HYBRID IMAGING: A NEW FRONTIER IN MEDICINE

Abstract

Medical imaging facilitates the visualization of the internal organs and tissues in the human body. It helps to monitor the anatomy, morphology, and physiology of the body, and diagnose any abnormalities. There are several imaging techniques which are being used for many decades such as ultrasonography, X-ray, positron emission tomography (PET), magnetic resonance imaging (MRI), computed tomography (CT), and single-photon emission computed tomography (SPECT). These imaging techniques offer a wide range of application ranging from diagnosis of cancer, neurological disorders, cardiovascular disorders, bone defects, gastrointestinal disorders, planning of radiation therapy for cancer, monitoring treatment progress and many others. However, these techniques have certain limitations which has led to the fusion of multiple imaging modalities. These hybrid imaging techniques provide better reliability, high resolution images, and detailed information while ensuring safety, specificity, and sensitivity. This chapter provides information on some of the hybrid imaging techniques used in modern medicine.

Keywords: Imaging, Diagnosis, PET, SPECT, MRI, CT.

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I. INTRODUCTION

Hybrid imaging is the amalgamation of two or more imaging techniques to create a multi model imaging technique. Hybrid imaging plays an important role in non-invasive diagnosis and treatment. These techniques employ a modified working principle which compliments one another to produce high resolution and detailed images [1]. Hybrid imaging involves combinations of anatomical imaging (ultrasound with MR or CT imaging), as well as combination between anatomical and molecular imaging (SPECT or PET) modalities. The application of these hybrid modalities is dependent on the availability of instruments, reliability of results, effectiveness of the instruments, trained operators with interpretation expertise. Single imaging modalities, such as ultrasound (US), X-rays, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and photon emission computed tomography (SPECT) are used for different clinical diagnosis and provide information on the location of a lesion, stage of cancer, blood flow, and soft tissues. The use of diverse imaging modalities on the same organs delivers diverse information. Hybrid imaging plays an important role in disease diagnosis as it provides anatomical and functional information about the same organs [2]. The fused image obtained by a hybrid imaging technique should fulfill the following requirements: (a) it should not have registration issues (b) it should preserve the detailed information of the input images, and (c) it should not have dots or scratches or other irregularities [3]. Different studies have suggested the importance of hybrid imaging research.

There are various studies which review hybrid imaging techniques and their classifications [4,5]. Each medical imaging technique has its individual characteristics, information, wavelength, and frequencies [6]. The magnetic field created by the MRIs triggers the protons in the body to align. The high-frequency range of CT and X-ray imaging methods makes them extremely radiative. Gamma rays used in PET and SPECT imaging have lower wavelength and higher frequency. It detects bioactivity in different organs. The X-ray, PET and CT scans are based on ionization, whereas the MRI and US are non-ionization-based [7]. Furthermore, each technique has its own image acquisition process. The X-ray, US, and CT produce images using internal sources whereas the SPECT, PET, and EMG use external sources.

The fusion of images requires combining two or more images obtained by using the same technique or by combination of techniques [8]. This step plays a major role in obtaining the required information from the input images. For example, SPECT and PET produce pseudo-color images with high spatial resolution which gives information about blood flow, soft tissues, and metabolism changes in the body, whereas US, MRI, and CT produce grayscale images with low spatial resolution which provide anatomical information of the body. To obtain hybrid imaging or fused imaging the input images are decomposed to acquire their coefficients utilizing proper fusion rules. These wavelet coefficients are processed by applying appropriate wavelet families and decomposition rules. Selection of low number of scales leads to loss of image information, whereas selection of high number of scales leads to blurriness of the image. Throughout the image fusion procedure, it is important that the fused image should not miss any information which was present in the input images, and there must not be any additional information which was absent in the input images. In a hybrid imaging technique firstly the desired organ of interest must be selected. Secondly, suitable imaging techniques should be selected. Validation of the fusion algorithm is necessary using performance measures. Consequently, an inverse action is employed to achieve the final fused image [9-12].

With further research in hybrid imaging, these technologies may be adapted for a wide spectrum of applications, which may have seemed impossible before the development of such prototype systems. Diagnostic field will have means to diagnose and monitor different complex diseases and will lead ways to provide healthcare solutions.

II. PET-CT

Positron emission tomography (PET) is a non-invasive imaging test that helps to detect abnormalities in the biochemical or metabolic functions inside the body. PET imaging involves injecting a positron emitting radioactive tracer into the veins. The tracer undergoes systemic distribution inside the body and accumulates in areas of the body with elevated levels of biochemical and metabolic activities. Computed tomography is another non-invasive and painless imaging technique that uses advanced X-ray equipment which takes a series of detailed images of bones, soft tissues, organs, and blood vessels inside the body. X-ray scans produce flat 2-D images where the body structures might overlap whereas CT scans revolve around the body and produce dozens of clear images without any overlapping. PET-CT hybrid imaging is the combination of both techniques which provides detailed and clear images of the affected regions. There are varieties of PET-CT scans which use various isotopes for detection, for example F18 FDG PET-CT [13,14], PSMA PET-CT [15,16] Cerianna (18F-FES) [17,18] and NetSpot (Gallium Ga 68 Dotatate) [19,20].

1. Procedure

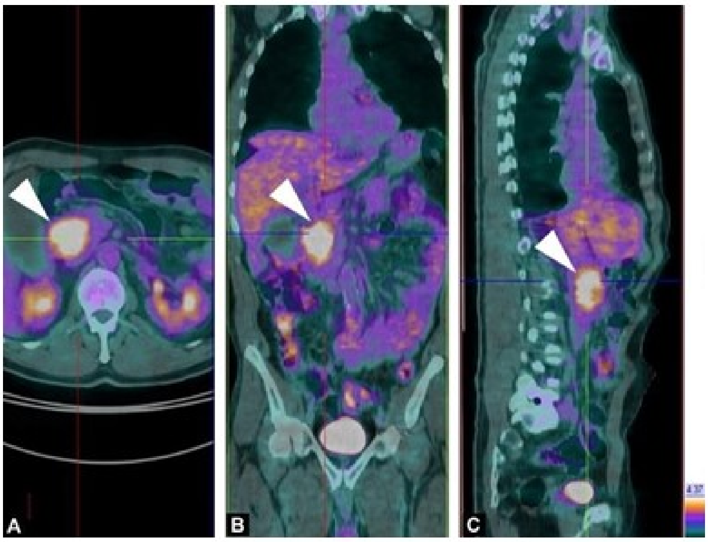

Figure 1: 56-year-old man with locally advanced ductal adenocarcinoma of the pancreatic head at initial staging. Fused 18F- fluorodeoxyglucose (18F-FDG) PET/CT images in the axial (A),coronal (B) and sagittal (C) planes show intense focal tumoral uptake of 18F-FDG (arrowheads).

At the beginning of a PET-CT, a radioactive sugar molecule called tracer is injected into the system. At the time of injection, it is important to ensure that the blood glucose level should be less than 200 mg/dL [21,22]. It takes about 30-60 minutes for the tracer to accumulate in the area of interest. The most commonly used sugar molecule is 18F-fluorodeoxyglucose (FDG). A CT scan is performed first which takes approximately 2 minutes and subsequently a PET scan is performed which takes about 20-30 minutes. Sometimes the PET scan is again followed by a CT scan with intravenous contrast. A PET-CT scan may be followed by other procedures and additional tests depending on the disease or condition. Some studies revealed contrast enhanced FDG PET/CT permits better and more accurate evaluation of distant metastasis [23]. Some other studies also indicated the prospects of using delayed FDG PET/CT images [24]. An example of 18F FDG PET-CT scan displaying advanced ductal adenocarcinoma is shown in Figure 1.

2. **Application of PET-CT Scan:** A PET-CT hybrid scan has a wide array of applications. Some of them are as follows:

- Diagnosis of cancer and detection of cancer relapse – It helps in detecting the initial staging in cancer and a relapse in a patient [25].
- Detection of cancer metastasis - FDG PET/CT can be used to detect distant metastases effectively in most studies, with a specificity range of 55% to 100% and sensitivity range of 85% to 89% [26,27].
- Planning a treatment - 18F-FDG PET/CT is useful in determining the active tumor volume in case radiation therapy or surgery planned [28].
- Selection of biopsy site - 18F-FDG PET/CT helps in choosing a biopsy site [29].
- Monitoring heart condition - PET/CT enables imaging of molecular developments within very small structures, such as the heart valves or the coronary arteries [30].
- Monitoring brain function and abnormalities – It helps detect and monitor brain abnormalities [31].
- Diagnosis of bone disorders – PET-CT scan is an important tool to identify bone infections and prosthetic joint infections [32,33].
- Diagnosis of infections and inflammations – It is also used to detect inflammations, fever, and infections in different parts of the body [34,35].

3. **Advantages of PET-CT**

- PET-CT scans have a high degree of accuracy as both the scans are carried out at the same time without moving the patient, thus reducing any chance of error.
- The combination of the two techniques allows a greater level of precision in diagnosis.
- It helps in detecting the early onset of a condition which allows the doctors to plan a treatment accordingly.
- It helps to identify irregularities at a cellular level.
- It is convenient for the patients as both the scans are carried out simultaneously.

4. **Drawbacks of PET-CT**

- PET-CT scans can be time consuming. The radiotracer requires time to accumulate in the desired area of interest.

- PET-CT scans are risky in diabetes patients as elevated blood glucose levels may negatively impact the results.
- The radiotracer is susceptible to quick decay; hence it becomes imperative to inject the molecule carefully and on schedule.
- The radiotracer injection might cause redness and pain.
- In some rare cases radiotracers might cause allergic reactions.
- It exposes the patient to a low level of radiation.
- PET-CT scans are not commonly used in pregnant women due to risk of radiation exposure in the fetus [36].

III. PET-MRI

PET-MRI is a hybrid technique that converges positron emission topography with magnetic resonance imaging. PET is a functional imaging technique whereas MRI is a soft tissue morphological imaging technique [37]. As discussed earlier, PET imaging requires a tracer which accumulates at the site of interest and helps to create clear images. On the other hand, MRI scans utilize a strong magnetic field to create comprehensive images of the body's internal structures. Shao et al. [38] developed the first hybrid PET-MRI detector in the late 1900s by placing scintillation crystals inside a 1.5T MRI scanner which was coupled to optical fibers resulting in traditional photomultiplier tubes outside the fringe magnetic field. Pichler et al. took a different approach and replaced the photomultiplier tubes with avalanche photodiodes to assemble a PET system which was compatible to MRI [39]. The first hybrid PET-MRI system involving avalanche photodiodes was developed recently for preclinical and clinical purposes [40,41]. PET-MRI offers substantial benefits, like outstanding resolution and contrast, 3D images and lowered ionizing radiation, compared to PET-CT.

1. Working of PET-MRI

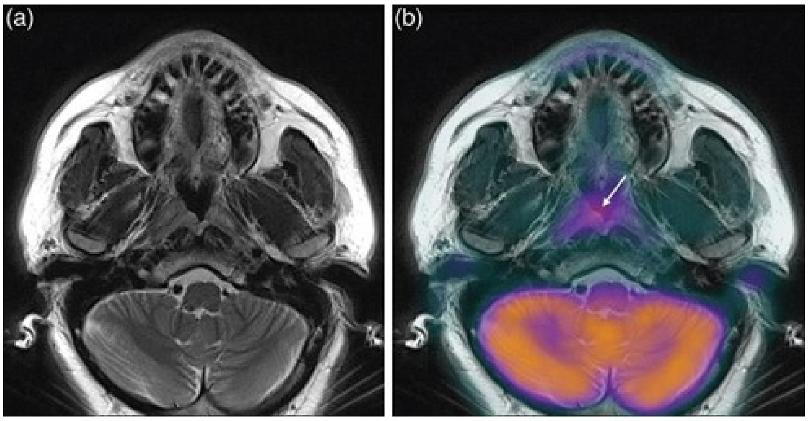

Figure 2: (a and b) A tumor of the fossa of Rosenmüller. (a) The small volume lesion is difficult to see on the T2 axial image, (b, white arrow) but demonstrates the uptake on the FDG PET/MRI image.

The PET-MRI procedure is similar to PET-CT. Initially, a radiotracer is injected into the vein of the patient. The affected cells absorb the radiotracer, and these areas look brighter during the scan. After the radiotracer accumulates in the desired area, the patient is made to lie down in the machine couch, which moves through the PET-MRI machine. As the patient moves through the machine, it takes images of the desired part of the body. In certain cases, the machine also scans the entire body and produces images [42]. Figure 2 demonstrates a PET-MRI image of a fossa of Rosenmüller tumor.

2. **Applications of PET-MRI:** PET-MRI scans are evolving as an important imaging technique in the present age of medicine. Some of its important applications are as follows:

   - Detection or tumor – It is used in detection of extramedullary diseases, bone metastasis and multiple myeloma [43].
   - Detection of neurological disorders – It is helpful in detecting epilepsy and other neurodegenerative diseases [44].
   - Cardiac imaging – It can be used to monitor cardiac conditions [45].
   - PET-MRI fuses the metabolic details of PET with the anatomical information provided by MRI offering better diagnosis and treatment plan.
   - PET-MRI images are of superior quality. It produces 3D images which are more detailed and clearer.
   - Since both PET and MRI scans are taken by a single machine, it is considered convenient.
   - It uses lower levels of radiation as compared to PET-CT [46].

3. **Drawback of PET-MRI**

   - It is expensive compared to PET-CT.
   - It takes longer than a PET-CT scan. A PET-CT scan takes about 30 minutes whereas a PET-MRI scan takes about 2 hours or more.
   - The scanning procedure is complex and requires a considerable amount of expertise [46].

IV. MRI-CT

Computed topography and magnetic resonance imaging are consistently used in radiologic assessment. MRI-CT is commonly used in planning radiation therapy (RT) for cancer treatment [47]. Magnetic resonance imaging -guided RT (MRIgRT) integrates MR imaging before and during radiation therapy. This provides high contrast of soft tissue images and other useful information. It enables doctors to identify the target before starting radiation therapy and track the stages of tumor during treatment [48]. However, MR images do not provide electron density information, hence, MRI images are converted to synthetic computed tomography (sCT). As modified CT-MRI instruments have not been developed, sCTs obtained from MRI images extend excellent assistance in planning and executing radiation therapy in cancer patients.

1. **Working of MRI-CT:** The sCT images are generated from MRI data using 3 methods – learning based, atlas-based, and segmentation-based. In the segmentation-based method, the MRI images are segmented into identified tissues and a CT value is assigned to each tissue. The precision of this method is dependent on the precision of segmentation.

Inaccurate assumptions of the tissue results in abnormal CT values. In the atlas-based method displacement vector field (DVF) involving new MRI scans and pre collected atlas values are calculated. These DVF values are applied to the CT images to obtain the sCTs. The precision of this method is dependent on the precision of the deformable registration. In the learning-based methods like deep learning, dictionary learning and random forest the integral correlations existing between MRI and CT images are demonstrated. Such correlations can be obtained mathematically or concluded by machine learning from data sets of MRI-CT images [49,50,51,52].

2. **Application of MRI-CT** Planning radiation therapy - MRI-CT is widely used in planning radiation therapy in cancer patients [53].

   - Monitoring therapy – It is used to monitor the progress in radiation therapy at different stages of treatment [54].
   - Altering therapy – MRI-CT detects failure in treatment plan and allows alterations in the treatment [53].

3. **Advantages of MRI-CT:** It is useful in planning and executing appropriate radiation therapy targeting specific cancer sites.

   - It offers the electron density information required for correct dose calculation in cancer treatment.
   - It provides high contrast images of the soft tissues and functional areas in the cancer affected regions [49].

4. **Drawback of MRI-CT** The accuracy of an sCT obtained from MRI depends on the method employed. It might result in an incorrect sCT owing to miscalculations [56]. The method of obtaining an sCT from an MRI is complex [56].

V. SPECT-MRI

Single-photon emission computed tomography (SPECT) is an imaging technique which uses gamma rays. It produces 3D images of the tissues using a gamma camera [56]. Similar to PET scans, a radioactive tracer is injected into the veins of the patient which travels to the affected tissue and gets accumulated. In contrast to PET, the radioactive tracers used in SPECT emit gamma radiation that can be measured directly. SPECT allows the clinician to assess the perfusion and functionality of specific tissues. SPECT images can provide information about the tissue functionality and physiology [57]. SPECT in combination with MRI is used as a hybrid technique in preclinical applications in small animals. SPECT provides tomographic images by measuring the intensity of γ-radiation radiated by the radio-nuclei supplemented to compound molecules present in a sample. MRI systems use signals emitted from the atomic nuclei which interacts with the magnetic field to produce tomographic images. An amalgamated SPECT/MRI system was first proposed by Breton et al. in 2007. He used an individual pinhole SPECT system together with a 0.1-T magnet [58].

1. **Working of SPECT-MRI** In line SPECT-MRI systems – This approach involves mounting the SPECT and MRI systems back-to- back on a platform. This allows to

obtain images from both SPECT and MRI one after the other in a short span of time. SPECT insertions in MRI systems have been developed to perform simultaneous SPECT and MR scans [59,60]. These systems have a fixed detector set-up and MRI-compatible

Side by side SPECT-MRI systems – In this approach the SPECT and MRI systems are positions side by side and the animals are shifted from one system to another after imaging. The animals are gently fixed to the bed using tape to prevent movement. Such systems require beds that can be efficiently installed on different scanners. Spatial coregistration is achieved by using multimodal reference markers

The current preclinical models of SPECT-MRI employ 2 approaches of producing images in small animals. detectors and collimators. However, these systems are in early development stages. attached to the animal/bed or a predetermined transformation matrix [61,62].

2. **Applications of SPECT/MRI:** There are various preclinical applications of combined SPECT / MRI. Some of the main applications include:

- Imaging of targets and probes – It can be used to produce images of the target tissues and the probes used for diagnosis or treatment [63,64,65].
- Tumor imaging – It produces detailed images of the tumor sites [66,67].
- Preclinical studies in small animals with neurodegenerative diseases – It can be used to monitor neurodegenerative diseases such as Alzheimer's or Parkinson's disease [68].
- Preclinical studies in small animals with cardiac diseases – It can be used to monitor heart conditions, such as, blood flow or blockage of arteries in the heart [69, 70].
- Biodistribution studies – It can help in studying the biodistribution of a drug inside the body without sacrificing large number of animal models [71,72].

3. **Advantages of SPECT/MRI**

- It can provide both morphological and functional data.
- It has better spatial and temporal resolution
- It is available in different configurations and produces trans-axial views, which permits imaging of varied range of small animals [73].

4. **Drawbacks of SPECT/MRI**

- Absence of synchronous SPECT-MRI for clinical studies results in individual and separate imaging by SPECT and MRI which is time consuming.
- The use of separate modalities of SPECT-MRI instead of an integrated system hampers the quality of images [73].

VI. SPECT-CT

SPECT-CT is an amalgamation of functional single photon emission computed tomography and anatomical computed tomography imaging. The conjunction of SPECT with CT permits spatial overlay of data obtained from SPECT on anatomical images obtained from CT. Installing diagnostic CT components into the SPECT/CT system makes the equipment cost efficient. The benefits of combining the two modalities are numerous. It not only improves specificity and sensitivity but also leads to better treatment monitoring and staging. The first commercial SPECT/CT hybrid model as a single unit was the GE Millenium™ hybrid SPECT/PET/CT, camera equipped with HawkEye™ single-slice CT. This model was the commercial execution of the successful research carried out by late Hasegawa et al. [74,75]. The hybrid imaging system such as SPECT-CT allows complete registration between images obtained from independent imaging technologies and produces high quality 3D images. The direct planar imaging technology involved in such systems can produce images of specific regions or the whole body to create bone scans as demonstrated in Figure 3

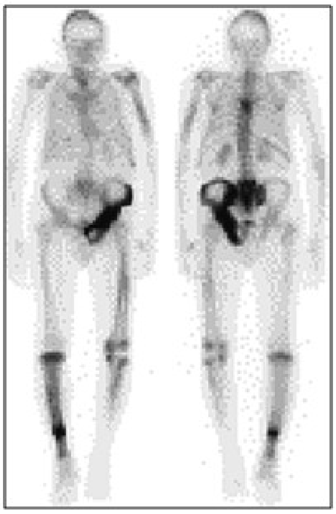

Figure 3: Whole body scan using 99mTechnetium-methylene diphosphonate (99mTc-MDP) showing involvement of Paget's disease [76].

1. **Procedure:** SPECT-CT also requires injection of a radioactive tracer. The most commonly used tracer in SPECT-CT scans is Technetium-99m (Tc-99m) [77]. The integrated SPECT-CT system is a large circular device with an embedded camera. After the tracer is accumulated in the area of interest the patient is made to lie down inside the device which rotates around the body and clicks pictures of the internal organs. SPECT-CT systems employ single head cameras which are rotated around the patient to create an image, or dual headed cameras which independently obtain data from its field of view. Initial SPECT systems applied ''image fusion technology" where images from SPECT and CT are fused separately, while current SPECT/CT systems have inbuilt CT systems allowing automatic image fusion and suitable tomographic correction. In some cases, 99mTc can be used in combination with biologically active compounds to track various physiological activities inside the body. 67Ga attached to specific compounds is used to monitor sites of chronic infections. Gallium 67 is specifically useful in imaging osteomyelitis excluding the spine. 111In attached to platelets can be used to detect thrombus. It can also be labelled with proteins or peptides to detect rare forms of cancer. 133Xe in the gas form is used for respiratory studies and for cerebral blood flow [78].

2. Applications of SPECT-CT

- Diagnosis of neurological disorders – SPECT-CT is used to differentiate between Parkinsons and other neurological disorders [79]. It also helps in diagnosis of cognitive impairment in the brain [80].
- Diagnosis of endocrinological disorders – It is used to diagnose hyperparathyroidism and parathyroid adenoma (PTA). The reported detection rate of PTAs using SPECT-CT ranges from 90 to 96% [81,82,83].
- Diagnosis of cardiovascular diseases – It is useful in the diagnosis of coronary artery disease. It detects the presence of coronary artery calcification (CAC) which is an indication of coronary atherosclerosis [84,85,86,87].
- Diagnosis of pulmonary embolism – SPECT-CT can detect acute and chronic pulmonary embolism [88,89,90].
- Monitoring of non-embolic diseases - It also helps to monitor non-embolic diseases such as regional changes in asthma, estimate regional lung function, optimization of radiotherapy in lung cancer, monitor lung function, assess irregularity of ventilation in emphysema patients [91].
- Diagnosis of bone diseases – It helps in the assessment of arthropathies [92]. It helps in detecting occult fractures and post-traumatic bone remodeling [93].
- Diagnosis of inflammation - SPECT–CT is applied in imaging of inflammation and infection [94].
- Diagnosis of cancer – It is useful in diagnosis of cancer, planning and management of radiation therapy and continuous assessment of different stages of cancer [95,96,97].
- Diagnosis of gastrointestinal disorders – It helps to diagnose GI injuries and bleeding [98]

3. Advantages of SPECT-CT

- It provides functional as well as anatomical data.
- It has a wide array of applications from diagnosis to monitoring of various diseases.
- It has improved localization properties.
- It has better specificity.
- It is highly sensitive.
- Integration of two modalities makes it cost effective.

4. Drawbacks of SPECT-CT

- It requires a long scan time.
- Improper positioning of the patient may lead to erroneous results.
- Spatial misalignment of the two modalities may lead to inaccurate findings [99].

VII. ULTRASOUND-CT/MR

Ultrasound (US) is another non-invasive imaging technique that displays internal body structures like organs and soft tissues in pictures or real time videos using high intensity sound waves with frequencies greater than 20kHz. The picture obtained from an ultrasound is called a sonogram. Unlike other techniques like X-rays, it does not employ radiation for imaging [100]. Ultrasound is used for prenatal imaging and diagnostic imaging. In prenatal imaging ultrasound is used to monitor the growth of the fetus, detect complications, and diagnose any abnormalities in the fetus [101]. Diagnostic ultrasound imaging is used to diagnose abnormalities in different parts of the body, for example, detection of kidney stones, liver disorders, cancerous growth etc. [102,103]. However, ultrasound cannot produce accurate images of the areas that are obstructed by vapor or air like intestines. It is also ineffective in producing images of the areas that are hidden under bones such as lungs or head or areas located deep in the body [104]. During such situations a CT or MRI scan is recommended by the doctors. In many cases real time-fusion of sonography with CT or MR images is proposed.

1. **Procedure:** The hybrid fusion imaging technique applies different tracking methods. The 3 major tracking methods are optical, electromagnetic (EM), and image-based [105]. Optical tracking is generally used in surgical procedures, EM tracking is broadly used for ultrasound-guided hepatic interventions and image-based tracking is used in vascular interventions. The general process of image fusion is as follows: Firstly, prior diagnostic MR or CT data were obtained and fed to the fusion system. Secondly, the MR or CT images that clearly exhibited both the target area and the surrounding anatomical landmarks were chosen by a radiologist. Lastly, co-registration was performed by positioning auto registration software (Samsung RS80A) utilizing a magnetic field generator. Two electromagnetic position sensors were linked to a position sensing unit. These were attached to a convex array transducer via a bracket. After an effective image fusion and registration was achieved, the registered CT/MRI images were concurrently shown along with the relevant ultrasound sectional plane [106].

2. **Applications of US-CT/MR**

   - US-CT/MR is used for transcutaneous hepatic intervention such as radiofrequency ablation (RFA) and biopsy [107].
   - It is used for percutaneous image-guided biopsy [106].
   - US-CT/MR hybrid imaging is used to monitor breast cancer [107].
   - US-CT/MR fusion imaging helps in the diagnosis and localization of lesions with low detection range.
   - It is helpful in detection of cystic and renal lesions [108].
   - It can be used to perform drainage of pancreatic necrosis [109].

3. **Advantages of US-CT/MR**

   - The success rates of biopsy were significantly higher in the fusion-guided biopsy compared to conventional US-guided biopsy [106].
   - The fusion-guided biopsy demonstrated reduced biopsy procedure times [106].
   - It is particularly beneficial in diagnosis and monitoring of hepatic disorders.

4. **Drawbacks of US-CT/MR**

   - It requires to synchronize the static images obtained from a CT or MR scan with the changing position and breathing motion of the patient [110]
   - Fusion of US-CT/MR techniques might lead to mistargeting a lesion [111].

- The periphery of the liver has very few anatomical landmarks. Thus, during fusion imaging any registration error particularly affects the peripheral areas of the liver [108].
- Visualization of the pancreas requires application of pressure with a probe on the upper abdomen which displaces the overlying hollow organs. This can affect the fusion between the US and CT/MR images [112].
- The synchronization between ultrasound and CT/MR image might exhibit discrepancies resulting in faulty data [113].
- It requires longer examination time.
- The fusion technique is expensive [114].

VIII. CT-ANGIOGRAPHY

Angiography is a medical imaging technique which involves x-ray imaging to examine the blood vessels of the body especially in the heart chambers, veins, and arteries. The word angiography originates from the Greek words angeion meaning 'vessel' and graphein meaning 'to write, record'. The images produced during an angiography are called angiograms. CT-Angiography (CTA) is a fusion of computed tomography and angiography and magnetic resonance and angiography. The fusion of angiography with CT and MR enhances the image quality and widens the detection range. CTA produces axial, or horizontal images, of blood vessels for diagnosis by utilizing x-rays and other softwares. Different post-processing techniques are used to interpret CTA results, such as maximum-intensity projections, multiplanar reformation, virtual coronary angioscopy or the angiographic view, and direct volume rendering [115]. CTA is progressively used to diagnose coronary disease or stable angina. Three common quality metrics required for a superior quality CT image in CT-Angiography are spatial resolution, temporal resolution, and volume coverage.

1. **Procedure:** Before initiating the scan, a contrast material is injected intravenously which helps to produce better images. During the scan the patient is laid back on the CT examination table. The radiologist ensures that the patient is positioned correctly to obtain clear images. During the scanning procedure, the table is placed at the starting point of imaging which will slowly move through the opening of the machine as the scan progresses. The rotating device emits beams of X-rays from different angles which pass through the body into the area of interest to produce cross sectional images. These images are later assembled by a computer to create 3D images. The majority of CTA uses helical CT with constant table motion and gantry rotation. The helical pitch determines rotation time along with the table speed which in turn determines the speed at which the volume is to be scanned. The helical pitch must match the table speed during the initial circulation of contrast material through the area of interest. Acquisitions with very high table speed and helical pitch outrun the iodine bolus and miss to acquire data when the contrast enhancement is at its apex [116]. During CTA of the heart, electrocardiogram (ECG) leads (sticky patches) are placed on the patient’s chest to coordinate CT scanning with the heartbeats [117].

2. Application

- It is useful to detect atherosclerotic plaques.
- It helps in the detection of aneurysms.
- CTA is used as a gold-standard for imaging the aorta [118,119].
- CTA can be used for imaging pulmonary arteries [120]
- CTA of the head and neck delivers high quality, 3D images to study cerebrovascular anatomy in any random plane [121].
- CTA is used in the diagnosis of fibromuscular dysplasia (FMD).
- CTA is used to acquire calcium scoring images without intravenous contrast. This allows optimal visualization and quantification of calcified plaque, which is a strong indicator of coronary artery disease [122].
- It is also used to diagnose deep venous thrombosis and varicose veins [123].
- CTA allows imaging of the renal arteries which are the common sites of atherosclerosis with associated aneurysms, stenosis, or occlusion [124].

3. Advantages of CTA

- CTA can eliminate the necessity of surgery.
- It provides accurate anatomical details of the blood vessels.
- It is noninvasive.
- It is less time-consuming.
- It can detect vascular obstruction and allow the physician to plan appropriate therapy [115].

4. Drawbacks of CTA

- It can cause allergic reactions to the contrast dye.
- Contrast materials containing Iodine cannot be used in patients with kidney disorders.
- It is not suitable for pregnant women.
- Excessive exposure to radiation can increase the risk of cancer [115].

IX. CONCLUSION

Extensive research is being carried out throughout the world to treat, monitor, and cure complex diseases such as, cancer, Alzheimer’s, Parkinsons, HIV etc. and to deal with novel diseases such as COVID-19. Treatment of such diseases requires persistent innovative approaches which demand the use of innovative technology, therapies, and novel drug molecules. Although new technologies are being developed, regulatory requirements mandate extensive clinical trials to be carried out for new drug molecules and devices before they can be marketed for use. While many hybrid imaging techniques are being developed for experimental purposes which offer immense potential, their incorporation into mainstream medical practice is slow. The hybrid imaging techniques that are currently being used for imaging like PET-CT, PET-MRI and SPECT-CT have revolutionized the diagnostic field. It produces detailed and high-resolution images of the affected areas which makes diagnosis and treatment planning much easier for the physicians, especially in diseases like cancer, neurodegenerative disorders, and cardiovascular disorders among others. In today’s medical practice there are a few hybrid imaging techniques where two imaging devices are integrated together which makes imaging easier. However, development of such integrated devices is met with financial challenges, which in turn makes imaging using such devices expensive. In other cases, images produced by two different imaging devices are fused together using computer programs. Such image fusion techniques present the risk of erroneous results due to miscalculation while using the computer program. Furthermore, in both scenarios a well experienced technical operator is of prime importance to carry out the imaging process.

In conclusion, hybrid imaging techniques play an important role in diagnosis, monitoring, and follow-up during treatment regime and further research, to develop cost effective, simple, and highly efficient hybrid imaging techniques is the need of the hour.

REFERENCES

[1] M. Laal, "Innovation process in medical imaging," Procedia Soc. Behav. Sci., vol. 81, pp. 60–64, June 2013.
[2] B. Rajalingam, R. Priya, "Review of multimodality medical image fusion using combined transform techniques for clinical application," International Journal of Scientific Research in Computer Science Applications and Management Studies, vol. 7(3), pp. 1-8, May 2018
[3] A.P. James, B.V. Dasarathy, "Medical image fusion: A survey of the state of the art," Inf. fusion, vol. 19, pp. 4-19, September 2014.
[4] H. Kaur, D. Koundal, V. Kadyan, "Image fusion techniques: a survey," Arch. Comput. Methods Eng., vol. 28, pp. 4425-4447, January 2021.
[5] O.S. Faragallah, H. El-Hoseny, W. El-Shafai, A.W. El-Rahman, H.S. El-Sayed, E.S.M. El-Rabaie, G.G. Geweid, "A comprehensive survey analysis for present solutions of medical image fusion and future directions," *IEEE Access*, vol. *9*, pp. 11358-1137, December 2020.
[6] B. Singh, R. Gautam, S. Kumar, S. Umapathy, "Application of vibrational microspectroscopy to biology andMedicine," Curr. Sci., vol. 102(2), pp. 232-244, January 2012.
[7] J. Andreu-Perez, C.C. Poon, R.D. Merrifield, S.T. Wong, G.Z. Yang, "Big data for health," IEEE J Biomed Health Inform., vol. 19(4), pp. 1193-1208, July 2015.
[8] S.U. Khan, Y.C. Wang, S.S. Chai, "A novel noise removal technique of X-ray carry-on luggage for detection of contraband/illicit object (s)," Int. J. Eng. Adv. Tech., vol. 2(3), pp. 94-99, January 2013.
[9] F.E.Z.A. El-Gamal, M. Elmogy, A. Atwan, "Current trends in medical image registration and fusion," Egypt. Inform. J., vol. 17(1), pp. 99-124, March 2016.
[10] D. O'Mahony, A.H. Gandjbakhche, M. Hassan, A. Vogel, R. Yarchoan, "Imaging techniques for Kaposi Sarcoma (KS)," J HIV Ther., vol. 13(3), pp. 65-71, September 2008.
[11] Y. Yang, Y. Que, S. Huang, P. Lin, "Multimodal sensor medical image fusion based on type-2 fuzzy logic in NSCT domain," IEEE Sensors Journal, vol. 16(10), pp. 3735-3745, May 2016.
[12] S.D. Ramlal, J. Sachdeva, C.K. Ahuja, N. Khandelwal, "Multimodal medical image fusion using nonsubsampled shearlet transform and pulse coupled neural network incorporated with morphological gradient," Signal, Image and Video Processing, vol. 12(8), pp.1479-1487, May 2018.
[13] R. Boellaard, R. Delgado-Bolton, W.J. Oyen, F. Giammarile, K. Tatsch, W. Eschner et al., "FDG PET/CT: EANM procedure guidelinesfor tumour imaging: version 2.0," Eur J Nucl Med Mol Imaging, vol. 42(2), 328-354, February 2015.
[14] S.J. Ahn, M.S. Park, J.D. Lee, W.J. Kang, "Correlation between18F-fluorodeoxyglucose positron emission tomography andpathologic differentiation in pancreatic cancer," Ann Nucl Med., vol. 28(5), pp. 430-435, June 2014.
[15] M.S. Hofman, N. Lawrentschuk, R.J. Francis, C. Tang, I. Vela , P. Thomas , et al., "Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study," Lancet, vol. 395, pp. 1208-1216, April 2020.
[16] M. Perera, N. Papa, M. Roberts, M. Williams, C. Udovicich, I. Vela et al, "Gallium-68 Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer-Updated Diagnostic Utility, Sensitivity, Specificity, and Distribution of Prostate-specific Membrane Antigen-avid Lesions: A

Systematic Review and Meta-analysis," Eur Urol, vol. 77, pp.403-417, April 2020.
[17] G.A. Ulaner, "16α-18F-fluoro-17β-Fluoroestradiol (FES): Clinical Applications for Patients with Breast Cancer," Semin Nucl Med., vol. 52(5), pp. 574-583, September 2022.
[18] C. Liu, C. Gong, S. Liu, Y. Zhang, Y. Zhang, X. Xu, H. Yuan, B. Wang, Z. Yang, "(18)FFES PET/CT influences the staging and management of patients with newly diagnosed estrogen receptor-positive breast cancer: a retrospective comparative study with (18)F-FDG PET/CT," Oncologist, 24(12), pp. e1277–e1285, December 2019.
[19] C. Pajak, L. Cadili, K. Nabata, S.M. Wiseman, "68Ga-DOTATATE-PET shows promise for diagnosis of recurrent or persistent medullary thyroid cancer: A systematic review," Am. J. Surg., vol. 224(2), pp. 670-675, August 2022.
[20] A. Kandathil, R.M. Subramaniam, "Gastroenteropancreatic Neuroendocrine Tumor Diagnosis: DOTATATE PET/CT," PET Clin., vol. 18(2,) pp. 189-200, April 2023.
[21] H.A. Jahromi, M.K. Fallahzadeh, A. Takalkar, J. Sheng, G. Zibari, A.H. Shokouh, "Impact of plasma glucose level at the timeof Fluorodeoxyglucose Administration on the Accuracyof FDG-PET/CT in the diagnosis of pancreatic lesions," Int. J. Endocrinol. Metab.,12(4), e16429, October 2014.
[22] K.H. Chung, J.K. Park, S.H. Lee, D.W. Hwang, J.Y. Cho, Y.S. Yoon, et al., "Lower maximum standardized uptake value of fluorine-18 flu-orodeoxyglucose positron emission tomography coupled withcomputed tomography imaging in pancreatic ductal adenocar-cinoma," Am. J. Surg. vol. 209, pp. 709-716, April 2015.
[23] T. Yoneyama, U. Tateishi, I. Endo, T. Inoue, "Staging accuracy of pancreatic cancer: comparison between non-contrast-enhanced and contrast-enhanced PET/CT," Eur. J. Radiol., vol. 83, pp. 1734-1739, October 2014.
[24] N. Kawada, H. Uehara, T. Hosoki, M. Takami, H. Shiroeda, T. Arisawa, et al., "Usefulness of dual-phase 18F-FDG PET/CT for diagnosing small pancreatic tumors," Pancreas, vol. 44, pp. 655-659, May 2015.
[25] P.Y. Salaün, R. Abgral, O. Malard, S. Querellou-Lefranc, G. Quere, M. Wartski, et al., "Update of the recommendations of good clinical practice for the use of PET in oncology," Bull Cancer, vol. 106, pp. 262-274, March 2019.
[26] Z. Wang, J.Q. Chen, J.L. Liu, X.G. Qin, Y. Huang, "FDG-PET in diagnosis, staging and prognosis of pancreatic carcinoma: ameta- analysis," World. J. Gastroenterol., vol. 19, pp. 4808-4817, August 2013.
[27] X.Y. Wang, F. Yang, C. Jin, Y.H. Guan, H.W. Zhang, D.L. Fu, "The value of 18F-FDG positron emission tomography/computed tomog- raphy on the pre-operative staging and the management of patients with pancreatic carcinoma," Hepatogastroenterology, vol. 61, pp. 2102- 2109, October 2014.
[28] A. van Baardwijk, B.G. Baumert, G. Bosmans, M. van Kroonenburgh, S. Stroobants, V. Gregoire, P. Lambin, D. De Ruysscher, "The current status of FDG-PET in tumour volume definition in radiotherapy treatment planning," Cancer Treat. Rev., vol. 32(4), pp. 245–260, June 2006.
[29] A. Noy, H. Schoder, M. Gonen, M. Weissler, K. Ertelt, C. Cohler, C. Portlock, P. Hamlin, H.W. Yeung, "The majority of transformed lymphomas have high standardized uptake values (SUVs) on positron emission tomography (PET) scanning similar to diffuse large B-cell lymphoma (DLBCL)," Ann. Oncol., vol. 20(3), pp. 508–512, March 2009.
[30] D. De Azevedo, J. Geers, O. Gheysens, M. Dweck, D. Vancraeynest, "18F-Sodium Fluoride PET/CT in Assessing Valvular Heart and Atherosclerotic Diseases," Seminars in Nuclear Medicine, Vol.53(2), pp. 241-257, March 2023.
[31] F. Akbik, M. Robertson, A.S. Das, T. Singhal, J.W. Lee, H. Vaitkevicius, "The PET sandwich: Using Serial FDG-PET Scans with interval burst suppression to assess ictal components of disease," Neurocrit. Care, vol. 33(3), pp. 657-669, December 2020.
[32] A.W.J.M. Glaudemans, P.C. Jutte, M.A. Cataldo, V. Cassar-Pullicino, O. Gheysens, O. Borens, et al., "Consensus document for the diagnosis of peripheral bone infection in adults: A joint paper by the EANM, EBJIS, and ESR (with ESCMID endorsement)," Eur. J. Nucl. Med. Mol. Imaging, vol. 46(4), pp. 957-970, January 2019.
[33] A. Signore, L.M. Sconfienza, O. Borens, et al., "Consensus document for the diagnosis of prosthetic joint infections: A joint paper by the EANM, EBJIS, and ESR (with ESCMID endorsement)," Eur. J. Nucl. Med. Mol. Imaging, vol. 46(4), pp. 971-988, January 2019.
[34] A.O. Ankrah, I.O. Lawal, R.A.J.O. Dierckx, M.M. Sathekge, A.W.J.M. Glaudemans , "Imaging of invasive fungal infections-The role of PET/CT," Semin. Nucl. Med., vol. 53(1), pp. 57-69, January 2023.
[35] M.F. Neuville, P. Lovinfosse, A. Jadoul, M. Thys, L. Seidel, R. Hustinx, F. Jouret, "The use of a visual 4-point scoring scale improves the yield of 18F-FDGPET-CT imaging in the diagnosis of renal and hepatic cyst infection in patients with autosomal dominant polycystic kidney disease," Eur. J. Nucl. Med. Mol. Imaging, vol. 48(1), pp. 254-259, January 2021.

[36] M. Gill, W. Sia, M. Hoskinson, E. Niven, R. Khurana, "The use of PET/CT in pregnancy: A case report of malignant parathyroid carcinoma and a review of the literature," Obstet. Med., vol. 11(1), pp. 45-49, March 2018.
[37] G. Antoch, A. Bockisch, "Combined PET/MRI: a new dimension in whole-body oncology imaging?," Eur. J. Nucl. Med. Mol. Imaging, vol. 36(S1), pp. 113–120, December 2008.
[38] Y. Shao, S. Cherry, K. Farahani, R. Slates, R. Silverman, K. Meadors, A. Bowery, S. Siegel, P. Marsden, P. Garlick, "Development of a PET detector system compatible with MRI/NMR systems," IEEE Trans Nucl Sci., vol. 44, pp. 1167–1171, December 1997.
[39] B. Pichler, E. Lorenz, R. Mirzoyan, W. Pimpl, F. Roder, M. Schwaiger, S. Ziegler, "Performance test of a LSO-APD PET module in a 9.4 Tesla magnet," IEEE Nucl Sci Symp., vol. 2, pp. 1237–1239, November 1997.
[40] M.S. Judenhofer, H.F. Wehrl, D.F. Newport, C. Catana, S.B. Siegel, M. Becker et al., "Simultaneous PET-MRI: a new approach for functional and morphological imaging," Nat Med., vol. 14, pp. 459–465, April 2008.
[41] H.P. Schlemmer, B.J. Pichler, M. Schmand, Z. Burbar, C. Michel, R. Ladebeck, et al., "Simultaneous MR/PET imaging of the human brain: feasibility study," Radiology, vol. 248, pp. 1028–1035, September 2008.
[42] T. Vitor, K.M. Martins, T.M. Ionescu, M.L. da Cunha, R.H. Baroni1, M.R.T. Garcia, et al., "PET/MRI: a novel hybrid imaging technique. Major clinical indications and preliminary experience in Brazil," Einstein, vol. 15(1), pp. 115-118, January-March 2017
[43] K. Barley, A. Chari, "Diagnostic advances in multiple myeloma," Curr. Hematol. Malig. Rep., vol. 11(2), pp. 111-117, April 2016.
[44] C. Spick, K. Herrmann, J. Czernin, "18F-FDG PET/CT and PET/MRI perform equally well in cancer: evidence from studies on more than 2,300 patients," J. Nucl. Med., vol. 57(3), pp. 420-430, March 2016.
[45] S.G. Nekolla A. Martinez-Moeller, A. Saraste, "PET and MRI in cardiac imaging: from validation studies to integrated applications," Eur. J. Nucl. Med. Mol. Imaging, vol. 36(Suppl. 1), pp. S121–130, March 2009.
[46] M.C.M. Gammel, E.L. Solari, M. Eiber, I. Rauscher, S.G. Nekolla, "A Clinical Role of PET-MRI in Prostate Cancer?," Semin. Nucl. Med., in press.
[47] R. Kashani, J.R. Olsen, "Magnetic Resonance Imaging for Target Delineation and Daily Treatment Modification," Semin. Radiat. Oncol., vol. 28(3), pp. 178-184, June 2018.
[48] S. Aouadi, A. Vasic, S. Paloor, R.W. Hammoud, T. Torfeh, P. Petric, N. Al-Hammadi, "Sparse patch-based method applied to mri-only radiotherapy planning," Phys. Med., Vol. 32(3), pp. 309, September 2016.
[49] X. Zhou, W. Cai, J. Cai, F. Xiao, M. Qi, J. Liu, L. Zhou, et al., "Multimodality MRI synchronous construction based deep learning framework for MRI-guided radiotherapy synthetic CT generation," Comput. Biol. Med., Vol. 162, 107054, August 2023.
[50] A. Bahrami, A. Karimian, H. Arabi, "Comparison of different deep learning architectures for synthetic CT generation from MR images," Phys. Med., Vol. 90, pp. 99-107, October 2021.
[51] Y. Lei, H.K. Shu, S. Tian, J.J. Jeong, T. Liu, H. Shim, et al., "Magnetic resonance imaging-based pseudo computed tomography using anatomic signature and joint dictionary learning," J. Med. Imaging (Bellingham)., vol. 5(3): pp. 034001-1 -034001-12, July 2018.
[52] X. Yang, Y. Lei, H.K. Shu, P. Rossi, H. Mao, H. Shim, et al., "Pseudo CT Estimation from MRI Using Patch-based Random Forest," Proc. SPIE. Int. Soc. Opt. Eng., vol. 10133, pp. 1-9, February 2017.
[53] S.H Hsu, Y. Cao, K. Huang, M. Feng, J.M. Balter, "Investigation of a method for generating synthetic CT models from MRI scans of thehead and neck for radiation therapy," Phys. Med. Biol., vol. 58, pp. 8419–8435, December 2013.
[54] J.M. Edmund, T. Nyholm, "A review of substitute CT generation for MRI-only radiation therapy," Rad. Onc., vol. 12(28), pp. 1-15, January 2017.
[55] Y. Lei, J. Harms, T. Wang, S. Tian, J. Zhou, H.K. Shu, et al., "MRI-based synthetic CT generation using semantic random forest with iterative refinement," Phys. Med. Biol., vol. 64(8), pp. 085001, pp-1-29, April 2019.
[56] J.W. Scuffham, "A CdTe detector for hyperspectral SPECT imaging," IOP J. Instrum., vol. 7(8), pp. 1-13, August 2012.
[57] O. Israel, O. Pellet, L. Biassoni, D.De Palma, E. Estrada-Lobato, G. Gnanasegaran, et at., "Two decades of SPECT/CT - the coming of age of a technology: An updated review of literature evidence," Eur. J. Nucl. Med. Mol. Imaging, vol. 46(10), pp. 1990-2012, September 2019.
[58] E. Breton, P. Choquet, C. Goetz, J. Kintz, P. Erbs, R. Rooke, et al., "Dual SPECT/MR imaging in small

animal," Nucl. Instrum. Methods Phys. Res. A., vol. 571, pp. 446–448, February 2007.
[59] J-W. Tan, L. Cai, L-J. Meng, "A prototype of the MRI-compatible ultrahigh resolution SPECT for in vivo mice brain imaging," I.E. Nuclear Science Symposium Conference Record, pp. 2800–2805, December 2009.
[60] D. Meier, D.J. Wagenaar, S. Chen, J. Xu, J. Yu, B.M. Tsui, "A SPECT camera for combined MRI and SPECT for small animals," Nucl. Instrum. Methods Phys. Res. A., vol. 652, pp. 731–734, October 2011.
[61] C. Ji, F.V.D Have, H.G.V. Andel, R. Ramakers, F. Beekman, "Accurate coregistration between ultra-high-resolution micro- SPECT and circular cone-beam micro-CT scanners," Int. J. Biomed. Imaging, vol. 2010(1), pp. 654506, October 2010.
[62] P.L. Chow, D.B. Stout, E. Komisopoulou, A.F. Chatziioannou, "A method of image registration for small animal, multi-modality imaging," Phys. Med. Biol., vol. 51, pp. 379–390, January 2006.
[63] C. Muller, "Folate based radiopharmaceuticals for imaging and therapy of cancer and inflammation," Curr. Pharm. Des., vol. 18, pp. 1058–1083, 2012
[64] E. Ruoslahti, S.N. Bhatia, M.J. Sailor, "Targeting of drugs and nanoparticles to tumors," J. Cell Biol., vol. 188, pp. 759–768, March 2010.
[65] K. Movahedi, S. Schoonooghe, D. Laoui, I. Houbracken, W. Waelput, K. Breckpot, et al., "Nanobody-based targeting of the macrophage mannose receptor for effective in vivo imaging of tumor-associated macrophages," Cancer Res., vol. 72, pp. 4165–4177, 2012.
[66] D. Hanahan, R.A. Weinberg, "Hallmarks of cancer: the next generation," Cell, vol. 144, pp. 646–674, March 2011.
[67] D. Hanahan, R.A. Weinberg, "The hallmarks of cancer," Cell, vol. 100, pp. 57–70, January 2000.
[68] J.D. Lee, Y.H. Chu, C.W. Chen, K.J. Lin, "Multi-image registration for evaluating the 99mTc-TRODAT-1 of Parkinson's rat model," Annu Int Conf IEEE Eng Med Biol Soc., vol. 2009, pp. 5801-5804, September 2009.
[69] A. Ruggiero, D.L. Thorek, J. Guenoun, G.P. Krestin, M.R. Bernsen, "Cell tracking in cardiac repair: what to image and how to image," Eur. Radiol., vol. 22, pp. 189–204, July 2012.
[70] J. Knuuti, P.A. Kaufmann, "Hybrid imaging: combination of PET, SPECT, CT, and MRI," The ESC Textbook of Cardiovascular Imaging, 2nd ed., Oxford, pp. 89-98, 2015.
[71] R. Madru, P. Kjellman, F Olsson, K. Wingårdh, C. Ingvar, F. Ståhlberg F, et al., "99mTc-labeled superparamagnetic iron oxide nanoparticles for multimodality SPECT/MRI of sentinel lymph nodes," J. Nucl. Med., vol. 53, pp. 459–463, March 2012.
[72] W. Bult, S.G. Kroeze, M. Elschot, P.R. Seevinck, F.J. Beekman, H.W. de Jong, et al., "Intra tumoral administration of Holmium-166 acetylacetonate microspheres: antitumor efficacy and feasibility of multimodality imaging in renal cancer," PLoS One, vol. 8(1), pp. e52178,January 2013.
[73] M.R. Bernsen, P.E.B. Vaissier, R.V. Holen, J. Booij, F.J. Beekman, M.de Jong, "The role of preclinical SPECT in oncological and neurological research in combination with either CT or MRI," Eur. J. Nucl. Med. Mol. Imaging, vol. 41(1), pp. S36–S49, April 2014.
[74] B.H. Hasegawa, K.H. Wong, K. Iwata, W.C. Barber, A.B. Hwang, A.E. Sakdinawat, et al., "Dual-modality imaging of cancer with SPECT/CT," Technol. Cancer Res. Treat., vol. 1, pp. 449–458, December 2002.
[75] Y. Seo, C.M. Aparici, B.H. Hasegawa, "Technological development and advances in SPECT/ CT," Semin. Nucl. Med., vol. 38, pp. 177– 198, May 2008.
[76] G.J.R. Cook, "Miscellaneous indications in bone scintigraphy: metabolic bone diseases and malignant bone tumors," Semin. Nucl. Med., vol. 40(1), pp. 52–61, January 2010.
[77] W.W. Lee, K-SPECT Group, "Clinical Applications of Technetium-99m Quantitative Single-Photon Emission Computed Tomography/Computed Tomography," Nucl. Med. Mol. Imaging, vol. 53, pp. 172-181, June 2019.
[78] L.K. Appelgren, "Methods of recording tumor blood flow," Tumor Blood Circulation: Angiogenesis, Vascular Morphology and Blood Flow of Experimental and Human Tumors, 1st ed., CRC Press, 2020, pp. 87–101.
[79] K. Yokoyama, E. Imabayashi, K. Sumida , D. Sone , Y. Kimura , N. Sato et al., "Computed-tomography-guided anatomic standardization for quantitative assessment of dopamine transporter SPECT," Eur. J. Nucl. Med. Mol. Imaging, vol. 44, pp. 366–372, March 2017.
[80] F. Welz, J.C. Sanders, T. Kuwert, J. Maler, J. Kornhuber, P. Ritt, "Absolute SPECT–CT quantification of cerebral uptake of 99mTc-HMPAO for patients with neurocognitive disorders," Nuklearmedizin, vol. 55, pp. 158–165, August 2016.
[81] H. Tokmak, M.O. Demirkol, F. Alagöl, S. Tezelman, T. Terzioglu, "Clinical impact of SPECT-CT in the diagnosis and surgical management of hyper-parathyroidism," Int. J. Clin. Exp. Med., vol. 7, pp. 1028–

1034, April 2014.
[82] C.N. Patel, H.M. Salahudeen, M. Lansdown, A.F. Scarsbrook, "Clinical utility of ultrasound and 99mTc sestamibi SPECT–CT for preoperative localization of parathyroid adenoma in patients with primary hyperparathyroidism," Clin. Radiol., vol. 65, pp. 278–287, April 2010.
[83] A-M. Woods, A.A. Bolster, S. Han, F-W. Poon, D. Colville, J. Shand, J.B. Neilly, "Dual-isotope subtraction SPECT-CT in parathyroid localization," Nucl. Med. Commun., vol. 38, pp. 1047–1054, December 2017.
[84] R. Detrano, A.D. Guerci, J.J. Carr, D.E. Bild, G. Burke, A.R. Folsom, et al., "Coronary calcium as a predictor of coronary events in four racial or ethnic groups," N. Engl. J. Med., vol. 358, pp. 1336–1345, March 2008.
[85] R.J.M.W. Rennenberg, A.G.H. Kessels, L.J. Schurgers, J.M.A. van Engelshoven, P.W. de Leeuw, A.A. Kroon, "Vascular calcifications as a marker of increased cardiovascular risk: A meta-analysis," Vasc. Health Risk Manage, vol. 5, pp.185–197, April 2009.
[86] M.J. Budoff, R. Young, V.A. Lopez, R.A. Kronmal, K. Nasir, R.S. Blumenthal, et al., "Progression of coronary calcium and incident coronary heart disease events: MESA Multi-Ethnic Study of Atherosclerosis," J. Am. Coll. Cardiol., vol. 61, pp. 1231–1239, March 2013.
[87] M.J. Budoff, J.E. Hokanson, K. Nasir, L.J Shaw, G.L. Kinney, D. Chow, et al., "Progression of coronary artery calcium predicts all-cause mortality," JACC Cardiovasc. Imaging, vol. 3, pp. 1229–1236, December 2010.
[88] H. Gutte, J. Mortensen, C.V. Jensen, C.B. Johnbeck, P. von der Recke, C.L. Petersen et al., "Detection of pulmonary embolism with combined ventilation-perfusion SPECT and low-dose CT: Head-to-head comparison with multidetector CT angiography," J. Nucl. Med., vol. 50, pp. 1987–1992. December 2009.
[89] M. Tamura, Y. Yamada, T. Kawakami, M. Kataoka, Y. Iwabuchi, H. Sugiura, et al., "Diagnostic accuracy of lung subtraction iodine mapping CT for the evaluation of pulmonary perfusion in patients with chronic thromboembolic pulmonary hypertension: Correlation with perfusion SPECT–CT," Int. J. Cardiol., vol. 243, pp. 538–543, September 2017.
[90] T. Derlin, C. Kelting, K. Hueper, D. Weiberg, K. Meyer, K.M. Olsson, et al., "Quantitation of perfused lung volume using hybrid SPECT– CT allows refining the assessment of lung perfusion and estimating disease extent in chronic thromboembolic pulmonary hypertension," Clin. Nucl. Med., Vol. 43, pp. e170–e177, June 2018.
[91] J-P. Collart, V. Roelants, D. Vanpee, M. Lacrosse, J-P. Trigaux, L. Delaunois, et al., "Is a lung perfusion scan obtained by using single photon emission computed tomography able to improve the radionuclide diagnosis of pulmonary embolism?," Nucl. Med. Commun., vol. 23, pp. 1107–1113, November 2002.
[92] J. Kim, H-H. Lee, Y. Kang, T.K. Kim, S.W. Lee, Y. So, W.W. Lee, "Maximum standardised uptake value of quantitative bone SPECT– CT in patients with medial compartment osteoarthritis of the knee," Clin. Radiol., vol. 72, pp. 580–589, July 2017.
[93] M.W. Huellner, K. Strobel, "Clinical applications of SPECT–CT in imaging the extremities," Eur. J. Nucl. Med. Mol. Imaging, vol. 41(1), pp. S50–S58, 2014.
[94] L. Filippi, L. Uccioli, L. Giurato, O. Schillaci, "Diabetic foot infection: Usefulness of SPECT–CT for 99mTc-HMPAO-labeled leukocyte imaging," J. Nucl. Med., vol. 50, pp. 1042–1046, July 2009.
[95] R. Nakamoto, Y. Nakamoto, T. Ishimori, K. Togashi, "Clinical significance of quantitative 123I-MIBG SPECT–CT analysis of pheochromocytoma and paraganglioma," Clin. Nucl. Med., vol. 41, pp. e465–e472, November 2016.
[96] A. Jimenez-Heffernan, A. Ellmann, H. Sado, D. Huic, C. Bal, R. Parameswaran, et al., "Results of a prospective multicenter International Atomic Energy Agency sentinel node trial on the value of SPECT–CT over planar imaging in various malignancies," J. Nucl. Med., vol. 56, pp. 1338–1344, September 2015.
[97] K.E. Goffin, S. Joniau, P. Tenke, K. Slawin, E.A. Klein, N. Stambler, et al., "Phase 2 study of 99mTc-Trofolastat SPECT–CT to identify and localize prostate cancer in intermediate- and high-risk patients undergoing radical prostatectomy and extended pelvic LN dissection," J. Nucl. Med., vol. 58, pp. 1408–1413, September 2017.
[98] Y. Otomi, H. Otsuka, K. Terazawa, M. Yamanaka, Y. Obama, M. Arase, et al., "The diagnostic ability of SPECT–CT fusion imaging for gastrointestinal bleeding: A retrospective study," BMC Gastroenterol., vol. 18, pp. 183, December 2018.
[99] L. Livieratos, "Technical Pitfalls and Limitations of SPECT/CT," Semin. Nucl. Med., vol. 45(6), pp. 530-540, November 2015.
[100] R. Novelline, Squire's Fundamentals of Radiology, 5th ed., Harvard University Press. 1997, pp. 34–35.
[101] J. Siddique, D.S. Lauderdale, T.J. VanderWeele, J.D. Lantos, "Trends in prenatal ultrasound use in the

United States: 1995 to 2006," Med Care., vol. 47(11), pp. 1129-1135, November 2009.
[102] V.L. Piloni, L. Spazzafumo, "Sonography of the female pelvic floor:clinical indications and techniques," Pelviperineology, vol. 26(2), pp. 59–65, June 2007.
[103] F.J.F. Herth, R. Eberhardt, P. Vilmann, M. Krasnik, A. Ernst, (2006). "Real-time endobronchial ultrasound guided transbronchial needle aspiration for sampling mediastinal lymph nodes," Thorax, vol. 61(9), pp. 795–798, May 2006.
[104] A. Andreas, et al., Grainger & Allison's Diagnostic Radiology: A Textbook of Medical Imaging, 7th ed., vol. 2. Elsevier, 2021.
[105] M. Maybody, C. Stevenson, S.B. Solomon, "Overview of navigation systems in image-guided interventions," Tech. Vasc. Interv. Radiol., vol.16, pp. 136-143, September 2013.
[106] S.J. Ahn, J.M. Lee, W. Chang, S.M. Lee, H-J. Kang, H-K. Yang, J.K. Han, "Clinical Utility of Real-time Ultrasound-multimodality Fusion Guidance for Percutaneous Biopsy of Focal Liver Lesions," Eur. J. Radiol., vol. 103, pp. 76-83, June 2018.
[107] M.W. Lee, "Fusion imaging of real-time ultrasonography with CT or MRI for hepatic intervention," Ultrasonography, vol. 33(4), pp.227- 239, October 2014.
[107] G.Y. Yoon, H-J. Eom, W.J. Choi, E.Y. Chae, J.H. Cha, H.J. Shin, et al., "Feasibility of supine MRI (Magnetic Resonance Imaging)- navigated ultrasound in breast cancer patients," Asian J. Surg., vol. 43, pp. 787-794, August 2020.
[108] J. Rubenthaler, K.J. Paprottka, J. Marcon, M. Reiser, D.A. Clevert, "MRI and contrast enhanced ultrasound (CEUS) image fusion of renal lesions," Clin. Hemorheol. Microcirc., vol. 64(3), pp. 457–466, 2016.
[109] H. Zhang, G.Y. Chen, L. Xiao, X. Ma, L. Shi, T. Wang, et al., "Ultrasonic/CT image fusion guidance facilitating percutaneous catheter drainage in treatment of acute pancreatitis complicated with infected walled-off necrosis," Pancreatology, vol. 18(6), pp. 635–641, September 2018.
[110] M. Gulati, K.G. King, I.S. Gill, V. Pham, E. Grant, V.A. Duddalwar, "Contrast enhanced ultrasound (CEUS) of cystic and solid renal lesions: a review," Abdom. Imaging, vol. 40(6), pp. 1982–1996, August 2015.
[111] M.F. Meloni, A. Smolock, V. Cantisani, M. Bezzi, F. D'Ambrosio, M. Proiti, et al., "Contrast enhanced ultrasound in the evaluation and percutaneous treatment of hepatic and renal tumors," Eur. J. Radiol., vol. 84(9), pp. 1666–1674, September 2015.
[112] A. Helck, M. D'Anastasi, M. Notohamiprodjo, S. Thieme, W. Sommer, M. Reiser, D.A. Clevert, "Multimodality imaging using ultrasound image fusion in renal lesions," Clin. Hemorheol. Microcirc., vol. 50(1–2), pp. 79–89, 2012.
[113] L. Sandulescu, A. Saftoiu, D. Dumitresc, T. Ciurea, "Real-time contrast-enhanced and real-time virtual sonography in the assessment ofbenign liver lesions," J. Gastrointestin. Liver Dis., vol. 17, pp. 475-478, December 2008.
[114] F.L. Giesel, S. Delorme, R. Sibbel, H.U. Kauczor, M. Krix M., "Contrast-enhanced ultrasound for the characterization of incidental liver lesions - an economical evaluation in comparison with multi-phase computed tomography," Ultraschall Med., Vol. 30, pp. 259-268, June 2009.
[115] B. Stinn, J. Fornaro, D. Hibbeln, L. Desbiolles, S. Wildermuth, S. Leschka, "Evaluation of a Computed Tomography Coronary Angiography Scan - Advantages and Disadvantages of Different Post-processing Techniques," Eur. Cardio. Review, vol. 6(4), pp. 10, January2010.
[116] W.A. Kalender, W. Seissler, E. Klotz, P. Vock, "Spiral volumetric CT with single-breath-hold technique, continuous transport, and continuous scanner rotation," Radiology, vol. 176(1). pp. 181–183, July 1990.
[117] K. Nieman, B.J. Rensing, R.J. van Geuns, J. Vos, P.M. Pattynama, G.P. Krestin, et al., "Non-invasive coronary angiography with multislice spiral computed tomography: impact of heart rate," Heart, vol. 88(5), pp. 470–474, 2002.
[118] R.G. Hayter, J.T. Rhea, A. Small, F.S. Tafazoli, R.A. Novelline, "Suspected aortic dissection and other aortic disorders: multi-detector row CT in 373 cases in the emergency setting," Radiology, vol. 238 (3), pp. 841–852, March 2006.
[119] S. Yoshida, H. Akiba, M. Tamakawa, N. Yama, M. Hareyama, K. Morishita, T. Abe, "Thoracic involvement of type A aortic dissection and intramural hematoma: diagnostic accuracy--comparison of emergency helical CT and surgical findings," Radiology, vol. 228(2), pp. 430– 435, August 2003.
[120] P.D. Stein, S.E. Fowler, L.R. Goodman, A. Gottschalk, C.A. Hales, R.D. Hull, et al., "Multidetector computed tomography for acute pulmonary embolism," N. Engl. J. Med., vol. 354(22), pp.2317–2327, June 2006.
[121] H.M. Silvennoinen, S. Ikonen, L. Soinne, M. Railo, L. Valanne, "CT angiographic analysis of carotid artery stenosis: comparison of manual assessment, semiautomatic vessel analysis, and digital subtraction

angiography," Am. J. Neuroradiol., vol. 28(1), pp. 97–103, 2007.

[122] A.S. Agatston, W.R. Janowitz, F.J. Hildner, N.R. Zusmer, M. Viamonte Jr, R. Detrano, "Quantification of coronary artery calcium using ultrafast computed tomography," J. Am. Coll. Cardiol., vol. 15(4), pp. 827–832, March 1990.

[123] W.E. Saad, N. Saad, "Computer tomography for venous thromboembolic disease," Radiol. Clin. North Am., vol. 45(3), pp. 423–445, May 2007.

[124] U.D. Patil, A. Ragavan, Nadaraj, K. Murthy, R. Shankar, B. Bastani, S.H. Ballal, "Helical CT angiography in evaluation of live kidney donors," Nephrol. Dial. Transplant, vol. 16(9), pp. 1900–1904, September 2001.