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Analysis and Detection of Diabetic Nephropathy based on basement membranes of capillaries in kidney

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Abstract: Diabetic Nephropathy(DN) is one of fast growing disease. The survey tells that 41312 peoples are under treatment of end stage renal disease in 2001.$22.8 are spend to take care of them.15% national health budget is spend on Diabetic Nephropathy if it at last stage that end stage renal disease(ESRD) then it is serious so the proposed research will helpful because here we are trying to detect DN at early stage by analyzing capillaries basement membrane and implementation will be done in Python a new approach for image processing as this research will contain image data of various DN patients.

Keywords: DN, Glomeruli, ESRD, Nephron

I. INTRODUCTION OF RESEARCH AREA

Medical imaging:-It is technique used in early 1970's which is mainly concerns with capture of images or visual representation of internal organ of human body, enhancement of images for tomography clinical analysis and medical intervention. Here images captured are via advance sensors and computer technology. Biomedical image processing uses either technologies Computerized tomography(CT), radioactive pharmaceutical, such as Positron emission tomography(PET), sound (ultrasound), through transmission electron microscope(TEM) or scanning electron microscope(SEM),magnetic resonance imaging (MRI),light(OCT) 3-D modeling technique i.e. computer generated images etc. In Computerized tomography(CT) ring of detectors encircles an object(or patient) and X-ray source concentric with the detector ring, rotates about the object and are collected at the opposite end by the corresponding detectors in the ring. As source rotated, this process is repeated. Now a day's physicians can watch real-time X-rays on monitor using technique X-ray fluoroscopy.

PET is nuclear medicine, functional imaging technique that produces three dimensional image of functional process in the body. In nuclear medicine radioactive material taken inside body or orally. In functional imaging metabolic changes like blood flow are detected and measured. PET scans enable researchers to compare, for example, brain activity during periods of depression based on the chemical activity in the brain. Optical molecular imaging can used to image human cells and molecules. contrast or imaging agents that attach to specific molecules, disease processing such as cancer, can be spotted before diagnose in pathologically.

Optical coherence tomography(OCT) is newer form of CT being used in research, which construct images from light that is transmitted and scattered through body.

In MRI imaging radio waves are used. Here patient is places in powerful magnet and passes radio waves through body in short pulses. Each pulse cause reverse pulse from patient's tissues. The location of these signals and strength are determined by a computer, which produces two dimensional picture of section of patient.MRI can produce picture in any plane.3-D.Application of MRI imaging ranging from image of star of pulsar to human brain activity, MRI of human knee, Kidney, heart, spine, internal organs and tissue.

In Acoustic imaging (using sound) also called ultrasound imaging finds application in geological exploration for oil and mineral detection, in medicine etc. For image acquisition over land, strength and speed of returning sound waves are captured by computer. In geological application low end of sound spectrum(hundreds of Hz.)is used while ultrasound imaging uses(millions of Hz.).In marine acquisition 3-D image model can be used to trap oil and or Gas.

Ultrasound imaging is best to determine the health of unborn baby for their development. Here ultrasound system transmit high frequency sound pulses into human body and hit boundary between tissues(e.g. (between fluid and soft tissue, soft tissue and bone) and reflected back to receiver i.e. ultrasound probe. Waves picked are relayed on computer. The machine calculates the distance from

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probe to the tissue or organ boundaries using speed of sound(1540m/s) and time of each echo's return. The system displays the distances and intensities of the echoes on screen forming a two dimensional image. Ultrasound imaging can also used in Thyroid detection, images of muscle layers. Depending on imaging technique and what diagnosis being carried, image processing and analysis can be used to determine the diameter, volume and vasculature(arrangement of blood vessels in organ) of tumor or organ, flow parameter or other fluids and microscopic changes which may lead major disorders in future.

II. DIABETIC NEPHROPATHY

Diabetes:-Carbohydrates that we eat, get converted into useful energy, but instead of becoming energy if Carbohydrates or sugar are directly enters into blood unprocessed then it increases level of sugar in blood. It causes high blood sugar, which damages nerves and blood vessels, this condition in body is called Diabetes. It has two types Type-I and Type-II, both can't allow blood sugar to turn into energy . Normally, eating sugar causes an organ called the pancreas to release the hormone insulin. This insulin turns the sugar into energy. Then it signals cells to store this energy for use. In type I diabetes, the pancreas doesn't make any insulin. It leaves the body with no way to process sugar. In type II diabetes, the pancreas makes insulin, signals cells to store the energy, but the cells do not respond. Because the cells resist the insulin, type II diabetics are said to be "insulin resistant." Of the two types of diabetes, type II is much more common. Ideal blood pressure is below 120/80. High blood sugar is is 140/80 [8].

Kidney:-Kidney cause blood to carries oxygen and nutrients to your organs and tissues and carries waste products out of body. Functions of Kidney i)balance of water ii) controls activity of making oxygen iii)controls on making red blood cells and acidic nature of blood ,blood pressure iv)filter your blood and throw waste product through urine via urinary bladder. The fundamental unit of kidney is nephron as in fig[1].

Diabetes causes injury to small blood vessels throughout the body. Small blood vessels in the kidney are often involved. This causes protein to spill into the urine. One type of protein, albumin, is detected in the urine even during early kidney disease. If it continues then disease develops in kidney blood vessels, the kidneys cannot function normally and kidney failure develops as in figure [4].

Diabetic Glomerular Disease:-The tiny structures that do the work in your kidneys are called nephrons. Each nephron has 3 parts: 1) a small blood vessel that brings in unfiltered blood 2) glomerulus that filters the blood 3) a small blood vessel that returns filtered blood to the body. The earliest detectable change in glomeruli is thickening of the thin basement membrane. This is part of the filter that separates the blood from the urine. Damage to this membrane causes proteins to leak from the blood into the urine. Damage to the membrane can be identified in a kidney using an electron microscope to show thickening of the membrane as in fig[3][4].

Diabetic nephropathy :-

is damage to human kidneys caused by diabetes. or Diabetic nephropathy nodular OR diabetic glomerulosclerosis is a progressive disease caused by angiopathy of capillaries in Kidney glomeruli as in fig[1]. Angiopathy is disease of arteries veins and capillaries. There are two types of angiopathy: microangiopathy and macro angiopathy. In microangiopathy, the walls of small blood vessels become so thick and weak that they bleed, leak protein, and slow the flow of blood. For example, diabetics may develop micro angiopathy with thickening of capillaries in many areas, including the eye.[9].It is micro vascular disease of the glomerulus that affects patients with Type I and Type2 diabetes[3].as in fig[5][6].

Related work and Contribution :-

There have been many Literatures showing significance of biomedical image processing which focused on Diabetic nephropathy. Biomedical image processing is very broad field, which covers signal gathering and image forming techniques and clinical imaging devices such as radiological imaging which includes radiography, ultrasound, thermograph, nuclear medicine and functional imaging[2].Here X-ray computed tomography (X-ray CT) is excellent. for static anatomical images. It also shows that nuclear imaging is best for metabolism, Heart imaging. It reflects special biomedical image processing languages and packages. Here white cell analyzer is developed. Large efforts have been taken for automation of cancer detection. But work need to be done in automation histology[2].

Diabetic nephropathy is a micro vascular disease of the glomerulus that affects patients with type 1 and 2 diabetes. Pathological changes in the glomerulus include diffuse thickening of the GBM accompanied by steady decline of the glomerular filtration rate. The pathogenesis of this alteration is poorly understood. It correlates with proteinuria and may be related to abnormal podocyte function.[4]. Kidney is part of urinary system which excretes waste products and maintains balance of water and electrolytes in the blood. In Kidney all functions perform by unit called nephron which contains renal corpuscle and renal tubules. The renal corpuscle includes Bowman's capsule and glomerulus where the filtering of selected blood components occurs[3] croosref [1][2]. The filtering action within glomerular is performed by endothelial cells,the glomerular basement (GBM).The typical width of GBM is in range of 300-350nm [3] crossref [1][2].In this paper methods for semiautomatic and user-guided methods are proposed, using split and merge (SAM) algorithm.[3] crossref. [1], morphological image processing [3] crossref. [17] and skeletonization [3]crossref. [16][18][19] and statistical analysis of width

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of GBM [3]crossref.[15][20].These methods are applied for data of five patients only and GBM width is analyzed one with thin GBM,one with normal GBM,two with thick GBM.Above mentioned methods and algorithms are applied and GBM width is calculated and statistically using cumulative histogram,mean ,mode and deviation is observed[3].

Here 34TEM images of renal biopsy samples are taken. Image processing methods such as edge detection, morphological image processing, contour modeling, skeletonization are used, statistical analysis of width of GBM is done and distribution of GBMS with thin, normal, abnormally variable and abnormally thick GBM width demonstrate[4].It is suggested that Additional work is required on the development of improved edge detection algorithms to minimize the manual steps of wall construction in the proposed procedure[4].

Here patients with proteinuria and isolated ultra-structural diffuse thickening of the glomerular capillary basement were studied focusing on possibility of diabetes. It is observed that the level of proteinuria and hematuria were similar in patients with isolated thick basement membrane and with diabetes. It is not co-related with age, smoking body weight, and hypertension. However blood tests are positive for diabetes in 20% of patients at biopsy, in 40% at 6 months and 70% at 24 months follows up while seven patients shows no sign of diabetes on follow-up. So patients with proteinuria and isolated thick membrane must be differentiated from minimal change nephropathy from theoretic implications for managing early diabetes[5].

Diabetic Kidney disease(DKD) affect many Type I diabetes patient. There is no cure if it is diagnose but early treatment of sub-clinically stage that is by diagnosing high urinary albumin execration rate(AER),it can be avoided [6].

Pathological classification exist for several renal disease, including IgA Nephropathy, focal segmental glomerulosclerosis and lupus nephritis. Biopsies diagnosed as diabetes nephropathy are classified as class-I glomerular basement membrane thickening, class-II mesangial expansion, class-III nodular sclerosis (Kimmelstiel-wilsenlesions), class-IV advanced diabetic glomerulosclerosis[7].Here it is put that upper limit of normal GBM thickness in adult is 520nm and 471nm in female it gives various directions to detect diabetic nephropathy using advance computer technology[7].Here it is discovered that if GBM>395nm in female and 430nm in male individuals of 9 years and older by electron microscopy(EM)[7].

Objective:-

From the enriched literature available till date shows that Diabetic nephropathy is damage to human kidney. The Objective of proposed research is to detect diabetic nephropathy based on membrane size of capillaries or nodules in kidney.

Methodology:-

Image acquisition:- In medical imaging various sources of images are available like CT(Computed Tomography), MRI (Magnetic Resonance imaging), PET(Positron Emission Tomography) or TEM(Transmission electron microscopy)etc. In Mat-lab software resolution, dimensions as per requirement cab be changed or clinically proven live data of patients from pathology cab be used later.

Image segmentation and analysis:-Image processing methods like segmentation using split and merge method to separate the capillaries boundaries, as per ref[3] or different edge detection methods can be used, statically results will calculated. All work will be implemented in Mat-lab or python software.

Features of Python:-

1) Python is free and open.
2) Object-oriented programming (OOP) in Python is simple and superior, and offers power/flexibility comparable to that of C++.
3) Unlike Matlab, which uses end statements as closures (i.e., to indicate the end of a block), Python determines the scope of a block based on its indentation. This forces Python programmers to indent code blocks, which is good practice anyway. (And, unlike programmers working in most other languages, no Python programmer ever wastes time hunting for a missing end statement).
4) Python code is more compact and readable than Matlab code.
5) Python offers more choice in graphics packages and toolsets.
6) Python is high level, easy to learn, and fast to develop.

features of Python used for bio Medical Image Processing

1) In Research ,Scientific computing is essential for developing mathematical models and quantitative analysis for putting final result.
2) Python having two modules **scipy** and **pylab** serve for scientific computing and can be imported as from scipy import * from pylab import *
3) Pylab offers good quality GUIs in addition to publication quality plots.
4) There are two modules for image processing .The first is Python imaging library**(PIL)** and package in scipy called **ndimage**. Both contain module for image acquistion, processing and writing. In medical imaging there is reading, filtering, classifying, segmenting and interpreting medical images such as CT image, MRI image, retinal image, angiograms .
5) Both ndimage and PIL can be used with minimum amount of coding for processing medical images as

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both support variety of image formats like .jpg .png, .pgm etc

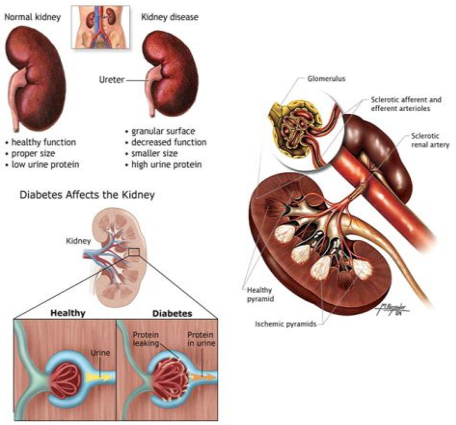
Scope of study:-

Diabetic nephropathy(DM) affecting 5-10% of the world populations and rising rapidly in young generation including children and adults[ref].In last decade DN is leading cause of end stage renal disease(ESRD).Type2 diabetic patients are mostly under renal dialysis treatment[5].Diabetes mellitus is chronic disease that affect 366 million people worldwide that is 6.4% of adult population and it is rise to 552 million by 2030[5] crossref[1] so diabetes care may include 15% of national health budgets[5] crossref[2].In 2008 1.3 million death were associated with diabetes[5] crossref [3].Diabetes results in both micro vascular and macro vascular complications, diabetic kidney disease is one of serious with significant impact on mortality and quality of life[5] crossref[4].Using proposed research diabetic nephropathy can be detected earlier due to analysis of capillaries in kidney, then this research will helpful for saving 15% of national health budget, improve mortality rate, can lower death rate. So this research will helpful to improve quality of life.

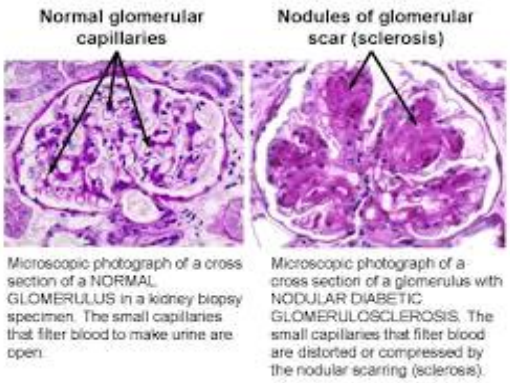
Tentative chapter schemes included in PHD thesis

1) Introduction:-In this chapter a brief description to introduce the area of the proposed research work will included.
2) Literature Review: In this chapter review of the relevant and up to-date literature like journals, conferences, seminars, technical reports, forum, reference books etc which reflect the work done previously in the area of proposed research so that to plan further research effectively. The information given will be supported by references.
3) Design of the system:-In this chapter graphs, figures, images or snapshot taken at the time of implementation are given. Methodology:-In this chapter information of data collection methods, data analysis methods, implementation tool or software used and statistical tools used in proposed research are given.
4) Experiment analysis and result: Here result of proposed work statistically computed will be shown in tabular or graphical format.
5) Conclusion and future work: In this chapter based on chapter 5, brief description of conclusion and finding of proposed research will be given. It may contain limitation and future scope.

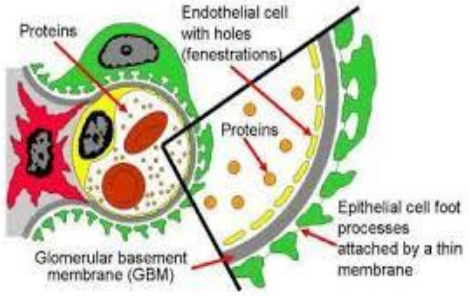
Figures and snapshots



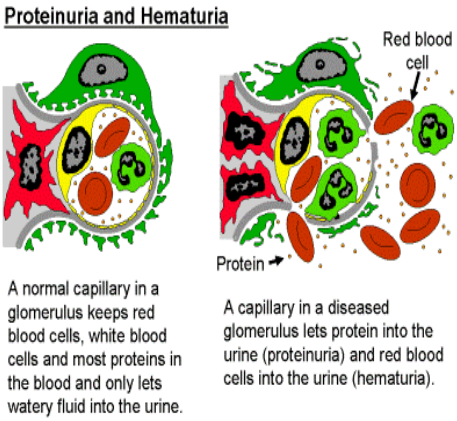
fig[1]



fig[2]



Fig[3]



fig[4]

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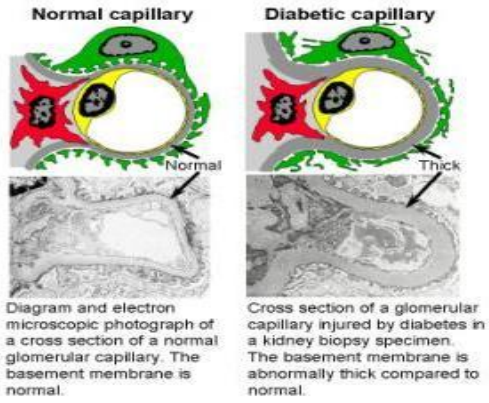
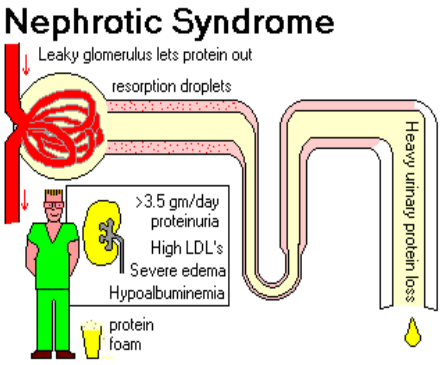


fig[5]



fig[6]

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BIOGRAPHY

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