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Anisotropic Median Diffusion Based Molecular Images Denoising For Detection of Breast Cancer

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Abstract: *Presently breast cancer detection is a very important role for world young women to save and extended to the life. The new proposed technology is anisotropic median diffusion filter for denoising low-signal-to-noise molecular images. This filter, which incorporates a median filter into the diffusion steps, is called an anisotropic median-diffusion filter. This hybrid filter achieved much better noise suppression and reduced Gaussian noise, spikes compared with the anisotropic diffusion filter when it was tested on an image created based on a molecular image model. We prepare an algorithm to detect of Brest Cancer early with molecular imaging ADME uses to the (i.e) uses of the density of molecular in this study we develop a mathematical model for ADME and together with the breast cancer molecular image and analysis that performance.The anisotropic median-diffusion filter also achieved good smoothen in the inner area and outer area boundary of the molecular images. In this filter particularly useful for nonlinear molecular images.*

Keywords: AMDF, Denoising, Breast Cancer, Molecular Images.

INTRODUCTION

Breast cancer is a malignant cell growth in the breast. If left untreated, cancer spreads to other areas of the body. Breast cancer is cancer that develops from breast tissue. Breast cancer usually starts off in the inner lining of milk ducts or the lobules that supply them with milk. A malignant tumor can spread to other parts of the body. A breast cancer that started off in the lobules is known as lobular carcinoma, while one that developed from the ducts is called ductal carcinoma. The vast majority of breast cancer cases occur in females. This article focuses on breast cancer in women. We also have an article about male breast cancer.

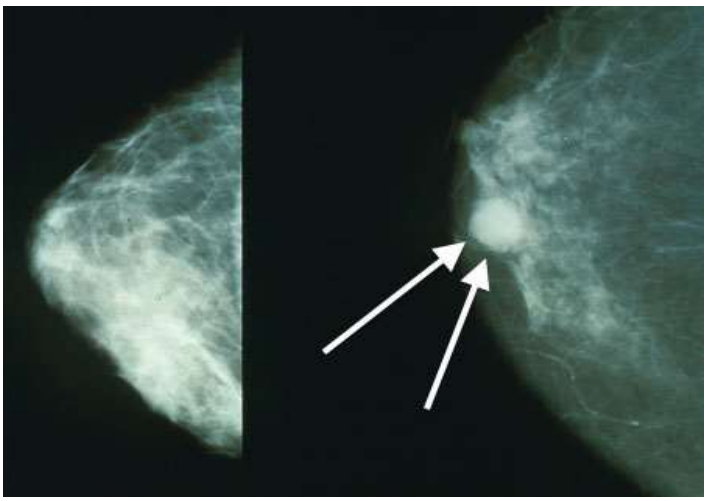


Fig 1 Breast cancer

BREAST CANCER IN INDIA

In India, we are now witnessing more and more numbers of patients being diagnosed with breast cancer to be in the younger age groups (in their thirties and forties). The horizontal line lowers down represents the age groups: 20 to 30 years, 30 to 40 yrs and so on. And the vertical line represents the percentage of cases. The blue colour represents the incidence 25 years back, and maroon colour represents the situation today. 25 years back, out of every 100 breast cancer patients, 2% were in 20 to 30 years age group, 7% were in 30 to 40 and so on. 69% of the patients were above 50 years of age. Presently, 4% are in 20 to 30 yrs age group, 16% are in 30 to 40, 28% are in 40 to 50 age group. So, almost 48% patients are below 50. Increasing numbers of patients are in the 25 to 40 years of age, and this definitely is a very disturbing trend. Of course, one particular reason for higher numbers of younger patients is our population pyramid, which is broad at the base and middle and narrow at the top, which means that we have a huge population in the younger age group and much lesser in older age group.

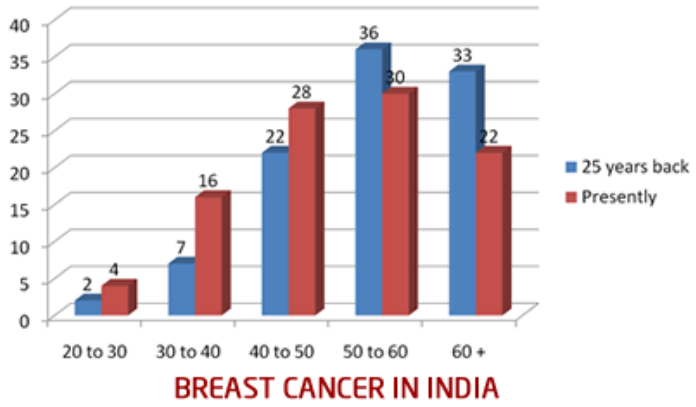


Fig 1.2 Breast cancer in India

CAUSES OF BREAST CANCER

Experts are not definitively sure what causes breast cancer. It is hard to say why one person develops the disease while another does not. We know that some risk factors can impact on a woman's likelihood of developing breast cancer. These are:

Getting older

The older a woman gets, the higher is her risk of developing breast cancer; age is a risk factor. Over 80% of all female breast cancers occur among women aged 50+ years (after the menopause.

Genetics

Women who have a close relative who has/had breast or ovarian cancer are more likely to develop breast cancer. If two close family members develop the disease, it does not necessarily mean they shared the genes that make them more vulnerable, because breast cancer is a relatively common cancer.

Having had certain types of breast lumps

Women who have had some types of benign (non-cancerous) breast lumps are more likely to develop cancer later on. Examples include atypical ductal hyperplasia or lobular carcinoma in situ.

Estrogen exposure

Women who started having period's earlier or entered menopause later than usual have a higher risk of developing breast cancer. This is because their bodies have been exposed to estrogen for longer. Estrogen exposure begins when periods start and drops dramatically during the menopause.

Obesity

Post-menopausal obese and overweight women may have a higher risk of developing breast cancer. Experts say that there are higher levels of estrogen in obese menopausal women, which may be the cause of the higher risk.

Alcohol consumption

The more alcohol a woman regularly drinks, the higher her risk of developing breast cancer is. The Mayo Clinic says that if a woman wants to drink, she should not exceed one alcoholic beverage per day.

Radiation exposure

Undergoing X-rays and CT scans may raise a woman's risk of developing breast cancer slightly. Scientists at the Memorial Sloan-Kettering Cancer Center found that women who had been treated with radiation to the chest for a childhood cancer have a higher risk of developing breast cancer.

HRT (hormone replacement therapy)

Both forms, combined and estrogen-only HRT therapies may increase a woman's risk of developing breast cancer slightly. Combined HRT causes a higher risk.

Certain jobs

French researchers found that women who worked at night prior to a first pregnancy had a higher risk of eventually developing breast cancer.

Canadian researchers found that certain jobs, especially those that bring the human body into contact with possible carcinogens and endocrine disruptors are linked to a higher risk of developing breast cancer. Examples include bar/gambling, automotive plastics manufacturing, metal-working, food canning, and agriculture. They reported their findings in the November 2012 issue of Environmental Health.

SIGNS & SYMPTOMS

The earliest sign of breast cancer is an abnormality that shows up on a mammogram before it can be felt by the woman or her health care provider. When breast cancer has grown to the point where physical signs and symptoms exist, a breast lump, or tenderness; skin irritation or dimpling; and nipple discharge and/or pain, scaliness, ulceration, or retraction may be noticed. Breast pain is commonly due to benign conditions and is not usually the first symptom of breast cancer.

MOLECULAR IMAGE IN BREAST CANCER DETECTION

Molecular imaging has become part of standard care for many types of cancer. By allowing scientists and physicians to see what is happening in the body at a cellular level, molecular imaging provides unique information to assist in the detection, diagnosis, evaluation, treatment, and management of cancer.

MOLECULAR IMAGING

Molecular imaging is a type of medical imaging that provides detailed pictures of what is happening inside the body at the molecular and cellular level. Where other diagnostic imaging procedures—such as x-rays, computed tomography (CT) and ultrasound—predominantly offer anatomical pictures, molecular imaging allows physicians to see how the body is functioning and to measure its chemical and biological processes.

WORKING OF MOLECULAR IMAGE

When disease occurs, the biochemical activity of cells begins to change. For example, cancer cells multiply at a much faster rate and are more active than normal cells. Brain cells affected by dementia consume less energy than normal brain cells. Heart cells deprived of adequate blood flow begin to die.

As the disease progresses, this abnormal cellular activity begins to affect body tissue and structures, causing anatomical changes that may be seen on CT or MRI scans. For example, cancer cells may form a mass or tumor. With the loss of brain cells, overall brain volume may decrease or affected parts of the brain may appear different in density than the normal areas. Similarly, the heart muscle cells that are affected stop contracting and the overall heart function deteriorates.

Molecular imaging excels at detecting the cellular changes that occur early in the course of the disease, often well before structural changes can be seen on CT and MR images.

Most molecular imaging procedures involve an imaging device and an imaging agent, or probe. A variety of imaging agents are used to visualize cellular activity, such as the chemical processes involved in metabolism, oxygen use or blood flow. In nuclear medicine, which is a branch of molecular imaging, the imaging agent is a radiotracer, a compound that includes a radioactive atom, or isotope. Other molecular imaging modalities, such as optical imaging and molecular ultrasound, use a variety of different agents. Magnetic resonance (MR) spectroscopy is able to measure chemical levels in the body, without the use of an imaging agent.

Once the imaging agent is introduced into the body, it accumulates in a target organ or attaches to specific cells. The imaging device detects the imaging agent and creates pictures that show how it is distributed in the body. This distribution pattern helps physicians discern how well organs and tissues are functioning.

MOLECULAR IMAGE MODEL

A molecular image illustrates the distribution of a certain molecule. Since the molecules are usually limited to certain areas, a molecular image can often be divided into several regions. A region with a high molecular concentration appears bright while regions with low molecular concentration appear dark. The intensity within a region usually changes gradually while the average intensities between the different regions are quite dissimilar. For such an image, we can use a piecewise-smooth model to describe

$$f(x,y) = \sum_{i}^{n} s_i(x,y)$$

it,

Where the $s_i(x,y)$ indicates a smooth region of f(x,y). We create a 128x128-pixel phantom according to the model. This phantom, illustrated in figure 1, represents a molecular image of a cell. In the phantom, the image is divided into five regions: the background, the cytoplasm, the nucleus, the mitochondria, and the endoplasmic reticulum (ER). In the phantom we assume the "interesting" molecules are distributed in the cell nucleus, mitochondria, and ER regions, but not in the cytoplasm region. The concentration of the molecules in the nucleus region is Gaussian distributed. The concentration of the molecules in the ER region is linearly distributed, with the highest concentration at the right end. The concentration of the molecules in the mitochondrial region is uniform. The entire image has a Gaussian distributed background illumination. A (noiseless) piecewise-smooth image is usually insensitive to a median filter. This is because a median filter eliminates primarily sudden, transient spikes while leaving sudden, sustained edges undisturbed. Moreover, the median filter does not significantly perturb the intensities in smooth regions. Figure 2 shows the result of the piecewise image shown in figure 1 following filtering by a 3x3 median filter. Except at the corners of the ER and mitochondrial regions, no features in this piecewise-smooth image were corrupted by the median filter. The quality index Q of the filtered image relative to the original image is 0.997 (in a range from -1 to 1, where 1 is the best possible). Moreover, the filtered image does not degrade much if the median filter is applied repetitively.

DENOISING USING ADMF

Anisotropic diffusion filtering schemes based on nonlinear diffusion developed for image enhancement. Since first proposed by Perona and Malik in 1990, anisotropic median diffusion has been developed and applied to different areas of image processing. To avoid blurring at the edges, instead of using the constant diffusion coefficients based on the original linear anisotropic diffusion, an edge stopping function was proposed to estimate the diffusion coefficients, which ensures the diffusion process taking place mainly inside of the regions rather than at their boundaries and thus the smoothing happens only in the interior of regions without crossing the edges.

The main target of efficient adaptive anisotropic diffusion algorithms in medical image processing is to remove noise via exponential diffusion function based on proposed a new edge –stopping function

ANISOTROPIC DIFFUSION FILTER

The anisotropic diffusion filter, first proposed by Perona and Malik, is a nonlinear filter which purports to smooth a noisy image without blurring the edges. The diffusion equation for image *u* is given by

$$\frac{\partial u}{\partial t} = div\,[c(\nabla u)\cdot\nabla u],$$

Where ∇u is a local image gradient and $c(\nabla u)$ is the diffusion coefficient, which is a function of the local gradient. The anisotropic diffusion filter has been broadly used for edge detection, image segmentation, and noise smoothing, often yielding better results than traditional filters such as the moving average or median filters or other edge-preserving filters. The idea behind the anisotropic diffusion filter is to evolve from a noisy image $g(x,y)$ a family of increasingly smooth images $u(x,y,t)$, indexed by diffusion parameter t, to estimate the original image. The diffusion coefficient $c(\nabla u)$ in the equation is sometimes called the "edge-stopping" function, which largely dictates the behaviour of the filter. The diffusion coefficient is set such that the filter in equation diffuses the image more in smooth areas and less near the edges. The diffusion coefficient has an argument, the local image gradient, which measures the local edge strength. However, the response of the gradient to the noise element may compete with or exceed the edge response, in which case the diffusion function cannot distinguish between image structure and noise contribution. Therefore, the basic anisotropic diffusion filter in equation usually fails to deliver adequate results as low SNR filter.

Anisotropic diffusion filter has been oriented toward understanding the characteristics of the diffusion coefficient and then improving the performance of the diffusion filter.In this model *Tukey biweight norm* as the diffusion coefficient proposed by Black *et al*. The normalized (magnitude) Tukey biweight diffusion coefficient is defined as

$$c(\nabla u, K) = \begin{cases} \frac{25}{16K}\left[1-\left(\frac{\nabla u}{\sqrt{5}K}\right)^2\right]^2, & |\nabla u| \le \sqrt{5}K \\ 0, & \text{otherwise} \end{cases}$$

The diffusion coefficient and the flux function are in figure 31. This plote together with and suggests that when the local gradient between a current pixel and its neighborhood pixel is smaller than the threshold, the neighborhood pixel is classified as belonging to the same smooth region as the current pixel. Therefore, the neighbourhood pixel is actively involved in the smoothing of the current pixel. However, when the local gradient is greater than but less than, the neighbourhood pixel is considered to be more distant from the pixel being analyzed in the current smooth region, therefore, such a neighbourhood pixel will have less contribution in the smoothing of the current pixel. When the local gradient is greater than, the neighbourhood pixel is determined to belong to another region, possibly on the other side of an edge. Thus, the involvement of this neighbourhood pixel in the smoothing is eliminated to avoid edge blurring. Determining a good value of for a noisy image is critical for the performance of these filters. Perona and Malik suggested using Canny's "noise estimator" to determine Torkamani-Azar and Tait used the mean of the absolute gradient as Black etal, determined from the median absolute deviation. All of these methods intend to separate the gradient generated by the noise from the gradient generated by the edges. However, in low-SNR images, the average gradient generated by the noise is comparable to determining a proper to smooth the noise while retaining the edges is quite difficult. Taking to be too small will result in a filter that fails to satisfactorily eliminate the overall noise element, especially large noise spikes or even larger than the edge gradients.

MEDIAN FILTER

The median filter is a nonlinear digital filtering technique, often used to remove noise. Such noise reduction is a typical pre-processing step to improve the results of later processing (for example, edge detection on an image). Median filtering is very widely used in digital image processing because, under certain conditions, it preserves edges while removing noise

ANISOTROPIC MEDIAN DIFFUSION FILTER

A molecular image, which displays the distribution of molecules. Such an image can be modeled as a piecewise-smooth image, which can be divided into several regions. Each region is chosen such that the changes in molecular concentration within the region are small and gradual. The intensities between the different regions are quite dissimilar because of the significant difference in molecular concentration. For these kinds of piecewise-smooth images, the anisotropic median diffusion filter was found 37 to be a suitable denoising filter.

MATHEMATICAL MODEL IMPLEMENTATION

Anisotropic median-diffusion filter which is specifically intended for denoising low-SNR images and which is particularly suitable for molecular smooth images such as those encountered in molecular imaging. A molecular image model is described. Based on this model, a molecular image is created as the test image for the modified anisotropic median diffusion filter. Use of the universal image quality index to measure the effectiveness of image denoising. And reduce the large spikes and smoothing inner and outer area boundary.

The anisotropic median diffusion filter is described as:

$$g^{(n+1)} = g^{(n)} + \lambda/4\left[c_N\nabla_N g + c_S\nabla_S g + c_E\nabla_E g + c_W\nabla_W g\right]^{(n)},$$

For median filter,

$g(n+1) = MedianFilter(g(n+1), Window)$,

Where *(n)* and *(n+1)* are the number of iterations, and $\lambda \in [0,1]$ controls the rate of the diffusion. The idea behind the anisotropic median-diffusion filter is to evolve from the recorded noisy image *g(0)* a family of increasingly smooth images *g(n)* to estimate the original image. The letters *N,S,E,W* in Eq. 3 are mnemonics for North, South, East and West; they describe the direction of the local gradient. The anisotropic median-diffusion filter is especially useful to smooth images with low signal-to-noise ratio, such as the Raman images. It can effectively reduce the Gaussian noise without blurring the edges on the images. A quantitative study has shown that the anisotropic median-diffusion smoothed images are very close to the original images in correlation, mean luminance and contrast. The local gradient is calculated using nearest-neighbor differences

$$\nabla_N u_{i,j} = u_{i-1,j} - u_{i,j}$$
$$\nabla_S u_{i,j} = u_{i+1,j} - u_{i,j}$$
$$\nabla_E u_{i,j} = u_{i,j+1} - u_{i,j}$$
$$\nabla_W u_{i,j} = u_{i,j-1} - u_{i,j}$$

The diffusion process was proposed as an alternative to smoothing images by a Gaussian kernel, which does not preserve edges. Since it derives from a process of equilibrating concentration differences, it can be expressed through a continuity equation of Fick's law

j = -D •Ñu
dt = div(D •Ñu)

D is called the diffusion tensor, a positive definite symmetric matrix which represents the relation between the concentration gradient Ñu and the flux which aims to compensate this gradient. In image processing, the concept of concentration is replaced by that of grey level. The diffusion tensor may be replaced by a positive scalar-valued diffusivity g. If j and Ñu are parallel, the diffusion is called isotropic. In the anisotropic case, j and Ñu are not parallel.

The last equation is called the diffusion equation. If the diffusion tensor is space-dependent, then the diffusion is called inhomogeneous, while a constant diffusion tensor is related to a homogeneous diffusion.

ALGORITHM STEPS

Calculate local gradient (∇*u*)

Calculate diffusion co efficient (c(∇*u*)

$$\frac{\partial u}{\partial t} = div\,[c(\nabla u)\cdot\nabla u],$$

Calculate flux density

$$\phi(\nabla u, K) = c(\nabla u, K)\cdot\nabla u.$$

Normalised diffusion co efficient

$$c(\nabla u, K) = \begin{cases} \frac{25}{16K}\left[1-\left(\frac{\nabla u}{\sqrt{5}K}\right)^2\right]^2, & |\nabla u| \le \sqrt{5}K \\ 0, & \text{otherwise} \end{cases}$$

Where k constant

CORRECTION OF NON-UNIFORM ILLUMINATION

After reducing the noise, the non-uniform illumination *i(x,y)* needs to be corrected. A flat field image is used as a reference image to correct the lateral non-uniform illumination. The effect of illumination difference in the axial direction is considered in PSF. According to the image model, a recorded flat-field reference image (after smoothing) can be expressed as:

$$r(x,y) = [h(x,y) * K_{flat}] \times i(x,y) \times t\,,$$

Where K_{flat} is a constant. The residue noise after smoothing is ignored in Eq. 6 for simplicity. The OTF of a microscope system is usually a low-pass filter (for example, the microscope system used in this research has a lateral cut-off frequency of 0.57 μm-1 and an axial cut-off frequency of 0.15 μm-1). Therefore, Eq. 6 can be simplified to

$$r(x,y) = K_{flat} \times i(x,y) \times t\,,$$

3-DIMENSIONAL IMAGE DECONVOLUTION

The objective of three-dimensional deconvolution is to restore the blurred image by using the PSF of the imaging system. After the deconvolution, it will reduce the focus- plane blurs caused by the limited aperture of the system as well as the out-of-focus plane

blurs resulted from the limited depth-of-field of the system. Many three-dimensional deconvolution algorithms have been developed, including the inverse filter, the Wiener filter, the Nearest-Neighbor deconvolution, the constrained iterative method, and the expectation-maximization maximum-likelihood(EM-ML) deconvolution. When restoring an image with all the information at the neighborhood planes available and no noise present, the deconvolution results from all these algorithms are very similar. However, in practice, some amount of noise always exists in a recorded image, even after smoothing by the anisotropic median-diffusion filter. In addition, there are often only a few images that can be recorded at different defocus planes within a limited period of time. Especially in the case of molecular imaging of living cells, we were only able to get one image (at a specific focal plane) to represent the drug distributions using the current instrumentation. This is again due to the relatively long exposure time required for molecular imaging.

Under this no-neighborhood condition, the three-dimensional deconvolution can be performed after replicating the recorded image as the neighborhood images. This simplification is based on the assumption that there is no abrupt change among the neighborhood images. However, if the assumption is not true, the three-dimensional deconvolution will not effectively remove the blurred information from the neighborhood planes.

Different deconvolution algorithms were compared to a three-dimensional cell model under the no-neighborhood condition 39. The EM-ML deconvolution was found to achieve better results when compared with the other algorithms. The EM-ML deconvolution was derived from the Bayesian theory with Poisson noise model. An iterative algorithm of the deconvolution, developed by Richardson and Lucy 40, 41, is described as follows:

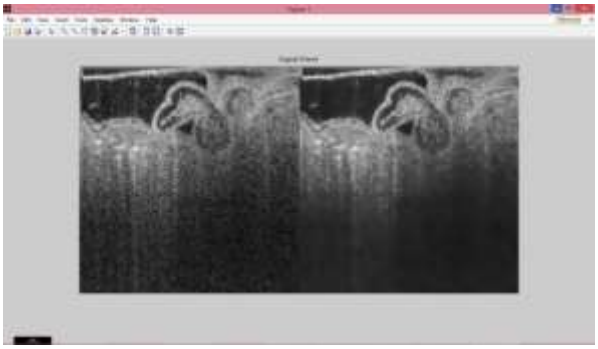
$$f^{(n+1)}(x,y,z)=\left[\frac{g_c(x,y,z)}{h(x,y,z)*f^{(n)}(x,y,z)}*h(x,y,z)\right]f^{(n)}(x,y,z), \quad (10)$$

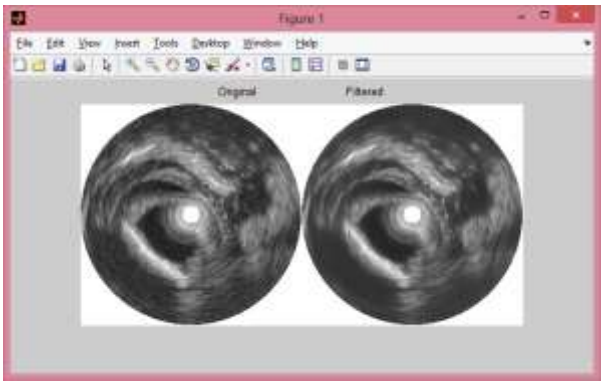
and $f^{(n+1)}(x,y,z)\geq 0$.

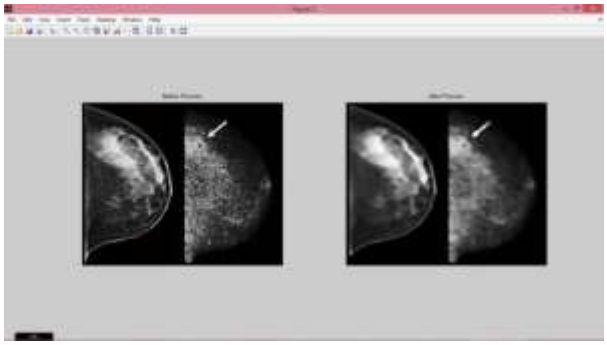
where *gc(x,y,z)* is a stack of two-dimensional images recorded in the experiment, *f(n)(x,y,z)* is the restored images at *n*th iteration, and *h(x,y,z)* is the PSF of the imaging system. The non-negative constraint is applied to the restored images after each iteration. Under the no-neighborhood condition in this study, the *gc(x,y,z)* is composed of an image recorded at the focal plane plus the neighborhood images created by replicating the focal plane image. All these images go through the denoising and non-uniform illumination correction procedures as described above. It is also important to subtract the background, or the "DC" value from the images prior to performing the deconvolution. Studies 42, 43 have shown that the background intensity has a critical influence on the performance of the EM-ML deconvolution. This is because the existence of the background makes the nonnegative constraint less effective.

In this study, the image background could be the fluorescence from the aqueous solution, which can be assumed uniform across the image. This background was subtracted from *gc(x,y,z)* before deconvolution.

SIMULATION







CONCLUSION

A medical image was enhanced by denoising it using a new anisotropic median diffusion filter. The behavior of the new anisotropic median diffusion depends heavily on the choice of the "denoising ". The function is a nonnegative molecular image, which should result in low SNR values at image edges that have large gradients, and high coefficient values within image regions that have low gradients. The experiments revealed that better results of noise reduction using molecular image were achieved with much smoother in the flat areas and sharper in the edgy regions after a small number of iterations. It is denoised inner and outer area boundary in the 3d image. Therefore the behavior of the proposed function is the best. The main advantages of this filter with new function is that it will work for most types of noise (besides additive Gaussian noise, it also gave good results on multiplicative speckle noise, impulse noise), also it gives significant improvement of image denoising, edge enhancement with little number of iterations over previous schemes results include performance measures PSNR, and SNR. The results are presented as table's graphs and images.

FUTURE TRENDS

There are several implemented techniques, which bring n improvements in the field of medical imaging. For future trends too early detection of breast cancer and working with Raman microscopy. This new filter is particularly useful for low-SNR molecular images such as fluorescence, Raman, isotope radiation, and positron emission images. Moreover, although the resulting images they provide look quite impressive, it has not been definitely proved that radiologists work better on these images. Therefore, there is sufficient room for improvements and further developments in image processing.

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