and 6.5(b) depicts the vertical and the horizontal score function plots contrary to the distances from the top and left of the image, correspondingly**.**

As depicted in Figure 6.5(a) and 6.5(b) we notice the rising and falling situation of score plots that are supportive us to know the severity of intensity levels in the bounding box of brain image.

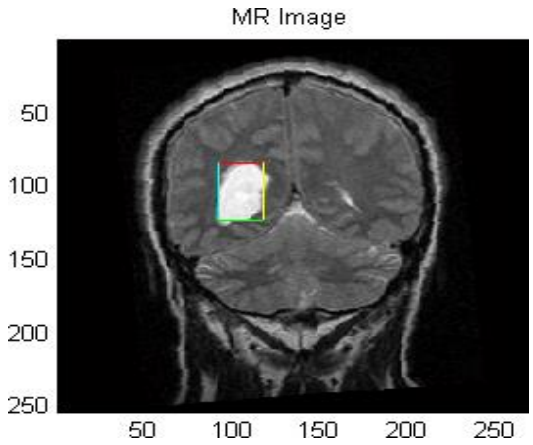


Fig 6.4 (a): Tumor on the left side of the brain on a T1C (enhanced T1) MR slice.

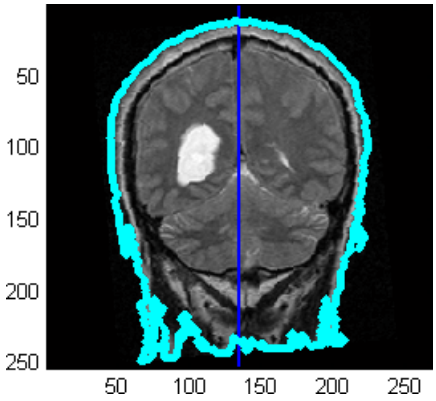


Fig 6.4 (b): Skull boundary detected by automatic global thresholding and subsequent post- processing.

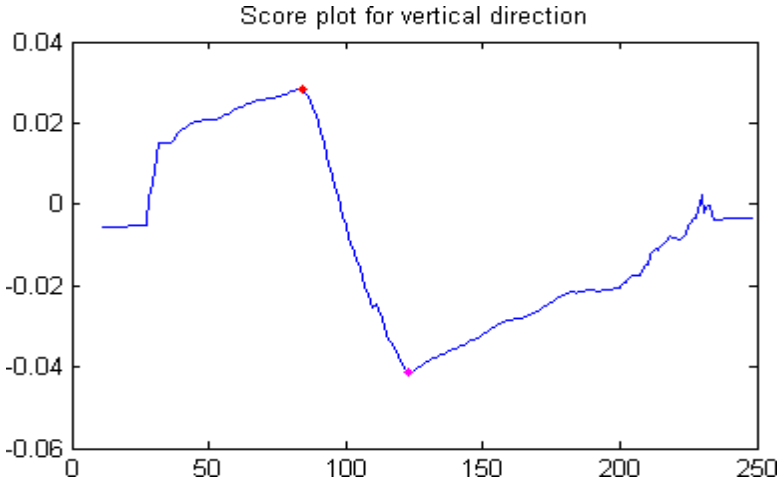


Fig 6.5 (a): Score plot for vertical detection

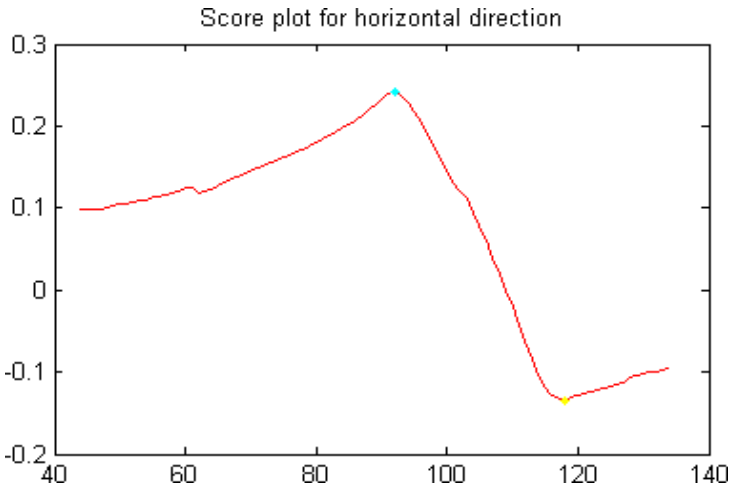


Fig 6.5 (b): Score plot for horizontal detection

Figure 6.5 (a),(b) Vertical and the horizontal score function plots contrary to the distances from the top and left of the image, correspondingly.

From Figure 6.6 we aim to know the presence of tumor location on the image by examining the averag intensity levels of bounding boxes on either sides of image and tumor existence can be known easily having mean intensity level at higher value at tumor location inside bounding box.

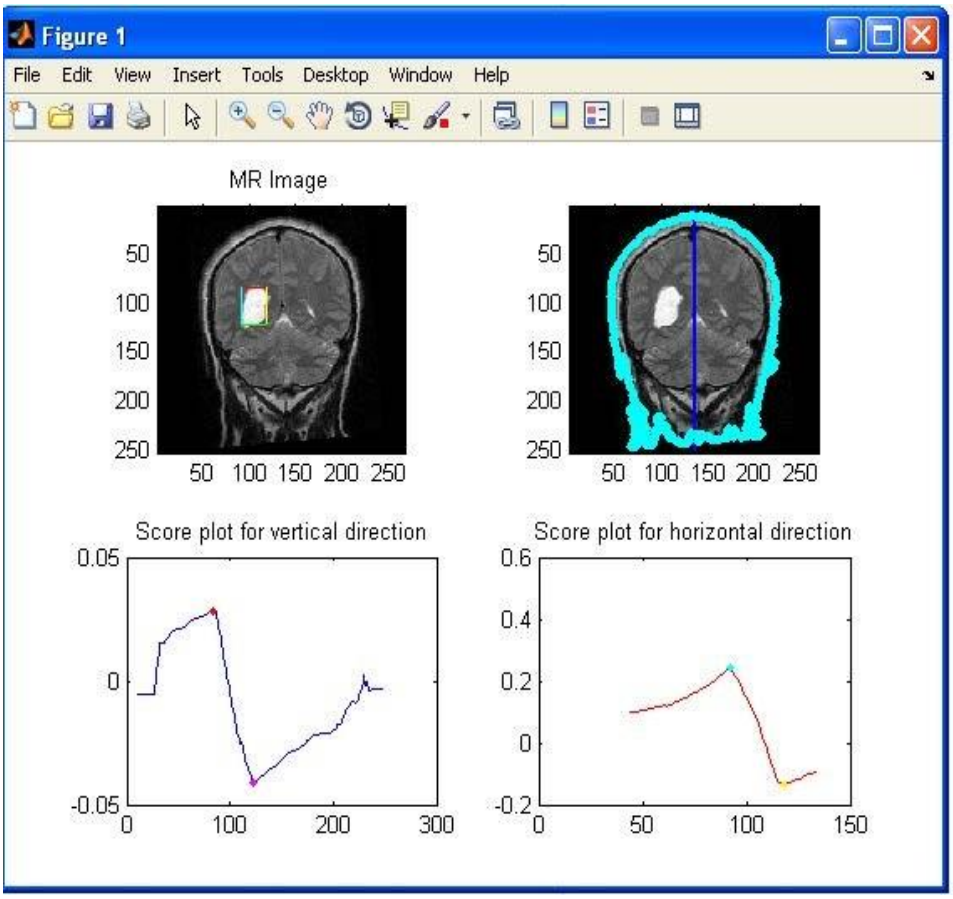


Fig 6.6: Segmentation with score plots.

CHAPTER 7

CONCLUSION

In current work a fully automatic method for brain tumor segmentation of MRI images that has three folds, first phase is a pre-processing stage in which unusable parts of human brain are detached and anisotropic diffusion filter is applied to remove noise present in MRI images by embedding 8-connected neighborhood. In the second phase to know the tumor location we used FBB (Fast Bounding Box) process**,** and one class SVM is opted for substantial training sample set usage. Finally by opting the one class SVM classifier involving the Radial Basis Function (RBF) kernel is employed for locating exact Tumor portion and isolates it from useful healthy texture region in MRI images.

FUTURE SCOPE

- **Application/Improvements:**

Segmented tumor obtained with precision are very useful for radiologists and specialists to had good idea of estimating tumor position and size with great dealt with ease and without any prior information.

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