UNIVERSITI PUTRA MALAYSIA

LIVER SEGMENTATION ON CT IMAGES USING RANDOM WALKERS AND FUZZY C-MEANS FOR TREATMENT PLANNING AND MONITORING OF TUMORS IN LIVER CANCER PATIENTS

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By

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LIVER SEGMENTATION ON CT IMAGES USING RANDOM WALKERS AND FUZZY C-MEANS FOR TREATMENT PLANNING AND MONITORING OF TUMORS IN LIVER CANCER PATIENTS

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October 2017

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Liver and liver tumor segmentation from Computed Tomography (CT) images and tumor burden analysis play an important role in the choice of therapeutic strategies for liver tumor treatment planning and monitoring. Furthermore, accurate segmentation of the blood vasculature structure can result in improved diagnosis and easier liver tumor treatment planning. Although many methods have been proposed, this segmentation remains a challenging task due to the lack of visible edges on most boundaries of the liver coupled with high variability of both intensity patterns and anatomical appearances in pathological livers. In this thesis, a new segmentation method for liver, liver tumors and liver vasculature structure from contrast-enhanced CT imaging is proposed. As manual segmentation for liver treatment planning is both labor intensive and time-consuming, a more accurate and automatic segmentation is desired. The proposed method is fully automatic, requiring no user interaction. The proposed segmentation is evaluated on real-world clinical data using publicly accessible benchmark clinical liver datasets containing one of the highest numbers of tumors and pathological livers utilized for liver tumor and vasculature segmentation. The proposed method is based on a hybrid method integrating random walkers algorithm with integrated priors and particle swarm optimized spatial fuzzy c-means (FCM) algorithm with level set method and AdaBoost classifier.

Based on the location of the lung, the liver dome is automatically detected and the liver is then extracted by random walkers method and refined using a fuzzy level set method. This is followed by the clustering of the liver tissues using particle swarm optimized spatial FCM algorithm. Then, these tissues are classified into tumors and blood vessels by an AdaBoost classification method based on tissue features extracted utilizing first, second and higher order image features selected by a minimal-redundancy maximal-relevance feature selection approach. Finally, the segmentation is refined using level set method.

The proposed method is able to segment all tumors and blood vessels with a largest axial diameter of over 5mm and 3mm, respectively. In comparison, RECIST standard commonly used in evaluation of tumors suggests a minimum largest axial diameter of 10mm for tumors and has no recommendations for the minimum largest axial diameter of blood vessels. The proposed method showed high accuracy on segmenting livers with a mean overlap error of 6.3% and mean absolute relative volume difference of 1.9%. In the case of liver tumor segmentation, with a mean overlap error of 19.6% and mean absolute relative volume difference of 11.2%. For liver vasculature segmentation, a mean overlap error of 35.9% and mean absolute relative volume difference of 16.7% was achieved by using the proposed segmentation method, making it amongst the most accurate liver vasculature segmentation methods. The medical applicability of the proposed method was further validated by a consultant radiologist where in 80% of the segmented tumors, the segmentation by the proposed method was preferred over the provided ground truth segmentation in the dataset. In case of liver envelope segmentation, the consultant radiologist suggested that the liver segmentation by the proposed method is clinically acceptable.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

SEGMENTASI HATI PADA IMEJ CT MENGGUNAKAN PEJALAN RAWAK DAN FUZZY C-MEANS UNTUK PERANCANGAN DAN PEMANTAUAN TUMOR DI KALANGAN PESAKIT KANSER HATI

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Segmentasi hati dan ketumbuhan hati daripada yang dikelaskan dari imej Pengiraan Tomografi (CT) memainkan peranan penting dalam strategi terapi bagi penyakit hepatic dan juga jenis rawatan yang akan diberikan. Tambahan lagi, segmentasi yang tepat melalui struktur vaskular akan dapat membantu diagnosis dan juga ketepatan pembedahan hati serta perancangan berkaitan. Walaupun banyak teknik yan bole digunakan, proses segmentasi ini adalah amat sukar kerana kurangnya bucu yang kelihatan berdasarkan sempadan paru-paru dengan variasi tertinggi oleh corak dan struktur atomi patologi paru-paru. Di dalam tesis ini, proses segmentasi untuk paru-paru, ketumbuhan hati dan juga bentuk struktur hati dari kiraan kontras paparan imej CT yang lebih maju dicadangkan. Berdasarkan segmentasi manual yang memerlukan intensif kerja dan keperluan masa dan juga ketepatan maka segmentasi automatik tetap diperlukan. Cadangan proses segmentasi ini dinilai, dengan data klinikal sebenar dan boleh dibandingkan bersama penilaian data set klinikal hati yang mengandungi ketumbuhan tumor dan struktur patologi hati yang digunakan dengan struktur segmentasi vaskular, berdasarkan teknik hibrid melalui integrasi algoritma pejalan rawak dan juga berdasarkan faktor yang diintegrasikan dengan algoritma zarah paya dioptimumkan spatial kabur c-means dengan kaedah tahap yang ditetapkan dan klasifikasi AdaBoost.

Berdasarkan kepada lokasi hati, kubah hati dikesan secara automatik dan bahagian hati ini kemudiannya diekstrak dengan kaedah pejalan rawak dan ditapis menggunakan kaedah tahap set yang kabur. Ini diikuti dengan pengelompokan tisu hati menggunakan algoritma c-means fuzzy spasial zarah paya. Kemudian, tisu-tisu ini diklasifikasikan ke dalam tumor dan saluran darah oleh kaedah klasifikasi AdaBoost berdasarkan ciri-ciri tisu yang diekstrak dengan menggunakan imej pesanan pertama, kedua dan lebih tinggi ciri yang dipilih dengan pendekatan pemilihan ciri maksimal-perkaitan yang minimum-pertindihan. Akhirnya, segmentasi disempurnakan menggunakan kaedah set peringkat.

Kaedah yang dicadangkan dapat mensegmenkan semua tumor dan saluran darah dengan diameter paksi terbesar lebih daripada 5mm dan 3mm, masing-masing. Sebagai perbandingan, standard RECIST yang lazim digunakan dalam penilaian tumor menunjukkan diameter minimum maksimum paksi 10mm bagi tumor dan tidak mempunyai cadangan minimum diameter paksi pembuluh darah yang paling kecil. Kaedah yang dicadangkan menunjukkan ketepatan yang tinggi terhadap pemisah dengan kesilapan pertindihan sebanyak 6.3% dan perbezaan purata perbezaan antara 1.9%. Dalam kes pembahagian tumor hati, dengan kesilapan sebanyak 19.6% dan perbezaan min purata relatif 11.2%. Bagi segmen vaskulatur hati, kesilapan bertindih sebanyak 35.9% dan perbezaan min purata relatif 16.7% dicapai dengan menggunakan kaedah segmentasi yang dicadangkan, menjadikannya di antara kaedah segmentasi hati yang paling tepat. Pemaparan perubatan kaedah yang dicadangkan kemudiannya disahkan oleh ahli radiologi perunding di mana dalam 80% daripada tumor yang disegmentasi, segmentasi dengan kaedah yang dicadangkan lebih disukai berbanding segmen kebenaran permukaan yang disediakan dalam dataset. Dalam kes segmentasi sampul hati, perunding radiologi mencadangkan supaya segmentasi hati oleh kaedah yang dicadangkan diterima secara klinikal.

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

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LIST OF ABBREVIATIONS

AUROC	Area under Receiver Operating Characteristics
AvgD	Average Surface Distance
CAD	Computer-Assisted Diagnosis
CCT	Contourlet Coefficient Texture
CT	Computed Tomography
DFT	Discrete Fourier Transform
DSC	Dice Similarity Coefficient
DWT	Discrete Wavelet Transform
ELM	Extreme Learning Machine
EM	Expectation-Maximization
FCM	Fuzzy C-Means
FDCT	Fast Discrete Curvelet Transform
FN	False Negative
FP	False Positive
GC	Graph-Cut
GLCM	Gray Level Co-Occurrence Matrix
GLDM	Gray Level Difference Matrix
GLRLM	Gray Level Run Length Matrices
GVF	Gradient Vector Flow
HAP	Hepatic Arterial Phase
HU	Hounsfield Unit
KNN	K-Nearest Neighbor
LBP	Local Binary Patterns
LUT	Look-Up Table
MAP	Maximum a Posteriori
MaxD	Maximum Symmetric Surface Distance
MI	Mutual Information
MICCAI	Medical Image Computing and Computer-Assisted Intervention
MP	Max Probability
MPNN	Modified Probabilistic Neural Network
MRI	Magnetic Resonance Imaging
NN	Neural Network
NPV	Negative Predictive Value
PA	Probabilistic Atlases
PCNN	Pulse Coupled Neural Network
PDE	Partial Differential Equation
PDF	Probability Distribution Function
PNN	Probabilistic Neural Network
PPV	Positive Predictive Value
PSO	Particle Swarm Optimization
PVP	Portal Venous Phase
RBF	Radial Basis Kernel Functions
RECIST	Response Evaluation Criteria in Solid Tumors
RMSD	Root Mean Square Symmetric Surface Distance
ROC	Receiver Operating Characteristics
RVD	Relative Volume Difference
SIRT	Selective Internal Radiation Therapy
SMOTE	Synthetic Minority Over-Sampling Technique

SSM	Statistical Shape Models
SVM	Support Vector Machines
TAE	Trans-arterial Embolization
TBE	Tumor Burden Error
TEM	Texture Energy Measures
TP	True Positive
VOE	Volumetric Overlap Error

CHAPTER 1

INTRODUCTION

Cancer is one of the leading causes of death worldwide. It was responsible for 8.2 million deaths in 2012 and the number of cancer deaths is estimated to raise over 11 million by 2030 (Globocan, 2016). Amongst the main cancer types, liver tumor is one of the most frequent cancer types (especially in South East Asia) and have caused approximately 745000 deaths in 2012, being the 6th most deadly cancer in the world (Globocan, 2016). Therefore, 3D analysis and interpretation of images from various imaging modalities play a crucial role in diagnosis and treatment planning for liver tumor. Medical 3D imaging is used in many medical tasks such as diagnosis, follow-up, and treatment planning or evaluation of the patients. However, the amount of data produced by these 3D imaging modalities makes handling and interpretation of images by humans difficult without the aid of automatic or semi-automatic image processing techniques and computer aided analysis.

This treatment planning requires liver and tumor volume measurements, the vessel topography and the relation of tumors to these structures. In addition to these, analysis can also be used for monitoring purposes for patients undergoing different cancer management related medical treatments. Accurate segmentation from 3D image data can be considered as the basis of almost all treatment options. Segmentation of the liver and tumors inside allows easier computation of this ratio, simplifying the planning for surgical resection. The identification of the regions to be removed becomes easier as tumors are well defined, the segmentation also provides a precise location of the tumors inside the anatomical segments of the liver simplifying the preoperational planning.

In addition, liver and tumor segmentation also offers several applications for treatment planning, such as thermal percutaneous ablation (Rossi et al., 1996), percutaneous ethanol injection (PEI) (Livraghi et al., 1995), radiotherapy surgical resection (Albain et al., 2009) and arterial embolization (Yamada et al., 1983). Furthermore, in treatments such as Selective Internal Radiation Therapy (SIRT) the fractional dose calculation of the liver and tumors depend on the volume of the liver and tumors (Al-Nahhas et al., 2006). Hence, in order to calculate the dose delivered to the tumor, it is essential to segment the tumor from the background and calculate the volume of the tumor region.

Although many liver segmentation methods have been proposed, there is still room for improvement especially in pathological livers where irregular liver shape and intensity patterns make automatic segmentation challenging. Furthermore, tumor and blood vessel segmentation methods are even less developed and researched. On the other hand, Computer-assisted Diagnosis (CAD) systems for livers are amongst the least developed compared to some other medical CAD systems available. While most of these CAD systems utilize state of the art machine learning methods, they use either manual segmentation steps or are based on simple segmentation methods.

1.1 Problem Statement

During the last century, many tools have been developed for detailed body imaging. Started by imaging the body using a 2D approach (X-Ray, Ultra-Sound) and more recently as a series of 2D images of the body represented as 3D volumes using non-invasive 3D imaging modalities such as Computed Tomography (CT) or Magnetic Resonance Imaging (MRI). Medical 3D imaging is used in many medical tasks such as diagnosis, follow-up, and treatment planning/evaluation of the patients. However, the amount of data produced by these 3D imaging modalities makes handling and interpretation of images by humans difficult without the aid of automatic or semi-automatic image processing techniques and computer aided analysis.

Furthermore, outlining multiple organs for applications such as radiotherapy can take up to or more than one hour making manual segmentation a time-consuming and tedious task. Additionally, most of the time, a non-trivial inter- and intra-observer variability can be observed, depending on the point in time or the level of user experience, different persons or even the same person may outline the organ boundaries differently (Göçeri et al., 2015). Therefore, a need for robust and reliable automatic or semi-automatic segmentation and computer aided analysis for supporting the operator during diagnosis, treatment or operation planning exists.

Many tumors can appear inside the liver although in practice only a subset of tumors is measured to determine their growth and size. In order to standardize the procedure, the Response Evaluation Criteria in Solid Tumors (RECIST) standard has been proposed (Eisenhauer et al., 2009). Based on the RECIST standard, only tumors with the largest axial diameter of over 10mm are considered for measurement while a decrease of 30% or more in the diameter is considered as a partial response to the treatment and an increase of 20% or more is considered as a progressive tumor. The main critical problem with RECIST standard as stated by Bornemann et al. (2007) is the fact that a single measurement of a diameter cannot correspond to the size of a 3D object such as a tumor, as these tumors are not spherical in shape and are mostly asymmetrical. In practice, a tumor can grow significantly if measured in 3D but its largest axial diameter may not show a significant change. Some livers can have more than five tumors, while based on RECIST guidelines, a maximum of five tumors per liver are measured as an overall indicator of the patient's condition.

Furthermore, the size and dynamics of changes in the size of tumors during given time periods are the subject for a routine assessment in every hospital. Depending on the size of the hospital, the radiologist might be asked to assess tens of studies per day, which makes this task very tiring and time-consuming. Exact delineation of the tumor is, therefore, unrealistic in the light of the large number of cases to be reviewed. Radiologists have to check these CT scans at regular intervals to determine response to the treatment (every 4 to 6 months). An automatic tool would mean a time gain for these physicians. The contribution of an automatic segmentation method for liver tumors for tumor evaluation, either before or after treatment is obvious.

Manual segmentation of the blood vessel network inside the liver envelope can be a tedious task due to a high number of individual vessels inside a CT volume. Accurate segmentation of the blood vasculature structure can result in improved diagnosis and more accurate liver surgical and resection planning (Kirbas and Quek, 2003). In treatment options such as SIRT, knowing the 3D structure and branching of the blood vessels (especially those feeding the tumors) along with ability to display the liver and the tumor(s) in a 3D space can ease treatment planning as a more accurate map for the insertion point of the radioisotope can be generated (Gulec and Fong, 2007). While many methods have been proposed for this segmentation, vessel segmentation remains a very challenging task with many of the previously proposed methods achieving average segmentation accuracy.

1.2. Research Aim and Objectives

This thesis intends to develop an improved framework for segmentation of livers, liver tumors and blood vessels in computed tomography images with good accuracy by utilizing random walker, FCM and level set approaches combined with AdaBoost classifier. The objectives of the thesis are as follows:

i) To design an accurate liver, liver tumor and blood vessel network segmentation method with a focus on segmenting pathological livers using machine learning methods.

ii) To evaluate the accuracy of the proposed segmentation method and liver tumor detection rate using publicly accessible datasets.

iii) To provide liver volume, tumor volume and tumor burden for patient treatment planning and monitoring.

1.3. Scope and Contribution of the Thesis

In this study, publicly accessible datasets designed to be used as a benchmark for different liver, tumor and vessel segmentation methods has been utilized. To ensure clinical applicability of the proposed algorithm, the expertise of a professional radiologist with over thirty years of experience was utilized. The method was validated using one of the highest number of tumors used for validating liver tumor segmentation methods. Furthermore, the vessel segmentation performance of the proposed method was also validated using the one of the highest number of livers with vasculature map provided by expert radiologist(s). In this study, tumors with a largest axial diameter of over 5mm and blood vessels with a largest axial diameter of over 3mm are considered for the segmentation. In comparison, RECIST standard commonly used in evaluation of tumors suggests a minimum largest axial diameter of 10mm for tumors and has no recommendations for the minimum largest axial diameter of blood vessels.

First, an accurate liver and liver tumor segmentation can be used for measuring the liver and tumor volumes, increasing the effectiveness of various treatment approaches. Then, the proposed method is able to identify and segment all major blood vessels inside the liver. Finally, in addition to using these segmentations as an input for a liver related CAD system, they can be used to visualize the location of tumors and blood vessel network feeding the tumor.

Visualization of the anatomy of the liver and pathologies makes treatment planning more efficient, especially for liver resection surgery planning, living donor liver transplants and for identifying the optimum insertion point for treatments such as thermal ablation and SIRT. Moreover, planning for radiotherapy treatments becomes more efficient as not only the location of the tumor is defined, but also the location and orientation of the vasculature structure feeding the tumor(s).
In addition, the inclusion of liver vasculature is essential in liver transplants and is also beneficial in liver resurrection as surgery planning becomes easier and any complications that might arise from the possibility of puncturing major blood vessels inside the liver can be averted.

1.4. Outline of the Thesis

The organization of the remaining chapter of thesis is as follows:

Chapter Two acquaintances the reader with different imaging concepts related to medical imaging. Then, different problems faced during liver, tumor and vessel segmentations and different segmentation approaches proposed for these segmentations are reviewed. Finally, the positives and negatives of these approaches are discussed and different conclusions derived from previous works are discussed.

Chapter Three deals with the methodology behind the developed framework and discusses the main ideas and theories relevant to the implementation of the different approaches for the segmentation and classification of different tissues inside the liver.

Chapter Four deals with the medical evaluation of the obtained segmentation and highlights the performance figure of the developed framework. The developed algorithm is compared with the other methods in the literature, showing its performance along with its weaknesses.

Chapter Five summarizes the proposed algorithm and discusses the obtained performance figures and possible future enhancements.

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