DETERMINATION OF FIBROSIS SCORE IN THE VENTRICULAR ARTER BY USING IMAGE PROCESSING TECHNIQUES ON HISTOPATHOLOGICAL IMAGES

Dilek Sönmezer[1], Yasemin Benderli Cihan[2], Fatma Latifoğlu[3]

[1]Çukurova University, Faculty of Engineering and Architecture
Department of Biomedical Engineering
Adana, Turkey
dsonmezer@cu.edu.tr
[2]Department of Radiation Oncology
Kayseri Education and Research Hospital
Kayseri, Turkey
cihany@erciyes.edu.tr
[3]Erciyes University, Faculty of Engineering
Department of Biomedical Engineering
Kayseri, Turkey
flatifoglu@erciyes.edu.tr

ABSTRACT

Histopathological image analysis is an important area for pathological image analysis and diagnosis in medicine. Among cancer patients, radiotherapy is widely used for treatment modality. The aim of the radiotherapy is giving maximum dose to tumor tissue as well as maintaining normal tissue unaffected as possible. The increase of the radiation dose is parallel with local tumor control. However, risk of complication of normal tissue is also increased. Thus, controlling of the tumor depends on the normal tissue tolerant. In this study, we aim to support radiologists to detect and control radiation dose and its effects for the radiotherapy. Determining of the ventricular artery thickness by using image processing techniques can give information about radiation effects and dose. Using by image processing techniques, adventitia layer which of cardiac vessel layer thickness is measured. For this measurement, whole cardiac histopathological RGB image is cropped and studies are applied on this image. Then RGB image is converted to grayscale image and after converted the binary image. Adventitia layer is detected with edge detecting method. After segmentation of the adventitia layer, this layer thickness is measured to show effects of the radiation dose. Thus, with this study an optimal radiation dose can be adjusted according to the increase of the adventitia thickness.

Keywords: Histopathological images; cardiac tissue; radiotheraphy; fibrosis

INTRODUCTION

Histopathological image analysis is important for getting good results on therapy.

In this study, we aim to support radio therapist to detect radiological effects in cancer treatment. Treatment of radiation is used to kill cancer cells or to stop of cancer cells proliferation. At that time, determination of radiation dose limits depending on the layer of vessel wall can be a new approach in cancer treatment. Radiation damages the vessel wall, especially causes vessel wall fibrosis. Thus, radiation dose and its application are important for human health.

Image processing techniques for diagnosis of diseases are widely applied in medicine [1, 2]. Fibrotic Myocardial Tissue Mechanics, classification of cervical cancer, diagnosis of prostate cancer, morphological analysis of carotid artery plaque and a study related with coroner artery and many more studies about histopathological image analysis are present in literature [3-7]. Image processing techniques also used in enhancement of vessels on angiography images. [8]. Response of arterial injury is determined based on adventitia of artery wall layer [9]. Thickness of the adventitia layer increases with the increment of the arteriosclerosis [12].

Radiotherapy is usually used for treatment of cancer disease, but also late side effects which depends on radiation therapy become crucially important [10]. Toxicological effects on the cardiovascular system are resulted from radiotherapy used for treatment breast cancer. [Mc Chesney SI, Rad Res, 1991; 125].

The aim of this study is to investigate whether the use of radiotherapy (RT) has a contribution to the development of radiation fibrosis in the heart.

MATERIAL AND METHODS

In this study, experimental studies were conducted in Erciyes University Faculty of Medicine Hakan Çetinsaya Experimental and Clinical Research Center (DEKAM) after ethical aproval from the Animal Experiments Local Ethics Committee of Erciyes University Faculty of Medicine. Twenty healthy female Wistar Albino rats aged 8 weeks and weigthing 213±27 grams were used in the study. The rats were kept under standard laboratory conditions (12:12-hour light/dark cycle at 25±3 ^{o}C) and fed with standard commercial pelleted feed. The rats were divided into 2 groups with 10 animals in each group. The groups were designed as follows:

Group C: The control group. No treatment was administered. The animals were followed under similar conditions as the other animals.

Group RT: The radiotherapy-only group. The thoracic region was irradiated while the animals were under anesthesia.

Histopathological examination: Samples were taken from various regions of heart that were fixed in formalin. Following paraffin blocking procedure, serial cross-sections of 5 microns were obtained. They were stained with hematoxylin-eosin. Mean of the fibrosis scoring was obtained for the heart vessel of each rat. The fibrosis score was numerically assessed based on values from 0 to 4. The scoring system for the intensity of fibrosis is as follows:
Score 0: No fibrosis or minimal fibrosis in the vessel wall.
Score 1: Moderate fibrosis that does not cause marked structural damage on the heart.

Score 2: Increased fibrosis with definite damage to heart vessel and formation of fibrous bands or small fibrous masses.
Score 3: Fibrosis that causes severe distortion in the heart vessel and that has large fibrous areas.
Score 4: Total fibrosis.

The rats were divided into two equal groups as follows: Group C: control and Group RT: RT only. RT was administered heart region in a single fraction at a dose of 12 Gy using a Co–60 device. At the end of 24 weeks, the rats were sacrificed after sedation. The heart was removed and blocked in paraffin. After H&E staining, the level of fibrosis in each cross-section was assessed with the help of a scale. Histopathological images were obtained from vessels, which showed late toxic effect on the heart. Histopathological tissue preparats of cardiac vessel were used for imaging. These cardiac tissues were locally applied radiotherapy on healthy rats. Leica microscope together with Olympus 3.2 Megapixel, C-3020 200m camera was used for routine inspections.

Histological image dataset was cinsists of 10 image slides. Our approach proposes measuring the adventitia thickness in order to understand effects of the radiation therapy. Methods for measuring adventitia thickness were combined with image processing techniques. Firstly, RGB image of the histopathological image was converted to gray-level image. After that, optimal thresholding was carried out by Otsu method to create a binary image. Then, mathematical morphology operations were used to obtain adventitia layer. The proposed approach is based on measuring of the adventitia layer by segmenting of this layer on histopathological images. Obtaining an average of the adventitia thickness of two images was used to show effects of the radiotherapy.

Figure 1. shows the microscopic image of the vessel of the rat at 600x magnification. In this image low radiation dose was applied to rat cardiac. Segmentation of the outer layer is seen as blue color (Fig. 1).

In Fig. 1.A, histopathological preparats were imaged via light microscopy at 600x magnification. RGB image was cropped in order to show the related part of the vessel area in figure 1.B. Then, RGB image was converted to grayscale image and after that obtained grayscale image is converted to binary image as seen in figure 1.D. Vessel adventitia layer was detected with Sobel edge detection method (Fig. 1.E). Taking complementation of the edge was detected image and showed it on grayscale vessel image and RGB image (Fig. 1.G). Finally, adventitia layer was measured with using five points on the layer of the distance between outer and inner surfaces (Fig. 1.I).

RESULTS AND DISCUSSIONS

Radiotherapy is an important treatment for breast cancer and any other kinds of cancers diseases. Because of the side effects of the radiation can generate problems on cardiac tissue. Due to the success of mammography in early diagnosis and the advances in chemotherapy and radiotherapy, breast cancer is a type of cancer whose treatment techniques is changing rapidly and can be combined also. A multimodal treatment that includes surgery, radiotherapy, chemotherapy, and hormonotherapy is used in the treatment of breast cancer. After surgery, patients are initially treated with chemotherapy and then undergo RT. Although the optimal sequence of chemotherapy and RT is still controversial, the generally accepted approach is RT after chemotherapy is completed. It is still unclear whether hormonotherapy should be used sequentially or concurrently with RT.

For detection of the radiation toxicological effects on the cardiac vessels are examined with proposed method in healthy but applied radiation to rats. Therefore, an optimal dose of the radiation can be applied according to vessel damaged score. In this study, we aim to measure just adventitia layer using by histopathological vessel images.

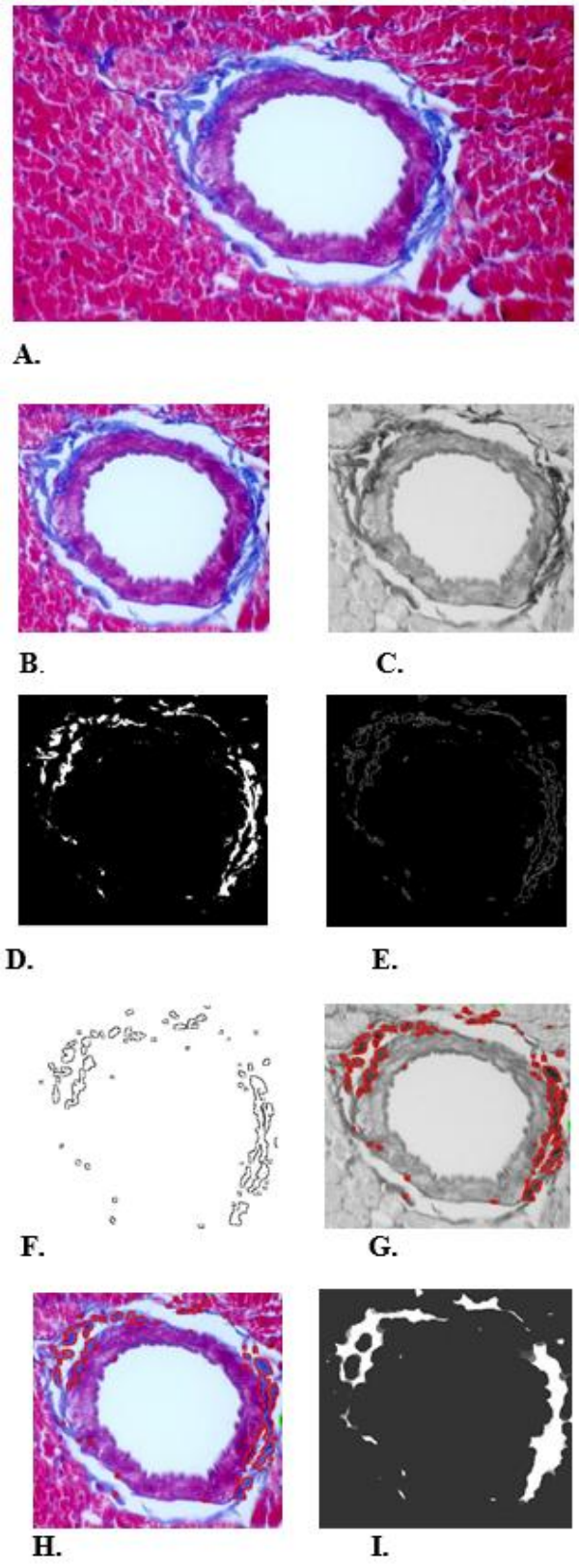

Fig. 1 Adventitia layer segmentation and measuring flowchart.

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