A novel approach for hepatocellular carcinoma detection with region merging segmentation method

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Abstract

We present a noninvasive method for the detection and an advanced segmentation of Hepatocellular carcinoma (HCC) based on Computed Tomography (CT) images. This proposed method basically starts with the processing of the data set. 60 CT images are prepared for the segmentation process. Image data is divided into two groups; 50 CT images of the HCC, and 10 CT images of the normal liver. The ground truth images are created with the specialist abdominal radiologist. Images are in 256x256 µm size in JPEG format. For the segmentation part, the Statistical Region Merging method is used. The proposed method consists of three main parts, these are thresholding, segmentation, and estimation of ROC parameters. By using the database and the ground truth, according to the simulation results, the average of the sensitivity, specificity, and accuracy are obtained as 0.7476 %, 0.9723 %, and 0.9502 %, respectively. In conclusion, HCC is the most common primary malignant tumor in the liver. It is considered an important and life-threatening disease. Early detection of liver cancer has become very important for the patients. The Region Merging Segmentation Method is a very useful liver segmentation technique for detection of the HCC.

Keywords: Liver cancer, diagnosis, computed tomography, statistical region merging method

Introduction

The increase in imaging methods used to evaluate the abdominal region has led to an increase in the detection of liver lesions. Small lesions have become identifiable as a result of technical developments in the field of radiology. Focal lesions detected in the liver can be benign and malignant lesions. Hepatocellular carcinoma (HCC) is the leading cause of cancer-related deaths and is the most common primary malignant tumor of the liver.

HCC is sixth in incidence and third in cancer mortality worldwide [1]. It is the most common primary liver cancer, with approximately 3/4 of cases occurring in Asia [2]. Despite advances in screening, diagnosis with treatment, incidence, and mortality continue to increase [3]. Early diagnosed lesions potentially have treatment options. Because the early diagnosis of HCC is very important.

Radiological imaging methods, biomarkers, and biopsy are used for diagnosis. Imaging plays a very important role in diagnosing HCC. In high-risk patients, noninvasive diagnosis can be obtained with imaging findings.

After analyzing the literature according to the topic of liver segmentation, results were classified. There are three techniques. The first technique is based on a common probability model used for the segmentation process. This technique explains the differences in liver structure [4]. The second technique is learning-based methods. This method is the process of defining and recognizing patterns in an image for segmentation via clustering, neural network, and support vector machine methods [5,6]. The other technique is a region-based method. In this method, the region is iteratively merged by comparing unallocated neighboring pixels to the region [7,8]. In this study, generally, HCC detection with the hybrid region merging segmentation algorithm is given and summarized in detail.

Materials and Methods

The clinical research ethics board approval was received from the
Non-Interventional Clinical Research Ethics Committee from the Institutional Ethics Committee.

Proposed Method

Statistical Region Merging block diagram is mainly given and information is given in detail (Figure 1).

![Proposed Statistical Region Merging Flowchart](Image)

**Figure 1.** Proposed Statistical Region Merging Flowchart

Image Acquisition

This proposed method begins mainly with the process of the dataset 60 CT images are prepared for the segmentation process. Indeed, the image database which is used was collected from the university hospital and the ground truth images are created with a specialist abdomen radiologist. The images are in JPEG format, and 256x256 µm in a size. The image data are divided into two sets; 50 images of HCC and 10 images of normal liver CT.

Thresholding Process

Mainly, the image resizing process is achieved. The proper data set choose the whole process started with thresholding of the liver images which are done by analyzing the histogram of the image dataset and advanced thresholding techniques which are contrast/ intensity-based and gray-scale image thresholding methods. The histogram processing of the image dataset to find the likelihood intensity of liver range is the most important part of the thresholding [9]. The histogram of the 60 gray images is also analyzed to find the range of liver. The liver pixels are separated from the abdomen CT image by using the two values k1 and k2, which represent the liver pixels, and the values before k1 and after k2 which represent the non-liver pixels will be assigned to zeros for elimination from the original image [10]. Finally, a binary image is obtained containing the liver pixel and all overlapping intensity with the liver pixel.

Statistical Region Merging Method

Because of the different shape of the liver, it is not possible to have an accurate segmentation in this step. The technique which is used in our proposed method is region merging that the pixel intensity is compared with a specific distance [11]. This technique starts with a definition of a specific pixel called the seed point. This can be chosen by using a common way. For each image, fixing a specific point in a way that will be very difficult for all images due to the liver shape variation [12]. Moreover, the region merging methods generally start by choosing a seed point. Then, the difference of a pixel’s contrast/intensity value between the mean value of the region is added to the Region of Interest (ROI). This process will continue until the intensity value between the region and a new pixel becomes greater than a certain threshold.

**Estimation of ROC Parameters**

The receiver operating characteristic (ROC) has been developed to assess the balance between accuracy and sensitivity between the correct detection rate and the false detection rate of a receiver in a noisy channel in the signal detection theory [13]. Testing is often used to define their accuracy and to make the most accurate comparison among tests. In addition to being used mostly in medical decision-making processes, it is also being used effectively in research such as machine learning and data mining [14]. The receiver operating characteristic curves provide a good basis for analyzing the performance of the interpreter. A distinction must be made among the criterion that is used by the interpreter to determine the presence or absence of a condition and the ability of the interpreter to determine the condition. More simply, the receiver operating characteristic is the ratio of true positives to false positives. When a positive class p and a negative class are considered a binary classifier consisting of only two classes represented by n, the instances in the problem are mapped to one of classes n or p. In the binary classification, there are four different situations for a given example, as shown in Table 1.

<table>
<thead>
<tr>
<th>True Positive (TP)</th>
<th>False Positive (FP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>True Negative (TN)</td>
<td>False Negative (FN)</td>
</tr>
</tbody>
</table>

That is, when a pixel is classified as a precise reference (TP), it is classified as a true positive (TN). If it is classified as a definite reference. When the segmentation is regarded as a vein on the images, the classification is classified as a true negative (TN). One pixel in two misclassifications, false negative in a vein (FN). The vein is a segmented image and vein non-vein (FP) false positive in the image marked as absolute classified reference. TPR shows the proportion of positive samples (positive classification) among all positive samples (1) and FPR represents the proportion of positive samples (false classification) among all negative samples (2). The accuracy of the classification (Accuracy, ACC) is calculated by the ratio of correctly classified samples to all samples (3), (Table 2). That is, the correct positive ratio (TPR) represents the fraction perceived as the correct pixel vessel. False positivity rate (FPR) represents the fraction perceived as a false pixel vessel. Accuracy (ACC) is measured by the ratio of the number of pixels in the view image area (the sum of true positive and true negatives) to the total number of correctly classified pixels. Sensitivity (SN) reflects the algorithm’s ability to detect pixels as veins. Specificity (SP) is the ability to detect non-vascular pixels.
Results

The proposed method for liver segmentation is applied to 60 CT images, respectively. These 60 images are divided into two parts. First, 50 liver CT images were used in different process training experiments, and 10 liver CT cases are used for the testing. During the thresholding process, some images are eliminated due to poor resolution and incorrect liver position. At the end of the process, excellent liver segmentation results are obtained from the approach. In Figure 2, one patient’s original CT image (a), the segmented image (b), a ground truth image (c), the result of the statistical region merging in grayscale illustration (d) are given respectively. In the part of the 20 patients’ estimation of ROC parameters, results which are sensitivity, specificity, accuracy is obtained and given in Table 3. It can be seen that the proposed segmentation method with adaptive thresholding and ROC result gives good results compared to manually segmented liver. Indeed, an average error percent of 5% for 10 test case studies is obtained and totally, the average success rate is calculated from the approach as approximately 95%. The sensitivity, specificity, and accuracy parameters are shown in a graph in detail (Figure 3).

Table 2. Calculation of sensitivity, specificity and accuracy

\[
Sensitivity = \frac{TP}{TP + FN} \tag{1}
\]

\[
Specificity = \frac{TN}{TN + FP} \tag{2}
\]

\[
ACC = \frac{TP + TN}{TP + FN + TN + FP} \tag{3}
\]

Table 3. The results of the sensitivity, specificity, accuracy

<table>
<thead>
<tr>
<th>Number of Image</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.693743</td>
<td>0.984806</td>
<td>0.955713</td>
</tr>
<tr>
<td>2</td>
<td>0.59835</td>
<td>0.969622</td>
<td>0.94248</td>
</tr>
<tr>
<td>3</td>
<td>0.862632</td>
<td>0.97253</td>
<td>0.933944</td>
</tr>
<tr>
<td>4</td>
<td>0.757023</td>
<td>0.886511</td>
<td>0.945052</td>
</tr>
<tr>
<td>5</td>
<td>0.739277</td>
<td>0.820258</td>
<td>0.939693</td>
</tr>
<tr>
<td>6</td>
<td>0.680059</td>
<td>0.834271</td>
<td>0.950778</td>
</tr>
<tr>
<td>7</td>
<td>0.723745</td>
<td>0.718544</td>
<td>0.968658</td>
</tr>
<tr>
<td>8</td>
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<td>0.861778</td>
<td>0.968915</td>
</tr>
<tr>
<td>9</td>
<td>0.802457</td>
<td>0.88118</td>
<td>0.950662</td>
</tr>
<tr>
<td>10</td>
<td>0.741146</td>
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<tr>
<td>11</td>
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<td>0.978815</td>
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<tr>
<td>12</td>
<td>0.752761</td>
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<td>13</td>
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<td>0.941906</td>
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<td>15</td>
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<tr>
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<td>0.953867</td>
</tr>
<tr>
<td>18</td>
<td>0.550336</td>
<td>0.931828</td>
<td>0.94036</td>
</tr>
<tr>
<td>19</td>
<td>0.829104</td>
<td>0.952399</td>
<td>0.962364</td>
</tr>
<tr>
<td>20</td>
<td>0.864051</td>
<td>0.937879</td>
<td>0.944117</td>
</tr>
</tbody>
</table>

Figure 2. Original image (a), segmented area (b), ground truth image, statistical region merging in colored illustration (c), and in gray-scaled illustration (d)
Today, in medical imaging techniques; early diagnosis, diagnosis, and treatment of diseases are performed with radiological modalities. The analysis and interpretation of medical images in clinical studies are mostly done by specialist physicians. However, in recent years, medical doctors began to benefit from computer-assisted diagnosis and treatment assistance. With the applications of artificial intelligence, computers have made significant progress in automatically analyzing and explaining complex data.1 In the field of medicine, imaging data analysis is needed, especially in radiology [5,6,15,16], pathology [17] dermatology [18], and ophthalmology [19]. It has been widely used in medicine.

HCC can be diagnosed by ultrasonography (US), contrast-enhanced US, CT, and dynamic magnetic resonance imaging (MRI). Also, computerized assistive methods can be very useful in evaluating liver lesions. In retrospective studies, using models based on dynamic contrast-enhanced CT images in the arterial phase and delayed phase, a very high diagnostic performance was obtained. [5,6,20]. With these methods, HCC, metastasis, cyst, hemangioma, and other benign lesions in the liver, sensitivity rates were reached of 70-85-90 %, and it was considered quite successful.

Segmentation of liver vascular structure with CT is very important in vascular disease, liver surgeries, radiotherapy planning, liver transplantation planning, and analysis of tumor vascularization. Manual segmentation is time-consuming and human error may be possible. The automation-oriented process and the application of deep learning models have been examined by some researchers. [6,21] The portal veins, hepatic veins, hepatic artery structures are revealed by automatic programs. It enables the detection of vascular anomalies and variations if any, and the measurement of liver mass volumes with minimal error. Thus, high-security data are obtained for donor and recipient in interventional procedures, surgical planning, especially liver transplantation. The most appropriate safety is provided in terms of radiation therapies. Artificial intelligence (AI) programs developed in these areas are rapidly becoming widespread. It is used in surgical clinics dealing with radiology, transplantation, and radiotherapy units. With these automatic segmentation methods, clinical treatment becomes easier, and more precise medical data are obtained. There is serious debate about the time required to fully apply artificial intelligence methods obtained by deep learning methods in clinics. The period discussed varies from a few years to more. Automatic methods based on deep learning aim to solve the most common clinical problems that require long-term expertise or are too complex for humans. They need to develop a more advanced deep learning algorithm to solve the problems of their methods. Currently, a common drawback of existing AI tools is that they cannot solve multiple problems at once. Currently, there is no comprehensive information system that can detect multiple abnormalities in the human body. The existence of too many different data and their inability to bring them together at the same time also makes it difficult to develop appropriate programs quickly. [22] However, data validation of some applications may necessarily be done by humans.

To achieve healthier practices in the future, it is necessary to collect information about different parts of the world and from different geographies, including different demographic characteristics, and make them useful by coordinating them. Different patient data, diagnosis, and treatment methods should be updated. Developing new methods will facilitate the work of specialist physicians in many other branches, especially radiology specialists. By using these methods, both time gain, and healthier diagnosis and treatment will be made possible. The line of success will rise rapidly. AI applications, especially deep learning, are quickly becoming a promising aid in liver imaging. It provides improved performance in detecting and evaluating liver lesions, facilitating clinical therapy, and predicting response to treatment. There is rapid progress towards becoming an integral part of specialist physicians. It is necessary to work with many different modalities to expand and spread applications in the field of radiology.

In conclusion, in this study, the average of the sensitivity, specificity, and accuracy are obtained as 0.7476%, 0.9723%, and 0.9502%, respectively for automatic liver segmentation. The goal of this work is to create a computer-assisted diagnostic system by gathering or combining different kinds of measurements. To serve patients more, it is necessary to work on the development and use of AI applications.

Conflict of interests
The authors declare that they have no competing interests.

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Ethical approval
Ethics committee approval received from the Institutional Ethics Committee of University.

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