Advances in Biomedical Imaging and Image Fusion

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ABSTRACT
Biomedical imaging is a series of procedures which create images of the human body, or parts of the body, to help screen for possible illness or injury, diagnose the likely cause of symptoms and monitor health conditions or the effects of treatment. The objective of the paper is to provide an overview about various bio medical imaging techniques used in detection and diagnosis of Cancer. Each of these imaging techniques provides information about the anatomy, chemical or physiologic phenomena of the human body which are studied independently by doctors to identify Cancer. The biomedical imaging systems, applications, benefits, drawbacks and research challenges are discussed. Image Fusion and its role in Bio medical imaging is also discussed. Image Fusion is the process of fusing two or more bio medical images which contain complementary information into a single composite image. These enrich image quality and avoid redundancy thereby increase the clinical applicability of medical images for cancer detection, prognosis and treatment planning of Cancer.

Keywords
CT, MRI, PET, SPECT, Ultrasound imaging, Biomedical Image Fusion

1. INTRODUCTION
Around 1.7 crore people suffer from cancer worldwide. India has approximately 20-25 lakhs cancer cases any given time and nearly half of them die every year. Around 7 lakh new cancer cases are diagnosed every year in India. The number of deaths per year is projected to shoot up to 1.2 million by 2035 [1]. The most common, nearly half of all are cancers of the lung and oral cavity in men, and of the breast and cervix in women. The rates of occurrences of breast and cervical cancers are 25.8 and 22. Almost three of five cancer deaths in India are associated with tobacco or infectious diseases. Tobacco use alone accounts for about 40 per cent of all cancers in India. Around 95 per cent of the medical colleges in India do not have comprehensive cancer care services, comprising Surgical, Medical and Radiation Oncology departments, in the same campus. Currently there are around 2,000 medical and radiation oncologists in India – one per 5000 newly diagnosed cancer patients – and in almost all remote or rural areas even the most basic cancer treatment facilities are non-existent. As a result, urban cancer centres are overcrowded and under-resourced, leading to long waiting times, delayed diagnoses, and treatment that comes too late for many patients.

Cancer is an abnormal growth of cells. In spite of space constraint, Cancer cells rapidly replicate and continue to utilize the nutrients shared by other cells. In addition to spreading in many areas of the body, Cancer cells do not function normally and look dissimilar from the normal cells. Oncology is the study of cancer. The tumors are classified into malignant and benign. The malignant tumor reproduces at a fast rate and can cause harm to the body, including death. Benign tumors grows slowly and do not spread to other parts of the body. The malignant tumors may be locally invasive or metastatic. The locally invasive tumor can attack the tissues nearby it, whereas, the metastatic tumor can send cells into other tissues in the body which are distant from the original tumor or primary tumor. The blood (circulatory system) or lymphatic system transports the cancerous cells to other parts of the body to form secondary tumors. Studies indicate Liver is the first organ to get affected earliest with secondary tumors.

Based on their origin, cancer can be classified broadly into 5 categories. Carcinomas are cancerous cells that have an effect on the tissues, organs and glands which account for 80%-90% of all cancers. The cancers found in cartilage, fat, muscle, tendons and bones are called Sarcoma. Examples of Sarcoma are osteosarcoma (bone) and chondrosarcoma (cartilage). Lymphoma is found in the glands of the lymphatic system. It can affect the organs like brain and breast. Leukemia is cancer of bone marrow. Myeloma is found in the plasma cells of bone marrow. In some cases, it forms a single tumor called Plasmacytoma and collects in one bone.

Biomedical Imaging has seen a lot of technological developments in the last few decades [2]. The most vital contributor in early detection of cancer lies with imaging along with the patient's history and physical examination. A single imaging technique cannot achieve cancer detection and may provide ambiguity, resulting in false positives which call for reiteration of imaging techniques. A biomedical imaging technique is competent, if it can verify or eliminate the presence of cancer. Furthermore it is used to examine the growth, plan and evaluate the efficacy of treatment. Biomedical Imaging techniques like Computed Tomography (CT), Magnetic resonance imaging (MRI), Positron-Emission–Tomography (PET), Single-Photon Emission –Tomography (SPECT), and Ultrasound (US) are crucial in diagnosis, treatment and prognosis of cancer.

2. BIOMEDICAL IMAGING TECHNIQUES
Cancer is been dignosed and treated followed by a number biomedical imaging techniques. This section discusses an overview of biomedical imaging techniques.

2.1. Computed Tomography (CT)
Computed Tomography (CT) produces a cross-section ("slices") of anatomy of the human body. Radiographic beams are made incident on the human body. The reflected radio beams create a detailed computerized picture taken with a specialized X-ray machine. CT is more precise than a standard X-ray, and provides a clearer image. Figure 1 shows a CT scan of transverse view of the brain.

The CT system consists of a power-driven table which moves the patient through a circular opening. An X-ray source and a detector assembly within the system rotate around the patient. A single rotation typically takes a second or less. A fan-type X-ray passes through the patient's body. Detectors are placed opposite the X-ray source absorb the energy and creates an image [3, 4]. Many "snapshots" (at many angles through the patient) are collected during one complete rotation. For each rotation of the X-ray source and detector assembly, the image data are sent to a computer to rebuild all of the individual "snapshots" into one or multiple cross-sectional images (slices) of the internal organs and tissues [5]. Figure 2 shows the CT images for multiple slices of the brain. The minimum and maximum number of CT slices range from 1 to 64 and 320 [5, 6]. CT is one of the most commonly used imaging modality for diagnosis of pulmonary diseases, coronary artery calcification, and metopic craniosynostosis diagnosis of pediatric CT scans of head , Change assessment for spine imaging [7-10]. CT is also used in radiation therapy and planning prostate cancer radiotherapy [7, 11]. The latest research trends in CT are in areas of registration, segmentation of veins, tumors in brain, lesion in liver, aorta, prostrate, reconstruction of CT images, generation of 3D CT images, superposition of cone-based CT images and generation of synthetic 4D CT images for image guided surgery [4,12-22].

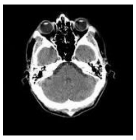

Fig. 1 Transverse views - CT scan of Brain

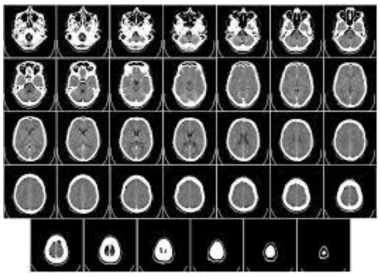

Fig.2 Multiple slices of CT scan of Brain

CT accurately outlines the bone, some soft tissue and blood vessels inside body; it is geometrically accurate, with short scan times and high resolution. CT fails to characterize tissue, transverse slices and there is a restriction on intensity of X-rays for short scan times and lastly the radiation can be harmful and not recommended for patients diagnosed with cancer or pregnant women [12, 23].

2.2 Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging (MRI) is a noninvasive diagnostic test that takes detailed images of the soft tissues of the body. MRI employs magnetic fields and radio waves to create the images. The human body is made up of 80% water which contains millions of hydrogen atoms which are magnetic. The magnetic field and radio waves disrupt the orientation and polarity of the hydrogen atoms [24-26]. The time taken by the hydrogen atoms to return to their original alignment is measured by a detector. In brief, MRI measures the water content (or fluid characteristics) of different tissues, which is processed by the computer to create a black and white image. Figure 3 indicates a MRI image for a side view of the brain.

MRI provides in depth image indicating the smallest abnormality. The thickness of slice can be of quarter inch size. A contrast dye which has magnetic properties may be injected into the bloodstream to make the image more distinct. MRI imaging cannot detect blood in arteries and this creates black holes on the image. Angiogram MRI is another form of MRI which can be used to view arteries and veins. Contrast dye may also be used here to image the veins and arteries. Figure 5 shows a MRA scan for the head. MRA can detect aneurysms, blockages of the blood vessels, carotid artery disease, and arteriovenous malformations.

Bone marrow, spinal fluid, blood, liver and soft tissues can be effortlessly imaged with MRI. It is one of the primary diagnostic imaging techniques for detection of brain tumors, spinal cord injury, hypertension, multiple sclerosis, the causes of headache, Crohn's diseases, liver diseases, Alzheimer's disease, dementia [27-34]. Figure 6 displays a MRI image of lumbar spine.

MRI is totally safe as it does not involve any radiation. Some people are sensitive to the contrast dye used and may develop an allergic reaction. MRI scans cannot be used for people with cardiac pacemaker or artificial heart valve metal plate, pin, or other metallic implant piercings (particularly body piercing) intrauterine device, such as Copper-7 IUD, insulin or other drug pump aneurysm clips and during pregnancy. Any metallic substance in the body can affect the quality of the images. Some promising research in MRI Imaging is 3D segmentation, multi-spectral segmentation, MRI guided surgery, MRI guided radiation therapy, Compressed Sensing, MRI/PET hybrid systems and content based image retrieval [35- 37].

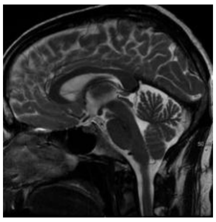

Fig. 3 MRI of the brain

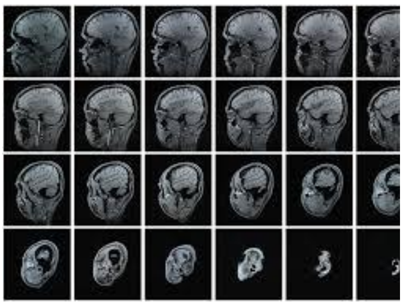

Fig. 4 MRI scans of the human brain.

Fig.5 MRA of the brain arteries

Fig.6 MRI of the lumbar spine

2.3 Positron Emission Tomography (PET)

Cancer is a biological processes and molecular imaging cannot be detected with CT or MRI. PET is used to find the progress of cancer cells. The diagnostic accuracy of PET is 8-43% higher than conventional scans and also affects the treatments planning [38]. A PET scan uses a small amount of radioactive material like FDG (fluorodeoxyglucose) called tracer, which is injected intravenously [39]. The tracer reacts with the cells to produce positrons which cause radiation. With the help of large tunnel shaped scanner, radiation emitted by the positrons is measured and images are generated with the help of a computer. The color variation is seen due to variation in the number of positrons. Figure 7 shows a PET scan of the neck, chest and abdomen region. A PET provides the functional information of organs and tissues. PET scans are very helpful in detection and treatment planning of Epilepsy, Alzheimer's disease, lung and liver cancer and breast cancer and Heart diseases [40-46].

PET imaging is frequently used in both clinical and biological research applications as it can detect cellular changes at a very early stage and the radio tracer used is very safe since it does not involve any kind of radiation [47]. However, PET imaging takes a longer time than CT or MRI because the radio tracer has to travel to all parts of the body and the resolution is less and the images are blurring [48].

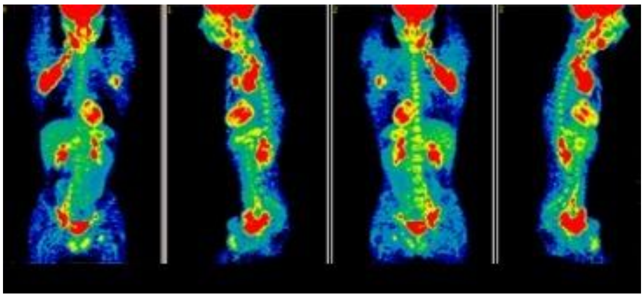

Fig.7 PET scan image

Future work in PET Imaging is generation of high resolution PET images, engineering the next generation PET Detectors, design of hybrid PET scanners, generation of 4D images and design of compact PET scanners [49-54].

2.4 Single Photon Emission Computed Tomography (SPECT)

SPECT uses different radioactive tracers and generates three-dimensional image based on its distribution and detection of single photons acquired from multiple planar images. SPECT integrates CT and PET technologies. SPECT provides both functional and anatomical information. For example, brain injuries have reduced or increased blood flow to some parts, which can be easily detected with SPECT. Figure 8 shows some SPECT images of the brain [55-58].

SPECT used to detect seizures, stress, spondylolysis, ischemic areas, thyroid cancer, Alzheimer's disease, Parkinson's disease, Bone imaging and Epilepsy [59-63].

Moreover, the observation time for SPECT lies between several hours to several days. The radioactive tracer used is rightly registered in space and time which gives good sensitivity with spatial and temporal resolution. Sensitivity of SPECT imaging is limited by the scanner design because for every single photon must be detected, hence this calls for precise and accurate design of the scanner. Furthermore, there is cross-talk due to use of different radio tracers and segmentation is challenging [59]. Some of the research challenges involved in SPECT systems are to reduce acquisition time for dynamic imaging, design of compact SPECT scanners, better sensitivity and temporal resolution and compressive sensing [58-65].

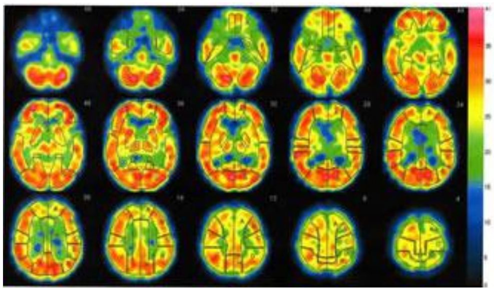

Fig.8 SPECT scan of Brain

2.5 Functional MRI (FMRI)

FMRI is a non-invasive imaging technique specifically used to understand the functionality of the brain. Small variation in blood flow is observed as a task is performed by the brain. FMRI detects the difference in the signal due to blood flow. In precise, FMRI detects the brain in action (e.g., speaking or moving) [66-68]. In particular, it indicates which part of the brain is handling critical functions such as thought, speech, vision, movement and sensation [69].

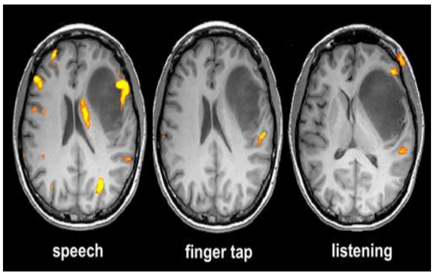

Fig.9 In FMRI, brain areas "light-up" when performing certain tasks

FMRI helps to understand the effect of tumor or stroke on the brain and detection of Alzheimer's disease. Also, helps in planning brain surgery. Figure 9 shows a sample FMRI scan of the brain. The colored areas indicated increased blood intake. Some research advances in FMRI include slice-timing effect and their effect on FMRI, effect of tumor on brain functionality, presurgical planning and extracting semantic data [70-74].

2.6 Ultrasound (US)

An ultrasound machine creates images called sonograms by passing high-frequency in the range of 1-20MHz sound waves through body [75]. Sound waves are reflected back from organs and tissues and transform to images are displayed on a computer [76]. The reflection of sound waves depends on density the tissue, cyst or tumor. Ultrasound can image soft tissues, fluid-filled cysts, tumors which go undetected with X-rays. Ultrasound has some limitations like low sensitivity and limited coverage as cannot pass through bones.

Unlike other blood flow imaging techniques, Color Doppler US is a special non invasive technique that does not use contrast dye, but can produce colored images based unequal blood flow in tumors compared to that in normal tissue. It can indicate the spread of cancer in other parts like liver and pancreas. It is also used to diagnose problems of the liver, gallbladder (such as gallstones), pancreas, thyroid gland, lymph nodes, ovaries, prostrate, kidneys, bladder, breast, abnormal widening of blood vessels (aneurysms), cysts and tumors [77,78].

Ultrasound is a very safe procedure as does not involve any kind of radiation or nuclear elements. It cost much less than CT or MRI. The efficacy of the results depends on expertise of the doctor, which is not the case with CT or MRI. Good images are harder to get in people who are obese. The research challenges in ultrasound imaging is generation of 3-D images to accurately differentiate benign and malignant tumors and ultrafast ultrasound imaging (4D imaging) for moving organs like heart and liver [79-82]. Lastly use of ultrasound images in surgery and planning of cancer and molecular targeting is newest development in Ultrasound research [83, 84].

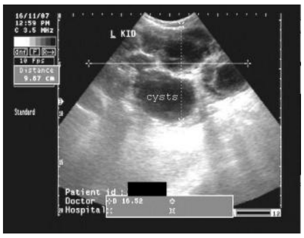

Fig.10 Ultrasound scans showing cysts in kidney

3. MEDICAL IMAGE FUSION

Medical image fusion is the process of combining two or more image modalities into a single image. The resulting image is more informative than the individual images. The quality of the resultant image is improved due to reduced uncertainty and redundancy. There is need of skilled personnel for interpretation of biomedical images. There are chances of incorrect interpretations from the images due to its inherent limitations. Moreover, a number of diagnostic tests may be done to make certain of medical problem. There is always a demand on the time for accurate diagnosis and treatment. This can be achieved by Medical Image fusion. Image Fusion provides comprehensive morphological and functional information which reflects physiological and pathological changes. The images which can be fused may have the same information from different views or images with complementary information can be considered for image fusion. With Image fusion, the clinical applicability for diagnosis and treatment of medical problem can be effortlessly developed. With advances in image processing, medical image fusion is an emerging stream of research in biomedical applications [2, 85].

Image Fusion can be performed on images acquired from different sources, at different times, with different resolutions and with different focus [86-90]. The images can be fused in 3 ways: pixel-level based image fusion, feature-level based image fusion and decision-making. In pixel level fusion, the input images are fused pixel by pixel followed by the information extraction. In feature level fusion, the certain features are extracted from each input image separately and then fused. Decision level fusion combines the results from multiple algorithms to yield a final fused decision [91-95].

Doctors make the most by analyzing the spatial and physiological relationships between the modalities, but this requires expertise. The incapacity to visually understand the different imaging modality separately is the main reason for evolution of biomedical image fusion. The images may contain different information like different color or shape. The same entity may appear different in different images. The fusion of these imaging modalities to one image is the ideal to interpret them well. Presently, Doctors still analyze images discretely. Image Fusion gives an amalgamated image which indicates all the details in one image. By means of biomedical image fusion, all images are stored in digital form and this helps in easy management of patient's database for the hospitals. This helps the doctors in earlier diagnosis and treatment planning. The cost of CT, MRI and ultrasound scanners is high and since they work on different concepts, it is complex to integrate all the three imaging techniques in one machine. Also, not many hospitals have all these facilities at one place. This is a good reason for considering biomedical image fusion, which will be a software technique and not much hardware is involved.

Image fusion will also play a major role in planning radiation therapy and radiosurgery [96]. Despite the many advantages of image fusion is not being used as yet in India. Limiting factors include: (i) cost intensive investment in hardware and software, (ii) time-consuming fusion procedures (10 to 45 min.), (iii) new 3D visualization techniques are needed to communicate the results to the clinicians, (iv) image registration and fusion tools are still evolving and are more computation intensive, and (v) CT, MRI, and PET data sets must be easily be transferred to one common imaging workstation. Finally, the objective and quantitative evaluation of spatial errors is an important task for image fusion is to gain clinical impact [104].

4. APPLICATIONS OF IMAGE FUSION

Medical Image Fusion has been used in detection, diagnosis and treatment planning of brain tumor and breast cancer. The following section discusses the various imaging techniques and to evaluate the performance of different image fusion.

4.1. Brain Tumor

Brain Tumor is a group of abnormal cells found in the brain cells, membranes around the brain, nerves and glands of the brain. Tumors can directly destroy brain cells, producing inflammation, placing pressure on other parts of the brain and increasing the pressure on the skull. CT, MRI, PET and SPECT are some of the commonly used imaging techniques. CT has been the keystone in detection of brain tumor in biomedical imaging. It is the easiest imaging technique with highest resolution but fails to show the essential differences in physiology. MRI is performed to study the damage caused to the soft tissue of the brain and fails to provide information about bones or skull. The fusion of these two imaging techniques will be of great help for radiotherapy planning as planning is done on CT images and localization is better with MRI images. The fused image improves diagnostic accuracy and localization of tumors all available in a single image [105-107].

The metabolic activity of the tumor cells can be studied by PET imaging. However, it fails to provide higher-resolution and anatomic information. For many years, separate procedures were carried for CT and PET scans. An expert would provide his views based on his mental synthesis of the images. There are multitude problems with these imaging techniques such as different positioning of the patient and different procedures. More recently, computers perform the fusion of these images. Nowadays, with the state-of-art scanners, CT-PET scans are performed in one machine and hence it is easier to get the images which are in the same form with minimal misregistration. Early detection of brain tumors is possible on MRI and CT but tumor grading remains a difficult task [98]. FDG- PET can differentiate between high-grade (hyper metabolic) and low-grade (hypometabolic) tumors with high accuracy; however, it does not distinguish between low-grade tumors and some benign lesions. Another multi-modality image fusion technique is PET-MRI, which can be used to define biopsy targets and separate the tumor cells from the affected cells. This also helps to determine the residual tumors and predict recurrence of tumors [103]. In radiation therapy of brain tumor, SPECT is used to differentiate the functional areas and non-functional areas of the brain. SPECT ensures to avoid high dosages of radiotracer element to functional parts of the brain [86].

Tan Haibo, Chen Limin, Guan Yihui and Lin Xiangtong et al compared MRI, PET and PET/CT imaging techniques for 55 patients with suspected brain tumor. The sensitivities of were 87.2%, 76.2% and 92.3% respectively and their specificities were 81.3%, 62.5% and 87.5% respectively for the 3 imaging techniques [99,-101]. Michael A Fisher et al evaluated the diagnostic accuracy of whole body MRI and PET/CT imaging techniques. Sixty-eight patients underwent PET/CT for staging of malignancy. PET/CT revealed 48/64 (75%) cases of cancer. The Detection rates and positive predictive value of MRI alone was 64% and 84% and for PET/CT it was 57% and 93%. Detection rates and PPV for side-by side analysis without and with fused images were 72% and 89% and 74% and 91% respectively [102].

Christian Buchbender, Till A Heusner et al have compared multi imaging modalities like PET/MRI and PET/CT. Cerebral metastases represent the most frequent brain tumor which occur in 20% - 40% of cancer patients. PET alone cannot compensate the shortcomings of CT or MRI. PET could detect only 61% of metastases compared to that were detected by MRI. PET/CT was found weak in terms of maximum sensitivity, specificity and accuracy of 50%, 97% and 76% when MRI was used as a benchmark [103]. Figure 12-14 indicates CT, MRI, CT/ MRI fused, MRI, PET and MRI/PET fused images [104].

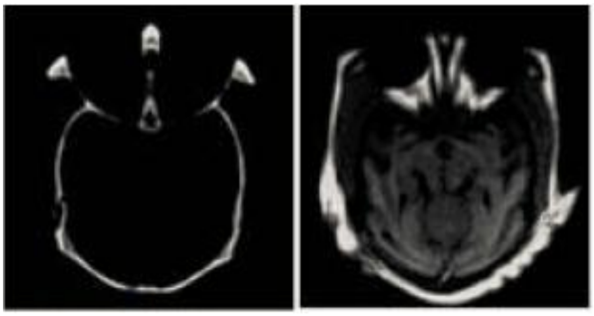

Fig.11 CT and MRI Image

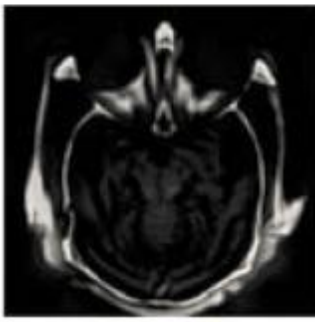

Fig.12 Fused CT & MRI Images

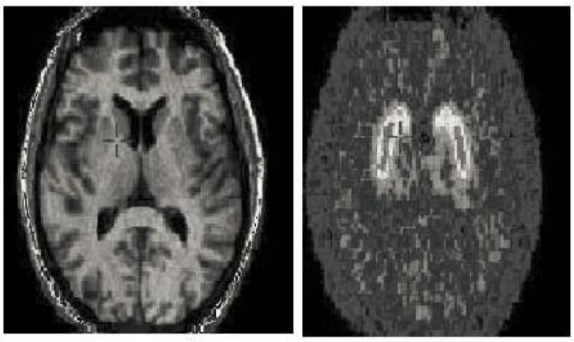

Fig.13 MRI and PET Images

Fig.14 Fused MRI/PET Image

4.2 Breast Cancer

Mammography, Breast Ultrasound, Digital tomosynthesis mammography, Breast Thermography, MRI and PET are some of commonly used imaging techniques for detection of Breast Cancer. Mammography is similar to X-rays, but uses low doses amplitude X-rays. Cancerous cells appear brighter o the mammogram. A modification of mammography which generates 3D view of the breast is called Digital tomosynthesis mammography. In cases, cancers go undetected with Mammography. Breast Ultrasound is used in case dense breast tissue. The drawback with Ultrasound Imaging is that the resolution is less. For grading of breast cancer, PET is widely used imaging technique.

Linda Moy et al evaluated the fusion of MRI and FDG-PET images for detection of breast cancer. They considered 36 women (i.e. of age range of 24 – 65years and mean age 43years) with 90 lesions detected on MRI. They found the following results - Sensitivity of MRI alone ne was 95%, FDG-PET alone was 57% and fusion was 83%. The specificity increased from 57% to 97%. The false-negative rate on FDG-PET alone was 26.7% and after fusion was reduced to 9%. The positive predictive value (PPV) in MRI was 77%, increased to 98% with fusion [105].

PET-CT is another multi modality imaging technique used in detection of Breast Cancer. Isabelle Segaert, Felix Mottaghy et al have evaluated the accuracy of PET-CT against PET and CT individually in conventional staging in breast cancer. Sensitivity of PET/CT was 97.1% against 87.5% in case of PET. The nodal status was increased to 87.5% from 62.5%. Specificity and negative predictive value for nodal status were 100% and 66.6%, respectively. PET/CT is able to visualize most clinical stage IIB and III primary breast cancers. PET/CT is superior to conventional staging for detecting internal mammary chain nodes and metastatic disease, but not for axillary staging. [106]. T A Heusner et al studied the accuracy of PET MRI mammography (MRM) for 58 breast lesions. The sensitivity, specificity, PPV, NPV and accuracy were 93%, 60%, 87%, 75% and 85% for MRM, respectively. For FDG-PET/MRM they were 88%, 73%, 90%, 69% and 92%, respectively. Figure 15-17 indicates MRI, PET and fused MRI/PET images [107,108].

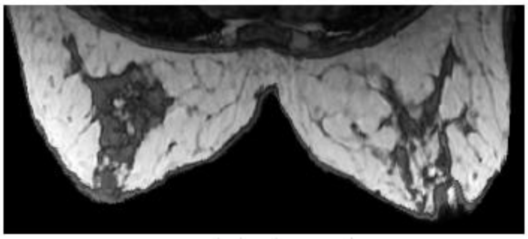

Fig. 15 MRI Image of Breast

Fig. 16 PET image of breast

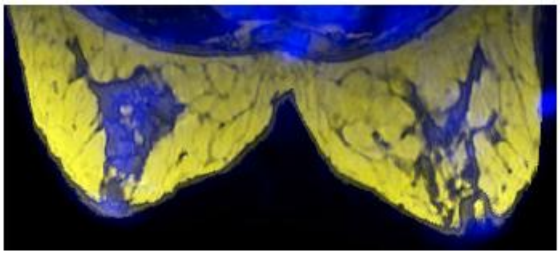

Fig. 17 MRI/PET Fused image with color mixing

5. CONCLUSION

The commonly used biomedical imaging techniques for diagnosis and treatment of Cancer were discussed in detail along with their applications, advantages, disadvantages and research challenges. The need for biomedical image fusion is discussed and the various modalities used for image fusion was discussed. It is seen that results of fused images are better than individual imaging techniques.

6. ACKNOWLEDGEMENT

I would like to acknowledge Dr.Rajesh, Specialist in Radiology, for his valuable inputs in the domain of Biomedical Imaging. I would also like to thank Dr.Jaydatt, Oncology India to provide inputs in diagnosis of Cancer and some real time benefits Image Fusion would provide in Cancer management.

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