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Un esquema para el realce de imágenes de neoplasias malignas en tejidos formados a partir del endodermo embrionario

A scheme for enhancing images of malignant neoplasms within tissues formed from the embryonic endoderm

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RESUMEN

El impacto de los artefactos y el ruido en las imágenes de tomografía computarizada determina la calidad y la comprensión de los procedimientos computacionales de análisis de imágenes médicas. En la evaluación automática de los tumores cancerosos, el realce de la imagen es una tarea preliminar necesaria para los métodos de segmentación utilizados para localizar el tumor y cuantificar los volúmenes de las neoplasias. En este documento, se describe un procedimiento para evaluar la capacidad de un conjunto de filtros de suavizado utilizados para disminuir el impacto de los artefactos y el ruido en las imágenes de tomografía computarizada de pulmón, hígado y estómago en presencia de tumores cancerosos. La determinación de los mejores filtros de mejora se realiza mediante una función de puntuación basada en la fusión de medidas de mejora de imagen de referencia completa y de referencia ciega.

PALABRAS CLAVE: Realce de imágenes, filtros de suavizamiento, tomografía computarizada, neoplasias malignas, endodermo embrionario.

ABSTRACT

The impact of artifacts and noise in computed tomography images determines the quality and understanding of medical images computational procedures of analysis. In the automatic assessment of cancer tumors, the image enhancement is as a necessary preliminary task for the segmentation methods used for locating the tumor and quantifying neoplasms volumes. In this paper, a procedure to assess the ability of a set of smoothing filters used to diminish the impact of artifact and noise in computed tomography images of lung, liver and stomach in presence of cancerous tumors is reported. Determination of the best enhancement filters is performed using a score function based on merging of full–reference and blind–reference image enhancement measures..

KEYWORDS: Images enhancing, smoothing filters, computerized tomography, malignant neoplasms, embryonic endoderm

INTRODUCTION

The embryonic endoderm has as main function to construct the linings of the digestive and respiratory tubes within the body (Zorn , Wells 2009). The lining of the digestive tube and its glands is generated from the endodermal cells; meanwhile the lungs are a derivative of the digestive tube. The glandular epithelium of the liver is also formed from the endoderm (Gilbert 2000). Morphogenetic movements that appear after the granulation process transform the naïve endoderm into a primitive gut tube surrounded by mesoderm. This tube becomes segmented into the broad fore gut, midgut, and hindgut. The fore gut forms the esophagus, trachea, stomach, lungs, thyroid, liver, biliary system, and pancreas; whereas the midgut gives rise to the small intestine and the hindgut becomes the large intestine (D'Amour , Agulnick , Eliazer , Kelly O, Kroon , Baetge 2005).

The classification of the malignant tumors located in tissues formed from the embryonic endoderm, as all types of cancer, is based on the International Classification of Diseases for Oncology (ICD-O) with coding systems for both topography and morphology. (Fritz , Percy , Jack , Shanmugaratnam , Sobin , Parkin , Whelan 2013). The ICD-O considers the histological examination (tissue samples under a microscope) (Sobin 1989), macroscopic sassessment (DiMarino , Benjamin 2002) , and the topographic codification (National Cancer Registrars Association 2004), for establishing the biological behavior of the tumor and the stage of the disease or stage of evolution.

Computerized tomography (CT) imaging improves the detection of tumors of the lungs, abdomen, liver, kidneys, pancreas and pelvis (Fass 2008). The fast speed of image acquisition, the ability to minimize artifacts in an image caused by patient motion, breathing or involuntary wavelike contraction of gastrointestinal organs are characteristics that position the CT as the typically method of choice for imaging cancer tumors (Barrett , Keat 2004). Currently, CT is increasingly used to guide tumor biopsy to assess whether the neoplasm is benign or malignant (Schiavon, Tyng , Travesso , Rocha , Schiavon , Bitencourt 2018).CT image degradation due to noise, artifacts and detail blurring is a universal issue that has not yet been overcome basically by hardware restrictions (McWilliams , Murphy , Golestaneh , O'Regan , Arellano , Maher , O'Connor 2014).

CT images require a conditioning stage before starting the diagnostic process of neoplasms (Diwakar, Kumar 2018). At this stage, a specific image enhancement technique is applied for improving the image quality to a better and more understandable level. The visual appearance and the quality of CT images for future data processing, such as analysis, detection, segmentation and recognition are improved (Paranjape 2009). In order to improve the contrast of CT images, the contrast enhancement methods that have been used include the gamma correction, global histogram equalization, dynamic histogram equalization, adaptive histogram equalization. Denoising and deblurring methods are also proposed to increase the quality of CT images (Al-Ameen , Al-Ameen , Sulong 2015).

The main objective here is to establish a useful improvement scheme as an image processing procedure to attenuate noise and artifacts in the volumes of CT data and improve the information associated with malignant neoplasms present in the volumes. To achieve a robust and reliable image improvement scheme, seven imaging strategies are compared. A score function is proposed for quantifying the effectiveness of the image enhancement schemes compared. Such measure is availed to determine the smoothing filter that greater impact on improving the information associated with medical images. The robustness of the enhancement scheme determined is validated by performing the segmentation of three-dimensional cancer tumors from CT images.

1. MATERIALS AND METHODS

1.1. Data Source

The datasets used in this research correspond with a part of the Cancer Genome Atlas (TCGA) that contains the comprehensive, multi-dimensional maps of the key genomic changes in 33 types of cancer. The TCGA initiative of the National Cancer Institute (NCI) is managed throughout the project The Cancer Imaging Archive which manages a full featured cancer imaging archive service in order to support NCI–funded research activities and the cancer research community at large (Clark , Vendt , Smith , Freymann , Kirby , Koppel , Moore , Phillips , Maffitt , Pringle , Tarbox , Prior 2013). The computed tomography images in the data collections, consider on the Cancer Genome Atlas Stomach Adenocarcinoma (TCGA–STAD) (Lucchesi FR, Aredes ND 2016), the Cancer Genome Atlas Lung Adenocarcinoma (TCGA–LUAD) (Albertina , Watson , Holback , Jarosz , Kirk , Lee , Lemmerman 2016), and the Cancer Genome Atlas Liver Hepatocellular Carcinoma (TCGA–LIHC) (Erickson , Kirk , Lee , Bathe , Kearns , Gerdes , Lemmerman 2016), are considered in this research.

1.2. Image Smoothing Filters

1.2.1. Median Filter

This is an image nonlinear filter class (Yin , Yang , Gabbouj , Neuvo 1996). The filter does not consider a convolution with a denoising kernel for noise attenuation. The values in a neighborhood (m×m×m) of an original image are sorted in an array, after, the median of this array is determined, and then this value is replaced in the current voxel (Gonzalez R, Woods R (2006) The filtered image results from iteratively applying the procedure described above.

1.2.2. Gaussian Filter

The application of this linear filter generates a blurred version of the input image. The convolution kernel of size n corresponds with a discrete Gaussian distribution with σi, σj and σk as the standard deviations applied at each dimension (Pauwels E, Frederix G. 1999).

1.2.3. Dilate Filter

Dilate filter is also known as a minimum filter and constitutes the morphological operation of dilation whereby the object boundaries in the image are extended and smoothed, and holes and gaps are closed. The image is transformed considering a non–linear operation of minimum between the elements of the original image and a set of additional points known as structuring element22.

1.2.4. Erode Filter

This filter corresponds with a maximum filter and it is the morphological operation of erosion. This operator causes objects to shrink, it smoothes object boundaries and removes peninsulas, fingers, and small objects. The non–linear maximum operator requires also a structuring element (Pauwels E, Frederix G. 1999).

1.2.5. Gradient Anisotropic Diffusion Filter

It is formulated to attenuate unwanted information while preserving the specific characteristics of the images (Serra. 1983). The method transforms the original image as a function of its derivatives in a higher dimensional space, this transformation represented the solution of the heat equation (Perona , Malik .1990). The conductance corresponds with a function of the gradient magnitude of the image at each point.

1.2.6. Curvature Anisotropic Diffusion Filter

It is also a diffusion anisotropic filter (Serra. 1983). The proposed filter considers a modified curvature diffusion equation for performing the anisotropic diffusion. This equation allows to enhance the contrast of edges rather than to exhibit the properties of edge improvement of classical anisotropic diffusion.

1.2.7. Curvature Flow Filter

This filter implements an anisotropic diffusion method useful for smoothing information and preserving the objects edges in the images. However, the diffusion is parallel to the image contours, the filter spreads the curvature along a contour, rounds the corners and reduces the distance of the contours (Cañero , Radeva . 2003)

1.3. Score Function for Enhancement Assessment

The measure proposed is based on merging of full–reference and blind–reference image enhancement measures. The score function is the average of the weighted sum of the image enhancement measures normalized between zero and one.

Let's consider the vector ηi whose components are the considered image enhancement measures (see second column of Table 1). Let ωi the vector of weights whose components take values −1 or +1. ωi is +1 if the value of the corresponding metric calculated for enhanced image has the expected variation (decrease ↓/ increase↑) with respect to the original image. ωi is −1 otherwise. Table 1 describes the metrics. The score function (1) is the average of the weighted sum of the measures.

$$SFEM = \frac{1}{l}\sum_{i=1}^{l} \omega_i \, \overline{\eta}_i \qquad (1)$$

where $\overline{\eta}_i$ is the vector of the normalized image enhancement measures and l is the number of image enhancement measures that varies from 1 to 12. A high value of this score function is associated with an effective enhancement.

1.4. Experimental Setup

The filters considered for filtering scheme are computationally implemented using the VolView 3.4 for Linux 64 bit (Gabarda, Cristóbal 2007), as a visualization tool. VolView is an application for the visualization and analysis of three-dimensional images. Table 2 shows the parameters required for the implementation in VolView for each of the filters considered and it also shows the confidence interval of each parameter.

Table 1. Expected variation of the image enhancement measures in cardiac MSCT images

Measure	η_i	**Variation**
Mean	η_1	Decrease ↓
STD	η_2	Decrease ↓
Entropy	η_3	Increase ↑
MSE	η_4	Increase ↑
MAE	η_5	Increase ↑
PSNR	η_6	Decrease ↓
EME	η_7	Increase ↑
EMEE	η_8	Increase ↑
AME	η_9	Increase ↑
AMEE	η_{10}	Increase ↑
SDME	η_{11}	Increase ↑
MSSIM	η_{12}	Decrease ↓

The confidence intervals are sampled using a probability sampling method which assures that the different values in the intervals have equal probabilities of being chosen.(Wang , Bovik 2009) Such sampling is applied in order to establish 27 experiments for each filter, that is, for each filter 27 sets of different parameters are chosen. Thus, a total of 189 experiments are considered.

Table 2. Parameters of the filters.

Filter	**Parameter**	**Set of values**
Median (S_1)	kernel size i kernel size i kernel size i	[1-5] [1-5] [1-5]
Gaussian (S_2)	σ_i σ_j σ_k	[0-4] [0-4] [0-4]
Dilate (S_3)	kernel size i kernel size i kernel size i	[1-5] [1-5] [1-5]
Erode (S_4)	kernel size i kernel size i kernel size i	[1-5] [1-5] [1-5]
Gradient anisotropic diffusion (S_5)	Number of iterations Time step Conductance	[1 - 100] [0.01 - 1] [0.1 - 10]
Curvature anisotropic diffusion (S_6)	Number of iterations Time step Conductance	[1 - 100] [0.01 - 1] [0.1 - 10]
Curvature flow (S_7)	Number of iterations Time step	[1 - 100] [0.01 - 1]

Regarding the management of data, computed tomography images in the data collection are expressed in Hounsfield units and they require a specific window and level for analyzing (Wang, Li, 2011)28, therefore it is considered an intensity scaling for representing the intensities in 12 bits in which the black corresponds to 0 and the white to

4095.

1.5. Enhancement Scheme

The proposed procedure to assess the ability of a set of smoothing filters to diminish the impact of artifacts and noise in CT image analysis consist of following steps:

- Performing the intensity scaling of the CT images
- Filtering the scaled images using the 189 configurations of smoothing filters
- Quantifying the score function for each processed image
- Determining the 10% of the configurations of smoothing filters with the higher values of the score function
- Analyzing sensitivity as the percentage of enhancement features with a condition that the enhancement scheme in CT images has correctly verified and that effectively has that feature.
- Analyzing the specificity as the probability of the proposed scheme of correctly identifying, solely from among images whose are known not to have an enhancement feature, all those who do indeed not have that feature.

2. RESULTS

For computed tomography images of lung cancer, the score function obtained (mean ± standard deviation), for each filtering strategies is shown in Table 3.

Table 3. Score function for lung images.

Filtering Strategies	Statistics		
	mean ± std	**Maximum**	**Minimum**
S_1	14.72 ± 0.49	15.41	14.46
S_2	14.71 ± 0.77	15.56	14.02
S_3	14.39 ± 0.09	14.41	14.24
S_4	**15.02 ± 0.70**	**15.77**	**14.37**
S_5	2.23 ± 0.95	3.47	2.01
S_6	3.37 ± 0.56	4.05	2.29
S_7	14.25 ± 3.63	14.69	8.18

Tables 4–5 shown the values of score function for liver and stomach computed tomography images, respectively.

The enhancement features considered for the sensitivity and sensitivity analysis are blurring the edges, noise, darkness, brightness and artifacts. These features are visually inspected from the processed CT images. This analysis is performed at 10% of the images with the highest value of the score function, regardless of which filtering strategy they belong to and the organ that contains the malignant tumor. Filtered images with erosion filter configurations occupy this 10%.

Table 4. Score function for liver images.

Filtering Strategies	Statistics		
	mean ± std	**Maximum**	**Minimum**
S_1	15.17 ± 1.51	16.32	13.32
S_2	16.63 ± 0.68	17.69	16.42
S_3	18.12 ± 1.17	18.21	16.14
S_4	**18.59 ± 0.96**	**19.46**	**17.55**
S_5	5.14 ± 1.22	6.49	2.99
S_6	8.43 ± 2.11	11.28	5.19
S_7	14.22 ± 2.13	16.54	12.29

Table 5. Score function for stomach images.

Filtering Strategies	Statistics		
	mean ± std	**Maximum**	**Minimum**
S_1	16.44 ± 0.40	16.48	15.68
S_2	16.35 ± 0.41	16.62	15.81
S_3	16.34 ± 0.59	16.82	15.65
S_4	**17.15 ± 1.23**	**18.35**	**15.87**

S_5	11.24 ± 2.31	13.67	9.22
S_6	10.45 ± 1.59	14.33	9.76
S_7	15.97 ± 0.68	16.87	15.54

The correspondence between the established features and the visualized enhanced features is estimated from the positive predictive value, and it is about 92.04%. Meanwhile, negative predictive value is about 92.18 %, which indicates that the filtering strategies present a high percentage of assessment of non–specific features of images enhancing. The sensitivity and the specificity computed in order to estimate the enhancement agreement are 92.38% and 93.71%, respectively.

In order to validate the results obtained from the enhancement scheme, a segmentation stage using a clustering method is used for obtaining the malignant neoplasms morphology39. The CT images enhanced using the erode filter (S4) are considered to be segmented. The corresponding unprocessed images are also considered. The volumes quantified from the tumors segmented using the procedure based on a region growing technique are as follow: lung filtered 61.28×103 - lung unprocessed 45.72×103; liver filtered 27.31×103 – liver unprocessed 29.15×103; and stomach filtered 51.38×103 - stomach unprocessed 49.06×103.

3. CONCLUSIONS

The strategy that attains the best results is S4, which corresponds to erode filter. This strategy generates the higher values of the score function for all computerized tomography images processed, and achieves high values of sensitivity and specificity for certain enhancement features. Secondly, the segmentation results obtained for a strategy with no one enhancement scheme compared with those achieved using remaining strategies suggest that application of an appropriate enhancement scheme is necessary.

In any event, the image enhancement scheme allows improving the interpretability or perception of information in images for oncology clinicians and providing better information as input for automated image processing techniques. In the computing sense, since image processing is one of the branches of computing, the image enhancement scheme reported is based on specific mathematics and computational criteria for modifying attributes of an image to make it more suitable for a given task and for the specific observer in this case.

The impact of specific factors of the observer such as the human visual system and the observer experience which introduce a great subjectivity into the choice of the image enhancement methods is diminished with the introduction of a metric of enhancement. An aspect not considered in the present work is related to the computational cost of smoothing filters which may play a critical role in choosing an enhancement algorithm. Despite the effectiveness of the erode filter, in practice it is possible to devise a combination of strategies to achieve more effective enhancement.

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