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Review article

Studies on abnormality analysis in typical medical modalities based on biomedical simulation tools

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ABSTRACT

Abnormality in medical images is an ill healthy or unnecessary growth or deterioration of a minute part in any organ. The most common form of defect is Cancer, Bleed, Edema, Infarct, Tumor, and Aneurysm in any part of the body. Among these abnormalities of High-risk factor Cancer (Malignant Tumor), Large Tumor (Benign) and Aneurysm are treated as exceptional cases. Region Of Interest (ROI) confirms Abnormality Of Interest (AOI) in various locations of cancer, tumor, and aneurysm images. Cancer and tumor have interdependence and imperial relationship. Using Segmentation ROI of any AOI is identified by subtracting the background from the foreground The case studies of cancer or tumor interest are known as Oncological Studies. The associated research related to Aneurysm is Homodynamic or Haemodynamic analysis. This paper provides qualitative information of all the three abnormalities. It first describes different kinds of abnormalities in brief and later, a particular focus on three abnormalities (Cancer, Tumor, and Aneurysm) and their Symptoms, Types, Treatment, Associated medical image modalities. Later, it concentrates on the Opportunities and challenges in these studies via different databases/data sets for diagnosis, tools for their modeling and analysis which provides professional growth in Medical academia, Research and Development (R&D) and Medical-surgical interventional community.

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INTRODUCTION

In this section, various types of abnormalities, Role of segmentation in the abnormality treatment and available segmentation methods are presented. Most general forms of abnormalities are five types as shown in Figure1. There is an apparent discrepancy among these anomalies. The tumor may be Harmful (Malignant type) or non-harmful (Benign nature). Malignant tumor means a cancerous tumor which spreads into the remaining part of the body whereas a benign tumor is a non-cancerous tumor. An aneurysm is a significant bulge part of any vessel. Tumors at different positions have different clinical presentations which are not clear. Many recent research findings indicate that tumor location based statistics are one of the critical factors for prognosis So in order to have proper diagnosis, we use multiple scans/slices of different modalities like Ultrasound, Computed Tomography (CT), Magnetic Resonance Imaging (MRI), functional MRI (f-MRI), X-ray micro modulated luminescence tomography (XMLT), Single Photon Emission Computed Tomography (SPECT), Positron Emission Therapy (PET), etc. Different types of Magnetic Resonance Angiography (MRA), Computed Tomography Angiography (CTA) are used for the diagnosis of aneurysms. Thresholding, Watershed (Combination of edge detection & morphology), Region Growing, Classifier, Clustering, Bayesian approach, Mean Shift Algorithm, Markov Random Field (MRF) Models, Deformable Models, Artificial Neural Networks (ANN), Atlas-Guided Approaches, Normalized Cut, Graph Partition Algorithm, Model fitting using ellipse or parabola and Deformable organisms are most widely used image segmentation methods [1].

Figures 1, 2,3,4,5 and 6 illustrates the classification of aneurysms.

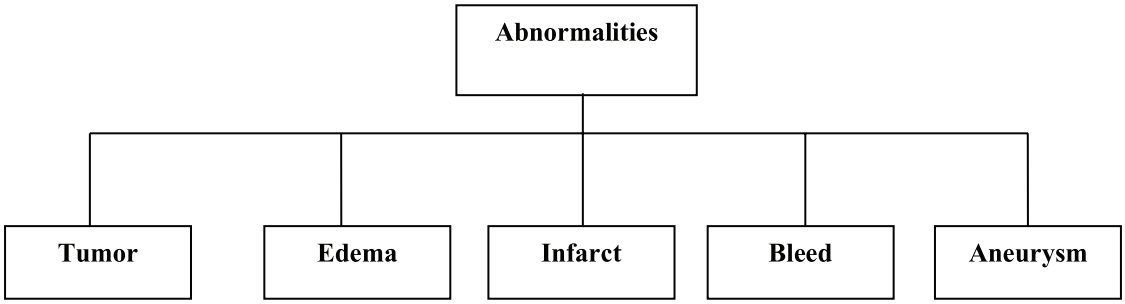

Figure 1. Types of abnormalities.

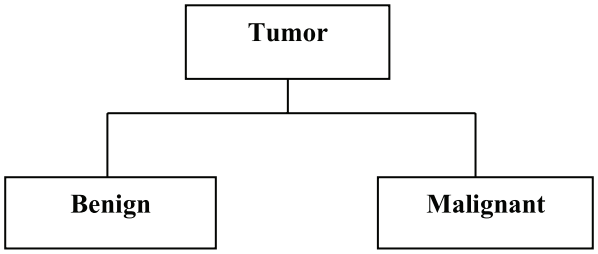

Figure 2. Types of tumors.

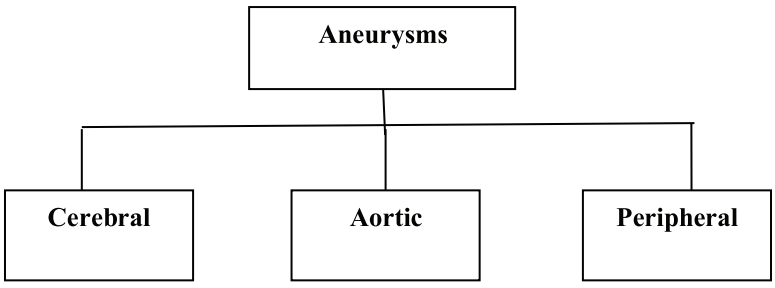

Figure 3. Types of aneurysms based on location.

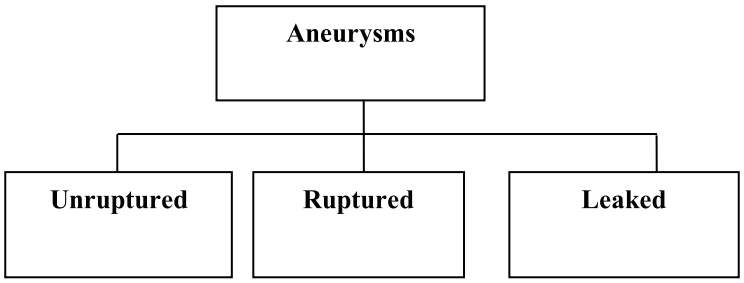

Figure 4. Types of aneurysms based on status.

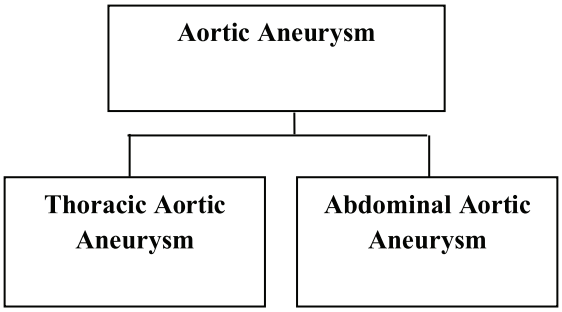

Figure 5. Types of aortic aneurysms.

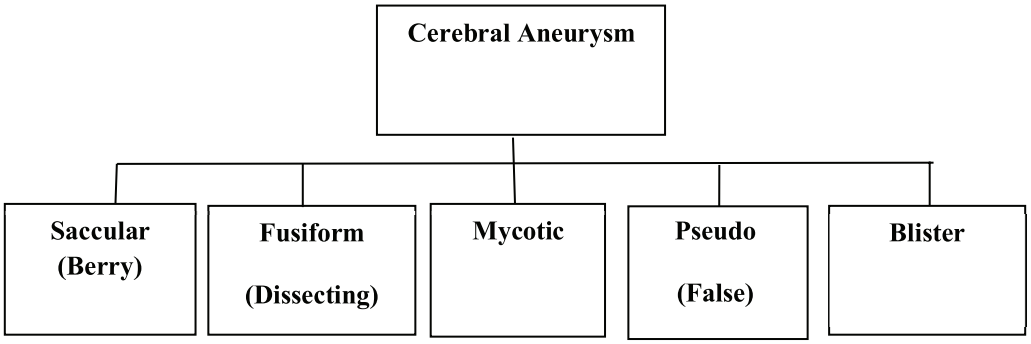

Figure 6. Types of cerebral aneurysms.

But, many of them suffer from the issue of over-segmentation. Also, management of diagnosis and prognosis details by a radiologist is cumbersome, and an expert radiologist is a prime requisite for proper identification of tumor type. Efficient firefly algorithm is used to overcome this problem. In this algorithm, the combination of image properties and modularity optimization is applied [2]. Currently, Convolution Neural Networks (CNN) and Deep Neural Networks (DNN) are the high-end neural network models to do medical image segmentation. Hence there is a necessity of algorithm which gives excellent tumor identification and its location statistics irrespective of its position in the Scans. This delineation ceases as regions of interest in an image is identified. Segmentation guides location based tumor pathology in case of high-risk tumor cases. Nowadays Healthcare systems of hospitals, clinics, and community agencies need automation to assist telemedicine facilities. Therefore, these automation services require image processing algorithms especially image segmentation algorithms. Image segmentation is also useful in applications such as multispectral images used for clinical monitoring, Post-processing of image acquisition tools, mobile devices for image acquisition through cameras or other types of scanners, assistance applications useful for disabled people, collaborative virtual environments for physicians which require image analysis support, and so on. Methods such as Traditional grayscale segmentation (in case of single image scheme) and Multispectral segmentation, semi-automatic and fully automatic image segmentation techniques are applied mainly on MRI data.

Image segmentation can be integrated into many applications regarding healthcare systems guidance, such as devices using a particular image sensor (e.g., a thermal camera) with built-in segmentation software or equipment equipped with a standard camera (e.g., a Smartphone) can be used as diagnostic devices for a cutaneous condition or oral medicine. Moreover, image segmentation can support telemedicine software for the elderly care or in the domestic environment of frail patients, to perform the segmentation of medical images to highlight lesions or other pathologies. The challenges and opportunities in this arena are remote support for medical diagnosis using image segmentation, image segmentation for healthcare devices, clinical monitoring and management using image segmentation techniques, clinical equipment including software and hardware, advances in medical imaging including segmentation/interpretation, mobile applications and low cost systems, telemedicine systems for elderly care, diagnosis support systems and fluoroscopy guided treatment & surgery.

In the recent past, Vitro studies are prominent than vivo studies in the stent or graft making to suit the real blood vessel characteristics. Its prime merit is to dissolve in it in their future course in case of critical aneurysm treatment. Cells or biological molecules outside their normal biological context and microorganisms are the means for vitro studies.

3D printing encourages these studies in a novel way. Tissue histology and Blood flow Fluid dynamics are critical factors for Patient-specific geometry, Uncertainty quantification, Non-Intrusive Spectral Projection in case of abnormality treatment.

The organization of the remaining part of the paper is as follows: In Section 2 Various image modalities are discussed. Section 3 covers Brief description of types of tumors, cancers, and aneurysms. In Section 4 Various tools and database information for pursuit medical students and research community are provided. Section 5 discusses treatment procedures for considered three abnormalities (tumor, cancer, and aneurysm). Section 6 includes Sample results of Segmentation of tumors, and analysis of aneurysms using tools like Matrix Laboratory (MATLAB), Analysis Systems (ANSYS), Materialise Interactive Medical Image Control System (MIMIC), 3-Matic, Image Processing Insight Segmentation Tool kit (ITK) SNAP. Section 7 gives the Concluding remarks.

MEDICAL IMAGE MODALITIES AND OTHER DIAGNOSIS AIDS

This section covers a brief review on various modalities & other diagnosis aids in three different subsections. In critical abnormality management, type of imaging modality plays a vital role. Biomedical imaging supports all aspects of cancer treatment management, i.e., screening, prognosis, biopsy guidance for detection, stage identification cum prediction, therapy planning - guidance - response, recurrence, and palliation. Imaging biomarkers are used to identify the tumor stage, presence of any cancer, and studies of response to therapy [3]. The advantages of biomedical imaging are the possibility of measurements without destruction of any tissues via minimal or no invasiveness, a feature of live monitoring of the whole organ, and the availability of various working modes such as multi-time & size scales. Interaction of electromagnetic radiation with body fluids and tissues is the working principle of all imaging modality systems except ultrasound modality in which sound waves scattering, reflection, and frequency shift means for scanning. Contrast agents are exogenous and provide images of many contrasts.

Medical Modalities

Comparative study of various medical modalities is made using below table 1.

Table 1. Comparative study between Different medical modalities

Type of Modality	Description & features	Merits & Demerits
MRI	LowIn 1973 significant developments are made in MRI by Lauterbur (who got the noble prize for his research) using local gradient fields [4]. Perfusion imaging, Relaxivity based imaging, Diffusion-weighted imaging, MR elastography, Endogenous & Exogenous spectroscopy, Stray field imaging (STRAFI) for Solid material and Blood Oxygen Level Determination (BOLD) are various types of MR imaging methods [4,5]. There are two unique techniques used along with MRI are MRA and Nuclear magnetic resonance (NMR) spectroscopy. MR images may be T1 or T2 weighted, Inversion Recovery (IR) and Fluid Attenuation Inversion Recovery (FLAIR) [6].	Merits include non-invasiveness, short span image acquisition around a second, few micrometers spatial resolution in all three dimensions and few mmole/kg sensitivity. Demerits are image contrast is effected by Coherent flow, Liquid mobility, Chemical Potential, and Diffusion coefficient [7].

Table 1. Comparative study between Different medical modalities (*continued*)

Type of Modality	Description & features	Merits & Demerits
CT	CT is used more in the detection of myocardial metastases compared to MRI [8]. It is a noninvasive diagnostic test which uses X-Ray systems along with Computer work station. Typical CT images have a sensitivity of millimole/kilogram. All this treatment information is provided according to the May field clinic health bulletins.	Merits are it uses contrast agent so clearer scans are provided compared to MRI. 3D CT can provide different scans of tumors, head injuries, hydrocephalus, hemorrhage, blood clots, and spinal stenosis and bone abnormalities using a contrast agent. 4D CT of Image Modulated Radiotherapy (IMRT), the tumor is at radiation field center, so that neighborhood tissue applications in the thorax can also be characterized efficiently [9, 10]. Main demerit is in Whole body CT screening is vague in some instances due to false negatives.
PET	PET has Superior diagnostic capability compared to SPECT. This nuclear or molecular imaging detects and tracks cancer by monitoring metabolic processes using a tracer (nuclide) injected into a vein. PET and SPECT detects Stroke detection in heart and brain, i.e., used for myocardial perfusion exams of heart or neurological diseases like Alzheimer's and other strokes. Sensitivity is of the order of nanomole/kilogram. Radiological Society of North America (RSNA) and American College of Radiology (ACR) provide valuable resources of PET, SPECT, their merits and demerits.	Integration of anatomical data of MR and metabolic data of PET gives new PET/MRI modality. In PET/CT hybrid modality metabolic data of PET is combined with a temporal/spatial resolution of CT. f-MRI and MR Spectroscopy (MRS) combination improves the diagnostic value of each method. PET/ MRI FDG (2-(18F)-fluoro-2-deoxy D-glucose) is another combination in the assessment of therapy response and TNM cancer staging (with three stages known as T staging, N staging, and M staging) [11].
SPECT	Improved image clarity cum resolution is possible in SPECT. It is possible with good image reconstruction software, detector technology, and radiotracers. It uses photomultiplier tubes, and scintillation detectors such as Bismuth germinate Oxyorthosilicate (BGO) or Lutetium Oxyorthosilicate (LSO). What amount of tumor cell consumes glucose and how it is happening is the working principle of PET imaging. viz., FDG with F-18 label's (analog of 2-deoxyglucose) increased accumulation is due to (i) Tumor effected by enhanced glucose transporter molecules and (ii) Increased concentration and/or action of hexokinase [12].	It is especially useful for cardiac imaging than a PET with improved resolution of 12 to 15 mm. SPECT tracers such as technetium-99m and rubidium-82 have a relatively long half-life. UltraSPECT is the new Iterative Reconstruction (IR) software which gives an image with improved Signal to Noise Ratio (SNR) [13, 14].
f-MRI	An area of neurology called function neuroimaging is used to map the brain activity to mm spatial resolution via fMRI. Neural activity is usually associated with variations in blood oxygenation, deoxygenation, and blood flow. Level of blood oxygenation's various signals can be studied using BOLD MRI pulse sequence, i.e., when blood is oxygenated hemoglobin is diamagnetic whereas paramagnetic if deoxygenated. Changes in Electromagnetic signal, Changes in Hemodynamic and Metabolism are observed efficiently with a neural activity using this modality.	It gives both the functional and anatomical information with monitoring of instantaneous fluid flow variations in the organ of interest All the rapid changes can be monitored and measured faithfully with Electro Encephalo Graph (EEG)/ Magnetic Encephalo Graph (MEG). Hybrid Modalities EEG/f-MRI, MEG/f-MRI are promising modalities for neurofunctional imaging. MEG has higher temporal and spatial resolutions whereas EEG has higher temporal and inferior spatial resolutions [7, 12].
Hybrid Imaging	PET/MRI, PET/CT, SPECT/CT, Ultrasound/MR, and EEG/fMRI, MEG/fMRI are popular Hybrid imaging systems in functional neuroimaging branch.	Main Merits is Longitudinal studies of response to desired therapy are studied using modalities such as PET/MRI and ultrasound/MR efficiently [15]. PET/CT is used to identify the active metabolic region to assist biopsy guidance [10].
Digital Mammography	Mammography is the breast X-ray imaging technique. The imagery on film is known as mammography films whereas images stored directly in the computer are known as digital mammography. Most of the radiation centers now use digital mammography rather than films. Sensitivity and Specificity are the study measures used.	Its merit is useful to identify tumors and aneurysms in heavy breast women.

Table 1. Comparative study between Different medical modalities (*continued*)

Type of Modality	Description & features	Merits & Demerits
Ultrasound	Ultrasound interacts with image tissue elasticity. Small elasticity tissues represent Cancer tissues. Ultrasound elastography investigates prostate cancer, liver fibrosis, breast cancer, etc. whereas pancreatic masses, adrenal, lymph nodes, submucosal tumors, liver fibrosis, etc. are diagnosed by Endoscopic Ultrasound Elastography. The chief merit of all these methods is to avoid needle aspiration biopsies [4].	At a glance, these procedures provide various pathological things like excessive fluids, excessive growths, stone formations, and dilations. The whole abdomen can be better visualized using Ultrasound image modality. But its main demerit is it is not that much useful for brain functional imaging.
Optical Imaging	This imaging is superficial catheter-based diagnosis process. How various body tissues and fluids absorbs and scatters the light is the working principle of this modality. Multispectral endoscopy, Confocal microscopy, multiphoton microscopy, and diffuse reflectance are various optical imaging modalities. Generally used optical imaging systems include Bioluminescence and Preclinical fluorescence-based optical imaging systems.	It is portable, cost-effective, endoscopic and non-invasive imaging for biomedical applications. It is one of the vital modality to study eye abnormalities, retinal malfunctions, diabetic retinopathy, and microaneurysms. Multispectral optical imaging is used to study breast imagery of abnormalities like breast carcinomas and skin lesions [4].
Thermal imaging	Thermal imaging is one of the night vision methods which improve the visibility of objects in a dark environment, i.e., It translates heat (thermal energy) into visible light to analyze surroundings and preparing image information based on it. Near-infrared illumination, low light imaging, and thermal imaging are different technologies of night vision. Primarily there are few algorithms/methods for ROI segmentation &classification such as head/neck thermogram temperature study, pain medicine, diabetics, banana classification, pre-processing of maximal similarity-based region merging method, etc. for utensil segmentation using thermal imaging [16,17,18]. Medical Thermal Imaging (MTI) is a technique which searches for inflammation non-invasively via scanning the human body.	MTI measures temperature emitted by the body through medical-grade night-vision technology. Therefore, this is also called as Thermography and the resultant images are called thermograms. Usually, Mammograms with thermal imaging Procedures are segmented efficiently using different methods [19]. Often thermal imaging is superior to optical imaging, but low contrast of thermal sensors and high SNR are its limitations.
Angiography	Physicians use angiography as a minimally invasive catheter-based medical test to diagnose blood vessels by using MR or CT or X-ray technologies in major organs. Nephrological case studies and diabetic nephropathy are better studied using Renal Angiography. MRA and CTA are the most commonly used methods. Usually, MRA diagnoses the abnormalities such as occlusions, aneurysms, stenosis, etc. Discussion about various techniques of MRA such as Contrast-enhanced MRA, Non Contrast enhanced MRA, Time-Of-Flight (TOF) Non Contrast enhanced MRA, Gadolinium-based Contrast agent and Phase contrast MRA are provided in [20]. In [21] Intravascular contrast agents & their effect on MRA are discussed. Usually, the diagnosis of the thoracic aorta and peripheral artery diseases is carried out by ECG- gated CE-MRA and ECG-gated 3D NCE-MRA techniques respectively. CTA can be used to scan arteries and vein in 2D whereas CTA provides a chance to rotate 3D reconstructed image in different view angles to obtain associated pathology. In this modality, a CT Diagnosis system is used along with a contrast agent like rich Iodine to observe blockages (such as atherosclerotic plaque disease and other stroke-related problems), aneurysms, and the flow of blood in the vessel and associated tissues via a small catheter.	The prime merit of these methods is to reduce the aliasing artifacts even with the usage of more number of coils. Dwight G. Nishimura et al. discussed temporal subtraction and canceling excitation methods of blood flow in case of MRA. NCE-MRA method is the widely used method of cerebral imaging. TOF MRA is efficient in studying cerebral aneurysm blood flow even compared to Hybrid modality of CTA/DSA. DSA stands for Digital Subtraction Angiography [22]. The main advantage of these methods is the disclosure of significant arterial stenoses without any exogenous contrast media.CTA is used to investigate blood vessels in major organs such as the brain, whole abdomen, heart, etc. to minor parts of the body like legs, neck, hand, etc. It helps in surgery like coronary bypass, Stenting, kidney transplantation, etc. For patients with health problems such as diabetes, :;; Chronic Kidney Disease (CKD) and other factors like obesity, contrast material allergies CTA can't be preferred. The patient needs to take food and allergy-related precautions according to may field clinic manuals during scanning.
Non-Ionizing Electro Magnetic Radiation Imaging Techniques	At a glance Electrical impedance spectroscopy or tomography, Near-infrared spectroscopy, Microwave imaging spectroscopy, Photo, and thermoacoustic imaging and non-electromagnetic radiation imaging modalities of breast like mammography [4].	Still lot of research is going on to address various issues

Other Diagnosis Aids

Apart from several discussed modalities, there are some other services/aids like Imaging Mass Spectrometry and Targeted Agents for further diagnosis.

Imaging Mass Spectrometry

It is a vitro ultra-high-resolution imaging technique used in tumor tissue samples to describe the spatial distribution of peptides, proteins, and drugs. An inverse problem of any modality occurs due to little noise getting converted into significant statistical and unpredictable changes in the image. Sensitivity to noise artifacts is a measure to know the quality of anatomical and pathological changes of any abnormality. Regularization methods are a remedy to associated inverse problems of any modality.

Targeted Agents

Targeted agents for cancer markers include Carcinoembryonic antigen (CEA), MelanoCortin-1 receptor (MC-1R), Somatostatin receptor (SSTR), Vascular Endothelial Growth Factor (VEGF), Epidermal Growth Factor Receptor (EGFR), Prostate Stimulating Membrane Antigen (PSMA), Transferring and folate receptor (TfR), etc. CEA is a blood test helpful in the diagnosis of the large intestine and rectum abnormalities. EGFR and tyrosine kinases receptors degraded signaling are indications of Alzheimer's disease while overexpression of them is associated with tumor growth & progression. Melanocyte Stimulating Hormone (MSH) of the pituitary gland (available in the cell membrane) invokes MC1R protein. Its infections cause different hair colors, pain, and, sepsis after any trauma, etc. SSTR is also known as Somatotropin Release- Inhibiting Factor (SRIF). It is a hypothalamic, pancreatic hormone and acts as central cum peripheral neurotransmitter. It has a wide distribution throughout the central nervous system as well as in peripheral tissues in the pituitary, pancreas, and stomach. It may be SSTR1, SSTR2, SSTR3, SSTR4, and SSTR5. TfR is a carrier protein which forms an intracellular iron concentration.

The use of different imaging agents, modalities, biomarkers [23], integrated technologies of independent and uncorrelated imaging provides efficient diagnostic orthogonality with improved sensitivity and specificity features. Development of tracers for various modality techniques and agents for nano-based treatment is a million dollar issue in oncology studies.

ABNORMALITIES

In this section, Major part of the discussion is about abnormalities such as Cancer, Tumor, and Aneurysm in brief according to the type of organ and its location. We considered only a valid summary of Brain tumor for discussions; as it is a large study. Dead cells will come into the picture if any of the cells are becoming older and infected due to any reason. New cells will occupy the place of dead cells. But in some different situations, the old cells are not getting vanished, but new cells formed rapidly. This kind of unnecessary growth of new additional cell forms an abnormal tissue mass called a tumor whereas, in medical terminology, Edema is a localized swelling due to injury/inflammation. Lose blood from the body as a result of injury or illness is called bleed. Brain hemorrhage is a different kind of stroke due to bleed in the brain according to WebMD [4], i.e., A ruptured artery causes localized bleeding in neighborhood tissue and kills the cells. Brain Infarct or a cerebral infarction or Ischaemic stroke is necrotic tissues region of the brain due to blocking or narrowing of arteries which supply blood and oxygen.

Tumor

According to 2017 online survey of National Brain Tumor Society with 1463 respondents, variousbrain tumor types observed in the diagnosis in the following proportion: glioblastoma is 36 %, meningioma is 18 %, astrocytoma is 17 %, oligodendroglioma is 11 % and a 29 % mix of other types with 2% of unsure diagnosis [24]. Neuroblastoma, Astrocytoma, Meningioma, Glioma, and Metastatic are various types of malignant tumors. All of them are different according to their position, size, and shape. The common tumor that occurs mainly in children is neuroblastoma which appears at outside the nerves of the brain. It is a brain tumor that occurs in the proximity of nerves of adrenalin by neuroblasts. The highest probable tumor of brain is Astrocytoma. It happens at two locations irrespective of gender in people above the age of 45. It uses star-shaped cells called astrocytes, hence the name. Commonly it appears at the brain's biggest part called cerebrum and also sometimes appears at the back part of the brain, the cerebellum. Common symptoms in the early stage include behavioral changes, Amnesia, Severe headache, and Seizures. Meningioma is another type of tumor that forms inside the skull via inner membranes of the spinal cord and brain. Meninges are three-layered structure of membranes. Early signs are Blurred vision, Headache, Weakness in arms/legs, Speech Problems and Seizures. Astrocytoma is rapid growing and Meningomia is slower growing. Next cancerousglial cells cause a brain tumor known as glioma which occurs from the mono cell of the nervous system with chemical imbalance (which grows exponentially to form tumor). Dizziness, Changes in behavior and Paralysis are early indications of it. Metastatic type is one in which the first site of disease spread to the remaining part of the body due to Symptoms such as Bone pain, broken bones, and Weakness in the legs or arms. We can find secondary malignant tumors.

Gastrointestinal stromal tumor, Pancreatic NeuroEndocrine Tumor (NET), skin tumor, soft tissue tumor, liver, and rectal tumor are various other types of tumors. Computer-assisted image investigations of

histopathology case studies provide a prime location, the enhanced portrayal of infections, abnormal growths, clots, bleeding, current location, etc.

Cancer

According to World Health Organization (WHO) fact sheet, an estimated 9.6 million deaths occurs in 2018 due to cancer. Cancer is the second main reason for the highest global mortality rate. In low- and middle-income countries it is prominent and causes 70% of deaths. The most severe cancers which has highest mortality are Lung, Colorectal, Stomach, Liver and Breast respectively [25].

Cancer can occur at any tissue of the body, i.e., It may occur in various areas like Throat, Prostate, Bone, Eye, Gall bladder, Pancreas, Glands, Kidneys, Liver, Large or small intestine, Lung, Mouth, Tongue, Blood, Thyroid, Colon, Skin (common in both male and female) whereas Breast, Fallopian tube, Ovaries, Cervix, Oesophagus, Vagina (appears only in woman usually). But sometimes breast cancer may also come into picture in heavy chest boys. Testicular Cancer appears in male only. The list mentioned here are the essential types only. In an exact diagnosis scenario, there are a wide variety of cancers [26].

Aneurysm

According to the fact sheet statistics, 9,863 deaths are occurred in the USA in 2014 due to aortic aneurysms [27]. W.H.O. survey statistics reflects severe strokes by cerebral/ intracranial/brain aneurysms occur at the anterior cerebral artery leads to death. The most common type of another brain aneurysm usually occurs at an internal carotid artery.

Most common aneurysms are Cerebral, Heart, Aortic and Peripheral. Peripheral aneurysms occur in non-aorta arteries of the neck, groin, or behind the knees. Intracranial ruptured aneurysm causes a stroke in the brain just like the heart. Peripheral aneurysms form blood clots whereas Aortic aneurysms are usually ruptured or dissected. Meningitis also causes Peripheral aneurysms [28, 29]. Congenital aneurysms are usually Non-inflammatory aneurysms. They are aneurysms of medial dysplasia, berry, and medial degeneration. The heart aneurysms occur at ventricles, coronary arteries, and sinus of Valsalva.

Types of Brain aneurysms are Charcot–Bouchard, Cerebral, and Berry aneurysms. According to the statistics of a survey of Brain Aneurysm Foundation among 6 million US people, 1 in 50 people have unruptured brain aneurysm whereas around 30,000 people have a ruptured brain aneurysm. Rupture takes place for every 18 minutes. The annual rate of rupture is approximately 8 – 10 per 100,000 people. These are fatal in 40% of the cases. This survey noticed that in case of Subarachnoid Hemorrhage (SAH) cases mortality rate is 15% (before reaching the hospital). Even many patients have disabilities after ruptured brain aneurysm treatment, i.e., 4 out of 7.

Loss of Perception/balance, Fatigue, Double vision and Speech problems are the symptoms of Unruptured Cerebral aneurysm whereas Loss of vision, Double vision, severe headaches, stiffness and Pain above or behind the eyes are common causes of ruptured aneurysms in the presence of SAH [30].

Aortic aneurysms are either thoracic or abdominal type. Aorta is the large artery which pumps blood to the torso and chest via the heart. If a bulge which is in the form of the balloon occurs at aorta due to dissection or rupture, it is an aortic aneurysm. It may be of two types Abdominal Aortic Aneurysms (AAA) in arteries near kidneys location and Thoracic Aortic Aneurysm (TAA) in chest location behind the heart.

AAA indications usually are more than a TAA. High blood pressure and sudden injury are the main reason for TAA whereas infection/injury and hardened arteries (atherosclerosis disease) are causes in case of AAA. Symptoms of TAA are Pain in the buttocks, groin or legs, back or side Throbbing, Marfan and Ehlers-Danlos syndromes whereas in case of AAA breathing, swallowing problem and unbearable chest or upper back pain are symptoms [31]. Other risk factors include Chain smoking and high cholesterol. These aneurysms are usually asymptomatic.

Recent Genome-Wide Association Studies (GWAS) identifies a specific site on chromosome 9p21 increasing the risk for both intracranial and aortic aneurysms. According to Merck's manuals, 20 percent of peripheral arterial aneurysms are iliofemoral, and 70% are popliteal. At the legs, there is an indication of popliteal aneurysms.

According to their macroscopic shape and size, an aneurysm is Saccular and Fusiform type irrespective of location. Saccular aneurysms are due to High arterial flow (Arteriovenous malformations) and connective tissue syndromes which occur at Circle of Willis. This aneurysm is the primary and leading cause of SAH, and usually, it is ubiquitous in the woman.A renal aneurysm is another common type of aneurysm observed in humans. The aneurysms that occur in the kidney can be renal artery aneurysm or intraparenchymal aneurysm. Common symptoms are tenderness, Haematuria, hypovolemic shock, and Hypertension. The aneurysms which occur at Capillaries are specifically capillary type.

Risk of rupture increases as its size increases. Diseases such as Tuberculosis and syphilitic aortitis cause Rasmussen's aneurysms and Aortic aneurysms respectively. Copper deficiency decreases the activity of the lysyl oxidase enzyme. Hence vessel wall thinning appears due to affected elastin issue.

Various aspects of Abnormality analysis are shown with Figure 7.

Aspect 1:

First diagnose the scans of various organs in different image modalities to identify the presence of abnormality

Table 2. List of Abnormality Medicine & Surgery related books

Name of the Book / Chapter	Authors	Coverage	Publisher	Edition/ Other details	Ref. No
Digital image processing book for medical applications	Dougherty G	Tumor & Cancer related studies	Cambridge University Press	New York, 2009	3
Vascular Surgery	Rutherford R B.	Aneurysmal disorders& Vascular surgery Issues	PA:WB Sauders Elsevier	6th edition, Philadelphia, 2005	32
Cirurgia Vascular	Brito C J, Duque A, Merlo I et al.	Aneurysmal disorder &Vascular surgery Issues	Revinter	2 volumes ed., Rio de Janeiro, 2008.	33
DoençasVasculares Periféricas	Maffei F U, Lastória S, Yoshida W B, Rollo H A et al.	Aneurysmal disorder & Vascular surgery Issues	Rio deJaneiro: Guanabara Koogan	Volume1, 2008	34
Cirurgia Endovascular	Lobato A C, Araújo A P, Pereira A H et al.	Aneurysmal disorder & Vascular surgery Issues	São Paulo: Instituto de Cirurgia Vascular e Endovascular de São Paulo. Rio deJaneiro, Revinter.	2006	35
Decision Making in Vascular Surgery	Cronenwett J L, Rutherford R B.	Vascular surgery Challenges	PA:WB Sauders Elsevier	2001	36
Cirurgia Vascular	Haimovici H, Ascher E, Hollier LH et al.	Aneurysmal disorder & Vascular surgery Issues	Rio de Janeiro, Revinter,	5 ed., 2006	37
Mastery of Vascular and Endovascular Surgery	. Zelenock G B, Huber T S, Messina L M et al.	Vascular surgery Challenges	Philadelphia, PA: Lippincott Williams & Wilkins (LWW)	2005	38
Aneurysm	Simona Celi, Sergio Berti et al.	Recent advances of aneurysmal related disorder studies	Rijeka, Croatia, InTech	YasuoMurai. Editor, 2012	39
Case studies in medical imaging	Ahuja A TAntonio G E et al. Eds.	Wide variety of case studies	Cambridge University Press	2006	40

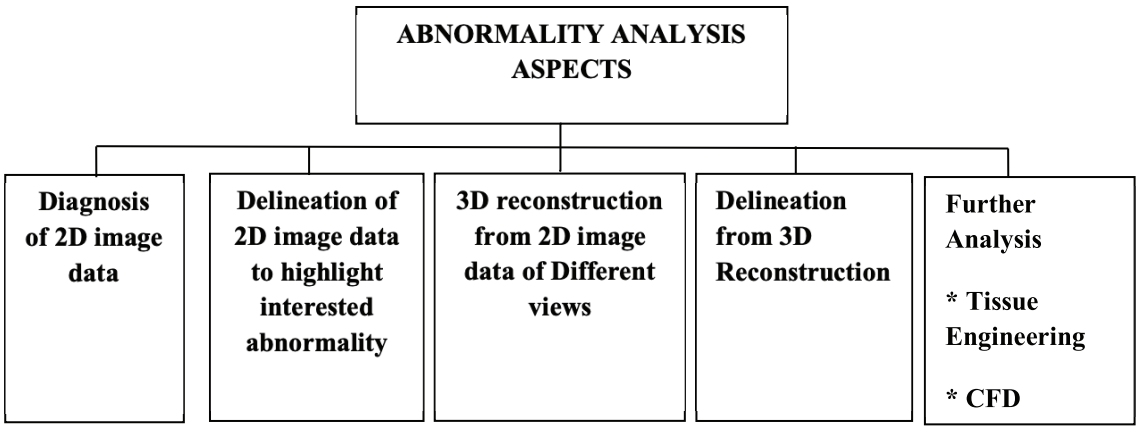

Figure 7. Different aspects of abnormality analysis.

such as tumor or aneurysm or any organ (if physician suggests any Scan for the patient).

Aspect 2:

Extract/Delineate/Segment the interested abnormality using various algorithms/methods. Many times, diagnosis from Image 2D data provides inadequate knowledge about abnormality. On the other hand Segmentation results only provide external geometry details of abnormality rather than internal geometry.

Aspect 3:

Objective is to reconstruct the Abnormality by stacking the layers of Axial (Transverse), Coronal (Frontal/ Perpendicular), and Sagittal (Longitudinal) orientations of that image modality. Hence, it provides the exact shape, size and dimensions of the abnormality by analyzing the external geometry. Sagittal plane separates the left and right sides of the Organ/Abnormality. Axial plane separates the upper (superior) and lower (inferior) halves of the Organ/ Abnormality Coronal Plane is a vertical plane running from side to side; divides the organ/abnormality or any

of its parts into anterior and posterior portions. 3D reconstruction model is constructed by combining all above 3 planes information.

Aspect 4:

Now, only select the ROI i.e. Abnormality using any segmentation techniques such as Dynamic Region growing, Thresholding, and Air free, coronary tool etc. using MIMIC. Innovation Suite, COMSOL tools etc.. Dimension analysis can be done using 3-Matic tool via length, distance, angle tools. Optimum mesh construction supports Finite Element Analysis (FEA).This provides an opportunity for making Additive manufacturing stencils of Organ/ Abnormality..

Aspect 5:

The 4 basic types of tissue are connective tissue, epithelial tissue, muscle tissue, and nervous tissue. Connective tissue supports other tissues and binds them together (bone, blood, and lymph tissues).Obviously, the engineering which studies these tissues is of vital importance. Among all epithelial tissues are very significant while studying the walls of any abnormality/organ. For example, epithelial tissues on walls of aneurysm prone vessel are important to fabricate stents/grafts. They also help in understanding the case studies of balloon angioplasty, ruptured aneurysm, blocks which cause myo-cardiac arrest, thickening/thinning of vessel walls. Anywhere in the human body presence of epithelial tissues identification is cumbersome task. Hence in Tissue Engineering and Regenerative Medicine., the challenging task is to transform scaffold growth to new functional tissues

A list of abnormality treatment & surgery literature books are provided for reference in table 2.

DATABASES AND BIOMEDICAL TOOLS

This section provides the details & prerequisites for student community who are trying to do research activity with various clinical imaging modalities. In this section, the first list of different databases and names of corresponding research institute are mentioned for awareness of different case studies, later in the second part, a brief discussion on various available tools for abnormality analysis are presented.

Databases

Awareness of related terminology and availability of ground truth images is essential to study, understand, and analyze the abnormalities, for this everyone needs to depend on various databases and research institutes which provide the valid, validated and accurate information. Here at this point of the study, we provide information about essential institutes and websites which help in this regard. For brain tumor studies please refer Societies of Neuro-Oncology and allied research institutes as discussed in table 3 & 4.

Biomedical Simulation Tools

The last aspect of the following subsection is to know a variety of software's or tools for adequate analysis of tumor, cancer, and aneurysm. MIMIC, AMIRA, Open Source Computer Vision (OPEN CV), FEBIO, ImageJ, Image Processing ITK, MATLAB, etc. are used for identification, location, and delineation of tumor and cancer. Aneurysm analysis can be carried out using AMIRA, ANSYS, ImageJ, ITK, MATLAB, MIMICS, OPEN CV, Solid Works, 3-, etc. MIMIC, Amira, ANSYS like software's do the flow analysis after identifying ROI by volume rendering.

Nowadays one can construct Virtual Models (VM) of Aneurysms using any Finite Element Analysis Software without volume rendering software later post flow processing is carried out via ANSYS, AMIRA, FEBIO, and MIMIC. With the help of 3D printing machines evolution, we can make a stencil/prototype of the virtual aneurysm with real constraints and necessary boundary conditions for relative comparison with VM to facilitate proper Aneurysm analysis with associated hemodynamics. Simulator of aneurysms is the Multidisciplinary framework of Electronic, Medical and Mechanical stream people. Comparison of various tools are provided in table 5.

TREATMENT PROCEDURES

According to severity, tumors may are Grade 1, 2, 3 and 4. Among the four, Grade 1, 2 are low grade non-harmful and 3, 4 are harmful high-grade ones. Grade 1 tumors are treated with continuous screening whereas Grade 2 tumors diagnosed and treated with repeat scans and we need to check for no recurrence during postoperative treatment. Grade 3 and 4 tumors are rapidly growing and harmful so that removal of them is Cumbersome. Hence during postoperative treatment chemotherapy, radiation,

Table 3. List of Useful databases

Database Name / Owner	Purpose	Web Site
Cybernet systems	Intagerealia free DICOM viewer which provides aortic aneurysm CT database in all views for the development of 3D model aneurysm	http://googleweblight.com/i?u=http://www.cybernet.co.jp/medical-imaging/english/&hl=en-IN
Cross cancer Research Institute/ Alberta cancer foundation databases	Tumor, Cancer, Aneurysm and also other organ databases	http://albertacancer.ca/cross-cancer-institute
Open Access Series of Imaging Studies (OASIS) database	Brain tumor databases	www.oasis-brains.org
Cancer imaging Archive	Oncological case studies like Brain tumor progression, Colonoscopic, Endoscopic, neck, Sarcoma, Breast, Kidney, Prostate imagery, Lymph nodes, data sets	https://wiki.cancerimagingarchive.net/
University of California's (UCLA), Los Angeles	Breast Cancer and other cancer databases	https://cancer.ucla.edu
Tusla relational brain tumor database resources	Tumor database	http://tumorsdatabase.altervista.org/
Laureate Institute for Brain Research (LIBR)	Neuro-Oncology and allied research	http://www.laureateinstitute.org/
Simulated brain database research resources of Brain web	Brain Axial, Coronal, Sagittal Case studies	http://brainweb.bic.mni.mcgill.ca/brainweb/
Public Internet Brain Segmentation Repository (IBSR)	Harvard Brain datasets	http://www.cma.mgh.harvard.edulibsr/
National Cancer Research Institute (NCI)	A-Z Cancers data catalog resources	https://www.cancer.gov/research/resources/data-catalog
Breast cancer Tumor agent breast cancer database	Breast cancer tumor, database translational research	https://link.springer.com/chapter/10.1007/978-3-540-36841-0_111,
DICOM (Digital Imaging and Communications in Medicine) library	Medical Image Databases	https://www.dicomlibrary.com
One-stop portal of CSIR's canceres	Various cancers databasesunder Biomedical Translational Research Initiative (BTRI)	http://crdd.osdd.net/raghava/canceres/db.php
PubMed (of NCBI)	Resources and tutorials and are useful for better understanding of vessels related diseases & abnormalities	www.pubmed.gov
Hemolab	3D Brain Aneurysm database	http://hemolab.lncc.br/3DBrainAneurysm/
Brain aneurysm foundation	Cerebral, Intracranial Aneurysm databases & treatment	https://www.bafound.org/about-brain- aneurysms/ brain-aneurysm-basics/brain-aneurysm- statistics-and-facts/
SciELO's	Electronic database of aneurysms, Synpic database of aneurysms	http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1677-54492014000400294&lang=en
Medline University	Medline Webinars & Surgery equipment information about aneurysm clips & clamps	https://www.medlineuniversity.com/
National Center for Biotechnology Information (NCBI)	It is a Part of NLM) which supplies different tools, kits, databases & tutorials of aneurysms	https://www.ncbi.nlm.nih.gov/ https://www.ncbi.nlm.nih.gov/guide/data-software/
May Field Clinic	Brain tumors, stroke, aneurysms, movement disorders related information & databases	https://www.mayfieldclinic.com
VHL Regional Portal	Open Educational Resources Repository Network CVSP / VHL	http://sites.bvsalud.org/rea/en/

Table 4. List of Useful Research Institutes

Institute	Purpose of Research	Web Site
U.S. National library of medicine	Tutorials and various Clinical trials	https://www.nlm.nih.gov/biomedical.html
American Stroke Association (ASA)	Ischemic &Hemorrhagic Stroke related information & resources	https://www.stroke.org
Open Access Series of Imaging Studies (OASIS) database	Brain tumor databases	www.oasis-brains.org
RSNA	Radiology Aspects	https://www.rsna.org
ARA Diagnostic Imaging (Austin Radiological Association)	Information about Interventional Radiology & Relative comparison study International Subarachnoid Aneurysm Trial (ISAT) of endovascular embolization and clipping	https://www.ausrad.com/
Indian Council of Medical Research (ICMR), New Delhi, India	Apex body in India for the formulation, coordination and promotion of biomedical research	https://www.icmr.nic.in
Indian Association for Cancer Research (IACR), New Delhi, India	To advance research in all aspects of cancer and promote interaction among scientists	www.iacr.org.in
Council of Scientific and Industrial Research – Indian Institute of Chemical Biology (CSIR-IICB), Kolkata, India	Engaged in research on diseases of national importance and biological problems of global interest, sophisticated state-of-the-art technology for life science research	https://iicb.res.in
Tata Medical Centre, Kolkata, India	. Cancer Bio-bank collects tissue, blood and other samples from patients at various time points during their treatment	https://www.tmckolkata.com
Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad, India	Research on Cancer Issues due to inheritance	www.cdfd.org.in
TIFR (Tata Institute of Fundamental Research), Mumbai, India	Cancer structural biology	www.tifr.res.in
TIFR Centre for Interdisciplinary Sciences (TCIS), Hyderabad, India	Cell & Cancer Biology, Fluid dynamics in Vessels, Material Science for Cancer	https://www.tifrh.res.in/

Table 5. Comparative study of Different Biomedical Simulation tools

Name of the Tool	Company / Vendor	Purpose	Options / Features
AMIRA	Thermo Fisher Scientificn collaboration with the Zuse Institute Berlin (ZIB)	Software platform for 3D and 4D data visualization, processing, and analysis.	Options include Mesh, Microscopy, Molecular, Neuro, Skeletonization, DICOM (Digital Imaging and Communications in Medicine) reader, VR, Very large data and Developer. https://www.fei.com/software/amira/ https://www.thermofisher.com › home › industrial › electron-microscopy
MIMIC	Materialise NV of Belgium nation	It is a 3D design and modeling software using image processing options [10].	It generates 3D ROI surface models via volume rendering process by using 2D image stacks of X-ray, Ultrasound, MR, CT, Micro CT, Confocal Microscopy, Traditional Angiography, MRA and CTA. It is used in Pulmonology, EndoVascular, Cardio Vascular, Craniomaxillofacial, Orthopedic Arthroscopy, etc. whereas it is also useful for rheology and other material science industries for understanding anatomical processes in nonmedical case studies [41]. https://www.materialise.com

Table 5. Comparative study of Different Biomedical Simulation tools (*continued*)

Name of the Tool	Company / Vendor	Purpose	Options / Features
ANSYS	ANSYS Inc.	ANSYS Fluent provides pressure based solver & density based solver for studying Computational Fluid Dynamics (CFD) in Vessels & Organ models as any modality cannot describe much about blood or fluid flow in it which affects its operation. User guide: ftp://ftp.energia.bme.hu/pub/Tuzelestechnika/MSc/flu_tg.pdf	Workbench is a single package that provides different suits for various ANSYS tools. ANSYS Fluent or CFD or CFX usually preferred for 3D Modeling and analysis. Student version is also available: https://www.ansys.com/en-in/academic/free-student-products
SOLID WORKS	Dassault Systems	It is an MS Windows-based Solid modeling Computer-Aided Design (CAD) and Computer-Aided Engineering (CAE) tool with Autodesk Inventor and Solid Edge on Parasolid-kernel [42].	Its files include drawing file (SLDDRW), part file (SLDPRT), assembly file (SLDASM) along with metadata sub-files and preview bitmaps [42]. https://www.solidworks.com/solution/job-functions/students
3 MATIC	Materialise	It integrates CAD tools and pre-processing capabilities. It also works on Stereo Lithography (STL) file (of an anatomic model) exported from MIMICS or any other software. It provides an opportunity to do real engineering on Anatomy. Hence medical research community calls this as Anatomical CAD.	Especially its role is significant in designing implants such as stents, grafts and surgical guides using 3D measurements and analyses. It is also useful for preparing the mesh for FEM. It offers better dimension results of diameter, curvature, etc. We can import this file to 3D printing. https://www.materialise.com › software › 3-matic https://www.materialise.com › medical › software › 3-matic
MATLAB	Matrix Laboratories	It is a Single integration package which carries out visualization, computation, and analysis via simple programming. It is a user-friendly object-oriented coding environment with plenty of built-in data structures, editing and debugging tools.	It uses mainly three windows called editor, graphical and command. Command Window provides a platform to write various commands via m-File Script or Function with extension .m. Command History and Workspace are its sub-windows. Editor window provides a secure platform to type and to modify the user programs. Graphics window generates various plots established by the user/programmer in the MATLAB Code. Graphical User Interface (GUI) Programming feature is also possible for better visualization. https://www.mathworks.com
OPENCV	Intel	It is a Programming function package with various SciPy, Numpy, Matplotlib are optimized libraries to assist computer vision, machine perception and learning. It is useful in Segmentation, Classification, and Clustering via statistical machine learning library [43].	It is developed in CPP with API bindings in MATLAB/OCTAVE, Java and Python. Similarly, it has C hash, Ch, Haskell, Ruby, Perl and Python wrappers. Useful OpenCV-Python tutorials are provided by K. Abid Rahman and Alexander Mordvintsev the intern and mentor of GSoC-2013 respectively for beginners [44,45]. https://opencv.org/
IMAGEJ	National Institutes of Health	It is a free image processing and analysis tool with JAVA. It is a convenient and intuitive Graphical User Interface (GUI).	It runs on any computer with Java Virtual Machine (JVM). A lot of tutorials for medical image processing with ImageJ are available in [3]. http://rsb.info.nih.gov/ij/

Table 5. Comparative study of Different Biomedical Simulation tools (*continued*)

Name of the Tool	Company / Vendor	Purpose	Options / Features
FEBIO	Gerard Ateshian's lab at Columbia University and Jeff Weiss' lab at the University of Utah	It is a software suite used to do nonlinear FEA. It studies deformation issues with the help of three packages called PreView, FEBio, and PostView in the areas of biophysics and biomechanics.	Preview package has Simple primitives to create desired geometry, Mesh editing tools to modify the designed geometry and Mesh repair tools to fix the common problems. It is a Finite Element Preprocessor with GUI option and allows the user to generate/import meshes, applying the desired boundary conditions along with wanted material characteristics, and in dearth analysis via a user-friendly graphical environment. FEBio package is a non-linear implicit Fluid Structure Interaction (FSI) and Growth solver with plenty of boundary conditions. It can't have any mesh generation capabilities, so it relies on the designed meshes of PreView. Postview is a package to visualize and analyze results of FEBio package via different plots like Plane cut, Vector, Surface, Iso Surface and tools such as TrackView, Summary, and Integration. https://febio.org
ITK	Insight Software Consortium	ITK is a cross-platform and open source tool of to do precise and straightforward image analysis. As the name suggests, it provides different 2D,3D edge segmentation/registration methods. C, C++, FORTRAN, and Python are the languages used for programming/coding. ITK-SNAP is a tool developed from SNAP in 2004 for segmenting anatomical structures in 2D or 3D medical images with a friendly and simple user interface [46]. Hence the name ITK-SNAP. Lot of ITK tutorials are available to understand its usage for a variety of applications [47].	ITK Snap provides active contour methods (ACM) based semi-automatic segmentation algorithms, manual delineation and image navigation via several features. Its unique merits for segmentation include Manual segmentation at once in three orthogonal planes, Flexible with concurrent or linked viewing of multiple images segmentation at a time and Rapid 3D cut-plane tool for ROI processing. It also supports working with multi-channel, color, and time-variant images. A Qt-based modern GUI of this tool supports all 3D image formats. Although ITK is a C++ application, many ITK functions are available in ImageJ through simple ITK Java compatibility layer. ITK Site https://itk.org/, ITK Snap site http://www.itksnap.org/pmwiki/pmwiki.php

targeted therapy etc. are preferred to know whether microscopic tumor cells grow back or not. These improve the lifetime of patients. Tumor pathology provides a chance for Appropriate Chromatography, Exact Chemotherapy, Precise Radiology, and Progressive Rehabilitation.

Study of brain tumors is necessary as it causes more mortality among the tumor deaths. For diagnosis and treatment, knowledge of the various kinds of brain tumours is essential. A brain tumour is usually diagnosed by neurological examinations, imaging studies such as CT or MRI scans, and occasionally a biopsy. Surgery, radiation therapy, chemotherapy, targeted therapy, or a combination of these may be used as a form of treatment, depending on the kind, location, and size of the tumour. There are several brain tumors such as Gliomas, Meningiomas, Pituitary Adenomas, Schwannomas, Medulloblastomas, Craniopharyngiomas, and Primary CNS Lymphomas. The most prevalent kind of primary brain tumours are gliomas, which develop from glial cells that support and shield neurons. According to the kind of glial cell from which they originate, they are categorised as Astrocytomas (Occurs as low grade/high grade due to astrocytes), Oligodendrogliomas (occurs at frontal and temporal lobes due to oligodendrocytes), Ependymomas (Occurs at ventricles ependymal cells).

Next, the meninges, which are the membranes that cover the brain and spinal cord, are the source of meningiomas. They are occasionally malignant. Pituitary Adenomas are due to pituitary gland malfunctioning and alters hormone production. Schwannomas are due to issues in Schwann cells, which create the myelin sheath (which protects nerve fibres). The most prevalent among them is vestibular schwannoma (acoustic neuroma) which causes hearing loss. Next in infants, the most prevalent malignant brain tumours is medulloblastoma spread to other areas of the brain and spinal cord rather than at cerebellum. Craniopharyngiomas are benign tumours in the proximity of pituitary gland and prevalent in old age people and children and changes hormone imbalance. Primary CNS Lymphomas are most uncommon, highly aggressive tumours that start in the Central Nervous system's (CNS) lymphatic system. They are more prevalent in individuals with compromised immune systems.

Oncology is a field of medicine which deals with the prevention of cancer. It can be Medical Oncology or Surgical Oncology or Radiational Oncology according to the type of treatment preferred to patient. Abnormality can be found using Chemetoradiography and External-beam radiation therapy Viz. Conventional radiation therapy, Stereotactic radiosurgery,3D & 4D IMRT, Proton therapy, 3D-CRT (3D radiation treatment), Fractionated stereotactic radiation therapy, etc [25, 48]. Prognosis, Surgery, Radiation Therapy, Chemotherapy, Immunotherapy (Natural Killer Cells), Photodynamic therapy, Digital Mammography, Targeted Therapy, Hemotherapy, Hormone Therapy, Stem Cell Transplant, Precision Medicine and Combinational therapy are alternative treatment methods for high- grade tumors and cancer. Surgical Treatments are preferable for benign tumors like Adenomas, Fibromas whereas Chemotherapy, Radiation therapy, Tumor Treating Fields and Targeted therapy are suitable for the treatment of high-grade malignant tumors. Nowadays cancer biomarkers, nano cancer research is also going on to increase the life span of patients.

Many researchers are trying to combine nanotechnology with molecular imaging to detect minute diseased part (abnormality) and to do accurate prognosis to give exact dose rate to tiny disease tissues. They provide a chance to vast vivo specific studies by Growth of tissue, arteries, parent/child blood vessels, muscles, and bones under repair. Quantum dots (qdots) are used to detect biochemical markers of cancer. They are usually are fluorescent nanoparticles.

To treat Aneurysms physicians use treatment aspects like Diagnosis, Prognosis based on appropriate dose rate and surgical treatment. Aneurysms treatment methods are nonsurgical and surgical. Surgical Intervention procedures include Open Surgical Repair (OSR), Clipping, Coiling (Endovascular Embolization), Stents, Grafting. Among these Coiling, Clipping is suitable for the treatment of Cerebral/Intracranial aneurysms whereas Stents used for the treatment of AAA/TAA.

Clipping is a surgical procedure employed to repair an aneurysm. A tiny metallic clip is placed across the neck of the aneurysm, ceasing the blood flow from it. Clips are made up of Titanium alloy, or Cobalt based alloys like MP35N (nickel/chromium/cobalt), Elgiloy/Phynox (cobalt/nickel/iron), and other non- or at most minimally ferromagnetic property materials. Its merit is it will avoid rupture of the aneurysm. This is carried out in Open cut surgery or open craniotomy in the skull and using a specialized microscope in case of cerebral/intracranial aneurysm. It is more risky compared to Coiling. So, 4 to 8 weeks are required to fully recover after clipping treatment. They are clipped temporarily removable or made as permanent implant.

Coiling is an endovascular procedure viz. the surgeon accesses the aneurysm through the vascular system. He or she will make an incision in the thigh and enter an artery of the leg. The surgeon will then use x-ray imaging and a special dye to guide a catheter to the site of the aneurysm in the brain/Aorta. Hence, it is also known as Endovascular embolization. Coils are made from Platinum/Kanthal (an iron-chromium-aluminum alloy), nichrome (a nickel-chromium alloy), stainless steel, titanium, and Ni200 (nickel). It offers permanent occlusion when deployed. Patient probably returns to his work or his normal routine in 3 to 7 days after coiling.

Neurosurgical clipping provides better results in terms of mortality, re-bleeding, and re-treatments. Endovascular coiling is a better surgical technique in terms of post-operative complications, favorable outcomes, and rehabilitation.

In Endo Vascular Aneurysm Repair (EVAR), A stent graft is sent along the catheter to the aneurysm. The stent graft is a tube made of a thin metal mesh (the stent), covered with a thin polyester fabric (the graft). This stent graft is opened inside the aorta and fastened in place. The stent graft stays in place, and blood flows through it.

Rehabilitation therapy is an excellent source of healing for aneurysm suffering patients. It increases the lifetime of patients. 3D simulator of the blood vessel with aneurysm prototypes provides an opportunity to study the realistic conditions in a cost-effective and invasive manner. It supports a high degree of Rapid Prototyping (RP) and Surgical Simulation (SS) in parallelism. Recent developments in Virtual, Augmented and Mixed Realities aid the surgical and nonsurgical treatments for aneurysm cure [49,50].

Various organizations like Brain Aneurysm Foundation, National Institute of Neurological Disorders and Stroke (NINDS), Joe Niekro Foundation are working for the neuro disorders awareness, rehabilitation and research whereas in cardiovascular area of medical research ASA efforts are uncountable.

RESULTS AND DISCUSSIONS

In this section, for the awareness of new researchers in the abnormality detection research area, the authors provided typical results through a variety of implementations

with different tools. It is a sequential framework which is lucid and result oriented. Steps are how to delineate an abnormality, change detection between different time (pre operative and post operative diagnosis scans or before and after treatment scans), how to reconstruct a 3D virtual model of the delineated abnormality of the interested organ with ANSYS/SOLIDWORKS for idea. Next based on Scan data develop the precise 3D model using MIMIC, How to extract the interested abnormality from whole 3D model, Then how to study the morphology of that abnormality with size & shape constraints and finally making a Replica with 3D Printing. Initially, the results of a Fast Aneurysm and Blood Vessel Delineation Method (FABDM) are provided using a MATLAB tool for delineation of abnormality boundaries [51, 52]. It is a level set based active contour algorithm on carrying out global segmentation without the usage of stability and termination criteria. Initially, define a curve (levelset) in the desired location (AOI), and later minimize the energy of the curve based on image details using various controlling parameters to fit on the abnormality boundary for its implementation. Speed and representing in the segmentation output in the white background are the merits of this method. The corresponding results are discussed using Figure 8 via four sub figures. FABDM process is explained in steps.

Step 1:

Consider original image u_0 of any angiography data sheet. Apply MICO algorithm to these images to avoid bias inhomogeneities (optional step) instead of conventional tensor fields. Hence, recommended for poor intensity or multiple intensity case studies.

Step 2:

Define an initial Contour c_0 in $u_{0.}$ Later it is guided towards ROI i.e. Aneurysm.

Step 3:

Initially define a mask which has the same dimensions of the input image. However, during execution it is controlled by four variables x, y, z and w to guide c_0. Define typical square mask via averaging kernel regression method to support multilayer, level and phase to generate Multi-Layer Deformable Models (MLDM). During regression, convolution of specified size of window is performed. This is the simple and widely used method for modifying the kernel estimate near the boundary.

Step 4:

Guide the mask towards boundary by evolved initial level set function ϕ_0 from c_0. Adopting various controlling and governing parameters to distinguish various vessel structures with different levels of intensity.

Step 5:

For segmentation and delineating the boundary of aneurysm and associated vessel structures level sets are varied to fit the boundary i.e. Mumford-Shah Energy functional is to be minimized. It is the sum of the three Statistical information terms viz., global term E^G, local term E^L and Penalization terms E^P

Step 6:

Cease the guided contour without any stability and termination phenomena such as Coudarnt Fredrich Levy

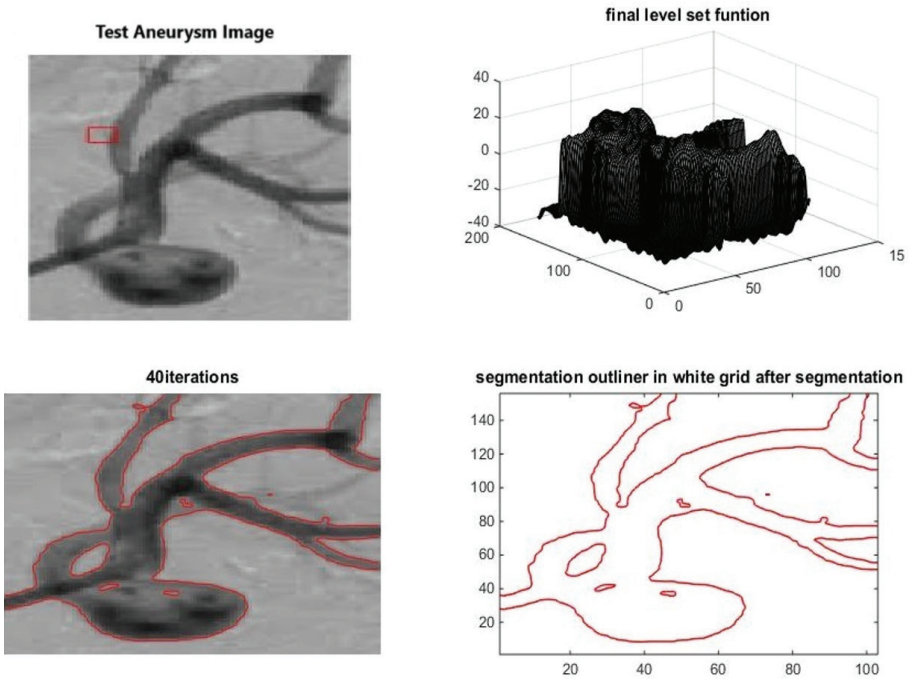

Figure 8. FABDM results using MATLAB.

(CFL) criterion [52] after capturing aneurysm along with nearby vessels which provides better achievement in terms of computational speed and convergence than the conventional level set ACM's.

FABDM is tested on different tumor case studies of GSL medical hospital, Radiopedia, Alberta University, TCIA etc. This is also tested on Cerebral Aneurysm case studies of Brain Aneurysm Foundation.

Aorta case studies of Basilar artery Phase Contrast MRA (PCMRA) of Kings College of London, 3 Dimensional Rotational Angiography (3DRA) AAA, Online Cybernet Systems Intage Realia, Hope International Hospitals, May field clinic etc. All the MATLAB Segmentation results are shown with four intermediate Steps for 3DRA Aneurysm Image: (Left top image (A): Test Image), (Left bottom Image (C): Segmented image), (Right top Image (B): Energy evolution) and (Right botom Image (D): Segmented Image in White Background).The white background helps us to identify the ROI precisely.

Abnormality under test may be Tumor, Infarct, Edema, Bleed, and Aneurysm. FABDM is also suitable to segment the coiled aneurysms to monitor the changes in the pre-coiled aneurysm and post coiled aneurysms as shown in below Figure 9.

Anterior communicating artery (ACA) cerebral aneurysm, Re-treatment Internal Carotid Artery (ICA) aneurysms, ICA bilateral aneurysm, DSA (Digital Subtraction Angiography), Carotid Cavernous Aneurysm (CCA), neupsykey aneurysm, Illustrative recurrence case of a ruptured Posterior communicating Artery (PcomA) aneurysm, May field clinic of Ohio's cerebral aneurysm etc.

The coiled aneurysm image is from brain aneurysm foundation resources Segmentation is carried out using MATLAB. Left image (A): Test image of Post coiled aneurysm and Right image (B): Segmented image after FABDM.

Next type of aneurysm study is Computational model designed from any imaging modality such as MR/CT or MRA/CTA scan findings from a patient as shown in the below figure using SOLIDWORKS/ANSYS tools. Viz. To find the associations between the growth, formation of aneurysms, and hemodynamic parameters [53].

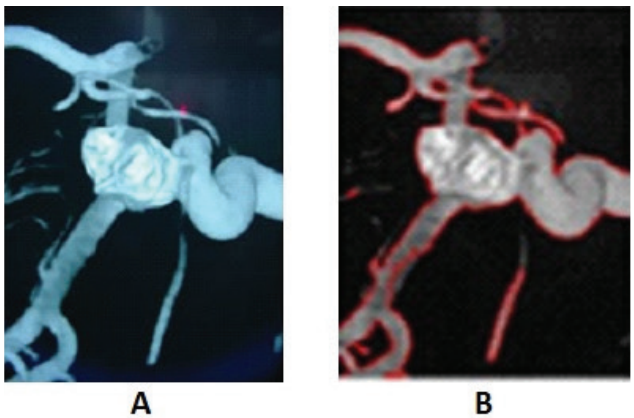

Figure 9. FABDM segmentation results for brain aneurysm with coiling.

In this Methodology Proposed Abnormal Vessel model is designed using ANSYS Design/Space Claim Modeler or SOLIDWORKS Profile Suite and subsequent CFD analysis is performed using ANSYS Fluent Workbench. Saccular and fusiform are two commonly found aneurysms of the abnormal vessel.

Design of fusiform aneurysm

Consider various circles by considering desired distance of diameter along with inner lay - outer lay structure. Draw these circles initially, first and last circles diameter must be high compared to middle circle diameter. Next, by using blend feature, connect all the circles in sequential manner.

Design of Saccular aneurysm

For Asymmetric Saccular aneurysm design, use alike process with tiny modification of all inner lay - outer lay circle structures must terminate at same bottom reference line. But this process may form asymmetry in blood vessel formation. For Symmetric design, Use mirror options. These models are designed in such a way to match different types y of realistic abnormal aortic vessels.

The flow simulations are carried out through FLUENT workbench of ANSYS. In this process, all exact conditions of Infected Aortic Aneurysm are imposed via 5-step procedure namely Geometry, Mesh, Set up, Solution and Results. The steps include, first design model via space claim model of geometry option. Second step is Mesh step. Entire prototype is divided to parts like Inlet, Outlet, Aortic wall and Fluid blood to incorporate various realistic environments to obtain precise model useful for subsequent steps. In third set up step three numerical simulation steps are carried out. General, Model options and Boundary conditions. In set up step select double precision option. Choose model as viscous – laminar profile. Material Selection for wall is Dacron (Solid) and for liquid input is Blood (Fluid). In the fourth step, select least squares method to solution model by assigning solution initialization parameters like Body forces, Density, Energy, Momentum and Pressure then go for Run calculation. The final result step is used for plotting various plots of Flow lines, Intra-aneurysmal velocity magnitude plots, Static pressure, Streamlines, and WSS for knowing the rupture or growth status of aneurysm.

In the below Figure 10, we have the flow parameter analysis of a Saccular and Fusiform aneurysms models (model 1 & model 2).

During flow analysis, a proper material, physical and boundary conditions are imported and adapted in a virtual scenario to suit real aneurysm environment. Row1 Figures A, B represents Pressures of Saccular (Model 1) & Fusiform (Model 2) aneurysms whereas Figures C, D (Row 2) shows Wall Shear Stress (WSS) plots. Saccular is one side swelled whereas fusiform is all side swelled aneurysm as shown in the figure for Saccular and Fusiform respectively.

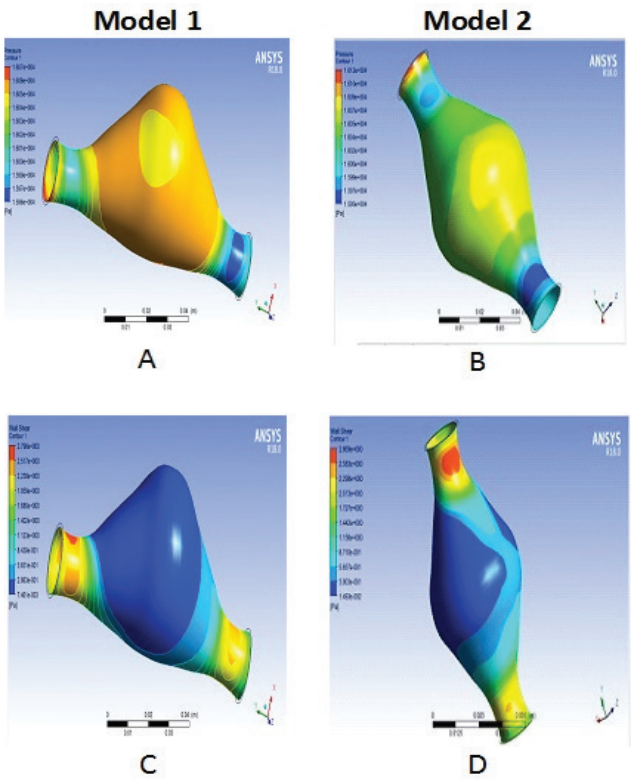

Figure 10. ANSYS analysis plots.

The parameter plots of Pressure, WSS are displayed in two rows called row 1 and row 2 respectively. WSS is a measure of stress which studies properties like friction, the viscosity of blood and endothelialization properties of tissues of the vessel. High WSS in blood vessel indicates aneurysm presence (periphery) and tells about rupture chances. WSS is low at aneurysm premises and high at walls. Whereas Pressure is high at aneurysm and low at remaining wall periphery.

For Precise and Robust modeling authors used the Materialise MIMIC Suite. It facilitates Virtual modeling of three-dimensional models of abnormality and without abnormality. Refer to Figure 11.

MIMIC Suite is a user-friendly tool. It requires data sets of three views Sagittal, Coronal, Axial. The whole model is developed by importing all the three view image sequences with desired ROI selection as shown in Figure 11. For further Analysis store it as a Project. It uses several segmentation procedures such as thresholding, region growing, live wire and airplane. Choose any of them to get a validated model to impose realistic conditions of the abnormality environment. There is a provision to save them in different file formats to import them to various tools like DS Solid works, ANSYS Fluent, 3-matic.

The best format to import it to ANSYS like tool is IGES or IGS storage format. The acronym for IGES is the Initial Graphics Exchange Specification. It is a computer-aided design compatible vendor-neutral file format that to share binary or any digital information of an associated

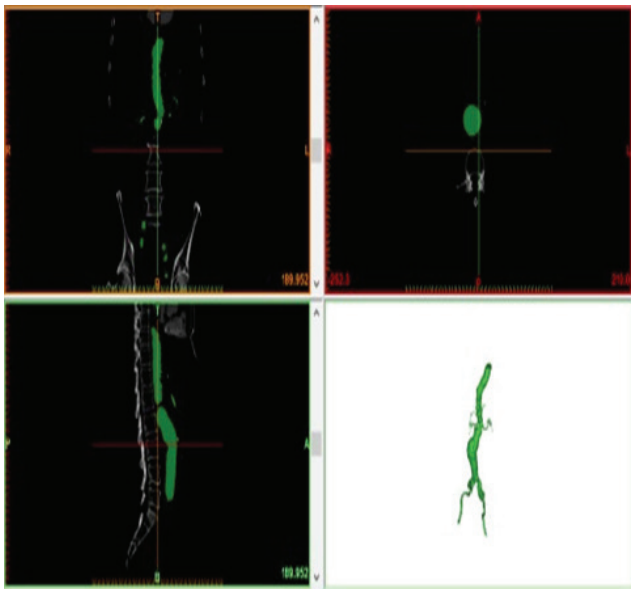

Figure 11. MIMIC tool developed virtual model of aortic aneurysm.

model. The Best Format to import it to 3-Matic, ANSYS, 3D Printers, other CAD, Computer Aided Manufacturing (CAM) software and systems is STL.

STL stands for STandard LithoGraphy. Also known as Standard Triangulation Language due to any model is represented as an abstraction of many triangles as layers. American Standard Code for Information Interchange (ASCII) or binary are two storage formats of STL files.

Procedure of Constructing Vessels using MIMIC Suite [54]

1. In the file menu, click on a new project.
2. A new project wizard is opened and then load CT DICOM dataset by selecting the concerned folder. Hence, it reads data and displays the data of the patient.
3. Use convert option so that it opens a window with 3 views viz. Coronal, Axial, and Sagittal.
4. Next in Segment menu chose dynamic region growing segmentation with fill cavities and multiple layer option as shown in Figure 11.
5. Click on the aorta part in the desired (axial view) to generate mask. Calculate the part from the created mask.
6. Export the part to 3-matic.
7. Use Hollow in Design menu to make a hole in the vessel.
8. Chose the part and apply.
9. Use Trim in Final menu
10. Chose the model and use Remove outer and draw a box on the model to remove the vessel outer the box. Click on Apply to create 3D model. Export this to STL for FEA.

The above Figure 11 is the screenshot of MIMIC result Left top, right top, left down to represent top, front and side aligned views called as Axial, Coronal, and Saggital. The figure at last Right bottom is the reconstructed vessel by using three views images sets of INTAGE Realia of CYBERNET

SYSTEMS medical imaging database site using dynamic region growing segmentation method.

Procedure for dimensional analysis using 3-matic [54]

Four-step process is used to determine dimensional parameters such as Aspect ratio, Dome to neck ratio, Inflow Angle (β), and Size ratio, Bottle neck factor etc. using 3-matic.

1. Open STL file and Cut the aneurysm into half via the trim option.
2. Draw line using line option of analyze option.
3. Use Distance option of Measure menu to measure the distance.
4. Use Angle option to find desired angles.

Figure 12 shows dimensions calculation by the 3-matic tool. Here blood vessel virtual models sections can be cut at desired places like aneurysm ends, bifurcations, etc. to find the desired parameters such as Aspect Ratio (AR), Dome to Neck Ratio, Size Ratio (SR), and Angle of Asymmetry (β).

Calculate the Length and diameter from the Virtual model of Aortic Aneurysm of INTAGE Realia CT database. Initially, draw a straight line using a line tool and later its value is annotated using the distance tool to measure the dimensions of aneurysm.

Ratio of the Perpendicular height to neck diameter is known as Aspect ratio. Dome diameter and Neck diameter ratio is known as Dome to neck ratio. Maximum perpendicular height and the Average diameter ratio is called as Size ratio. Inflow angle is the angle between flow line height and perpendicular height.

The below Figure 13 shows the Virtual model of the colon of TCIA image. Nowadays Colorectal cancer is the third cause of mortality throughout the globe [55]. The early detection of polyps is necessary in colonoscopy images. According versatile geometry Polyps are sessile, pedunculated, and flat [56].

Hence there is a necessity to reconstruct the 3D model of Colon CT images. Using ITK Snap's Color Auto segmentation 3D model can be generated using 3 steps Viz. Pre-Segmentation, Contour Initialization, and Curve evolution. In First choose desired abnormality part from any of the Coronal, Sagittal, and Axial images. Then do Pre-Segmentation with lower and upper thresholds. Initialize the contour by placing and adding number of bubbles in to image.

Select X, Y, Z Coordinates and radius for bubble by trial and error method. Configure different parameters for Curve Evolution via Differential Equation and number of iterations where to cease segmentation. Hence delineation will be completed and segmented part will be extracted. Manual Segmentation can also be carried out using Cursor Inspector, Polygon Inspector and Morphological Interpolation option features. TCIA colon and NIfTI (file format) | Radiology case studies are tested.

Figure 12. 3-matic tool based dimensions calculations.

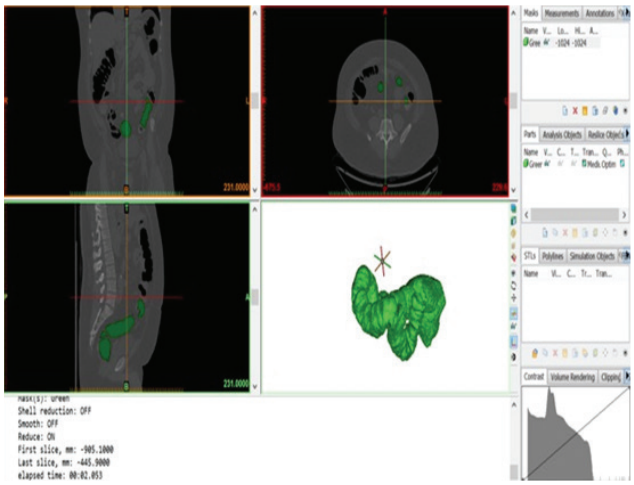

Figure 13. MIMIC tool developed virtual model of the colon.

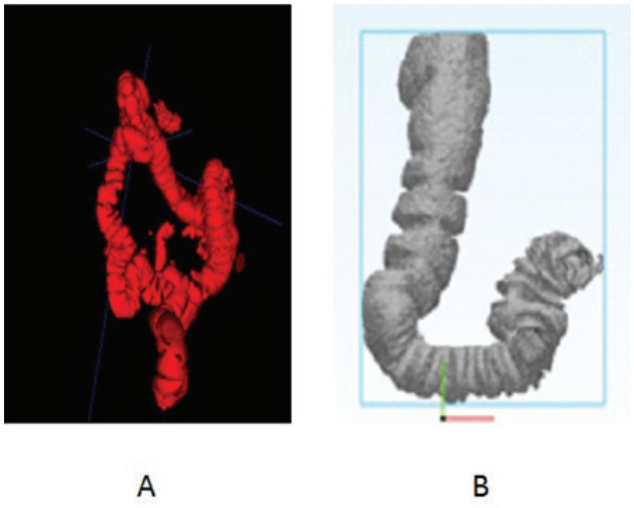

Figure 14. Colon part extraction using ITK Snap & 3 matic tool.

Figure 15. 3D printed blood vessel with a tiny aneurysm.

Above Figure 13 is a generated using image slice from Three Views (Coronal, Sagittal, and Axial) of CT COLON database from TCIA - The Cancer Imaging Archive.

Left side figure (A) shows Extracted Colon using ITK snap tool whereas Right side Figure (B) MIMIC tool's Extracted Colon using live wire segmentation

In Figure 14 the colon extraction results using ITK Snap (using Auto segmentation option) and MIMIC tool (using Dynamic Region Growing method) are shown on left & right figures respectively.

Additive manufacturing (3-D Printing) provides this prototype: 3D Printing is a process for making a physical object from a three-dimensional digital model, typically by laying down many successive thin layers of a material. It brings a digital object (its CAD representation) into its physical form by adding layer by layer of materials.

The above Figure 15 shows 3D Prototype of a Blood vessel with tiny Aneurysm.

First Vessel STL file is created from CT 3 view Image database of Intage Realia. STL file stores information about 3D models. This format describes only the surface geometry of a three-dimensional object without any representation of colour, texture or other common model attributes. These files are usually generated by a computer-aided design (CAD) program, as an end product of the 3D modeling process. Dynamic region growing segmentation method is used to get the Precise reconstruction model. Later generated the G-Code via Cura Ultimake slicer then given it to Hydra Fluid Deposition modeling (FDM) 3D printer (For Printing PLA (Polylactic acid) Black Spool is used) [54].

FDM is a 3D printing process that uses a continuous filament of a thermoplastic material. Filament is fed from a large coil through a moving, heated printer extruder head. Molten thermoplastic is forced out of the print head's nozzle and is deposited on the growing work. The print head is moved under computer control to define the printed shape. Usually the head moves in two dimensions to deposit one horizontal plane, or layer, at a time; the work or the print head is then moved vertically by a small amount to begin a new layer.

The speed of the extruder head may also be controlled to stop and start deposition and form an interrupted plane without stringing or dribbling between sections.PLA is Highly durable a biodegradable and bioactive thermoplastic aliphatic polyester derived from renewable resources, such as corn starch (in the United States and Canada), cassava roots, chips or starch (mostly in Asia), or sugarcane (in the rest of the world). Print temperature: 130-180 °C and Soluble in benzene, tetrahydrofuran, and dioxane.

CONCLUSION

Various abnormalities, their imaging science (modality types & sensitivity), note on associated segmentation (delineation) methods, modeling, database resources, typical case studies, tools of usage, various treatment procedures in different aspects of treatment (like diagnosis, prognosis, surgery, postoperative non recurrence remedies, rehabilitation etc.) and results of work carried out by authors using various tools are discussed in this manuscript. List of available books in the introduction section provides an in-depth insight into the recent trends in the specific abnormality diagnosis & treatment research. Briefly, this paper offers how to proceed to work on biomedical imaging based treatment, health care systems, segmentation algorithms, modeling of abnormal structures, Medical 3D printing, Reality opportunities cum challenges, etc. for beginners of medical, non-medical imaging science scholars and other concerned medical community. Results provide deep insight to beginners how they can use a particular tool for analysis of an abnormality to carry out a specific task. Viz. MATLAB is useful for delineation, ANSYS useful for flow analysis and MIMIC helpful for modeling of various abnormalities, Finally, How MIMIC, Cura Ultimake Slicer, Hydra 3D FDM printer with black PLA material used for developing Virtual prototype of the blood Vessel are also presented.

FUTURE SCOPE

Developing an AAA prototype simulator using the developed 3D printed replica of AAA to carry out the further noninvasive research to support surgical simulation. To develop a cost effective frame work for rapid prototyping of AAA and Stents/Grafts.

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AUTHORSHIP CONTRIBUTIONS

Authors equally contributed to this work.

DATA AVAILABILITY STATEMENT

The authors confirm that the data that supports the findings of this study are available within the article. Raw data that support the finding of this study are available from the corresponding author, upon reasonable request.

CONFLICT OF INTEREST

The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

ETHICS

There are no ethical issues with the publication of this manuscript.

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