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Analysis of Ventricular Contraction by Factorial Phase Imaging with Equilibrium Radionuclide Angiography

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***Abstract*— Equilibrium radionuclide angiography (ERNA) imaging of the heart is used to visualize and quantify the cardiac function. Phase image analysis has been used for the localization of several conduction and contraction abnormalities and has been proposed to evaluate cardiac resynchronization therapy. The ventricular contraction has been described with indices like mean, standard deviation, mode, synchrony and entropy with Fourier phase imaging (FoPI). Factorial phase imaging (FaPI) has been used for wall motion abnormalities analysis and on a cardiac phantom, but not for synchrony quantification. In this paper a comparison of several indices obtained with FoPI and FaPI for a normal population is presented. These indices were computed inside regions corresponding to left ventricle, right ventricle and the total ventricular area. A set of ERNA images from 23 normal volunteers was analyzed. The comparison of indices was carried out by paired Student's t test with a significance level of ($p<0.05$). The results show significant differences among FoPI and FaPI on the analysis of ventricular contraction in normal individuals and consequently, on the quantification of the synchrony of contraction. The indices obtained from FaPI can be used to characterize a normal subject population for the evaluation of ventricular contraction synchrony.**

I. INTRODUCTION

Equilibrium radionuclide angiography (ERNA) imaging of the heart is used to visualize and quantify the cardiac function. This imaging technique provides a sequence of images (frames) that represent a specific time of the distribution of a radiotracer throughout the whole cardiac cycle [1]. Several parametric images have been derived for the digital processing of this study [2]. Among these are the amplitude and phase images. The former represents a picture of pixel by pixel stroke volume, while the phase image represents a map of ventricular contractility and shows the progression of contraction [3]. Fourier phase image (FoPI) analysis has been used for the localization of several conduction and contraction abnormalities [4] and has been proposed to evaluate cardiac resynchronization therapy [5]. The ventricular contraction has been described with indices like mean, standard deviation, mode, synchrony and entropy with FoPI [6]. However, FoPI has limitations because it assumes that all the temporal evolutions of the time activity curves (TAC) are periodic and that the transition between the first and the last frames of the study is smooth; these limitations increase in regions with severe contraction abnormalities. Factorial phase imaging (FaPI) does not assume a specific behavior of the shape of TAC and considers any TAC like a weighted sum of a limited number of pure time activity evolutions, called physiological factors. A functional image is associated with each factor and the two most significant factors are used to reconstruct the phase image [7]. There exist some reports about the use of FaPI in wall motion abnormalities analysis [8] and on a cardiac phantom [9]; but none about synchrony quantification. In this paper we present the comparison of several indices obtained with FoPI and FaPI for a normal population: minumim value, maximum value, range, mean, standard deviation, mode, skewness, kurtosis, synchrony and entropy; these indices were computed inside regions corresponding to left ventricle, right ventricle and the total ventricular area.

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II. METHOD

A. Fourier phase imaging

If, for T frames per cycle, the value of the pixel (i,j) in the kth frame is $n(i,j,k)$, $(k=1,...,T)$, two images I_{cos} and I_{sin} are calculated using the following equations:

$$I_{cos}(i,j)=\sum_{k=1}^{T} cos\left[\frac{2\pi}{T}(k-1)\right]\times n(i,j,k) \quad (1)$$

$$I_{sin}(i,j)=\sum_{k=1}^{T} sin\left[\frac{2\pi}{T}(k-1)\right]\times n(i,j,k) \quad (2)$$

The Fourier phase image is defined by [4]:

$$I_{FoPI}(i,j)=tan^{-1}\frac{I_{sin}(i,j)}{I_{cos}(i,j)} \quad (3)$$

and the Fourier amplitude image by:

$$I_{FoAI}(i,j)=\sqrt{I_{cos}(i,j)^2+I_{sin}(i,j)^2} \quad (4)$$

B. Factorial phase imaging

Let $X(p,q)=n\left[(i,j),k\right]$, be a two-dimensional array of the (i,j)-th value of pixel in the kth frame, $(p=i\times j, q=k)$. The factors (F) that describe $X(p,q)$ with non-information redundancies are given by:

$$F=X_m\times V\times D \quad (5)$$

where X_m is $X(p,q)$ with the mean removed, V and D are the set of eigenvectors and a diagonal matrix containing the eigenvalues of the autocorrelation matrix of X_m respectively. The two most significant factors F_1 and F_2, determined by the two largest eigenvalues, have been associated with the

cosine and sine behavior as in FoPI. The factorial phase image is then defined by [7]:

$$I_{FaPI} = tan^{-1}\frac{F_2}{F_1} \quad (6)$$

and the factorial amplitude image by:

$$I_{FaAI} = \sqrt{2(F_1^2 + F_2^2)} \quad (7)$$

C. Studied population

The population under study consisted of 23 volunteers (18 men, 5 women, age 28± 5 years old) with a low likelihood of coronary artery disease and without history of heart failure, no rest ECG abnormalities and no contractility impairment as assessed by echocardiography. All laboratory examinations (sodium, potassium, creatinin, thyroid hormonology) and chest X-ray were normal. After cardiac evaluation, the heart was considered as normal. All subjects gave informed consent to participate in the study protocol.

D. Image acquisition

Red blood cells were labeled in vitro [10] with 740 to 925 MBq of technetium-99m (UltraTag kit©). The ECG was monitored continuously to ensure R-wave gating of the QRS complex. Elimination of premature ventricular beats was carried out with a window threshold of 20% around the mean RR interval during acquisition of projections. ERNA images were acquired in the left anterior oblique projection with a detector incidence between 30^0 and 60^0, to assure the best left (LV) and right (RV) ventricle definition. The images were acquired with a single-head gamma camera, equipped with a low energy and high resolution collimator. The projection was gated with the ECG to get 16 frames spanning the cardiac cycle.

E. Definition of indices

The acquired images were processed using *MatLab*© and filtered with a Gaussian low pass filter with a 5×5 kernel and standard deviation of 5. Fourier and factorial phase images were generated as described above. Each phase image was shifted $\pi/3$ to enhance the differences between auricles and ventricles. A threshold of 10% of maximal value on the Fourier amplitude image was selected to exclude background regions of noise and random phase angle. The phase images were displayed using a continuous color scale corresponding to phase angles from 0^0 to 360^0. The LV, RV and total ventricular region (Ventricles) were drawn manually upon each phase image by an expert unaware of the state of heart function. A histogram of the angles was generated, for each region of interest (ROI) evaluated, relating phase angle on the abscissa to the frequency of occurrence on the ordinate with a class interval of 6^0. Minimum value, maximum value, range, mean standard deviation, skewness and kurtosis were computed for all angles in the ROI. The Mode was computed as the most frequent value in the angle histogram. Synchrony (S) was computed as [11]:

$$S = \frac{\left|\sum_{i,j}^{N} I(i,j)\right|}{\sum_{i,j}^{N} |I(i,j)|} \quad (8)$$

where each element of $I(i,j)$ is a vector with amplitude $I_{FxAI}(i,j)$ and phase $I_{FxPI}(i,j)$, $x \in \{o,a\}$ for Fourier or factorial images. N is the number of pixels in the ROI. The Entropy (E) normalized for the number of phase angles in the ROI, was computed as a measure of the degree of randomness or disorder in the ROI [11], and was calculated as:

$$E = -\frac{\sum_{i=1}^{M} P_i log_2(P_i)}{log_2(M)} \quad (9)$$

where M is the number of phase angles in the ROI and P_i is the probability of occurrence of the i-th angle.

F. Statistical analysis

All measurements are reported as mean ± standard deviation and expressed in degrees. Comparison of indices was done by analysis of residuals for normality distribution test and by paired Student's *t* test with a level of significance p<0.05.

III. RESULTS

Fig. 1 shows the FoPI and FaPI for a normal subject with their corresponding histogram phase distribution. Fig. 2 shows FoPI and FaPI, with histogram phase distributions, for ventricular, LV and RV regions respectively. Of the twenty-three phase images, those generated by FoPI were visually more homogenous than FaPI. The FaPI angle values were higher in lateral and inferior areas compared with superior regions. Tables I, II and III show the values for each evaluated ROI. Indices marked with * were not statistically different (p>0.05). For all regions the minimum value, range, standard deviation, entropy indices by FoPI were lower and statistically diferent than those computed by FaPI. Synchrony computed by FoPI was higher and statistically diferent than FaPI synchrony.

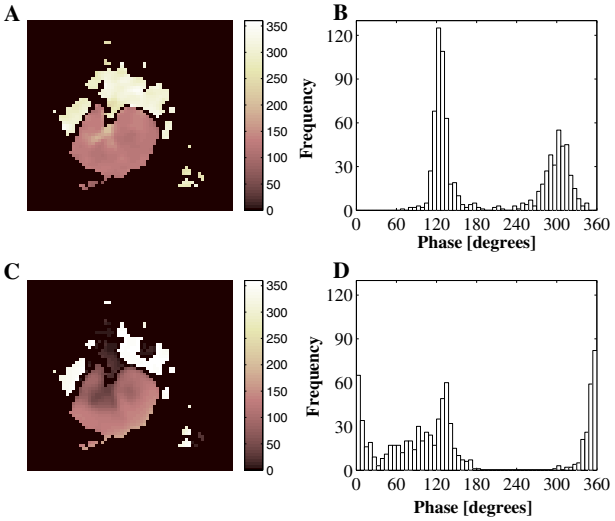

Fig. 1. Examples of Fourier (A) and factorial (C) phase images with histogram phase distribution (B) and (D) respectively, of a normal subject.

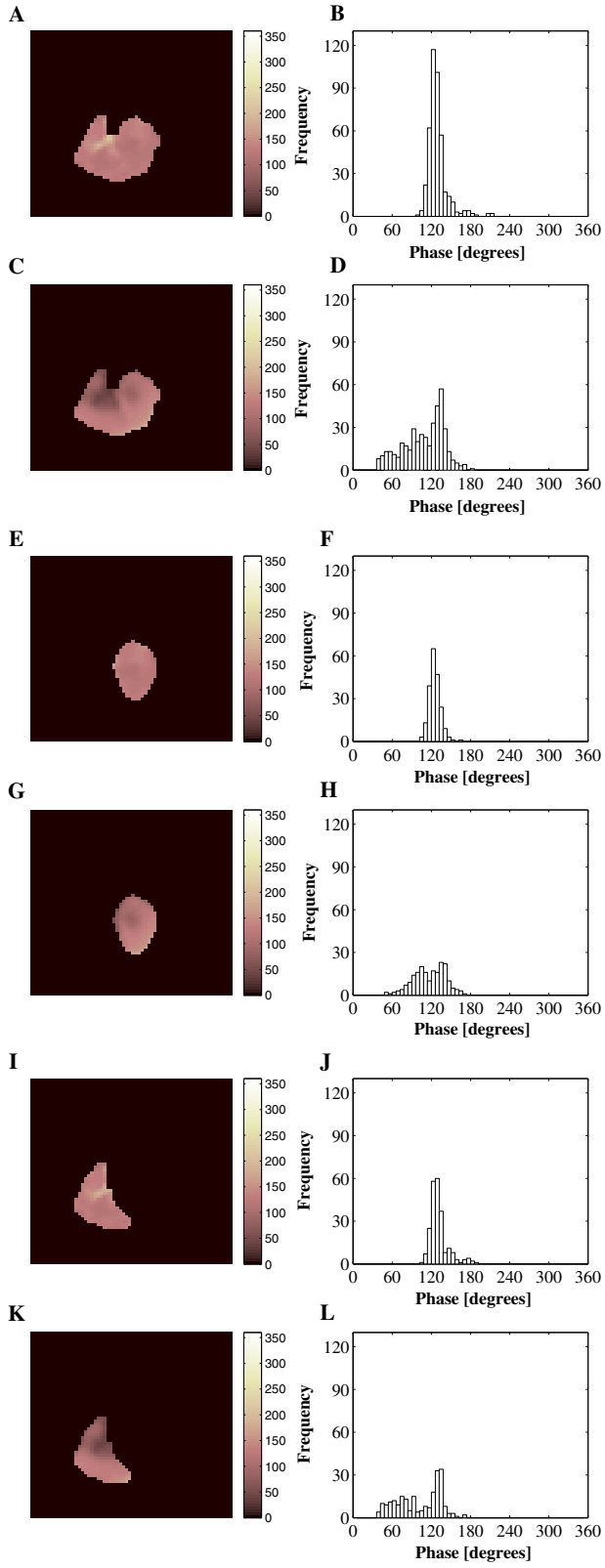

Fig. 2. Fourier and factorial images, with histogram phase distribution, for ventricles (A-D), left ventricle (E-H) and right ventricle (I-L) regions.

TABLE I

DESCRIPTIVE ANALYSIS FOR VENTRICULAR AREA.

VENTRICLES	FoPI	FaPI
Minimum value	76.98 ± 21.83	51.96 ± 11.60
Maximum value	151.37 ± 13.64	161.90 ± 19.84
Range	74.39 ± 20.86	109.94 ± 22.98
Mean	113.18 ± 11.93	116.02 ± 7.11*
Standard Deviation	10.43 ± 1.44	22.00 ± 4.00
Mode	109.30 ± 11.99	125.74 ± 9.31
Skewness	0.06 ± 0.77	-0.57 ± 0.36
Kurtosis	5.24 ± 2.74	3.04 ± 0.68
Synchrony	0.99 ± 0.01	0.94 ± 0.02
Entropy	0.77 ± 0.05	0.88 ± 0.03

TABLE II

DESCRIPTIVE ANALYSIS FOR LV AREA.

	FoPI	FaPI
Minimum value	88.18 ± 14.80	61.70 ± 18.66
Maximum value	140.91 ± 16.16	169.86 ± 32.22
Range	52.73 ± 14.69	108.16 ± 35.17
Mean	113.20 ± 12.45	121.87 ± 9.66
Standard Deviation	8.87 ± 1.80	19.76 ± 4.25
Mode	110.09 ± 11.67	125.74 ± 16.63
Skewness	0.01 ± 0.60	-0.28 ± 0.57 *
Kurtosis	3.94 ± 1.23	3.70 ± 1.63 *
Synchrony	0.99 ± 0.00	0.96 ± 0.02
Entropy	0.79 ± 0.05	0.86 ± 0.04

TABLE III

DESCRIPTIVE ANALYSIS FOR RV AREA.

	FoPI	FaPI
Minimum value	81.21 ± 15.35	55.20 ± 12.89
Maximum value	153.30 ± 21.57	148.10 ± 14.13*
Range	72.09 ± 21.67	92.90 ± 19.51
Mean	113.34 ± 12.06	109.17 ± 7.26*
Standard Deviation	11.54 ± 3.00	22.82 ± 5.36
Mode	109.04 ± 13.62	122.87 ± 8.84
Skewness	0.33 ± 0.75	-0.56 ± 0.23
Kurtosis	4.72 ± 1.63	2.47 ± 0.61
Synchrony	0.99 ± 0.01	0.92 ± 0.04
Entropy	0.79 ± 0.06	0.91 ± 0.04

IV. DISCUSSION

The propagation of ventricular contraction starts at the septum level, spreading to the apex and to lateral walls of the ventricles [12]. This behaviour was more evident with the image reconstructed by FaPI than FoPI for each ROI evaluated. The FaPI presents higher phase angle values around inferior and lateral regions than superior regions. Therefore, and according to the normal ventricular contraction, the indices kurtosis, entropy and standard deviation computed by FaPI are higher than FoPI, and reflect a more spread histogram distribution. Fauchier et al [6], found that the standard deviation index is a measure of dyssynchrony of ventricular contraction and is an indicator of illness severity. O'Conell et al [11], propose the synchrony and entropy indices, that relate the timing, the magnitude of contraction and the distribution of phase angles, to classify simulated

regions like abnormal, diffuse and with severe dissfunction. However these indices were computed in subjects, or regions, with severe abnormalities and is in this segments where FoPI has limitations. The synchronies computed by FoPI and FaPI are statistically different, but they were higher than 0.9 and their mean differences are minimal, therefore the synchrony values for both methods can be considered like normal. In this paper we propose reference indices for the description of normal ventricular contraction computed for a method that extracts the most representative information of ventricular contraction.

V. CONCLUSIONS AND FUTURE WORK

The main findings of the present study were that there are significant differences among Fourier phase image and factorial phase image on the analysis of ventricular contraction in normal individuals and consequently, on the quantification of the synchrony of contraction. A visually more detailed contraction pattern for lateral and inferior regions for each ventricle was generated by FaPI. It correlates with a normal ventricular activation pattern. In this work we propose reference values for a normal population computed for a method that does not assume a specific shape of the time activity curves and extracts the representative information of the region of interest. In the future we will evaluate the sensibility and specificity of factorial phase imaging, having minimal and controlled changes of ventricular contraction using a software phantom for radionuclide ventriculography image series. We will analyze the contribution of the third and fourth factors in the study of ventricular synchrony for abnormal ventricular contraction. We will use an automatic segmentation algorithm for the analysis of regional synchrony contraction, using a mechanical cardiac phantom. We will explore methods to classify different abnormal patient populations under cardiac resynchronization therapy or pharmacological treatment, according to their degree of synchrony and we will extend the FaPI analysis using tomographic images to avoid the effect of overlapping structures.

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