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Determination of Instantaneous Interventricular Septum Wall Thickness by Processing Sequential 2D Echocardiographic Images

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Abstract: Non-invasive quantitative analysis of the heart walls thickness is a fundamental step in diagnosis and discrimination of heart disease. Thickness measurements in 2D echocardiographic images have many applications in research and clinic for assessing of wall stress, wall thickening and viability parameters. Regarding to interventricular septum wall thickness measurement by conventional manual method is more dependent on sonographer experiment; this encouraged these researchers to develop a semi-automatic computer algorithm in accessing to interventricular septum segments thickness. We proposed and carried out a computerized algorithm for wall thickness measurements in 2D echocardiographic image frames. In this program, wall thickness measurement is based of intensity profile function and adaptive bilateral thresholding operation. For validation, thicknesses of septum base and mid segments were estimated in constituent image frames with use of proposed method and then were compared with conventional manual results at same images of the cardiac cycle by statistical methods. In our sample image frames (240 corresponding segments; with different rang of image quality), a bias of 0.10 and 0.12 mm with SD differences of ±0.81 and ±0.72 mm and correlation coefficients of 0.87 and 0.89 were found in base and mid segments, respectively. Interobserver variability using the Computer-Assisted Method (CAM) and Conventional Manual Method (CMM) were 4.0 and 4.7% for the basal and 2.8 and 3.9% for the middle segments. The method introduced in the present study permits precise thickness assessment of base and mid segments of the interventricular septum wall and has high concordance with CMM.

Key words: Echocardiography, interventricular septum, wall thickness, intensity profile

INTRODUCTION

Cardiovascular diseases are a major health concern world-wide. Since 1980, ultrasonic imaging of the heart from multiple tomographic planes with the two Dimensional (2D) echocardiography let to development of additional quantitative and qualitative methods (Waggoner and Davis, 1995). Nowadays echocardiography has become one of the most commonly used the heart diagnostic techniques, applicable to the assessment of a wide variety of the heart diseases (Shipton and Wahba, 2001; Ceylan *et al*., 2003; Chapa *et al*., 2005; Zoghbi *et al*., 2003; Ahmad and Awan, 2004). In recent years, computer and electronic techniques have been increasingly applied to echocardiography. The augmented capability and flexibility attendant with the utilization of this technology have been fruitfully applied to all aspects of 2D echocardiography, including image acquisition, manipulation and storage within the echocardiography, as well as to quantitative analysis of echo data using off-line systems (Skorton *et al*., 1985; Lang *et al*., 2005). Quantitative analysis of the heart walls thickness in echocardiographic images is a fundamental step in assessment and discrimination of the heart disease; for example: ischemic heart disease, hypertrophic cardiomyopathy, mitral stenosis, restrictive cardiomyopathy (Traill *et al*., 1978; Kushwaha *et al*., 1997) and so on. It should be noted that wall thickness measurements are small in value and it makes observer errors and also manual measurements are more dependent on sonographer experiment (Forcer and Parisi, 1986) that suffer from a considerable variability. Therefore, a computer-base analysis is highly desirable to obtain more objective and quantitative.

Measurement of changes in the thickness of the arterial and heart wall over time may allow not only the

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evaluation of the viability, wall stress and wall thickening but could also be used to study the effect of therapeutic methods to prevent or control of the heart disease (Cwajg *et al*., 2000; Grossman *et al*., 1975; Kanai *et al*., 1997). Beach *et al*. (1989) used intensity profile technique for measurement of superficial femoral artery wall thickness using ultrasound imaging and Pignoli *et al*. (1986) measured the distance between two echogenic structures in the normal arterial wall and related them to the sum of the intima-media thicknesses. Heart wall boundaries are imaged in echocardiograms as intensity edges which are points where the image intensity changes from one level to another. So early researchers used Sobel operator and approximation of the Laplacian operator to process echocardiographic images and then to threshold the gradient magnitude map. Duan *et al*. (2005) and Mokhtari-Dizaji *et al*. (2006) used optical flow correlation to predict the position of the detected edges in the sequential multiframe. Optical flow tracking refers to the computation of the displacement field of objects in an image, based on the assumption that the intensity of the object remains constant. In this context, motion of the object is characterized by a flow of pixels with constant intensity. Also there are a lot of literatures describing the application of active contour or snake to heart ultrasound. The approach was first proposed by Kass *et al*. (1988) to segment the contour of objects in 2-D images. Snakes, or active contours, are curves defined within an image domain that can move under the influence of internal forces coming from within the curve itself and external forces computed from the image data. The internal and external forces are defined so that the snake will conform to an object boundary or other desired features within an images (Xu and Prince, 1998).

In this study, we concentrate on 2D echocardiography, as it is ubiquitous and is the most widely used imaging method to assess the heart function. The techniques proposed for wall thickness measurement cannot be applied directly; because of the specific features of echocardiographic data especially the signal-to-noise ratio is relatively low and inhomogeneity. Therefore, in this research a computerized algorithm for regional border recognition and thickness information of the septum base and mid in 2-D echocardiographic images is presented. Our approach is relies on intensity profile drawing in septum regions manually and process of the resulted intensity profile automatically.

MATERIALS AND METHODS

In this research, we designed a new computerized algorithm and used it to measure interventricular septum wall thickness in 2D echo images throughout the cardiac cycle, in base and mid segments. This method is based on tracking of the heart walls echogenicity, ventricle-atrium interface. Heart wall edges in 2D echo images are regions in which image intensity change significantly so that the image in the wall regions has a higher density and in the ventricles and atriums has a brightness lower density (Fig 1a). In this research, septum wall thickness measured by using intensity profile technique (by improfile function) of Matlab7.0.4 image processing toolbox (Math software Co., Mathwork, USA) and Thresholding technique. Suppose that a intensity profile f can take κ possible levels 0, 1, 2, …, K-1. Define an integer threshold, T, that lies in the range of T ª {0, 1, 2, …, K-1}. The process of thresholding is a process of comparison: each pixel value in f is compared to T. Based on this comparison; a decision is made that defines the value of the corresponding pixel in an output intensity profile g (Bovik and Desai, 2000):

$$g(n) = \begin{cases} 0 & \text{if } f(n) \geq T \\ 1 & \text{if } f(n) < T \end{cases} \qquad (1)$$

We carried out proposed computer algorithm in Matlab7 software and then measurement accuracy of 2D echocardiographic images was assessed.

Echocardiographic data acquisition: Echocardiography studies were performed using a Vivid7 GE echocardiography System (GE, Milwaukee, Wisconsin, USA) with an ergonomically-designed M3S transthoracic sector transducer (1.5-4 MHZ) and 2D echocardiographic images were obtained as a multiframe movie of 12 healthy participant volunteers (mean age 52±6.5 year) using standard four-chamber view according to guide lines of the American Society of Echocardiography (Henry *et al*., 1980). The images with 50 frames per second were saved as a digital recording (with AVI format) at three cardiac cycles and then the electrocardiography were recorded simultaneously and acquired images transferred to a Pentium 4 personal computer for analysis.

Image analysis: For examining of presented method on sample images, first, we designed a simple program by using the Matlab software functions for converting AVI images to constructed gray scale frames and saved them as Bitmap single frame images (Fig. 1a).

For improving the quality of images, we used histogram equalization (Image Adjust Function) such that 1% of image data is saturated at low and high intensities of images. The idea behind it extends that not only should an image fill the available gray-scale range, but it should be uniformly distributed over that range (flat histogram).

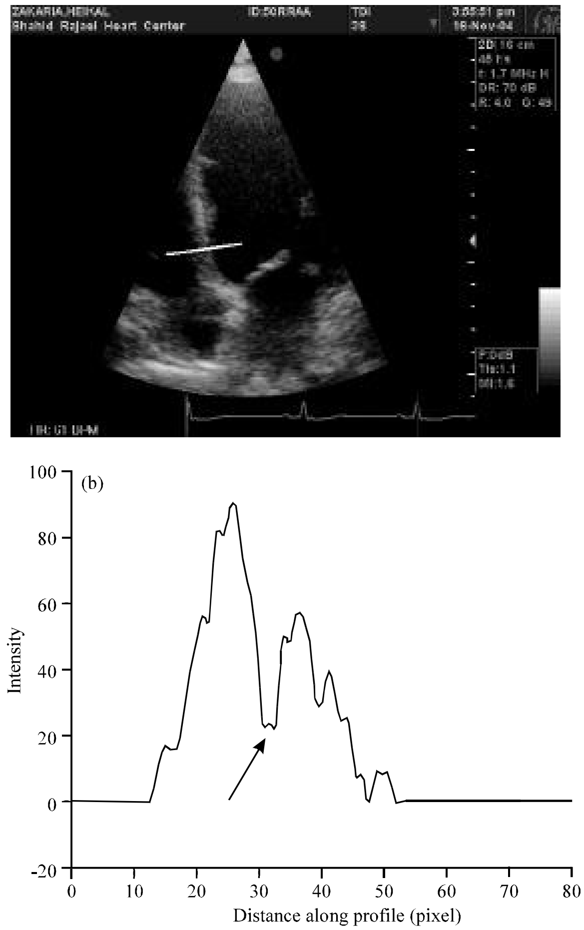

Fig. 1a: The line profile is drawn in septum basal segment of a 2D echocardiographic image frame and (b): The intensity profile and a gross change in data values along septum wall (black arrow)

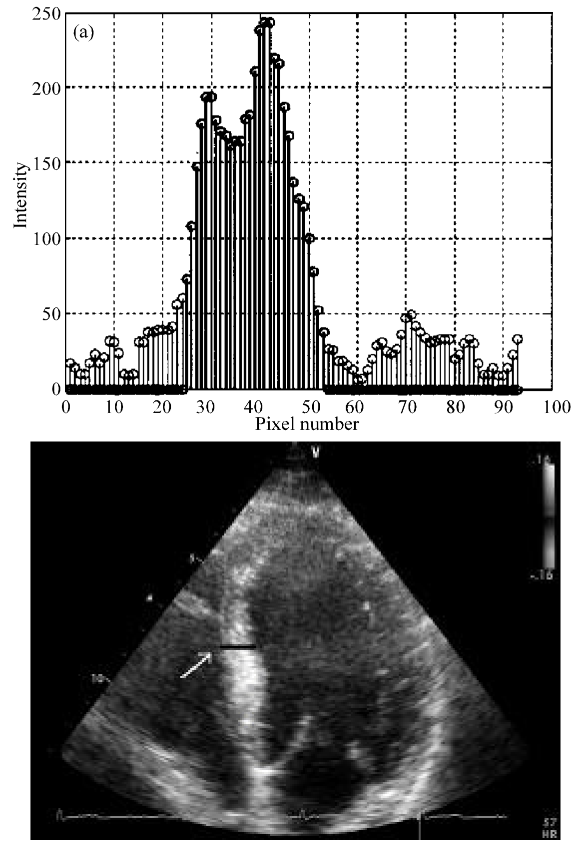

Fig. 2a: Visual evaluation of thresholding by use of graphical stems (thick stems show the use of pixels for thickness measurement) and (b): Superimposing used portion of the line profile on images (the black line which is indicated by white arrow)

There are good mathematical reasons for regarding a flat histogram as a desirable goal. For an image containing N×M pixels, the normalized image histogram is given by (Bovik and Desai, 2000):

$$p_f(k) = \frac{1}{N\times M} H_f(k) \tag{2}$$

For k=0, 1, 2, ..., K-1, where $H_f(k)$ is the number of pixels which have value κ. This function has the property that:

$$\sum_{k=0}^{k-1} p_f(k) = 1 \tag{3}$$

In histogram equalization the aim is to flat the histogram of the image i.e., make the $p_f(k)$ as a constant function. In this research, we primarily measured septum wall thickness in basal segment by use of presented computer program. Figure 1 shows the intensity profile was acquired from right to left ventricle in basal segment of interventricular septum. For examining this method, the intensity profiles were acquired in sequential 2D echocardiographic image frames throughout the cardiac cycles. Since there were significantly intensity changes in septum edges, thus we used Thresholding technique for determining area of edges.

Then the pixels between two edges of septum were counted and multiplied in pixel size for thickness calculating. In our images, the size of 0.4 mm was obtained for each pixel. Because the pixels values and contrast updates in different frames, we defined an adaptive threshold based on mean intensity value of left and right ventricular cavity and mean intensity value of the mid portion of septum wall in each segment. Adaptive thresholding selects an individual threshold for each pixel based on the range of intensity values in its local neighborhood of the resulted intensity profile. We have evaluated thresholding function visually by use of graphical stems and also superimposing used portion of line profile on images (Fig. 2a and b).

For increasing measurement accuracy, we used additional parallel intensity profiles automatically as well as central profile (above and below of central profile) at intervals of one pixel to each other. In our computer program, number of line profiles is arbitrary; however in each segment, we used 3 profiles for the thickness measurement. The mean and total mean of each measurement were reported automatically.

By proposed method, thickness measurements of the septum base and mid were examined on some of acquired images throughout the cardiac cycle and compared with the results of CMM. The results show that thickness measurement error in middle segment was very high and it is worthy of mention, we sometimes encountered an important problem due to gross changes of pixels value along septum wall (Fig. 1b) because of image noise and non-uniform intensity of the septum wall. Regarding to above mentioned problems, we improved presented algorithm via converting the gray scale images to binary images by use of image processing toolbox of Matlab software (Fig. 3).

However the septum edges in binary images appeared better than gray scale images, but measurement results are underestimated (due to abstraction of information) that we examined it by conventional measurements. The binary images for thickness measurement are not suitable because thickness data are loosed and residual data are related to middle portion of the septum wall. But by this characteristic, we do not need to the thresholding process along intensity profile in the middle of each segment and then the problem of intensity random changes reduce. We used it as an advantage for determining of primary septum edges with standard threshold function of image processing toolbox.

Fig. 3: A 2D Echocardiography image that converted to a binary image

We need to find the pixels belonging to septum thickness that were omitted and add them to primary determined thickness. At first, for reduction of noise effect, intensity profile values were smoothed by use of a moving average filter, as the name implies, the moving average filter operates by averaging a number of points from the input intensity profile to produce each point in the output intensity profile. In equation form, this is written (Smith, 2003; Khojastepour *et al*., 2004):

$$y(i) = \frac{1}{M} \sum_{j=0}^{M-1} x\,(i + j) \tag{4}$$

In this equation, x (i+j) and y (i) are the input and the output profiles respectively. M is the number of points used in the moving average. By comparing of mean values with threshold, we could determine pixels that belonged to septum wall thickness. In case that means (for example assume that mean is resulted from 5 pixels) were higher than threshold level, the first pixel are added to septum thickness and then means of second 5 pixels were compared with threshold level, in case that it was lower than threshold level. It means that residual pixels did not belong to septum thickness. Finally, we counted all computed septum pixels in each segment and multiplied it with image pixels size (0.4 mm in our study). The above mentioned method could semi-automatically measure accurate thickness in horizontal direction of intensity profile in sequential multiframe. For thickness measurement in oblique direction, we found coordination of pixels that were at the beginning and end of the used intensity profile and then equivalent distance calculated in terms of pixel based on Pythagoras equation automatically.

Statistical analysis: The all measurement results were analyzed using SPSS13 (SPSS Inc. Chicago, IL, USA). In this study twelve healthy males were included after having given written informed consent. All of them had a normal ECG, normal visual function in echocardiogram and no history of heart disease, angina, hypertension or diabetes. Their resting heart rates varied between 60 to 88 beat per minute (mean 72±9 bpm). The study protocol has been approved by the ethics committee of Tarbiat Modares University. We selected ten image frames of each healthy volunteer in random order (total 120 frames and 240 segments). Two measurements were taken with the each method on the same segments of the image frames. Only the first measurement by each method is used to illustrate the comparison of the methods, the second measurement being used in the study of repeatability. Pearson coefficients of correlation and

Limits of Agreement (LOA) were calculated for comparisons of the septum wall thickness results of the CAM and CMM. Intra observer variability for each method defined as differences between measurements expressed as a percentage error of the means.

RESULTS

To investigate validity and applicability of the proposed semi-automatic wall thickness analysis in 2D echocardiography images, the CAM and CMM were used on the same 120 image frames in the same segments and Pearson correlation analysis was applied for comparisons of the results between the methods. Pearson correlation coefficients were 0.87 ($p< 0.001$) and 0.89 ($p< 0.001$) for thickness of the septum base and mid, respectively. There were significant correlations between the measurements at each segment (Fig. 4).

It should be noted that the use of correlation alone may mislead and therefore in addition to it we used a scatter plot of the difference between measurements against the mean of the measurements was then constructed according to the technique for assessing agreement between two methods of clinical measurement described by Bland and Altman(1986) with 95% Limits of Agreement (LOA) (i.e., mean difference ± 2SD of the difference).

By means of this analysis means difference was 0.10mm (SD of differences = 0.81) and 0.12 mm (SD of differences = 0.72) for basal and middle segments, respectively (Fig. 5).

Interobserver variability for septum base and mid was found 4.0 and 2.8% for CAM and 4.7 and 3.9% for CMM, respectively. Both values in CAM are lesser than CMM for thickness of septum base and mid segments.

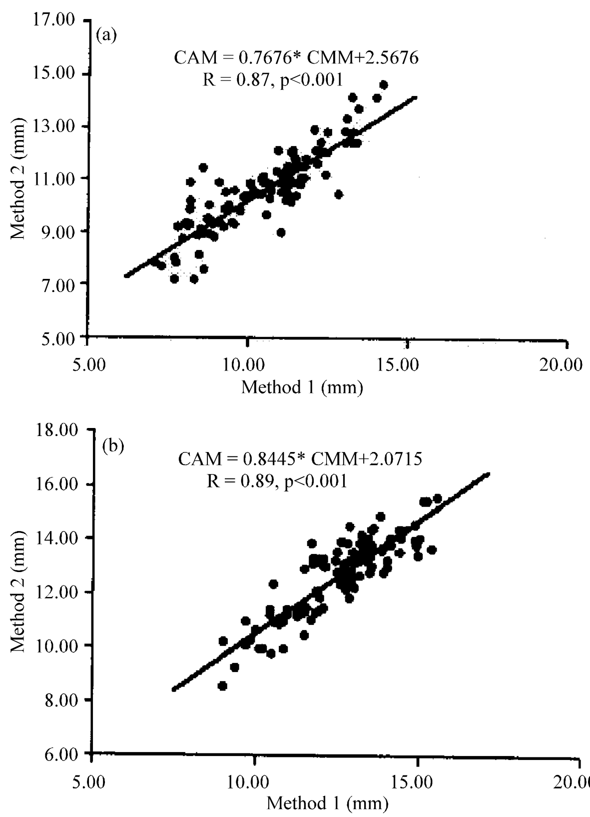

Fig. 4: Correlation between the computer assisted method (CAM) and conventional manual method (CMM) in (a) septum base and (b) mid segments

DISCUSSION

The 2D echocardiography images have poor signal to noise characteristics and low spatial resolutions. Numerous attempts have been made to develop different algorithms for quantitative analysis in these images in order to measure heart wall thickness, but as yet none have been developed adequately. As we have mentioned before, we have briefly surveyed some advances in the

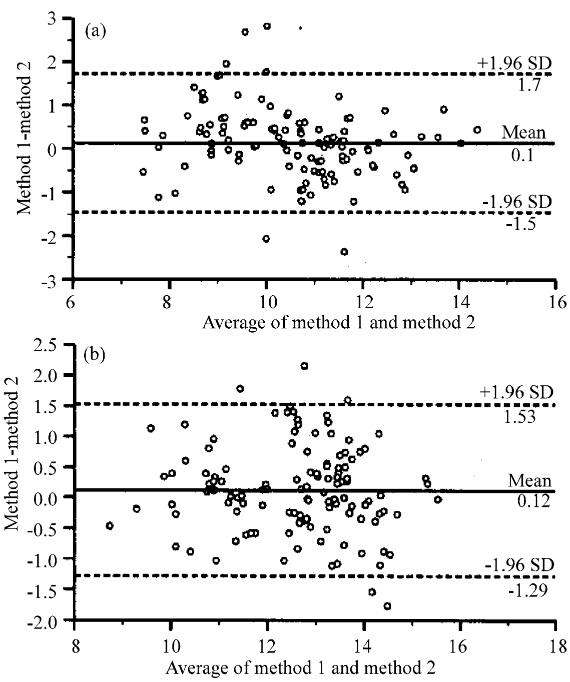

Fig. 5: Bland and Altman graph with the LOA for septum wall thickness measurements (mm) in the base (a) and mid segments (b) for 120 image frames separately (Method 1 and Method 2 are computer-assisted and conventional manual measurement methods, respectively)

fields of echocardiographic image processing and here we will talk about some of their characteristics and problems. The results turned to be that Sobel and Laplacian operators usually produced a large number of false responses while missing changes that vary less abruptly and detecting significant features has been more important when information derived from any stop frame in an image sequence is severely affected by noise (Yao *et al*., 2004). The optical flow approach has quite some advantages like that border recognition algorithms are no longer needed (Giachetti, 1998). Unfortunately these methods have problems which hinder their clinical usage. Optical flow methods are well known for being sensitive to image noise and since optical flow tracking refers to the computation of the displacement field of objects in an image, the assumption of intensity conservation is typically unrealistic for medical imaging applications.

Snakes are also unlikely to work well on low-quality images where noisy feature measurements will tend to make them wander into noisy areas of the image and there is a distinct possibility that different human operators would produce different results on the same data, through slightly different initializations (Giachetti, 1998).

What we wanted to prove in the paper is the idea that simple and effective method may also achieve the goal. This paper presented one approach for simultaneous extraction of the regional septum boundaries for thickness measurement from 2D apical four-chamber echocardiographic images and compared their performance with the CMM. The accuracy of the thickness measurement in poor quality images may need improving. The program can reliably estimate septum wall thickness in base and mid segments in our echo images and myocardial boundary recognition in desired wall segment is adaptive and autonomous and human input need only for initial estimation of the segments location. For this reason, Since in the most wall segments, the boundary features cannot be extracted by simple gray level thresholding, because of image noise and non-uniform intensity of the septum wall, therefore in our study, thickness measurement is achieved based on adaptive bilateral thresholding method to delineate the left and right endocardial interfaces separately by use of gray scale and binary images simultaneously. We evaluated the validity of the algorithm in comparison with CMM in the same image frames and approximately similar results are observed for two methods. Finally, we applied it to the regional thickness analysis of the septum. In this study, the paired thickness measurements closely agreed: The Bland-Altman analysis revealed a good agreement

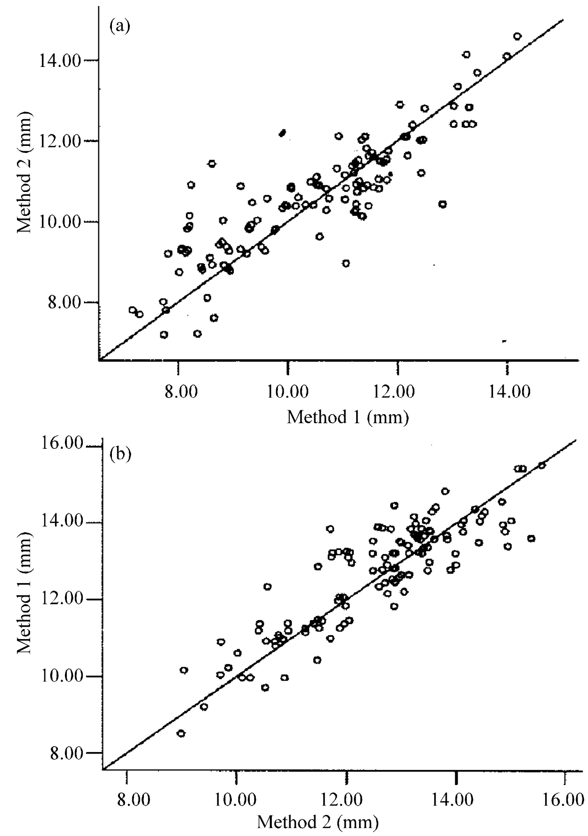

Fig. 6: Line of equality (a) for the septum base and (b) mid segments separately for 120 image frames (Method 1 and Method 2 are computer-assisted and conventional manual measurement methods, respectively)

between the used methods because 95% of differences lied between the mean plus and minus 1.96 SD (Fig. 5). Line of equality or identity on the scatter plots indicated that the thickness values measured by CAM in basal segment slightly underestimated the manual measured values in diastolic phase of the cardiac cycle and it seems because of mean intensity value decreases and threshold function did not act as well as systolic phase (Fig. 6).

The mean differences in thickness values that measured by means of the methods were small and were not statistically significant. There was a good correlation between methods. Also the comparison between the results shows that thickness measurement by use of presented method has brought about accurate results after smoothing of the intensity profiles.

The results confirm that computer-assisted semi-automatic measurement of wall thickness is applicable for 2D echocardiographic images and has measurement capability in these images.

We used presented method only for septum base and mid wall segments in healthy persons and these researchers are going to study applicability and capability of the proposed method in other left ventricular wall segments in normal and patients using 2D echocardiographic images in the future.

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