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ADVANCED DIAGNOSTIC TECHNOLOGY FOR BRAIN

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ABSTRACT

The quick development of diagnostic technology has fundamentally altered the field of medicine by allowing accurate and thorough evaluation of numerous physiological and pathological problems. This review article examines the crucial contribution that cutting edge diagnostic tools have made to the field of medicine, including Single photon emission computed tomography (SPECT), Positron emission tomography (PET), Magnetic resonance spectroscopy (MRS), Diffusion-weighted imaging (DWI), and Electroencephalography (EEG).We dig into the fundamentals and uses of each technology, emphasizing how they help to reveal the chemical, structural, and functional details of the human body and brain. Early disease detection and individualized treatment plan are now possible because to the development of powerful techniques like SPECT and PET for imaging metabolic processes and molecular interactions. We now have a better understanding of a variety of illness thanks to MRS's non-invasive insights into tissue composition and metabolic processes. In particular in neurological circumstances, DWI has played a significant role in measuring microstructural integrity and has also provided novel insights on tissue damage and recovery. EEG, on the other hand, has shaped our understanding of neural dynamics and neurological illness by providing vital real time data on brain activity and connectivity.

KEYWORDS: Brain, Diagnosis, Electroencephalography, Imaging, Positron Emission Tomography.

1. INTRODUCTION

Numerous neurological dysfunctions and multiple symptom clusters are linked to brain illnesses. For instance, research has revealed various neural dysfunctions, such as aberrant sub thalamic nucleus oscillations and alterations in cortical and cerebellar structures, even though Parkinson's disease (PD) is linked to decreased dopamine levels in the brain.[1] Additionally, a variety of motor symptoms, such as tremor, bradykinesia, akinesia, and medication-induced dyskinesia, are linked to Parkinson's disease (PD). These signs are bought on by a distinct kind of brain disorders. This is also true with Alzheimer's disease (AD), which has a variety of neurological abnormalities, such as damage to the neocortex and hippocampal regions, in addition to other symptoms clusters such as memory loss, apraxia, language impairment, and executive dysfunction.[2] Likewise, diverse neurological foundations underlie a variety of psychopathological symptoms that characterize mental diseases. For instance, among other behavioural symptoms, major depressive disorder (MDD) is linked to mood, somatic, and cognitive alterations. The World Health Organisation better known as WHO, divides brain tumors into benign and malignant categories, and then further divides each of these into four grades based on the rate of histopathological progression.[3] The characteristics of the patient population affect the incidence of tumour subtypes. Overall, almost frequent adult brain tumours.[4]

Many technological developments over the last ten years have made it possible to analyze the neurological system more accurately. The capacity to recognize diseases of the central nervous system has improved thanks to advancements in magnetic resonance imaging (MRI) technology, particularly functional MRI (fMRI) and high-resolution imaging. In order to assist in the diagnosis of conditions like neurodegenerative disorders, new wearable technologies and digital sensors gather real-time diagnostic data.[5] Furthermore, a growing number of clinical diagnostics, including those involving difficult neurological diagnoses, are employing whole-exome sequencing.[6] The best treatment plan must start with the accurate diagnosis, and neuroimaging is essential for diagnosis, prognostications, therapy planning, and management. Cross sectional images of human body using CT or MRI technology is the first stage in the development of brain tumour.[7-9] Nuclear medicine modalities like PET and CT with SPECT are extremely helpful for neuroimaging of brain tumours.

2. ELECTROENCEPHALOGRAPHY (EEG)

An electronic device that measures the impulses that are produced by the brain is regarded as an

electroencephalography sensor. The electrical signals produced repeatedly by dense cluster of neurons active close to the surface of the brain often recorded using EEG sensors. They function by increasing the electrical current, filtering it if essential and measuring the minute differences in electric current produced between the sensor electrode and the skin.[10] EEG devices can be classified in the communication and multi-sensor technology and it is further explained in the following:

2.1 EEG Devices Technology

2.1.1 Communications, both wired and wired less

Both of them use a cable, wireless, or Bluetooth connectivity connections to transfer informations to a computer, accordingly. While wireless connections allow for greater mobility, wired EEG connections are less mobile and tend to transfer less data in a given amount of time. Whatever the kind of connection, shifting cables and electrodes may hinder the connectivity between the electrodes and the scalp, which can lead to abnormalities in the EEG output.

2.1.2 Wet EEG Devices

The following section will examine various wet EEG equipment types:

(a) Dry

(b) Saline solution

(c) Gel based

Fig. 1: Types of EEG.

2.1.2.1 Soft-gel based: By putting conductive gel into each electrode's pocket, this connection enableelectrodes to make connection with the scalp. After the experiment is complete, it is crucial to evaporate, this is done frequently.

2.1.2.2 Saline solutions: For low impedance electric contact between the skin the sensor electrode in some EEG headsets, conductive gel is necessary. The above technique connects on EEG headsets by adding saline to each electrode

2.1.2.3 Dry: Dry EEG eliminates the need for salt or gel to fix the electrodes to the scalp, making it easier to collect EEG data without the assistance of an operator.[11,12] It also takes less time to set upthan wet ear buds.[11,12]

2.1. Multi-sensor EEG devices

Some EEG devices are made to record data on the brains as well as physiological variables likeblood pressure and muscular activity. For recording physiological signals like electrocardiograms (ECG), electrooculogram (EOG), photoplethysmograms (PPG), and electromyograms (EMG) these devices feature one or more channels. For the purpose of recording information in head and body motion, certain EEG equipment using accelerometers and other types of motion sensors.

3. MAGNETIC RESONANCE SPECTROSCOPY

It is a useful, non-invasive approach that does not require the injection of intravenous contrastand classifies lesions according to the component of their metabolic makeup (31P) MRS examines phosphorous-containing metabolites like phosphocreatine inorganic phosphate. Using the proton magnetic resonance spectroscopy (1H-MRS), it is possible to quantify the amount of tissue metabolites required for cancer growth.[15] The compound that MRS can identify often have low molecular weight, move around between organs and compartments, and exist in relatively high quantities that is more than few (mM). Some metabolites participate in the metabolic process that gives rise to tumours, such as the role of N-acetylaspartate (NAA) utilizes in the pathways of lipogenesis[16], choline (cho) in the Kennely pathways, which are involved in the production of phospholipid for cell membranes.[17], which makes magnetic resonance spectroscopy sensitive to the tumour atmosphere.[18] The two techniques acquire 1H-MRS data are single voxel magnetic resonance spectroscopy that produce signals from the lower areas of around a small cubic cm, and MRSI, that provides a better resolution than single voxel magnetic resonance spectroscopy.[19] Since none of the above method gives a sufficient clinical clarity and brain coverage with appropriate time, magnetic resonance spectroscopy is the region based acquisition and analysisstrategy.

3.1. Method

Either 1.5T or 3T can be utilized for clinical MRS procedures. Greater signal-to-noise ratios (SNR) and enhanced spectral resolution are made possible by higher field strengths. Proton MRS can employ either a single voxel approach or many voxels. Strong magnetic field homogeneity is quickly and easily provided by the single voxel approach inside the volume ofinterest. While it is possible to analyze entire big lesions and adjacent tissues or several lesions using the multi-voxel approach, these

task requires longer scans duration and are technically difficult.[20] Both the qualitative and quantitative MRS evaluation are possible. The presence or absence of specified metabolite peak is revealed by the qualitative analysis, it may be hampered false positive result. To avoid locations with bony features, necrotic or hemorrhagic foci ROI placement is essential (which would result in an underestimating of the choline peak), calcifications (which would result in an increase in field inhomogeneity), or muscle (which would result in an overestimation of the choline peak).

For tumour showing the voxel after five min. is positioned at the regions of delayed enhancement. The enhanced region of the tumour is addressed in ROI positioning.[21] The multiple voxel techniques have the potential to overcome the disadvantages of single voxel spectroscopy due to changes in voxel repositioning during post processing and grids that provide multiple voxels over a wide area of interest. 3T 16X16 spectral grating can be completed in about five min. using TR 1500ms 1.5cm^3 voxel resolution, average single-stage coding step, elliptical k-space sampling, and multi voxel spectral acquisition.[22-23] The accuracy of MRS for separating neoplastic from non-neoplastic tissue were reported to a high (92%) and it was enhanced when combined with the other advanced magnetic resonance imaging techniques like PWI (96%).[24] The most common use of MRS has been to distinguish between tumour progression and treatment-related MRI alterations (i.e., pseudo progression) when there is a known malignant brain tumour.[25]

4. DIFFUSION-WEIGHTED IMAGING

The DWI technique evaluates tissue circularity & cell membranes integrity by measurement ofthe diffusivity of the water molecules (Brownian motion).[26-29] In an inversely proportionate way, the amount of water molecule mobility in cellular compartments (extracellular, intracellular, trans cellular and intravascular) determines the DWI signal.[30] Water molecules cannot move through tissues with a high cell density, unbroken cell membranes, or tiny extracellular spaces. Since extremely vascularize lesions might have a considerable intravascular water molecule mobility, it is crucial to include this contribution to the DWI signal.[14,15] DWI interactions include spin echo, steady-state free precession, and echo-planner imaging (EPI). The single or multishot EPI, which has a quicker acquisition time and is less sensitive to movie artefact, is the most popular. By placing a region of interest (ROI), the ADC can be examined qualitatively or quantitatively. A parametric map is used to express the ADC. It is not required to use a specific number or size of ROI, and the evaluation of the maximum, minimum, and mean ADC is not standardized.[15]

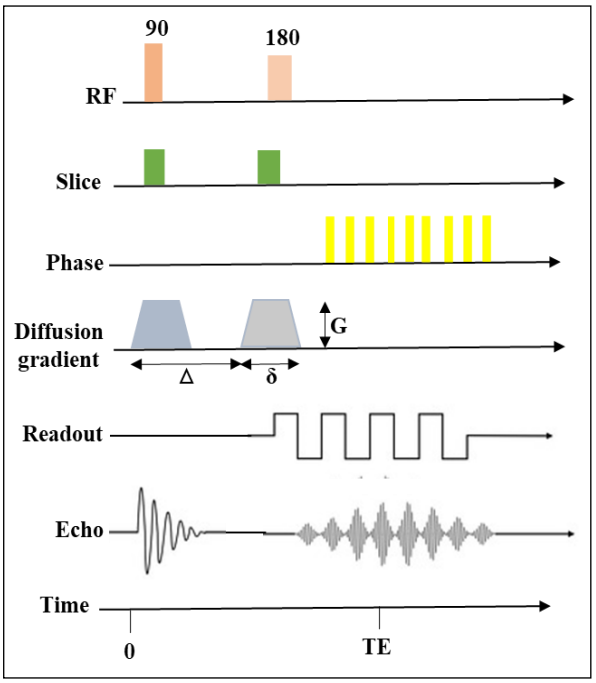

Fig. 2: Diffusion Weighted Image.

Consider Given that ADC values rise in vascularized tumours and cause an overlap in the values of ADC between benign and malignant tumours, it is crucial to consider tissue perfusionand the intravascular component of water. Utilizing perfusion-insensitive ADC values help prevent this.[31,33] The inherent low signal- to-noise ratio, low spatial resolution, artefacts from susceptibility (artefacts in correspondence with the blood products, tissues, or air) are the fundamental limitations of DWI.[32,33]

5. SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY

SPECT is a nuclear imaging method that quantifies flow of or labels specific brain chemicals using a radioactive tracer (radiopharmaceutical). The camera sensitive to photon emissions detects the single photon that are used to trace the radioactive tracers in SPECT EMIT. SPECT can be used to measure cerebral blood (as an indirect marker of neuronal activity) and cellular components of the nervous system, such as neurotransmitter receptor, neurotransmitter reuptake transporter, and other animals and humans with corresponding animal protein and human diagnosis.[34] Detecting, identifying & measuring gamma rays emitted from radiolabeled substances is the basic idea behind SPECT imaging. When the unsuitable isotope gets decayed and releases a photons, gamma ray emissions are created. An intravenous injection of the radiolabeled substances is given to an animal or persons, where it circulates to the brain. The gamma camerasystem is then used to find the photons that are radiolabeled chemicals has released. Compounds called as radiopharmaceuticals perfusion of SPECT, which helps to quantify the blood flow, pass the blood-barrier before dispersing inside the extracellular space proportionately to the flow of blood to an area. In order to successfully

traverse the blood-brainbarrier, a SPECT perfusion tracer needs to possess the right lipophilicity qualities, but it also needs to lack any specific binding to brain constituents.[35]

5.1. Synthesis of Radiopharmaceuticals

A radionuclide is the first step in the manufacture of SPECT radiopharmaceuticals. Technetium(Tc) which can be represented as (^{99m}Tc) and iodine (I) as (^{123}I) are the two radio nuclides that is more frequently utilized in SPECT imaging. The main method for producing SPECT radionuclides is to bombard atoms with charged particles. The radionuclide is then chemically coupled to an interesting pharmacological molecule, such as reuptake transporter binding ligand or neurotransmitter receptor, to produce the radiopharmaceutical. Due to the relative weight of ^{123}I, ^{99m}Tc, and other single photon emitting radionuclides, it is challenging to bind them to tiny, physiologically active molecules like glucose while maintaining their biological activity. Since big molecules won't cross the blood brain barrier, There are limited SPECT radiopharmaceuticals for rain imaging for the molecules having a weights of few hundreds.[36]

5.2. Construction of image

The creation of images required for the SPECT is the employment of the gamma camera, a unique detecting system that combines hardware and software techniques to produce images that display the tracer's location and intensity. Data were interpreted using mathematical models in single-photon emission computed tomography-driven molecular imaging and single- photon emission computed tomography perfusion imaging. This model takes into account the characteristics of the viewer, such as the speed of equilibrium in the brain and the absence of specific binding.[37]

5.3. Resolution

A hardware and software that makes up the gamma camera system play a big role in SPECT imaging resolution. Modern SPECT scanners have resolution of about 1 cm in routine clinical use, although specialized small animal studies using updated gear and software for image generation, SPECT scans can produce images with resolutions less than 1mm.[38]

5.4. Time course and availability

The half-life of two commonly used SPECT radionuclides, ^{123}I compounds and ^{99m}Tc compounds, is approximately 13 hours for ^{123}I compounds and approximately six hours for ^{99m}Tc compounds. Due to its stability, the SPECT ligand can be applied several hours before the screening procedure.[35]

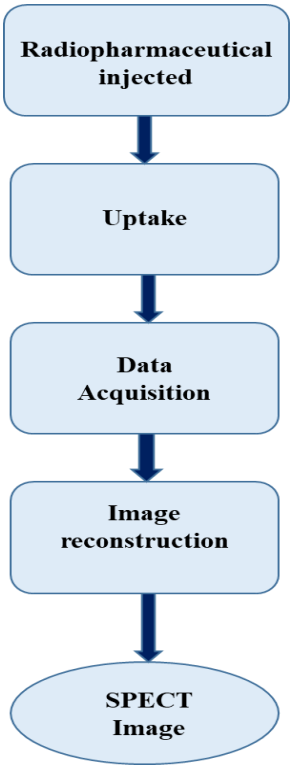

Fig. 3: Schematic diagram of workflow of a SPECT imaging.

6. Positron Emission Tomography

It is a nuclear medicine imaging which is non-invasive procedure that uses biochemical analysis to produce three dimensional images which shows the functional activity of a particular tissue. In clinical practice, it has been used to plan the treatments, diagnosis patients, and predict outcomes for a variety of disorders. One of its main uses has been to help understand complex neurological conditions like Dementias, Multiple sclerosis, Huntington's disease, and Parkinson's disease. The short lived radioactive tracers is injected into a person's circulation during positron emission tomography, often intravenously. This technique is based on physical principles. The procedure starts with the creation of hydrogen ions that are negatively charged in a machine known as a cyclotron. Particles accelerated in the vacuum chamber of specially designed electrodes create a static andelectric field.[39] The ion source emits a charged particle, often a proton or deuteron, which isthen propelled along a circular route by the electric field. The stable forms of elements like oxygen, nitrogen, and carbon become radioactive with them.

This radioactive state, known as a radioisotopes, primarily unstable because it has an excess of protons. The synthesized molecule of interest (tracer) is subsequently linked to radioisotopes using computer software in bio synthesizer component known as a hot cell. An isotope that emits positron, like carbon- 11 whose half-life is 20 min., nitrogen-13, oxygen-15, or fluorine-18 with half-life of 20 minute, 15 minute, 10 minute, 110 minutes respectively is used to mark the

target tracer. A computer system stores the digital radiation emission profiles that were obtained by PET detector equipment. Through the use of reconstruction procedure known as "filtered back projection". Which is a kin to computed tomography (CT), the computer system creates 3D images from this data.[40]

The scanning time of attenuations greatly decreased when PET scanners are used in conjunction with integrated CT technology (PET/CT). Positron emission tomography scannersmake this process possible by using a crystal detection technology that significantly improves the resolution of the PET camera. PET scanners feature great sensitivity, good spatial and temporal resolution, and a more sensitive 3D mode that can be used.[41] The advantage of 3 dimensional acquisition is that scans can may be made with around four times less radiation and still be as good as scan in two dimensional mode. The 3 dimensional mode enhances the possibility to undertake voxel based analysis instead of only region based ones. Presently, a range of design for 3 dimensional PET scanners are available with the improved sensitivity, signal-to-noise ratios, and spatial resolutions.[42-44]

A PET scan is not intended to show minute details of the anatomy of an organ, in contrast to other imaging modalities like magnetic resonance imaging. Instead, it shows images with varying levels of color intensity to convey information about the chemicals activity occurring within certain organs and tissues. Tran's axial planes of the subjects in the scanner are parallel to the line spanning the anterior-posterior commissure line, and they are laying supine. They are made comfy and their head position is maintained with the help of specially constructed holders of foam. Throughout the scans, position of head with regard to the laser light from the cameras is monitored, and if movement is noticed, the head is moved. When the subject is at rest, after a drug challenge hasbeen administered[45,46], or when the subject is performing specific tasks, PET scans can be conducted. Despite the non-invasive nature of positron emission tomography scanning, radiation exposure poses some safety risks.

However, the overall radiation exposure is quite low, frequently 7 mSv or less. Compare this to the 2.2 mSv average annual background radiation in the UK, the 0.02 mSv dosage from a chest X-ray, the 8mSv dose from a chest CT scan, and the 2 to 6 mSv dose that aircrew experience each year. There are other limitations to consider as well. Currently, widespread use of PET is limited by the high operating and maintenance costs of cyclotrons, the need to generate short wavelength radiation for PET scans, and the need for specialized electrical equipment to produce electrical equipment.[47-49] As an example, the simplified reference of tissue compartmental model (SRTM)[50] is frequently used, which employs cerebellum as the reference tissue for radiotracers like 11C raclopride.

The process of frame-by-frame realignment, also known as movement correction, is frequently used in positron emission tomography imaging analysis.[49,50] The term "specific binding "refers to the association of a radio ligand with a target as opposed to a radio ligand that is free of solution or unspecifically coupled with the other macromolecules elements. The equilibrium concentrations of a certain binding is measured byBP as a ratio to another reference concentration. Numerous techniques exist for stimulatingthe signal using reference concentration, which can be obtained from either arterial blood or a reference tissue free specific radioligand's binding.[48]

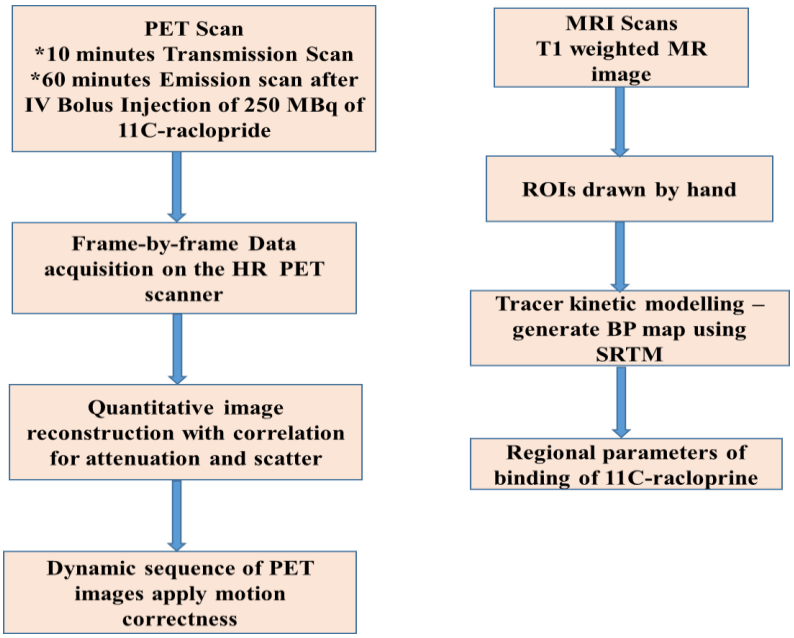

Fig. 4: An overview of the 11C-Raclopride PET study's analysis and scanningtechniques using a schematic flow chart.

7. CONCLUSION

The introduction of cutting-edge technologies like SPECT, PET, MRS, DWI, and EEG has significantly changed the landscape of the diagnostic medicine. Healthcare workers can now better understand the intricate workings of the human body and brain thanks to cutting-edge imaging and diagnostic methods that go beyond conventional limitations. These innovations have ushered in a new era of precision medicine thanks to their amazing capacities to offer precise structural, functional, and molecular insights. By showing metabolic activity and receptor interactions, SPECT and PET have transformed our understanding of cellular and molecular processes, facilitating the early detection and ongoing monitoring of a variety of disorders. A non-invasive analysis of tissue composition and metabolic pathways is now possible because to MRS, which has opened an unrivalled window into biochemical processes. In especially when it comes to neurological illnesses. DWI has become a cornerstone of neuroimaging, providing priceless insights into the microstructural integrity of brain tissues. In addition, EEG has continued to be crucial technique for researching brain connection and activity because it provides a real-time window into neural dynamics. A more thorough understanding of complex conditions, such as malignancies, psychiatric disorders, and neurodegenerative diseases, has been achieved through the integration of various technologies, opening the door to specialized therapeutic strategies that focus on the underlying pathophysiology.

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