Journal of Medical Systems (2019) 43: 43
https://doi.org/10.1007/s10916-019-1164-1

IMAGE & SIGNAL PROCESSING

Clinical Study of Diffusion-Weighted Imaging in the Diagnosis of Liver Focal Lesion

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Received: 12 November 2018 / Accepted: 9 January 2019 / Published online: 16 January 2019

Abstract

Apparent diffusion coefficient (ADC), derived from diffusion-weighted magnetic resonance images (DW-MRI), measures the motion of water molecules in vivo and can be used to quantify tumor response so as to determine the best therapy approach. In this paper, our goal was to determine whether the DW-MRI can be used for qualitative and quantitative liver cancer analysis, where an automated method will be proposed for improving the accuracy of liver segmentation in DW-MRI to increase the ability of diagnosis of disease. We firstly analyzed the research status of liver cancer diagnosis, especially on the issues of liver image segmentation technology in MRI. Then, the imaging mechanism and image features of the DW-MRI were analyzed, and the initial DW-MRI slice was segmented by graph-cut algorithm. Finally, our obtained result from the liver DW-MRI image is quantitatively and qualitatively analyzed. Experimental results show that DW-MRI has a great advantage in the diagnosis, the DWI images of benign lesion group was lower than that of malignant lesion, thus DW-MRI is segmented by graph-cut algorithm can provide important additional information regarding differential diagnosis of specific liver cancer to some extend.

Keywords Liver segmentation · Diffusion weighted imaging · Apparent diffusion coefficient · Segmentation contour · Graph cut · B-value

The liver features mainly include artificial features such as texture features, shape features, wavelet decomposition coefficient features, local feature descriptors, and visual word-bags. The generalization of artificial features is relatively poor, and it is difficult to select effective features. Therefore, scholars began to study the feature extraction based on machine learning, and obtain the internal structural features of the liver image by self-learn, which can better solve the poor generalization problem of artificial features. This has become a hot spot and trend of liver image feature research. In view of the problem of liver segmentation, extensive researches have been carried out, and can be roughly classified into a pixel-based method, an energy-based method, and a shape-based prior method. Pixel-based methods mainly include threshold method, region growing method and clustering method. Liu et al. proposed an improved liver segmentation model using a regional growth method based on adaptive filtering. The literature [1] proposed to use threshold, morphological operations, K-means clustering and Multi-Layer Perceptron Network (MLP) so as to segment the liver. The literature [2] proposed a regional growth-based liver MRI image segmentation method, using the Quasi-Monte Carlo algorithm to obtain the seed points and design region growth criteria of the region of interest. The literature [3] proposed an automatic liver segmentation method that combines a convex variable model with image brightness and local region features. However, since the gray-scale of the liver and its surrounding tissues are very similar, pixel-based methods such as the region growing method are easily misclassified into adjacent organs. In addition, intrahepatic tumors often cause grayscale inhomogeneity and mislead boundaries that interfere with liver segmentation.

Compared with the pixel-based method, the energy-based method has high stability, fast processing speed, and avoids errors caused by image discretization. In recent years, the graph cut algorithm has been widely used in image segmentation because of its advantages in the global optimal solution problem. In [4], the spatial energy correlation between adjacent slices is used to construct a graph cut energy function, which iteratively segment the entire MRI image. This method requires manual

This article is part of the Topical Collection on *Image & Signal Processing*

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segmentation of the initial slice and is less effective for image segmentation with lower contrast. In addition, statistical models based on prior information such as position and shape are also commonly used for segmentation of the liver in MRI sequences. This method usually requires a large amount of data to establish a rough liver position or shape model, so it takes a long time and is less effective for irregularly shaped liver segments. Yang et al. introduced a kernel function based on the traditional graph-cut theory, and proposed a liver segmentation algorithm based on kernel graph-cut model. However, the segmentation accuracy is closely related to the initial shape, so a priori information is usually considered to the graph-cut model when segmenting the liver [5]. Tang et al. used the statistical shape model to obtain the prior shape, and then used the improved graph cut algorithm to finely segment the liver [6]. Atsushi et al. used the training results of the statistical shape model to optimize the object energy function, and sought the optimal solution to obtain the optimal liver segmentation results [7]. Milletari et al. integrated a priori statistical knowledge obtained through Principal Component Analysis (PCA) into a convolutional neural network(CNN) to obtain robust predictions when dealing with corrupted or noisy data. The deep learning method is widely used because of its high accuracy, but it requires a large amount of sample data during training. Due to the particularity of medical images, the application in liver segmentation is affected [8].

As can be seen from the above analysis, most of the existing liver segmentation algorithms process MRI images [9]. But some problems demanding prompt solutions are still faced. For example, the tissues and organs adjacent to liver in the medical imaging have the similar tissue density, which leads to obscure boundary; the tumor should be segmented as part of the liver. However, there is a considerable intensity difference between both structures, which often leads to misclassification of the tumor as nonliver tissue. Figure 1 shows some examples of the various difficulties. Due to its highly varying shape, the liver is also a very challenging structure to describe with model-based approaches. In consequence, liver image segmentation in MRI is one of the most fundamental and challenging task.

Because of the MRI examination of abdominal organs, it is susceptible to breathing, heartbeat, large blood vessel pulsation, and intestinal peristalsis. Therefore, the application of MRI in the abdomen is limited. Diffusion-weighted magnetic resonance imaging (DWI or DW-MRI) is the use of specific MRI sequences as well as software that generates images from the resulting data, that uses the diffusion of water molecules to generate contrast in MR images. It is the only non-invasive inspection technique that reflects the functional status of living tissue. In recent years, the research and application of this technology [10–12] in the liver has attracted people's attention, especially in the differential diagnosis of liver occupying lesions, vascular and cystic lesions. The diffusion imaging sequence highlights the effect of diffusion motion on the MR signal by designing the imaging sequence. Due to the rapid development of DWI, echo planar imaging (EPI) technology is gradually applied to the examination of abdominal organs due to the short scanning time and the acquisition of a single image in a few milliseconds. EPI technology, especially single-shot EPI technology is currently the fastest imaging technology of MRI, the acquisition time is less than 50 ms, so the physiological activities that affect image quality can be eliminated [13, 14]. Even in the absence of breath holding, the image quality is less affected. According to the data and experiments, the diffusion-weighted image and apparent diffusion coefficient reflect the characteristics of the tissue structure at the microscopic level. Due to the different water content and cell density of various space-occupying lesions, and different liquid flow and viscosity in each tissue, their apparent diffusion coefficient values are also different [15, 16]. Qualitative diagnosis and differential diagnosis based on apparent diffusion coefficient are possible. Therefore, this paper aims to compare the segmentation results of DWI-MRI and MRI, and determine whether the DW-MRI can be used for qualitative and quantitative liver cancer analysis so as to develop an automated method for improving the accuracy of liver segmentation in DW-MRI and increasing the ability of diagnosis of disease [17, 18].

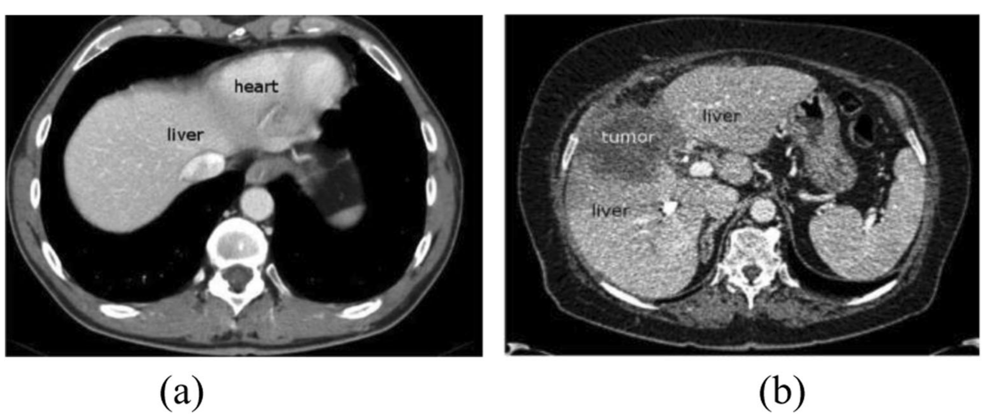

Fig. 1 Examples why liver segmentation is a challenging task

Diffusion weighted imaging

Diffusion-weighted magnetic resonance imaging (DWI-MRI) can be used for the clinical staging and evaluation of the early diagnosis of malignant tumors. It is a new technology of functional magnetic resonance imaging. It is currently an imaging method capable of non-invasive observation of the diffusion movement of water molecules inside living tissue cells. DWI can reflect the spatial structure inside human tissues at the molecular level, and can also reflect the functional status of water molecule exchange in human tissues under pathological conditions. It can reflect the physiopathology changes of lesions earlier than conventional MRI, which is an effective means of early diagnosis and evaluation of tumor treatment at the cellular level [19]. The DWI signal attenuation parameter, also known as the apparent diffusion coefficient (ADC) value, is a quantitative measurement index of DWI. The normal tissue cells have a complete cell membrane, and the cell membrane limits the free diffusion of water molecules inside and outside the cell. The diffusion of water molecules in the tissue is very low, the signal attenuation is also very small. The DWI image shows a higher signal, and the ADC value is lower. Malignant tumors grow rapidly, and the cells are large and dense, and the extracellular space is reduced, so the space for free diffusion of water molecules becomes smaller. The free diffusion of water molecules is significantly restricted, and the signal is high on the DWI image, while the ADC is significantly reduced. It can be seen that DWI can accurately reflect the changes of microscopic motion state of water molecules in tissues caused by tissue ischemia, local necrosis and cell proliferation, so as to observe and analyze the internal structure and characteristics of tissues. Through effective anti-tumor treatment, the cell membrane of tumor cells will be destroyed and the cell density will decrease. Therefore, the space for free diffusion of water molecules inside and outside the cell becomes larger, the diffusion of water accelerates, which makes the ADC value increases and the ADC value changes [20, 21]. The ADC magnitude is related to the effectiveness of its treatment. In the central nervous system diseases, the application of DWI has been more common, but it is restricted by the chemical displacement, respiratory movement and other factors in the treatment of chest and abdomen diseases. Nowadays, the literature on the evaluation of tumor efficacy using DWI is mostly concentrated on animal experiments. In the clinical evaluation of human tumors, more research is on glioma, rectal cancer and breast cancer. With the advancement of MR technology (such as planar echo imaging technology, respiratory gating and cardiac triggering imaging technology), not only shortening the scanning time, but also reducing the motion artifacts, DWI gradually applied to the body. In this paper, the effect of segmentation on liver cancer was evaluated by ADC image. The magnitude and changes of ADC values of liver cancer before and after chemotherapy were studied to determine the ADC value in MR diffusion-weighted imaging so as to predict and evaluate the chemotherapy efficacy of liver cancer.

The *b* value is one of the important parameters of DWI. On the one hand, the size of the *b* value can reflect the quality of the DWI image; on the other hand, the size of the b value can reflect the true diffusion coefficient value of the diffusion of water molecules. When the *b* value we choose is smaller, the greater the influence of T2 shine-through and blood perfusion, the higher the measured ADC value and the higher the mutation rate, while the higher the signal-to-noise ratio (SNR) of the lesion signal is; When we choose the larger *b* value, the influence of T2 shine-through and blood perfusion is the smaller [22, 23], so the more realistic reflection of the movement state between the intracellular and intercellular water molecules in the tissue is shown. The measured ADC value is closer to the true diffusion coefficient of the tissue, but the SNR on the DWI is significantly reduced, thus affecting the quality of the DWI image. Therefore, the principle of determining the *b* value should make the measured ADC value more accurate on the basis of ensuring the signal-to-noise ratio of the DWI image. The DWI is scanned with b = 700 s/m2 in paper, which can guarantee the quality of the image and ensure the accuracy of the ADC value.

Graph cut model for liver segmentation

The Graph-cut method was proposed by Boykov and Jolly for energy-based image segmentation. Its main purpose is about interactively finding the *s-t* cut of minimal total cost with 2 labels (binary labels) in iamge. In interactive graph-cut approach could only be segmented into two parts: object and background, with soft constraints on boundary and region. Graph-cut is a typical graph theory based algorithm, which transforms the image segmentation problem into the Min-cut problem of the graph. Its solution method of the minimum cut problem is relatively mature. The most commonly used method is the *maxflow* method.

Each image can be mapped into an undirected graph $G = <V, E>$ with weights. Each node $v \in V$ in the graph corresponds to each pixel in the image, and each edge $e \in E$ is connected with a pair of adjacent pixels. There are two special points in the graph cut: source point and sink point, which are respectively recorded as s, t, and are collectively referred to as terminal vertices. The non-negative weight w_e of each edge in the graph can be understood as the cost value. The vertices of the minimum cut graph are divided into two disjoint subsets S and T, where $s \in S, t \in T$, $S \cup T = V$. These two subsets actually correspond to the foreground and background, thus completing the segmenttation task.

Image segmentation is actually marking the each pixel in the image, usually with 0 and 1 representing the background and foreground, respectively. Then the segmentation of the image is actually looking for a set of labels $l = \{l_1, l_2, \cdots, l_p\}$, $p \in V \backslash \{s, t\}$ that minimizes the energy of the cost function

$E(l) = \lambda R(l) + B(l)$ where $R(l)$ and $B(l)$ are regional penalty item and edge penalty item, respectively. When converting image segmentation into minimum cut, the minimum value of the energy functional of graph-cut corresponds to the minimum value of the minimum cut problem. Thus, according to the expression of the energy functional of the graph cut, the weight of each side of the graph can be set, where pixels are point sets for the foreground and background seed, respectively, and the four connected domains are also adopted. Thus, once the structure of the graph-cut is done, the segmentation algorithm only needs to solve the equivalent flow problem.

Lesion contour analysis in DW-MRI

Apparent diffusion coefficient (ADC), derived from diffusion-weighted magnetic resonance images (DW-MRI), measures the motion of water molecules in vivo and can be used to quantify tumor response to therapy. In this paper, our goal was to determine whether the DW-MRI can be used for qualitative and quantitative liver cancer analysis so as to develop an automated method for improving the accuracy of liver segmentation in DW-MRI and increasing the ability of diagnosis of disease.

Apparent diffusion coefficient (ADC), derived from diffusion-weighted magnetic resonance images (DW-MRI), measures the motion of water molecules in vivo and can be used to quantify tumor response to therapy. The accurate measurement of ADC can be adversely affected by organ motion and imaging artifacts. As for image-based segmentation methods, it will be a great challenge to extract the liver and its vascular areas completely and accurately. For the under-segmentation at the edge of liver, the DW-MRI is very effect to get the accurate segmentation results.

The initial liver contour feature point is written as $\{p_1, p_2, \cdots, p_i, \cdots, p_k\}$, where k is the number of feature points. The starting characteristic points p_i and $p_j (j = i + t)$ are randomly chosen, where $\overline{p_i p_j}$ represents the straight line between point p_i and p_j; H_U represents the maximum distance from the liver edge pixel point to $\overline{p_i p_j}$, and I_{ij} represents the brightness value of the closed area formed at the liver edge between line $\overline{p_i p_j}$ and point p_i and p_j. Therefore, it is changed into the average brightness of the closed area. In order to obtain the best contour,p_i and p_j must meet the following three conditions: (a) $\overline{p_i p_j}$ does not pass through the liver region; (b) the length ratio of H_U to $\overline{p_i p_j}$ is greater than threshold $T\lambda$; (c) the average brightness I_{ij} is greater than the brightness value $a + b$. If both p_i and p_j meet the above three conditions, the concave region is considered to be the liver area. Combined the points p_i with p_j, the point p_i to the position of p_j, p_j to the position of p_{j+t}will be moved; otherwise, point p_i remains unchanged, point p_j moves back along the edge to the previous feature point p_{j-1}. If $j = i$, move p_i to the next feature point p_{i+1}, and p_j to p_{i+1+t} This process is repeated until all feature points on the liver contour have been calculated and the algorithm is over. In the experiment, *t is set as* half of the contour feature points, and the value of T_λ is 0.5.

Experiment results and analysis

The segmentation of the liver tissues is a key step in developing any non-invasive computer-aided diagnostic (CAD) system. This paper introduces a geometric (graph-cut)-based model approach for the liver segmentation from diffusion-weighted magnetic resonance imaging (DW-MRI). In this section, we will use the same graph-cut algorithm to process MRI and DW-MRI, which determines whether the DW-MRI can be adopted for qualitative and quantitative liver cancer analysis so as to develop an automated method for improving the accuracy of liver segmentation in DW-MRI and increasing the ability of diagnosis of disease.

Data set

To evaluate the value of quantized diffusion weighted magnetic resonance imaging(DWI) in diagnosis of focal liver lesions, a series of 2D 256×256 abdomen MRI images are used in experiment, which are taken with a GE Genesis Signa HiSpeed CT system from a third-Grade Class A hospital. A simulation analysis is performed in 206 patients with focal fiver lesions(FLL) and 35 cases of liver image data who have completed the examination using 3.0 T MR, including DWI and routine non-enhanced MRI. In order to cover the entire liver, each patient scan consisted of up to four separate DWI acquisitions resulting in a total of 52 different series for analysis. The DW-MRI images were acquired with fat suppression to visualize tumors with good contrast from their background. This in turn resulted in a robust segmentation of tumors. And the parameters are: slick thickness 15.0, repetition time 4.7, echo time 1.2, magnetic field strength 15,000, flip angle 60 degrees. The experiments are performed on a PC with i5 2.8Ghz, 8G RAM. We will show the result with two images. One is the abdomen DW-MRI, and the other is the same image with some missing parts. The initial prior shape is a similar but not exactly fit liver.

Evaluation criteria

To evaluate the quality of our given segmentation, we follow the empirical discrepancy approach. Segmentation in MRI and DW-MRI are compared to expert-generated references and rated according to detected deviations. There exists a multitude of different measures for this purpose,we selects the Dice coefficient was calculated between segmentation by one method and the ground truth.

The bigger the value is, the better the segmentation result. In addition, we employed five volume and surface based measures:the mean ratios of the volumetric overlap error (VOE), relative volume difference (RVD), average symmetric surface distance (ASD), root mean square symmetric surface distance (RMSD) and maximum symmetric surface distance (MSSD),which were proposed by MICCAI 2007 challenge in detail. The smaller the value is, the better the segmentation result.

Qualitative and quantitative comparison

On our dataset, the liver Dice results using our proposed model in MRI and DW-MRI is shown as Fig. 2 for each patient. It is obvious that segmentation quality using our model is higher than that of using the comparison MRI, which indicates that the former one could well represent soft tissue deformation. The overall median of liver Dice using our model increases significantly from 0.68 to 0.84, compared with the MRI.

Figure 3 shows the results of two sets of experiments randomly selected from the database, which is the results of two experiments randomly selected from different abdominal DW-MRI sequences. The Fig. 3(a) is the original MRI image. The areas marked by the closed curve in the Fig. 3(b) is the segmentation results obtained by using the graph cut algorithm (GC). The Fig. 3(c) is the original DW- MRI image. The areas marked by the closed curve in the Fig. 3(d) is processed by the same segmentation algorithm. It can be seen from the Fig. 3 that because the brightness inside the liver is not uniform in MRI, the graph cut algorithm can only effectively extract the liver parenchymal region, and the vascular region will be under-segmented. The contour optimization method proposed in this paper can effectively solve this problem so as to get a complete and accurate liver area. The segmentation result obtained by DW-MRI is obviously better than MRI.

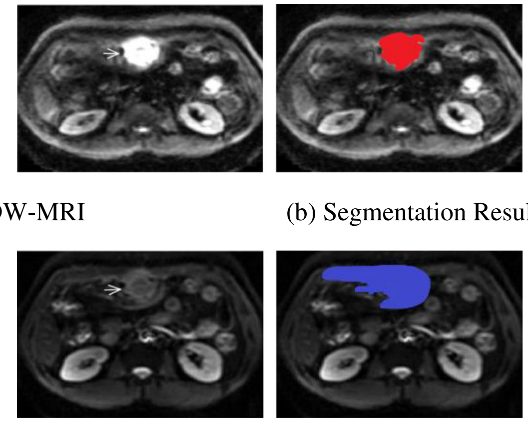

Fig. 3 Comparison for DW-MRI and MRI

The results of the 10 test sequences in database are statistically analyzed. The mean and standard deviation are shown in Table 1. Compared to the MRI, the RVD obtained by the DW-MRI has a large negative mean value, mainly because the method cannot include the liver blood vessels during the segmentation process. In addition, the method has the same mean and error for the other four evaluation indicators, which indicates that the method can effectively and completely segment the liver region in the DW-MRI sequence by combining graph cut, which has high accuracy and robustness. It can be seen large distance with the ground truth in the measures of ASD, RMSD, and MSD. ICV method obtained the best VOE and ASD due to a Level Set model for user interaction. Our results show slightly better performance than ICV method, which RVD, RMSD, and MSD are 1.03%, 1.68 mm, and 12.33 mm respectively.

Fig. 2 The comparison of Dice measure using original graph-cut and our algorithm

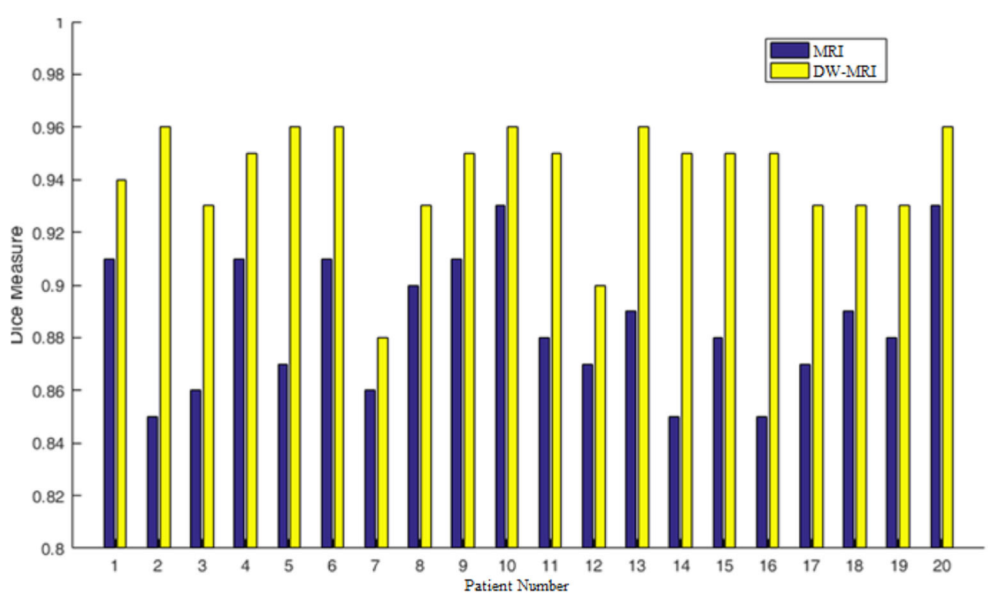

Table 1 Comparison quantitative results between MRI and DW-MRI

Source	VOE(%)	RVD(%)	ASD(mm)	RMSD(mm)	MSD(mm)
MRI	6.0±0.6	−2.3±1.8	1.1±0.2	1.5±0.5	27.1±8.6
DW-MRI	5.5±0.6	−0.2±1.1	0.9±0.5	1.5±0.3	22.0±3.2

Discussions

It is important to make a correct diagnosis of liver focal lesions to avoid unnecessary operative and invasive procedures. In this work liver cancer was the most common space occupying lesion. In existing researches of the liver have revealed poor lesional characterization regarding the signals intensity pattern as most of the benign and malignant focal lesions appeared iso-hypo intense at T1WI and hyper-intense T2WI. DW-MRI is a relatively existing technological improvement that expanded MRI capabilities and it could be helpful for identification, characterization, prognostic stratification and follow-up during treatment. We found that DW-MRI with ADC value measurements can provide in the differentiations of different liver focal lesions, which established that combination of DWI with MRI studies increase the accuracy of benign and malignant lesions characterization with accurate diagnosis.

The gray-scale features and boundaries of regions of interest (ROIs) segmented by graph-cut algorithm describe the spatial distribution of pixels, which can reflect the histological type and pathological features of lesions. They are often used in the medicine image analysis. Therefore, they have attracted more and more attention in the field of artificial intelligence medical imaging. MRI is to detect the emitted electromagnetic waves by applying a gradient magnetic field according to the different attenuation of the released energy in different structural environments inside the material, so its image is very smooth, and the accurate measurement of MRI can be adversely affected by organ motion and imaging artifacts. Thus, DW-MRI is more suitable for tumor segmentation than MRI, so as to get more accurate details.

In this paper, we use the same graph-cut algorithm to process MRI and DW-MRI, and the experimental results show that the DW-MRI can be used for qualitative and quantitative liver cancer analysis so as to develop an automated method. It can improve the accuracy of liver segmentation in DW-MRI and increase the ability of diagnosis of disease. In addition, the ADC value derived from a higher b-value provides a better sensitivity and specificity in discriminating liver cancer from space occupying lesion. We think that most disease diagnoses can be performed directly on DW-MRI images.

Conclusions

In this paper, our goal was to determine whether the DW-MRI can be used for qualitative and quantitative liver cancer analysis so as to develop an automated method, which will improve the accuracy of liver segmentation in DW-MRI and increase the ability of diagnosis of disease. We firstly analyzed the the research status of liver cancer diagnosis, especially on the issues of liver image segmentation technology in MRI. Then, the imaging mechanism and image features of the DW-MRI were analyzed, and the initial DW-MRI slice is segmented by graph-cut algorithm. Finally, our obtained result from the liver DW-MRI image is quantitatively and qualitatively analyzed. Experimental results show that DW-MRI has a great advantage in the diagnosis, and the DWI images of benign lesion group was lower than malignant lesion. Therefore, DW-MRI is segmented by graph-cut algorithm can provide important additional information regarding differential diagnosis of specific liver cancer to some extend.

Compliance with ethical standards

We declare that we have no conflict of interest. This article does not contain any studies with human participants or animals performed by any of the authors. Informed consent was obtained from all individual participants included in the study.

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