Brazilian Journal of Medical and Biological Research (2002) 35: 1285-1292
ISSN 0100-879X

Clinical assessment of the effect of digital filtering on the detection of ventricular late potentials

P.R.Benchimol-Barbosa[1,2], E.C. Barbosa[2], A.S. Bomfim[2], P. Ginefra[2] and J. Nadal[1]

[1]Programa de Engenharia Biomédica, COPPE, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brasil
[2]Divisão de Cardiologia, Hospital Universitário Pedro Ernesto, Universidade Estadual do Rio de Janeiro, Rio de Janeiro, RJ, Brasil

Abstract

Ventricular late potentials are low-amplitude signals originating from damaged myocardium and detected on the body surface by ECG filtering and averaging. Digital filters present in commercial equipment may interfere with the ability of arrhythmia stratification. We compared 40-Hz BiSpec (BI) and classical 40- to 250-Hz band-pass Butterworth bidirectional (BD) filters in terms of impact on time domain variables and diagnostic properties. In a transverse retrospective age-adjusted case-control study, 221 subjects with sinus rhythm without bundle branch block were divided into three groups after signal-averaged ECG acquisition: GI (N = 40), clinically normal controls, GII (N = 158), subjects with coronary heart disease without sustained monomorphic ventricular tachycardia (SMVT), and GIII (N = 23), subjects with heart disease and documented SMVT. Conventional variables analyzed from vector magnitude data after averaging to 0.3 μV final noise were obtained by application of each filter to the averaged signal, and evaluated in pairs by numerical comparison and by diagnostic agreement assessment, using conventional and optimized thresholds of normality. Significant differences were found between BI and BD variables in all groups, with diagnostic results showing significant disagreement between both filters [kappa value of 0.61 ($P<0.05$) for GII and 0.31 for GIII (P = NS)]. Sensitivity for SMVT was lower with BI than with BD (65.2 *vs* 91.3%, respectively, $P<0.05$). Filters provided significantly different numerical and diagnostic results and the BI filter showed only limited clinical application to risk stratification of ventricular arrhythmia.

Correspondence
P.R.B. Barbosa
Rua Pompeu Loureiro, 36/702
22061-000 Rio de Janeiro, RJ
Brasil
E-mail: pbbarbo@attglobal.net

Research partially supported by Faculdade de Medicina, UERJ (No. #5152/2001).

Part of these data were presented at the XXVIII International Congress on Electrocardiology, Guarujá, SP, Brazil, June 2001, as an Abstract and received the Young Investigator Award 2001 from the International Society of Electrocardiology.

Received December 14, 2001
Accepted August 12, 2002

Key words
- High resolution electrocardiogram
- Digital filtering
- Health technology assessment

Introduction

The ventricular late potentials (VLP) are low-amplitude and high-frequency electrical signals emerging from regions of damaged ventricular myocardium with slow and fragmented conduction (1). Usually detected by body surface high resolution ECG using techniques of signal amplification and averaging (SAECG), VLP are generally observed at the end of ventricular activation and often advance into the ST segment (1-3). They bear a precise temporal relationship with fragmented activities directly recorded from the epicardial surface and are considered the hallmark of several ventricular arrhythmic events of a

reentry nature (2,3).

Due to low amplitude (1 to 30 μV), VLP are covered by both low-frequency high-amplitude deflections of the surface ECG and by high-frequency interference, arising from biomedical instrumentation and muscular activity. Therefore, band-pass filtering must be applied not only to allow their visualization but also to permit measurements by automated techniques (4).

Recently, an expert consensus document from the American College of Cardiology and the American Heart Association endorsed the use of the bidirectional filter for the identification of VLP in the time domain (5,6). However, in view of the current level of development of electrocardiography, the committee does mention the study and implementation of zero-phase filters.

Among the classes of filters currently in clinical use for identification of VLP in the time domain, the spectral filters and the autoregressive-moving-average (ARMA) filters are the most important (4,7).

Spectral filters are transfer functions of analog or digital filters, which are applied to the ECG signal by means of the discrete Fourier transform (7,8). Depending on the shape of the filter, the generation of artifacts, mostly ringing, is almost unavoidable, restricting their clinical use.

ARMA filters are the time domain analog of spectral filters, developed by techniques of bilinear and *z*-transformation of their respective transfer functions. The most outstanding ARMA filter currently in clinical use is the so-called bidirectional filter, first introduced by Simson (1) in 1981. It solves the problem of artifact generation in the ST segment by a change in the phase of the filter. Among bidirectional filters, the Butterworth one is the most frequently employed for analysis of the VLP (4,6).

BiSpec is a spectral filter introduced in the early 90's with the aim of reproducing the effects of the Butterworth bidirectional filter. There is no information about its mathematical characteristics in the literature. In 1990, Mehta et al. (9) evaluated a group of 50 subjects and compared the effects of the BiSpec and the Butterworth bidirectional filters using SAECG. The authors proposed the validation of the BiSpec, but did not perform clinical comparisons of the diagnostic results of the two filters using control groups. Recently, Goldberger et al. (10) reported that paired differences of filtered QRS duration between the BiSpec and Butterworth bidirectional filters were not statistically significant, although there was a high variance of paired difference of the filters' output at 61.1 ms (2).

In a previous study (11), we presented a preliminary comparison of the diagnostic performance between the BiSpec and Butterworth bidirectional filters and found a reduced sensitivity of the former in identifying subjects with episodes of sustained ventricular tachycardia.

In order to evaluate several conflicting reports comparing the Butterworth bidirectional and BiSpec filters during the clinical application of SAECG, we determined the effect of filter choice on the diagnosis of subjects prone to life-threatening ventricular arrhythmias.

Material and Methods

In a cohort of 1580 subjects admitted for evaluation at the Arrhythmia Unit of the Department of Cardiology, Hospital Universitário Pedro Ernesto, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, RJ, Brazil, between December 1995 and February 2001, 221 subjects in sinus rhythm without bundle branch block from the high resolution electrocardiogram signals database (12) were evaluated in a retrospective, transverse, case-control, age-adjusted study.

The subjects admitted to the study had been referred to the Unit for clinical investigation of either a symptomatic episode considered as rhythm disturbance by primary

evaluation or documented cardiac arrhythmia. Subject information was collected from the Arrhythmia Unit's registry and by anamnesis, physical examination, 12-lead ECG, and echocardiogram. Subjects were divided into three groups (Table 1): group I (GI) contained 40 clinically normal individuals with normal 12-lead ECG and echocardiogram; group II (GII) 158 subjects with coronary heart disease without previous documented episodes of sustained monomorphic ventricular tachycardia (SMVT), and group III (GIII) contained 23 subjects with coronary heart disease, right ventricular dysplasia or Chagas' disease and previously documented episodes of SMVT. For admission to the study, all persons in GII and GIII presented documented heart disease with myocardial damage, and abnormal 12-lead ECG and echocardiogram. In GII, 37 subjects had anterior/anteroseptal myocardial infarction, 61 had inferior/inferoseptal myocardial infarction, 11 had myocardial infarction at other locations and 47 had chronic coronary heart disease without previous myocardial infarction. The median period after myocardial infarction was 924 days. In GIII, the inclusion criteria were diseases in which the mechanism of arrhythmia is classically defined by intramyocardial reentry circuits. Two subjects with Chagas' disease with ventricular arrhythmia originated by reentry circuits in the apical aneurysm located in the left ventricle were included. SMVT episodes were defined as more than 40 consecutive beats with the same morphology, heart rate above 100 bpm and QRS duration above 100 ms, documented at the coronary care unit or by 24-h Holter monitoring.

All subjects were submitted to SAECG with the Predictor IIc SAECG equipment (ART, Austin, TX, USA) using XYZ Frank leads averaged with the default parameters to a final noise of less than 0.3 μV. One SAECG was acquired for each subject. The SAECG was assessed for vector magnitude using the BiSpec filter at a cutoff frequency of 40 Hz and the Butterworth bidirectional band-pass filter with four poles and cutoff frequencies at 40 and 250 Hz applied to the averaged signal. The variables employed for analysis were: duration of total ventricular activation, duration of the potentials below 40 μV in the terminal region of the ventricular activation (LAS40), the root-mean-squared voltage of the last 40 ms of ventricular activation (RMS40) and the root-mean-squared voltage of the total ventricular activation (RMST). Measurements were automatic and were supervised by visual inspection. The presence of VLP was considered positive if at least two of the first three variables were out of the normal range. The reproducibility of the method has been tested and confirmed (13).

Data analysis was conducted in three phases: i) paired analysis of the vector magnitude variables, between Butterworth and BiSpec filters, in all groups; ii) assessment of the diagnostic agreement (positive and negative results) between both filters using the conventional thresholds of normality ≤38 ms for LAS40, ≥20 μV for RMS40 and ≤114 ms for duration of total ventricular activation, and iii) optimization of the normality thresholds for BiSpec, based on GI, using the Student *t*-probability density function, the one-tailed 95% confidence interval (95% CI), and reassessment of diagnostic agreement.

In the first phase, statistical analysis was carried out using the paired Student *t*-test, and one-way analysis of variance (ANOVA) for comparisons of the means and correlation coefficient analysis. To compare the results obtained for GIII with those reported in the literature, we also applied the *z*-test for mean comparison of Fisher transformation of the correlation coefficient (11). In second and third phases, to evaluate the ability of both filters to correctly identify the risk for life-threatening arrhythmia among subjects with coronary heart disease, the analyses were conducted comparing GII (referred to

Table 1. Characterization of normal subjects and patients.

	GI	GII	GIII
Number of patients	40	158	23
Age (years)	52.1 ± 11.9	56.5 ± 12.6	54.5 ± 15.9
Gender (M/F)	27/13	112/46	11/12
Assessment of clinical state	Clinically normal	Abnormal ECG/ECHO without SMVT	Abnormal ECG/ECHO with SMVT
Distribution according to heart diseases		Coronary heart disease (111 old MI and 47 chronic stable angina)	15 Coronary heart disease 2 Chagas' disease 6 ARVD

SMVT: at least one episode of sustained monomorphic ventricular tachycardia: more than 40 consecutive beats with heart rate >100 bpm, QRS >100 ms. MI: myocardial infarction; ARVD: arrhythmogenic right ventricular dysplasia.

Table 2. Comparison of means of vector magnitude variables between the filtering techniques used by the BiSpec filter (BI) and the Butterworth bidirectional filter (BD).

GI - Clinically normal individuals (N = 40)	BI	BD
Dur (ms)	95.2 ± 9.4	94.1 ± 8.5
LAS40 (ms)	29.3 ± 8.8	28.1 ± 6.4
RMS40 LNT (LN [μV])	3.8 ± 0.5	3.7 ± 0.6
RMST LNT (LN [μV])	4.2 ± 0.3	4.6 ± 0.3*
GII - Coronary heart disease without SMVT (N = 158)	**BI**	**BD**
Dur (ms)	106.5 ± 18.6	105.1 ± 18.8*
LAS40 (ms)	33.3 ± 16.5	35.1 ± 16.3*
RMS40 LNT (LN [μV])	3.3 ± 0.9	3.2 ± 0.9
RMST LNT (LN [μV])	4.2 ± 0.4	4.6 ± 0.5*
GIII - Coronary heart disease, with episodes of SMVT and RVD or with Chagas' disease (N = 23)	**BI**	**BD**
Dur (ms)	135.6 ± 37.3	140.6 ± 47.2
LAS40 (ms)	56.6 ± 31.4	60.7 ± 39.4
RMS40 LNT (LN [μV])	2.5 ± 0.9	2.3 ± 0.9
RMST LNT (LN [μV])	4.0 ± 0.5	4.3 ± 0.5*

Values are reported as mean ± SD. SMVT: sustained monomorphic ventricular tachycardia; RVD: right ventricular dysplasia; LNT: natural log transformed; Dur: duration of total ventricular activation (VA); LAS40: duration of the potentials below 40 μV at terminal region of the VA; RMS40 and RMST: root-mean-squared voltage of the last 40 ms and total VA, respectively (see text for details). *P≤0.02 compared to BI (two-tailed paired Student *t*-test).

as control group) and GIII (referred to as case group). We applied analysis of diagnostic performance (sensitivity, specificity and total accuracy), comparison of proportions, analysis of odds ratio, and the kappa statistics χ^2 test to determine diagnostic agreement (14,15). In the kappa χ^2 test, the null hypothesis tested was the absence of diagnostic agreement between both filters in GII and GIII as well. A sampling procedure was carried out to assure that the sizes of the case (GIII) and control (GII) groups were adequate to validate the study, using alpha and beta error levels of 0.05 and 0.20, respectively.

The variables RMS40 and RMST were transformed into their natural logarithm before analysis in order to normalize their asymmetrical probability distribution (4). The confidence level was fixed at 0.05. Data analysis was performed with EPI Info software version 6.04 (Centers for Disease Control and Prevention, Atlanta, GA, USA), MS Excel 2000 (Microsoft Corporation, Redmond, WA, USA) and Statgraphics Plus version 5.0 (Manugistic, Rockville, MD, USA).

Results

The age distributions of all subjects and patients were similar (Table 1). Paired comparisons of the data showed significant differences between some parameters, mainly RMST for all groups and duration of total ventricular activation and LAS40 for GII (Table 2). The correlations of LAS40 and of RMS40 between BiSpec and Butterworth filters in GI, and of RMST in GII were below 0.7 (Figure 1). In GIII, all correlations were above 0.8 for vector magnitude parameters.

Assessment of the diagnostic results using conventional thresholds of normality is presented in Table 3. The odds ratios of VLP as a marker of SMVT detected by Butterworth and BiSpec filters were 23.4 (95% CI [5.3-209.7], P<0.001) and 4.4 (95% CI [1.6-12.8], P = 0.002), respectively. The kappa statis-

tics of diagnostic disagreement between Butterworth and BiSpec filters for GII and GIII were 0.61 (P = 0.006) and 0.30 (P = 0.15), respectively.

The optimized normality thresholds based on GI 95% CI for BiSpec were ≤114 ms for duration of total ventricular activation, ≥15 µV for RMS40 and ≤47 ms for LAS40. Assessment of the diagnostic results is presented in Table 4. The odds ratio of VLP as a marker of SMVT detected by BiSpec after optimization was 4.1 (95% CI [1.5-11.3], P = 0.003). The kappa analyses of diagnostic disagreement between Butterworth and BiSpec filters for GII and GIII were 0.61 (P = 0.005) and 0.19 (P = 0.21), respectively. Results of application of both filters in subjects of GII and GIII are shown in Figure 2.

From analysis of BiSpec and Butterworth filter results based on conventional cutoff values, a worth detecting odds ratio of 4, assuming a 6.5 control-to-case ratio and 71% specificity among controls (GII) was defined. Based on this model, we calculated a sample size of 150 subjects for GII (controls) and of 23 subjects for GIII (cases).

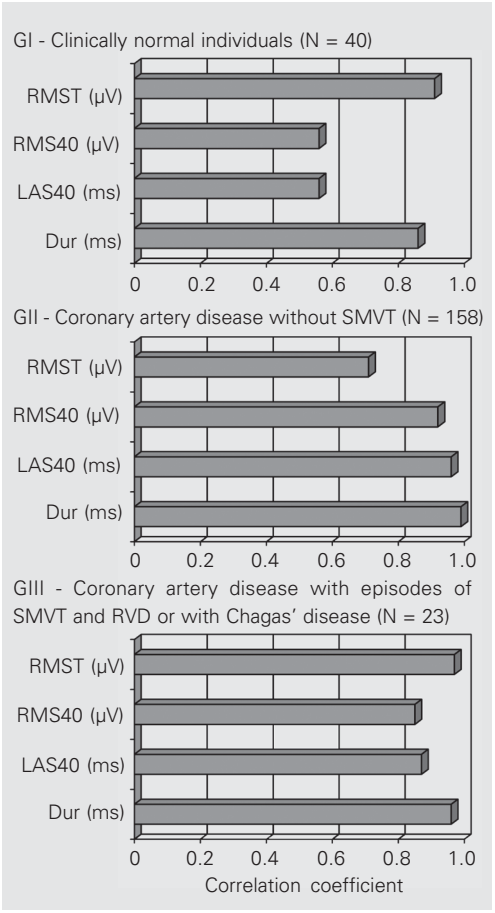

Figure 1. Correlation coefficients of vector magnitude variables between BiSpec (BI) and Butterworth bidirectional (BD) filters. For abbreviations, see legend to Table 2.

Discussion

The correct identification of VLP in subjects with SMTV is mandatory, since subsequent procedures, especially invasive electrophysiological tests, are frequently guided by SAECG. In post-myocardial infarction subjects without life-threatening ventricular arrhythmia, the presence of VLP may indicate the presence of a scar or a potential substrate for arrhythmia and represents a 5- to 50-fold increased risk for sudden death or life-threatening ventricular arrhythmia after one year (6,12,16). El-Sherif et al. (17) reported 17 to 29% positive predictive values of VLP for arrhythmic events after myocardial infarction. In coronary ischemic heart disease with stable or unstable angina, the prevalence of VLP is higher than in the normal population and similar to that observed

Table 3. Distribution of diagnostic results using conventional thresholds of normality as a function of patient group analysis.

GII - Coronary artery disease without SMVT (N = 158)			
	BD+	BD–	Total
BI+	35	12	47
BI–	14	97	109
Total	49	111	158
GIII - Coronary heart disease, with episodes of SMVT and RVD or with Chagas' disease (N = 23)			
	BD+	BD–	Total
BI+	15	0	15
BI–	6	2	8
Total	21	2	23
Diagnostic performance assessment			
	BD	BI	
Specificity (%)	69.0	70.3	
Sensitivity (%)	91.3	65.2*	
Total accuracy (%)	71.8	69.6	

BD: Butterworth bidirectional filter; BI: BiSpec filter; (–): negative exams; (+): positive exams. For other abbreviations, see legend to Table 2.
Kappa analysis compared diagnostic agreement between signal amplification ECG results. Kappa = 0.61 (P = 0.006); kappa = 0.30 (P = 0.15).
*P<0.05 compared to BD (chi-square test).

Table 4. Distribution of diagnostic results after optimization of BiSpec threshold of normality according to group analysis.

GII - Coronary artery disease without SMVT (N = 158)			
	BD+	BD–	Total
BI+	29	4	33
BI–	20	105	125
Total	49	109	158
GIII - Coronary heart disease, with episodes of SMVT and RVD or with Chagas' disease (N = 23)			
	BD+	BD–	Total
BI+	12	0	12
BI–	9	2	11
Total	21	2	23
Diagnostic performance assessment			
	BD	BI	
Specificity (%)	69.0	79.1*	
Sensitivity (%)	91.3	52.2*	
Total accuracy (%)	71.8	75.7	

BD: Butterworth bidirectional filter; BI: BiSpec filter; (–): negative exams; (+): positive exams. For other abbreviations, see legend to Table 2. Kappa analysis compared diagnostic agreement between filter results. Kappa = 0.61 (P = 0.005); kappa = 0.19 (P = 0.21).
*P<0.05 compared to BD (chi-square test).

in post-myocardial infarction subjects (12,18).

The BiSpec filter reduces the total energy of the vector magnitude and enlarges the filtered QRS complex of SAECG of subjects in GII. Variables calculated from the vector magnitude with the BiSpec filter correlated poorly with those calculated with the Butterworth bidirectional filter in control subjects of GI. The correlation coefficients obtained for GIII, 0.85 for RMS40 and 0.87 for LAS40, are significantly lower than those reported in the literature for arrhythmic events (7), i.e., 0.96 ($z = 6.2$, $P<0.01$) and 0.97 ($z = 7.2$, $P<0.01$), respectively. It is important to observe that the study conducted by Mehta et al. (9) compared the diagnostic results for 50 subjects submitted to invasive electrophysiological evaluation, while the present study assessed a larger number of clinically stratified subjects with heart disease and/or documented sustained rhythm disturbances.

The low correlation between variables in GI indicates the poor agreement of the diagnostic results obtained with conventional or optimized thresholds of normality, especially for GIII. When conventional thresholds were applied to GIII, kappa statistical analysis demonstrated that a diagnostic disagreement between BiSpec and Butterworth bidirectional filters could be ruled out. The odds ratio analysis showed that the Butterworth bidirectional filter has an independent and statistically stronger diagnostic value for SMVT than BiSpec after optimization (odds ratio 23.4, 95% CI [5.3-209.7]; odds ratio 4.1, 95% CI [1.5-11.3], respectively).

After threshold optimization, the BiSpec filter becomes less sensitive than the Butterworth bidirectional filter, affecting the analysis of VLP in subjects with SMVT. After optimization, kappa statistical analysis showed reduced diagnostic agreement and

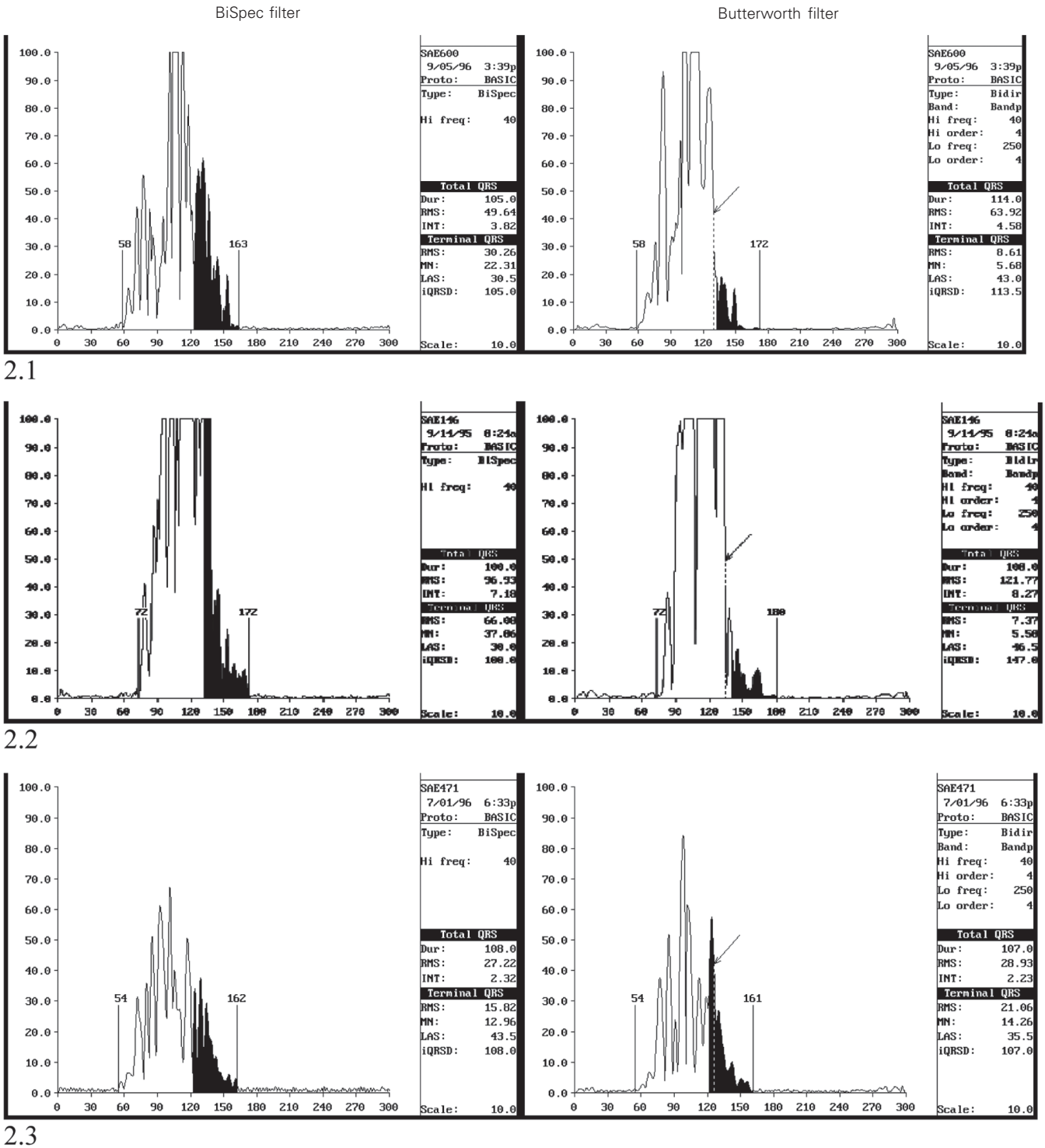

Figure 2. Vector magnitude analysis and variables obtained with BiSpec (BI) and Butterworth bidirectional (Bidir) filters for three patients: (2.1) BI-negative and Bidir-positive exam in a 57-year-old male from GIII after myocardial infarction with left ventricular aneurysm and 35% ejection fraction of the left ventricle (note the baseline noises in the BI filter covering late potentials); (2.2) BI-negative and Bidir-positive exams of a 67-year-old male from GII with dilated cardiomyopathy, and (2.3) BI-positive and Bidir-negative exams of a 78-year-old male from GII with coronary heart disease (note the reduction of the energy of the total activation and QRS terminal generating late potentials). Hi and Lo freq: higher and lower cutoff frequencies, respectively; INT: numeric integral of the whole ventricular activation; MN: numeric integral of the last 40 ms of the ventricular activation; Bandp: band-pass mode. For other abbreviations, see legend to Table 2.

modified the diagnostic value of BiSpec, as shown by a small reduction of the odds ratio. Data analysis was properly validated with the sampling procedure performed.

In conclusion, BiSpec is not recommended for VLP detection under conventional normality thresholds, and the filter algorithm must be further improved to be suitable for clinical application.

Acknowledgments

The authors wish to thank Dr. David Martin Simpson (Programa de Engenharia Biomédica, COPPE/UFRJ, and currently with the Institute of Sound and Vibration Research, University of Southampton) for assistance in analyzing our preliminary results.

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