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A REVIEW OF APPROACHES UTILIZED FOR MOLECULAR IMAGING TECHNIQUES

Shabber Hussain Y.B[1], Pakkirappa.K[2]

[1]M.Tech Scholar, [2] Assistant Professor,

Chiranjeevi Reddy Institute of Engineering & Technology, (India)

ABSTRACT

Medical Imaging is the technique or process of creating visual representations of the interior of a body for clinical analysis and medical intervention. It seeks to reveal internal structures, as well as to diagnose and treat disease. It also establishes a database of normal anatomy and physiology to make it possible to identify abnormalities. Medical imaging is often perceived to designate the set of techniques that non-invasively produce images of the internal aspect of the body. Positron Emission Tomography (PET) is a molecular Image technique that provides the information that how tissues and organs are functioning. It consists of feature of radio-nucleids that they decay via the emission of positrons. Kernel Density Estimation via Diffusion is considered to construct the histogram of PET images, which are allowed by smoothing. A novel segmentation frame work is proposed in this work to quantify Tuberculosis (TB) disease in small animals. The PET segmentation framework evaluates the robustness and accuracy yielded with computer-aided Quantification and visualization of abnormalities on PET-CT images of small animals infectious disease. The segmentation of diffuse will be well-suited by segmentation algorithm. Visualization of pathologies in three dimensions with PET functional information over laid for determining the optimal histology slice localization.

Keywords*: *Affinity Propagation, Interpolation, Molecular Imaging Techniques, Quantification, Rendering, Segmentation, Visualization.

I. INTRODUCTION

Molecular imaging techniques depend upon molecular mechanisms operative in vivo. This imaging technique encompasses the visualization, characterization and measurement of biological processes at the molecular and cellular levels in humans and other living systems. The techniques used include Positron Emission Tomography – Computed Tomography(PET-CT), nuclear medicine, Magnetic Resonance Imaging (MRI), Magnetic Resonance Spectroscopy (MRS), optical imaging and ultrasound. The selection of the imaging modality often is determined based on the temporal and spatial resolution, field of view, sensitivity of the imaging system, depth of the biological process, the molecular or cellular process to image, and the availability of suitable probes and labels than can be delivered to the imaging target.

II. MOLECULAR IMAGING MODALITIES

1.1 CT Imaging

Images in CT (spatial resolution of 50–100 μm) are obtained when component tissues differentially absorb x-rays passing through the body and are collected by high resolution CCD detectors. CT is essentially an anatomical imaging modality.

1.2 Nuclear Imaging

Nuclear imaging or also called as radionuclide scanning provides an effective diagnostic tools for the radiologists as it shows not only the structure of an organ but also the function of the organ. Nuclear imaging routine uses small amounts of radioactive material, or tracer for diagnostic purpose. Radioactive tracers used in nuclear imaging are in most cases is administered into a vein and some are given orally. After an administration of radioactive tracers, patient is required to rest for a certain period to allow distribution of radioactive tracer in the body. In the end, for imaging purpose, a specialized gamma camera is used to detect the radiation throughout the body.

Most commonly used techniques in nuclear imaging are positron emission tomography(PET) and single photon emission computed tomography (SPECT).

1.2.1 Positron Emission Tomography (PET)

Positron emission tomography or known as 'PET' is a rapidly developing nuclear imaging technique, with a clinical role that now exceeds almost 15 years. It is a quantitative tomographic imaging technique which produces cross-sectional images that are composites of volume elements. The signal intensity for PET images in each voxel is dependent upon the activity of radionuclide tagged with radioactive tracer which intravenously administered at the earlier stage before the scanning takes place. A scanner which usually called PET scanner employs a gamma photon coincidence detection system designed for oppositely directed annihilation photons emitted indirectly by the positron decay of PET radionu-clides.This logic allows acquisition of images that are quantitative three dimensional (3-D)maps of radio labeled tracers in tissue. The most commonly used PET radioactive tracer is the glucose derivative, 2-[18F]fluoro-2deoxy-D-glucose or commercially known as [18F]FDG, with numerous other tracers under development capable of highlighting a broad range of organ and tissue metabolic functions.

1.2.2 Single Photon Emission Computed Tomography (SPECT):

Similar to PET, single photon emission computed tomography (SPECT) also uses a radioactive tracer that is adminis-tered to the patient and a scanner to record data that a computer constructs into two or three dimensional images. SPECT technique employs a gamma camera that rotates around the patient to detect a radioactive tracer in the body. In contrast to PET this employs shorter half-lived tracers as opposed to the SPECT tracers. If a tumor is present, the antibodies will stick to it and thus allow for detection of timorous cells.

III. LITERATURESURVEY

3.1 Fundamentals of PET-CT Imaging

To obtain metabolic/functional information of tissues through PET scans, molecular imaging probes, such as18F-FDG and NaF, are used to interrogate specific targets such as cell surface receptors, enzymes, and

structural proteins. Given the low resolution in PET, the superior anatomic localization of a lesion is achieved by fusing the PET images to CT images such that the lesions identified on PET are then anatomically localized by analyzing the corresponding cross-sectional CT slices. To obtain anatomical and physiological information from tissues and organs, CT is usually used in small animal studies since it is the gold standard for clinical practice, particularly for lung studies. This dual-imaging modality approach provides a better understanding of the underlying disease by fusing both modalities into a single view.

3.2 What to Measure in CT?

Structural imaging methodologies (i.e., CT and MRI) provide detailed knowledge of anatomical structures such as their shape, numbers, dimensions, surfaces, geometric arrangements, locations, and relative positioning. Among these morphological measurements, the total lung volume and the fraction of lungs occupied by disease are common measurements used by clinicians and researchers to evaluate respiratory pathology. Abnormal CT imaging patterns (volume occupied by gas, tissue, and total number of alveoli) are also conventional measures frequently used by clinicians to evaluate disease state, severity, and progression of respiratory disorders; however, accurate, robust, and fast computation of these volumetric measurements require computer-aided lesion detection, image segmentation, and automatic quantification methods. Due to significant limitations in imaging (i.e., low specificity and similar appearances between normal and abnormal tissue), manual processing and computing the aforementioned metrics are still too time-consuming and difficult.

3.3 What to Measure in PET

PET imaging, as a functional imaging methodology, provides a way for making *in vivo* measurements of specific biochemical reactions. Conventionally, the standardized uptake value (SUV), a quantitative measure of tissue activity, is widely used in assessing PET images. SUV can be used either voxel-wise or over a region/volume; and particularly in the latter case, precise identification of the region of interest (delineation) plays a vital role in diagnostic decision systems. In addition, similar to the morphological metrics used in structural imaging methodologies, volume and area of activity regions, as well as its SUV-related indexes, are used to evaluate disease extent, characterization, and severity. In other words, the precise volume/surface information of uptake regions is needed due to two reasons: (a) total volume/surface occupied by radiotracer activity can be used independently to compare the fraction of the lung affected by the infection to the fraction of the abnormal anatomical structure having activity, because only a small percentage of the abnormal tissues (i.e., consolidation)may have high metabolic activity, depending on the disease pathology, and (b) the accurate computation of SUV-related evaluation metrics requires precise delineation of uptake regions from PET scans. Even small errors in delineation can distort SUV calculations by changing the margin of the uptake regions, and this can eventually affect the characterization of the disease, evaluation of response to therapy, and the therapy planning.

IV. METHODS

1. Kernel Density Estimation via Diffusion:

Generally, the histogram had been utilized to give a visual hint to the general state of the probability density capacity (pdf). The observed histogram of any image is the summation of histograms from numerous hidden

articles "covered up" in the observed histogram. Our proposed techniques expect that a top in the histogram relates to a moderately more homogeneous area in the image, it is likely that a top includes stand out class. The justification behind this supposition is that the histogram of items, in medical images, are ordinarily considered the summation of Gaussian curves, which infers a top compares to a homogeneous region in the image(s).

Because of the way of medical images, histograms have a tendency to be extremely boisterous with vast variability. This makes the optimal threshold choice for differentiating objects of interest troublesome. In the first place, the histogram of the image needs to be assessed in a hearty manner such that an expected histogram is less delicate to neighborhood local peculiarities in the image information. Second, the assessed histogram ought to be more delicate to the clustering of test values such that data clumping in certain regions and data sparseness in others–particularly the tails of the histogram–should be locally smoothed. To avoid all these problems and provide reliable signatures about objects within the images, herein we propose a framework for smoothing the histogram of PET images through diffusion-based KDE. KDE via diffusion deals well with boundary bias and are much more robust for small sample sizes, as compared to traditional KDE. We detail the steps of the KDE as follows:

Traditional KDE utilizes the Gaussian kernel density estimator, however it needs nearby adjustment; subsequently, it is sensitive to exceptions. To enhance neighborhood adjustment, a versatile KDE was made in view of the smoothing properties of linear diffusion processes. The kernel was seen as the transition density of a diffusion process, henceforth named as KDE via diffusion. For KDE, given N independent realizations, Xu∈{1,...,N }, the Gaussian kernel density estimator is customarily characterized as

$G(x,t) = x,X_u;t)$, x R;……(1)

Where

$(x,X_u;t) =$

is a Gaussian pdfat scale *t*, usually referred to as the bandwidth. An improved kernel via diffusion process was constructed by solving the following diffusion equation with the Neumann boundary condition

$g^{diff}(x,X_u;t) =]$...(2)

After KDE via diffusion, an exponential smoothing was connected to further decrease the noise; the crucial state of the histogram was saved all through this methodology. Data clumping and sparseness in the first histogram were removed, and any noise staying after KDE via diffusion was diminished impressively while as yet safeguarding the state of the pdf. The resultant histogram can now serve as a capable stage for the segmentation of the objects, the length of a powerful clustering methodology can place the valleys in the histogram.

V AFFINTY PROPAGATION

Clustering data by recognizing a subset of agent illustrations is essential for processing signals and identifying examples in data. Such "exemplars" can be found by arbitrarily picking a starting subset of information focuses and afterward iteratively refining it, however this functions admirably just if introductory decision is near to a decent arrangement. We contrived a strategy called "affinity propagation," which takes as info measures of likeness between sets of data focuses. Real valued messages are traded between data points until a high-quality set of models and comparing clusters continuously rises. AP is valuable on the grounds that it is effective,

insensitive to initialization, and produces groups at a low cluster rate. Essentially, AP partition the data taking into account the augmentation of the aggregate of likenesses between data points such that each one part is connected with its model (in particular its most prototypical data point. Dissimilar to other model based grouping systems, for example, k-centers clustering and k-means, Hence execution of AP does not depend on a "good" initial cluster/group. Rather, AP acquires exact arrangements by approximating the NP-hard issues in a significantly more productive and precise way. AP can utilize arbitrarily complex affinity functions since it doesn't have to inquiry or incorporate over a parameter space.

5.1 Background on AP

AP at first expect all data points(i.e., voxels) as models and refines them down iteratively by passing two "messages" between all focuses: ***responsibility*** and ***availability***. Messages are scalar values such that each one point makes an impression on all different focuses, showing to what degree each of alternate focuses is suitable to be its model. The primary message is called ***responsibility***, demonstrated by r(i, k), and is the way mindful point k is to be the model of point i. In ***availability***, indicated by a(i, k), each one point makes an impression on all different guides and demonstrates toward what degree the point itself is accessible for serving as a model. The ***responsibility*** and ***availability*** were defined in Frey and Dueck's original paper as

r(i,k)s(i,k) –

a(i,k)min{0,r(k,k)+}

where s(i, k) is the likeness between point i and point k, and k is all different focuses aside from i and k. Point k is not mindful to be the model for point i if there is an alternate point that portrays i better than k; subsequently, the most extreme quality for responsibility is arrived at. The whole of availabilities and responsibilities at any emphasis gives the current models and orders. At first, all focuses are thought to be conceivable models, which ensure all inclusive ideal arrangements. AP uses max-product belief propagation to acquire great models through maximizing the objective function $\text{argmax}_k[a(i, k) + r(i, k)]$.

5.2 Novel Affinity Metric Construction

We developed a novel affinity metric to model the relationship between all data points utilizing the precisely evaluated histogram with the principle supposition that closer force qualities are more prone to have a place with the same tissue class. As such, the information is made out of focuses lying on a few unique straight spaces; however this data is covered up in the image histogram, given that the histogram is deliberately evaluated in the past step. This segmentation processes recovers these subspaces and relegates data points to their individual subspaces. Simultaneously, likenesses among the voxels assume an indispensable part. Most clustering routines are centered around utilizing either Euclidean or Gaussian separation capacities to focus the likeness between data points. Such a separation is direct in execution; be that as it may, it drops the shape data of the hopeful circulation. Since both probability- and intensity-based differences of any two voxels convey profitable data on the determination of appropriate threshold determination, we propose to combine these two limitations inside with another affinity model. These constrains can basically be joined with weight parameters n and m as:

s(i,j) = -(|^n + ||^m)$^{1/2}$

Where s is the closeness capacity, d_ij^G is the registered geodesic separation between point i and j along the pdf of the histogram, and d_ij^xis the Euclidean separation between point i and j along x-axis.

The geodesic separation or distance between the two information focuses in the image naturally reflects the similitude because of the gradient information (i.e., voxel intensity differences). It likewise fuses extra probabilistic data through upholding neighborhood groupings for specific locales to have the same mark

= where j > i.

Once the similarity function is computed for all points, AP tries to maximize the energy function

E(c) = c_i) + ….(3)

An exemplar-consistency constraint δk (**c**) can be defined as

.(4)

This limitation authorizes substantial design by presenting a huge punishment if some information point i has picked k as its model without k having been effectively named as a model. In the wake of embeddings a novel affinity function definition into the vitality imperative to be expanded inside the AP calculation, we got the following objective function:

E(c) = -

+ ...(5)

All voxels are marked in light of the advancement of the target capacity characterized previously. Since the upgrade rules for AP compare to altered point recursions for minimizing a Bethe free-energy approximation, AP is effectively inferred as an occurrence of the max-entirety calculation in a factor graph portraying the requirements on the marks and the energy function.

VI. PLAN OF ACTION

1. Framework:

It is followed as,

- In this work PET and CT images of rabbit lungs are considered for investigation.
- PET and CT Images are acquired through database.
- Manual adjustments should be carried on the images when they are necessary.
- A GUI is used for Quantification analysis
- The Quantification analysis is to be carried out on CT and PET images such as
- Visualization
- ROI Segmentation
- 3D Rendering.
- Auto Reporting
- Quantification

VII. RESULT & ANALYSIS

In this project PET and CT lung images of a rabbit lung are considered as inputs for Quantification. A GUI framework called QAV-PET (Courtesy: QAV: PET by Foster and Bagci of NIH)is used.

QAV-PET analysis allows easy, intuitive and efficient visualization and quantification of multi modal medical images. This is carried out in different steps such as Visualization, Interpolation, segmentation, Rendering, auto-reporting and Quantification

The results for each step are given below:

7.1 Visualization

Functional (PET image) and Anatomical (CT image) images of rabbit are read into the framework. These images can be shown in three categories:

a) Fused image

b) Functional image

c) Anatomical image

The Figure 1(a), 1(b) 1, (c) shows the fused image(which is formed by fusion of pet and ct images), functional image(pet image) and anatomical image(ct image).

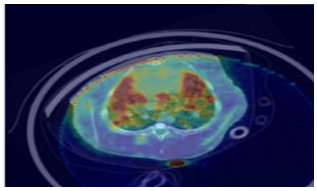

Fig 1(a): Fused Image

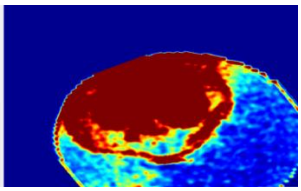

Fig1 (b): Functional Image

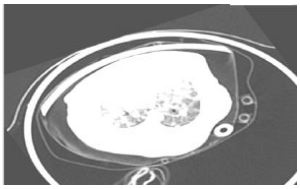

Fig1(c): Anatomical Image

7.2 ROI Definition

Region of Interest (ROI) is created to focus on specified area of lung mask to analyze the situation of image and quantify the image.

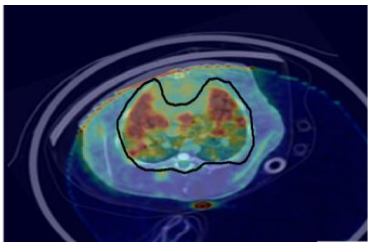

Fig2: ROI Defined in Fused Image

7.3 Interpolation

Once the ROI is created, the image is subjected to interpolation. This is shown in below figure.5. Interpolation is used for the calculation of the value of a function between the values already known. Here Interpolation is used to measure the values of already created ROI regions and this gives us the accurate measure.

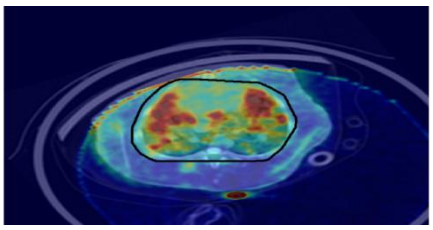

Figure 3: Interpolated Fused Image

7.4 Segmentation

Once the ROI is created, the segmentation process is carried out using Affinity Propagation Image segmentation. As a process the lesions formed due to Tuberculosis are segmented as shown in figure.

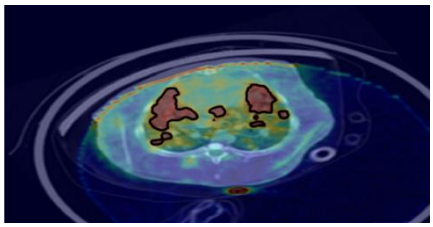

Figure 4: Image segmentation

7.5 Opacity

The process shown below in figure is used for changing the opacity between Functional and Anatomical images. Threshold is adjusted in order to remove the background areas for improved visibility of underlying anatomical image.

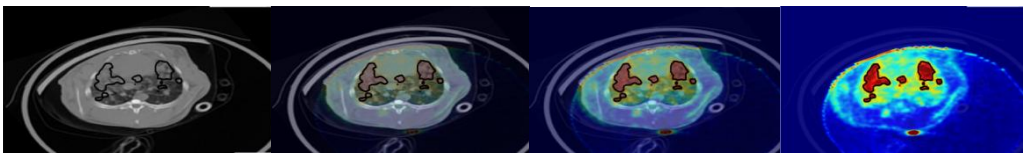

Fig 5 (a): 0 **Fig 5(b): 0.25** **Fig5(c): 0.50** **Fig5 (d):1**

Figure 5(a), (b), (c), (d): Representation of varying the opacity between PET and CT on the segmentations

- The opacity ranges from 0, fully anatomical (CT) information to 1, fully functional (PET) information.

7.6 Rendering

The Rendering process is done in 3D-visualization. The Rendering is carried out for both lung mask and AP segmented Image. The figure 9 which have the lung mask rendering shows the affected area in red color indicated by a color bar adjacent to image. The color bar represents the intensity of damage happened to the lungs.

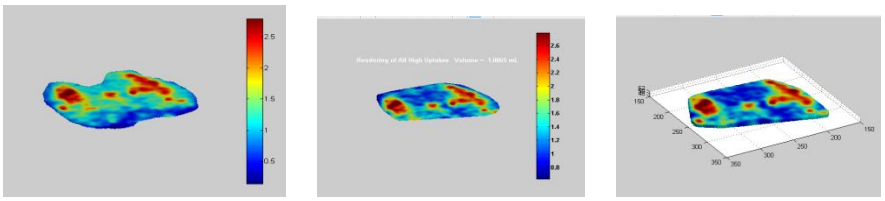

Fig6 (a) **Fig 6(b)** **Fig 6(c)**

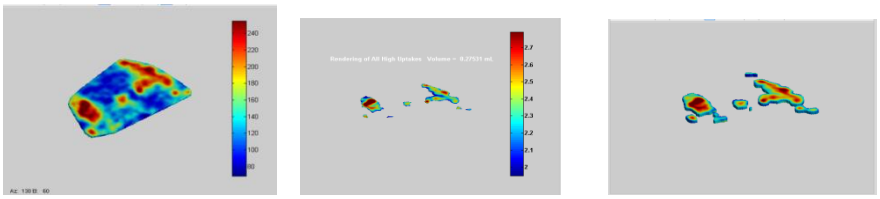

Fig 6(d) **Fig6(e)** **Fig6(f)**

Figure 6(a), (b), (c), (d), (e),(f),(g) shows rendering of lung mask, lesion rendering and interpolated image.

7.7 Auto-Reporting

It produces a report which includes the most important information needed for quantifying the disease and high uptake value regions. The report includes both Qualitative and Quantitative data. Quantitative data includes

SUV_{mean}, SUV_{max} and volume of current label and the location of SUV_{max} on axial, sagittal and coronal view of PET Image.

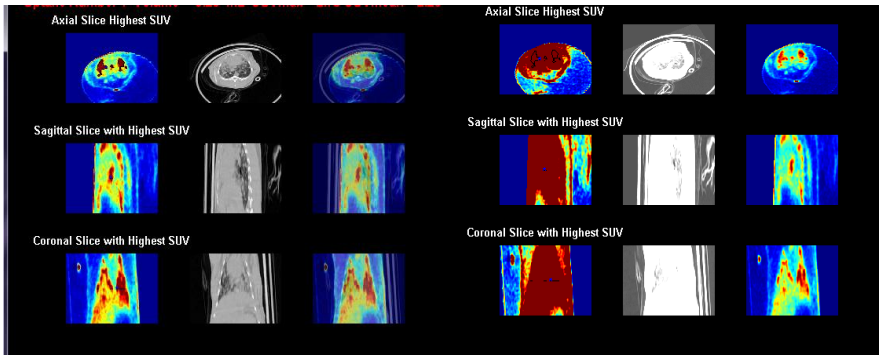

Fig7(a) **Fig7(b)**

Figure: These images represent the reporting for AP segmented images for different opacity values.

- After the Reporting process, we acquire the Qualitative metrics and they are tabulated below :

7.8 Tabular Column

VOLUME	SUV_{max}	SUV_{mean}
0.27400	2.7930	2.2540
0.27700	2.7930	2.2621
1.64600	2.7930	1.2930
1.68300	2.7930	1.2821

Table: Qualitative Metrics of Fused Images

	Range	Type of lesion
SUV Value	0 < 2 < 2.5	Benign
	> 2.5	Malignant

Table: Lesion Identification

These values represent the uptake values of lesions.

The report includes both quantitative and qualitative data. The quantitative data includes the SUVmax, SUV mean, and the volume of the current label, and, additionally, it provides the location of the SUVmax on the axial, sagittal, and coronal view of the PET image, the CT image and the PET-CT fused image All of this information allows the user to get a quick view of the highest uptake lesion, which is important for disease severity quantification.

VIII. CONCLUSION

This can be used for quantification and visualization of abnormalities on PET-CT images of small animal infectious disease studies. The segmentation algorithm that is implemented has been shown to be particularly well-suited for the segmentation of diffuse, multi-focal PET radiotracer uptakes that are commonly seen with

infectious diseases. It is used for visualization of the pathologies in three dimensions with the PET functional information overlaid for determining the optimal histology and slice localization. When taking histology slices from a diseased organ, this three dimensional view of the distribution of the disease will aid researchers in determining the best location to take the histology slices from for the best characterization. It includes a framework for quantification which can be easily manipulated and tuned to fit any medical imaging application..

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