radionuclide angiography derived indices synchrony and entropy identify responders to cardiac resynchroniza therapy?

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Introduction

The clinical importance of synchronous contraction was recognized two decades ago as an indicator of cardiac function and prognosis in patients with heart failure; despite many clinical trials, no specific measure of mechanical synchrony has yet been found. Finding a method to quantify ventricular contraction synchrony is an important goal for many clinical applications, like Cardiac Resynchronization Therapy (CRT) by biventricular pacing.

Aim

Aim of this study is to analyze two quantitative parameters recently proposed by O'Connell et al, i.e., synchrony (S) and entropy (E) derived from planar equilibrium radionuclide angiography (ERNA).
S (1.) and E (2.) are evaluated from phase and amplitude images obtained from first order Fourier fit of blood volume curve in the left vetricle region.
S and E are near 1 and 0 respectively in good synchrony condition, while S decreases, tending to zero and in the same time E increases, tending to 1 as the synchrony gets worse.

$$S = \frac{\left|\sum_{i}^{N} v_i\right|}{\sum_{i}^{N} |v_i|}$$

1. Synchrony; in left ventricle region, a vector v_i of components ($v_i\cos\varphi_i$; $v_i\sin\varphi_i$) is defined for each pixel i. S is the rateo of the amplitude of the vector sum and the sum of the amplitude of all the vectors (N = number of pixels in left ventricle region).

$$E = \frac{\sum_{i}^{M} P_i \log_2 P_i}{\log_2 M}$$

2. Entropy; Pi is the frequency of occurrence of all phase values φ_i along the phase histogram and M is the number of intervals in which phase histhogram is divided

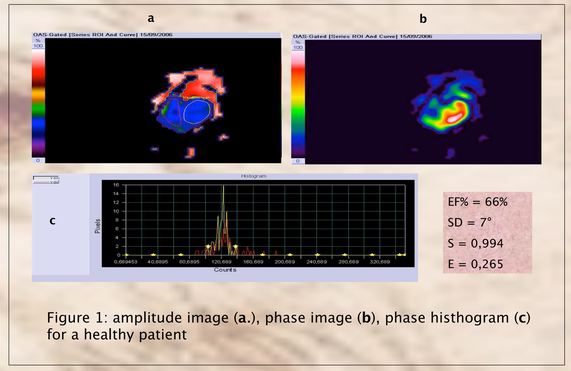

Figure 1: amplitude image (**a**.), phase image (**b**), phase histhogram (**c**) for a healthy patient

Methods

We studied 17 patients, mean age 70 years, with congestive heart failure (50% CAD) and optimal medical therapy who underwent biventricular pacemaker implantation. Clinical and nuclear data were obtained at baseline and after 8 months of follow-up (FU).
Control group consisted of 14 patients with no history of heart failure, who underwent ERNA before chemotherapy, in order to avoid additional cardiac toxicity of anthracyclines.
For each patient,phase histogram, standard deviation of phase angle (SD), synchrony (S) and entropy (E) were calculated.
S, E were evaluated from scintigraphic data, using a plug-in of the free software package, ImageJ, developed at Health Physics Unit of Belcolle Hospital, Viterbo, Italy. It calculates S,E after having drawn left ventricle region of interest (LVROI) on phase image.

Results (I)

Phase image analysis clearly showed the abnormal pattern of contraction in CHF patients with respect to control group. CHF patients were found to have significantly different values of all variables measuring intraventricular contractile synchrony (SD, S, E), as resulted from t-test ($p<0,0001$). Results of the comparison are given in table I.

Table I: comparison between control group (CG) and CHF patients

	CG	CHF	p value
SD	11.9 ± 4.8	50.0 ± 19.7	<0.0001
S	0.990 ± 0.006	0.910 ± 0.083	<0.0001
E	0.328 ± 0.072	0.578 ± 0.127	<0.0001

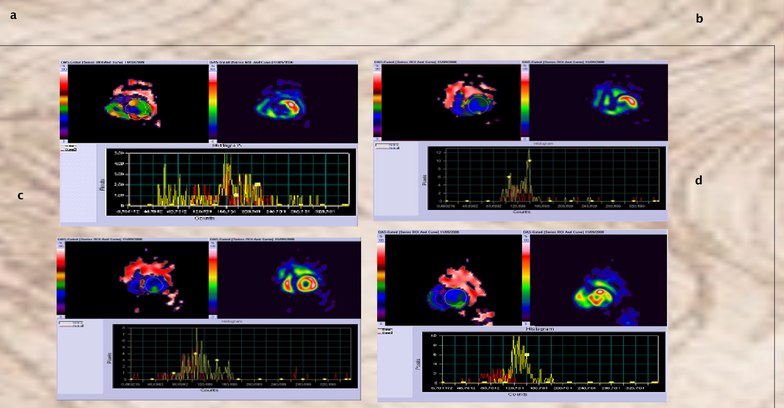

Figure 2: comparison of group A and B; figures a and b represent basal and follow up study for a patient of group A, figures c and d for a patient in group B

Table II: comparison between basal and follow up values for each group

	Group A (9 p)				Group B (8 p)		
	basal	FU	p value		basal	FU	p value
EF%	25.6 ± 7.5	38.5 ± 13.9	0.030	EF%	32.0±7.0	31.0±10.0	0.87
SD	56.3 ± 16.7	25.7 ± 13.3	<0.001	SD	42.0±21.0	48.0±21.0	0.59
S	0.869±0.094	0.950±0.058	0.05	S	0.955±0.032	0.914±0.062	0.13
E	0.641 ±0.112	0.495±0,109	0.01	E	0.510±0.110	0.600±0.120	0.12

Result (II)

Follow-up studies indicated an overall recover of contractile synchrony and improvement of NYHA functional class and ejection fraction EF before and after pace-maker implants. Nevertheless, RNA data varied in a non-homogenous way after CRT, so changes of SD, S, E for the whole study group were not significant, according to t-test.
Two different groups can be identified, one with patients in which an improvement in mechanical asynchrony was noted, with significantly different values of SD, S and E between baseline and follow up (group A), the other with patients showing no significant variations of the same variables (group B). Patients in group A also showed a marked increase of ejection fraction after implant, while in group B, EF remained more or less constant.
Results of comparison in table II.

Result (III)

Table III summarizes results of comparison between basal values of two groups. A significant difference between S and E values are observed, with S, E values lower in group A then B. EF an SD differences are not statistically different, with p-value for SD comparison clearly indicating that SD is substantially the same for group A and B.

Table III: comparison between basal values of two groups

	group A	group B	p value
EF%	25.6 ± 7.5	32.0 ± 7.0	0.12
SD	56.3 ± 16.7	48.0 ± 21.0	0.39
S	0.869 ± 0.094	0.955 ± 0.032	0.03
E	0.641 ± 0.112	0.510 ± 0.110	0.03

Conclusion

Synchrony and entropy derived from ERNA are suitable parameters to quantify ventricular contractile synchrony, and may represent a reliable alternative method to echocardiography.
Our preliminary results demonstrated that patients with a worse haemodynamic and dyssynchrony setting show a better improvement in LV mechanics with respect to less ill ones. Improvement in nuclear dyssynchrony was in agreement with EF improvement in group A. S and E seem to be promising in identifying responders to CRT, especially in the presence of the disappointing results of ultrasound techniques, which suffer high operator dependency.
Our results also demostrated that SD, although may be considered a good dissynchrony parameter, might not be suitable to identify responders to CRT.