Real-Time Analysis of Electrocardiographic Data for Heart Rate Turbulence

Final Report

NASA Faculty Fellowship Program – 2004

Johnson Space Center

Prepared By: E. Carl Greco, Jr., Ph.D.

Academic Rank: Associate Professor

University and Department: Arkansas Tech University
Department of Electrical Engineering
Russellville, AR 72801

NASA/JSC

Directorate: Space and Life Science

Office: Human Adaptation and Countermeasures

Mail Code: SK3

JSC Colleague: Todd T. Schlegel, M.D.

Date Submitted: August 13, 2004

Contract Number: NAG 9-1526 and NNJ04JF93A

ABSTRACT

Episodes of ventricular ectopy (premature ventricular contractions, PVCs) have been reported in several astronauts and cosmonauts during space flight. Indeed, the "Occurrence of Serious Cardiac Dysrhythmias" is now NASA's #1 priority critical path risk factor in the cardiovascular area that could jeopardize a mission as well as the health and welfare of the astronaut. Epidemiological, experimental and clinical observations suggest that severe autonomic dysfunction and/or transient cardiac ischemia can initiate potentially lethal ventricular arrhythmias. On earth, Heart Rate Turbulence (HRT) in response to PVCs has been shown to provide not only an index of baroreflex sensitivity (BRS), but also more importantly, an index of the propensity for lethal ventricular arrhythmia. An HRT procedure integrated into the existing advanced electrocardiographic system under development in JSC's Human Adaptation and Countermeasures Office was developed to provide a system for assessment of PVCs in a real-time monitoring or offline (play-back) scenario.

The offline heart rate turbulence software program that was designed in the summer of 2003 was refined and modified for "close to" real-time results. In addition, assistance was provided with the continued development of the real-time heart rate variability software program. These programs should prove useful in evaluating the risk for arrhythmias in astronauts who do and who do not have premature ventricular contractions, respectively.

The software developed for these projects has not been included in this report. Please contact Dr. Todd Schlegel for information on acquiring a specific program.

INTRODUCTION

Heart Rate Turbulence, HRT, is the sinus nodal response following an isolated premature ventricular contraction, PVC. Typically a short initial acceleration in heart rate immediately follows the PVC's compensatory pause. This initial acceleration is then later followed by a deceleration of the heart rate. Figure 1 depicts a typical electrocardiogram and arterial blood pressure response for a normal, healthy individual just prior to and following an isolated PVC.

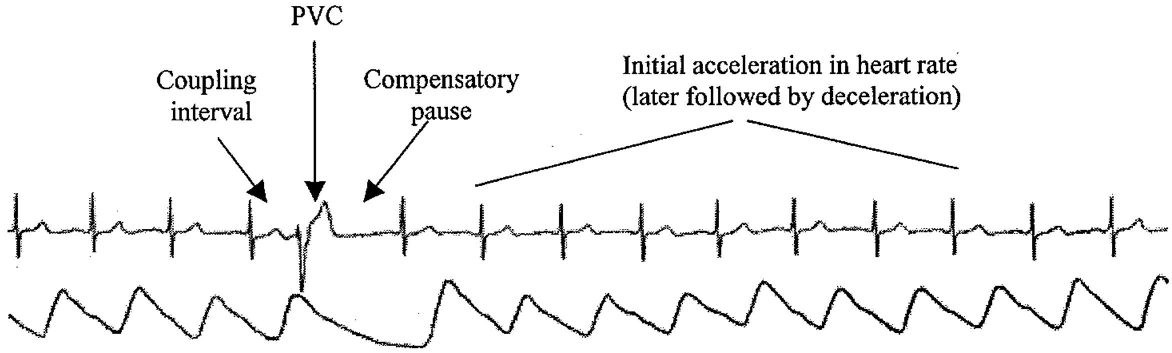

Figure 1: Electrocardiogram (upper trace) and arterial blood pressure preceding and following a single premature ventricular contraction, PVC[2]

Although the underlying mechanisms of HRT have not been fully identified, HRT likely represents a baroreflex response. The premature ventricular contraction causes a brief decrease in the mean arterial blood pressure. When the autonomic control system is intact, the change in arterial blood pressure elicits an instantaneous response in the normally conducted heartbeats that follow the PVC which result in HRT. If the autonomic control system is impaired, this reaction is either weakened or entirely missing. Two parameters have been used to quantify HRT: Turbulence Onset and maximum Turbulence Slope[1]. Turbulence Onset is a measure of the sinus acceleration following single PVC whereas the maximum Turbulence Slope is an indicator of the deceleration phase.

The HRT for a normal healthy individual is shown in Figure 2 and is represented by the RR intervals just preceding and following qualified PVCs. Beats –2 and –1 are the two normal sinus rhythm (NSR) RR intervals just prior to the PVC, beat 0 is the coupling RR interval between the last NSR beat and the PVC, and beat 1 is the compensatory pause RR interval between the PVC and the NSR beat immediately following the PVC. Beats 2 – 16 are all NSR RR intervals. Figure 2 depicts the average of five acceptable separate HRT responses from a total of seven PVC's. An HRT response is deemed to be acceptable if a predetermined number of normal sinus beats preceded and followed the single PVC. In this example, the acceptance criteria were 10 normal beat RR intervals proceeding and 15 following the PVC. Two of the seven detected PVCs were excluded based on these acceptance criteria. The total number of detected and acceptable PVCs was reported on the graphical display. Straight lines connect the average RR intervals between each consecutive beat relative to the PVCs' average coupling interval. The vertical bold line at each RR interval location spans the standard deviation of that PVC relative RR interval. The horizontal dashed line represents the mean of the RR intervals for the two pre-PVC NSR beats preceding all of the included PVCs.

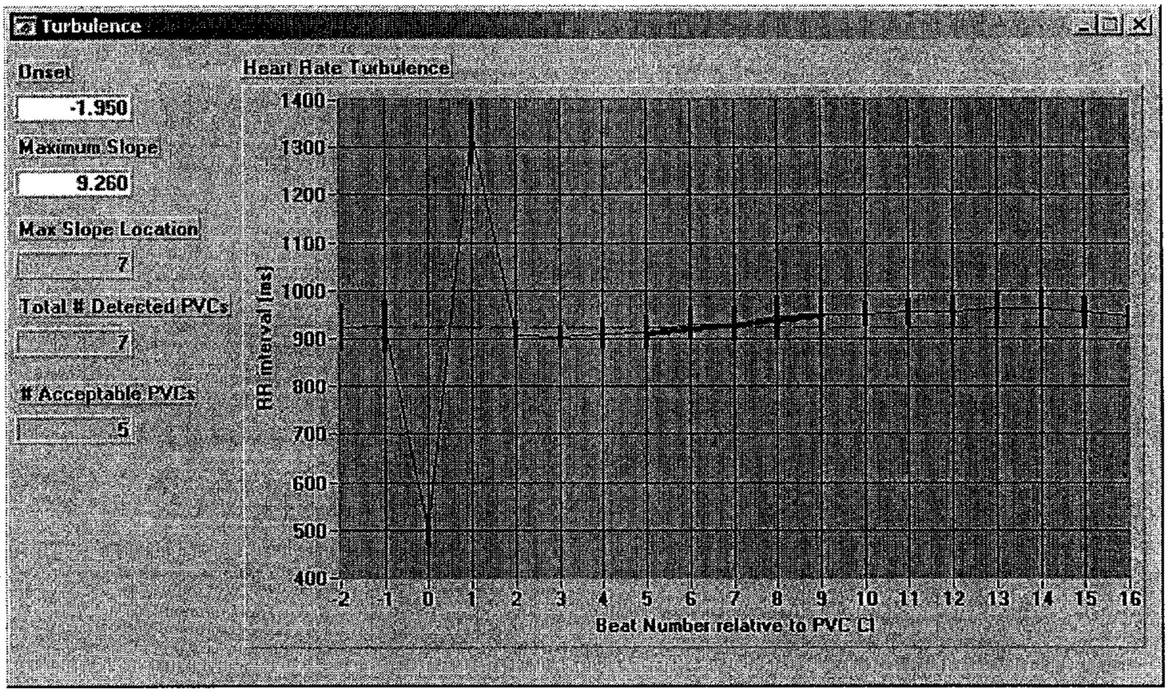

Figure 2: A typical HRT response

Traditional HRT analysis utilized long term data recording for example from 24-hour Holter recordings. The real-time online analysis approach described here evaluated the turbulence response for each identifiable PVC as it occurred.

HRT Parameters

HRT has been characterized by two parameters, Turbulence Onset (TO) and Turbulence Slope (TS) defined as follows:

Turbulence Onset:

$$TO = \frac{(RR_2 + RR_3) - (RR_{-2} + RR_{-1})}{(RR_{-2} + RR_{-1})} * 100\%$$

where RR_{-2} and RR_{-1} represent the two NSR beats intervals immediately preceding the single PVC's coupling interval, RR_0. The RR_2 and RR_3 intervals are the first two NSR beat intervals immediately following the PVC's compensatory pause interval, i.e., RR_1. Turbulence Onset represents the fractional (ms/ms) differential change (expressed in percent) for the two-beat NSR average prior to and following the PVC. TO was calculated for each individual PVC and averaged over all acceptable PVCs[2].

Turbulence Slope:

Turbulence slope was determined from the averaged RR interval response for all PVCs within a patient's record as the maximum slope of a five beat NSR sequence within a 15-beat interval following the PVC. The required normal sinus beat intervals window bracketing each PVC was designated by the operator prior to analysis. Linear regression was applied to each overlapping 5-beat sequence. For example, for the data shown in Figure 2 the slopes were found for the following eleven 5-beat number sequences:

[(2, 3, 4, 5, 6); (3, 4, 5, 6, 7); … (12, 13, 14, 15, 16)]

and recorded at the center beat number for each sequence, i.e., [4, 5, 6, …, 14]. The maximum slope for each of these five beat intervals was reported in ms/beat units and represented a measure of the deceleration in heart rate following the single PVC. A straight line drawn through the center point of the sequence with the maximum slope is shown in Figure 2. The maximum slope and its location were reported on the HRT display panel. In the online evaluation of HRT, the HRT display was updated following the prerequisite contiguous interval of normal sinus beats trailing each PVC.

Clinical studies utilizing 24 hr. Holter recordings have found significant predictive risks associated with abnormal turbulence parameters. Schmidt et al[1] used TO > 0% and TS < 2.5 ms/beat to stratify patients into a high risk group. The turbulence slope was found to be more significant of the two parameters for risk assessment. Taken together TO and TS were found to be the best predictors of mortality in their post myocardial infarction patient populations with reduced left ventricular ejection fraction. On the other hand, normal healthy individuals who have PVCs but who do not have structural heart disease have turbulence parameters in the normal range. For example, Diaz et al[3] found TO < 0 for all participants in a study of healthy subjects with PVCs. Values of TO ranged from -1.1% to –11.2%, with a mean of –4.9%. The TS values were not reported in this study.

METHODS

A real-time online HRT parameter estimation routine was developed in the JSC Neurosciences Laboratory to analyze an electrocardiogram obtained from the CARDIAX PC-based computerized ECG system. The CARDIAX system was developed by

International Medical Equipment Developing Co. Ltd. (IMED), Budapest, Hungary, and distributed by CardioSoft, Houston, Texas. The HRT program was written in the C programming language using the CVI system software integration and development environment from National Instruments. Data exchange between the CardioSoft/CARDIAX PC based system and the HRT/HRV application occurred via a named pipe shared memory communication channel as described in the MSDN Library. The HRT code was integrated into a system containing additional heart rate variability analysis routines[4].

The first stage of the HRT application was beat classification based on interval analysis to identify dysrhythmias resulting in significantly altered beat-to-beat intervals. With rare exception, single beat ectopic foci of ventricular origin produce an earlier than a normal conducted beat and result in a delayed compensatory pause recovery beat. The structural evaluation of the P and QRS complexes was not deemed necessary for beat classification requirements for HRT and was therefore not preformed[+]. Analysis of the normal sinus heart rate response that followed an isolated PVC was then performed.

HRT Beat Classification

The first step in the HRT process was the classification of individual beats. Two separate beat classification algorithms were investigated. The first was a modification of the technique developed last summer and was based on the algorithm described on the HRT website[2]. The second procedure was a subset of the one developed by Hamilton and Tompkins[5] and provided on their website[6]. Both beats classification algorithms were based on interval analysis. The HRT algorithm classified each interval as one of the following: normal; PVC coupling interval; PVC compensatory pause; artifact; and unknown. The i-th RR interval, RR_i, was designated a normal RR interval if all of the following conditions were met:

Normal beat requirements:

$$300ms \le RR_i \le 2000ms$$
$$|RR_i - RR_{i-1}| < 200ms$$
$$|RR_i - RA| < 0.20 * RA$$

where RA is the running average of the last 5 normal beats. Traditional classification of PVCs, as defined on the h-r-t website[2], was based on the following procedure: A PVC was defined as a sequence of two consecutive RR intervals wherein the coupling interval is 20% less than the running average and the compensatory pause is 20% greater, or

[+] Beat classification for HRT analysis was found to be less stringent than that required for ectopic beat exclusion in HRV parameter estimation. A small number of false negatives were acceptable in HRT but not in HRV analysis.

$RR_{i-1} < 0.80 * RA$ for a coupling interval

And

$RR_i > 1.20 * RA$ for a compensatory pause

RA was the running average or filtered average as define below. The user can choose the **HRT.org** analysis option using the switch in the upper right portion of the program initiation panel, as shown in Figure 3 below:

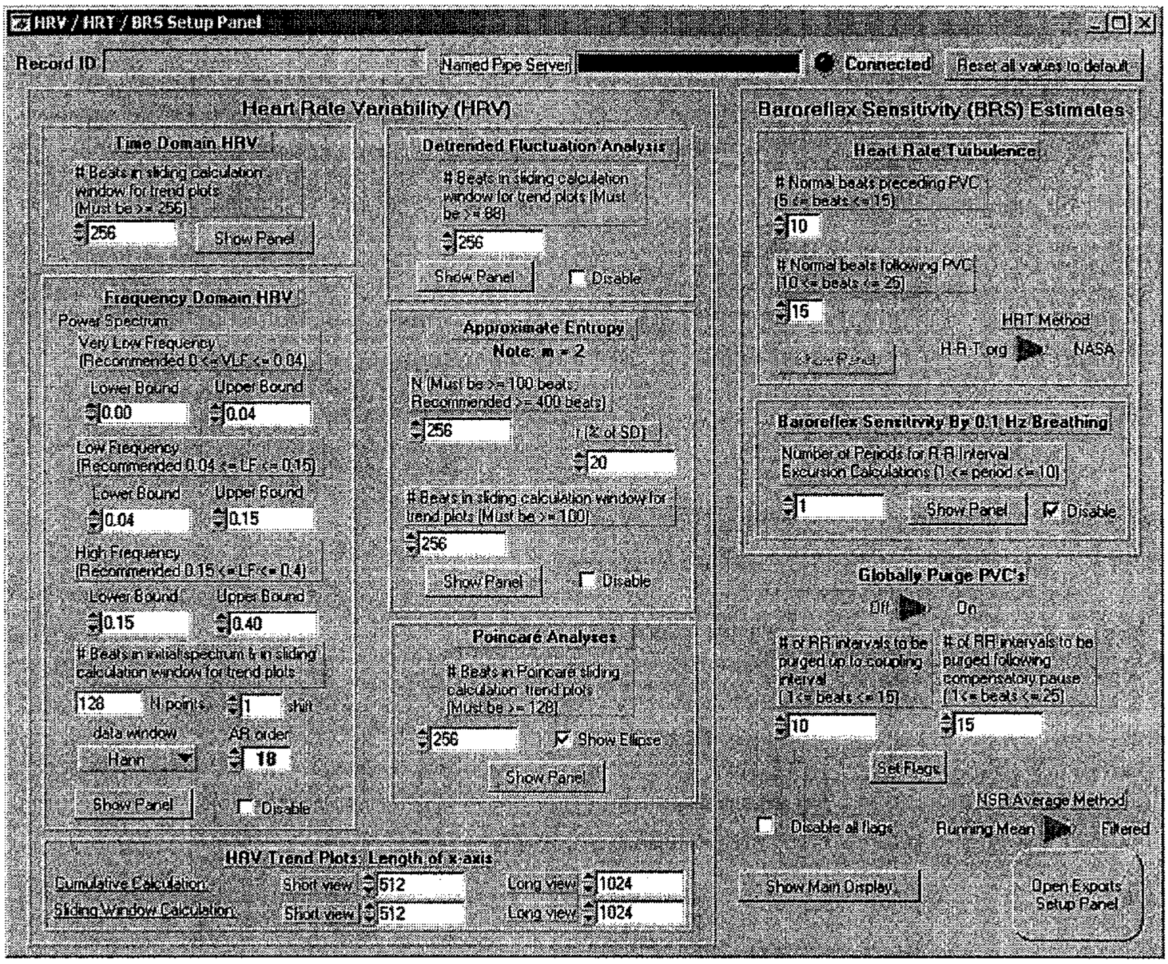

Figure 3: HRV Setup Panel showing the setting for HRT beat classification

A filtered running average for RA weighted the most recent NSR higher with the sequence [5^2, 4^2, 3^2, 2^2, 1] scaled to the sum of the coefficients. The switch in the lower right corner allows the user to select the standard or filtered option.

A slightly modified approach was developed to handle records where the coupling intervals were larger and compensatory pauses were smaller than the traditional criteria. This is designated as the **NASA** criteria on the initiation panel and is defined by the following:

$$RR_{i-1} < RA - RSD \qquad \text{for a coupling interval}$$

And

$$RR_i > \max\left[1.17 * RA, RA + RSD\right] \qquad \text{for compensatory pause}$$

where RSD is the running standard deviation.

An interval that does not qualify as a normal interval, coupling interval or compensatory pause is designated as an artifact. An "unknown" classification is necessary to label the first beat in the record since it does not have a preceding beat and cannot be classified as normal, PVC or artifact without it. The first beat was typically the only beat so designated.

Rhythm Check Beat Classification

The second algorithm investigated for beat classification was based on a subset of the algorithm development by Hamilton and distributed from his website as GPL code. RhythmChk, or rhythm check, compared the current interval to past seven intervals and their respective classification for a beat classification of the current beat. Intervals were classified as either normal, PVC or unknown. RhythmChk required a minimum of four intervals to begin. The first three intervals were designated as unknown. Subsequent unknown classifications were converted to artifact for integration into the HRV program.

PVC Qualification and Inclusion in HRT

RR intervals classified as a coupling interval followed by a compensatory pause were identified as individual PVCs. For inclusion in the HRT analysis, each PVC must also be evaluated to determine if it had the prerequisite number of normal sinus beats preceding and following it. The default values were 10 consecutive before and 15 consecutive NSR beats following each PVC. Otherwise the PVC was excluded from the HRT analysis. The program was written to allow the user to adjust these numbers within a specified range.

HRT Analysis

The TO and TS parameters were determined for all acceptable PVCs. If none were detected, a popup message was printed to the screen. Refer to Figure 2 for the format of the TO and TS parameters along with the total number of detected PVCs, acceptable

PVCs for analysis and a plot of the averaged HRT response. The maximum slope location is displayed and a line with this slope is drawn at that location (beat 7 in the above plot). If the TO and/or TS values are out of the normal range, they were highlighted in red on the display. The maximum slope for this record was 9.26 ms/beat and was in the normal range (> 2.5) and the TO value –1.95% was also in the normal range (<0%).

CVS

A version control system was installed for code maintenance and documentation. CVS required a CVS server installation to retain the code database and communicate with the user clients. The WinCvs[7] client and CVSNT[8] server package were installed. Both were licensed under GNU General Public License (GPL).

WinCVS

The WinCvs client interface provided the following features[7]:

- Sophisticated graphical user interface helps to utilize full power of CVS for experts and quickly learn basics for beginners.
- Native look-and-feel on Windows, Mac and Unix/Linux thanks to the use of popular GUI frameworks like MFC, Metrowerks PowerPlant and gtk+.
- Scripting support allows to easily automate, extend and customize common tasks.
- Realtime sandbox view with visual indication of the local state of files.
- Various filters to monitor any folder or all its subfolders in a flat view.
- Command line support makes any CVS commands or command options not directly handled by GUI possible.
- Repository tags, modules and files browser allows to easily enter command parameters.
- Changes in the files can be verified using diff command or external diff application.
- File revisions history can be displayed as a graph.
- Supports text, binary and Unicode file types.
- The type of the files is automatically detected upon import and add command.
- Reserved edits help to organize team work.
- Close cooperation with CVSNT project resulting in very dynamic and effective development of new features.

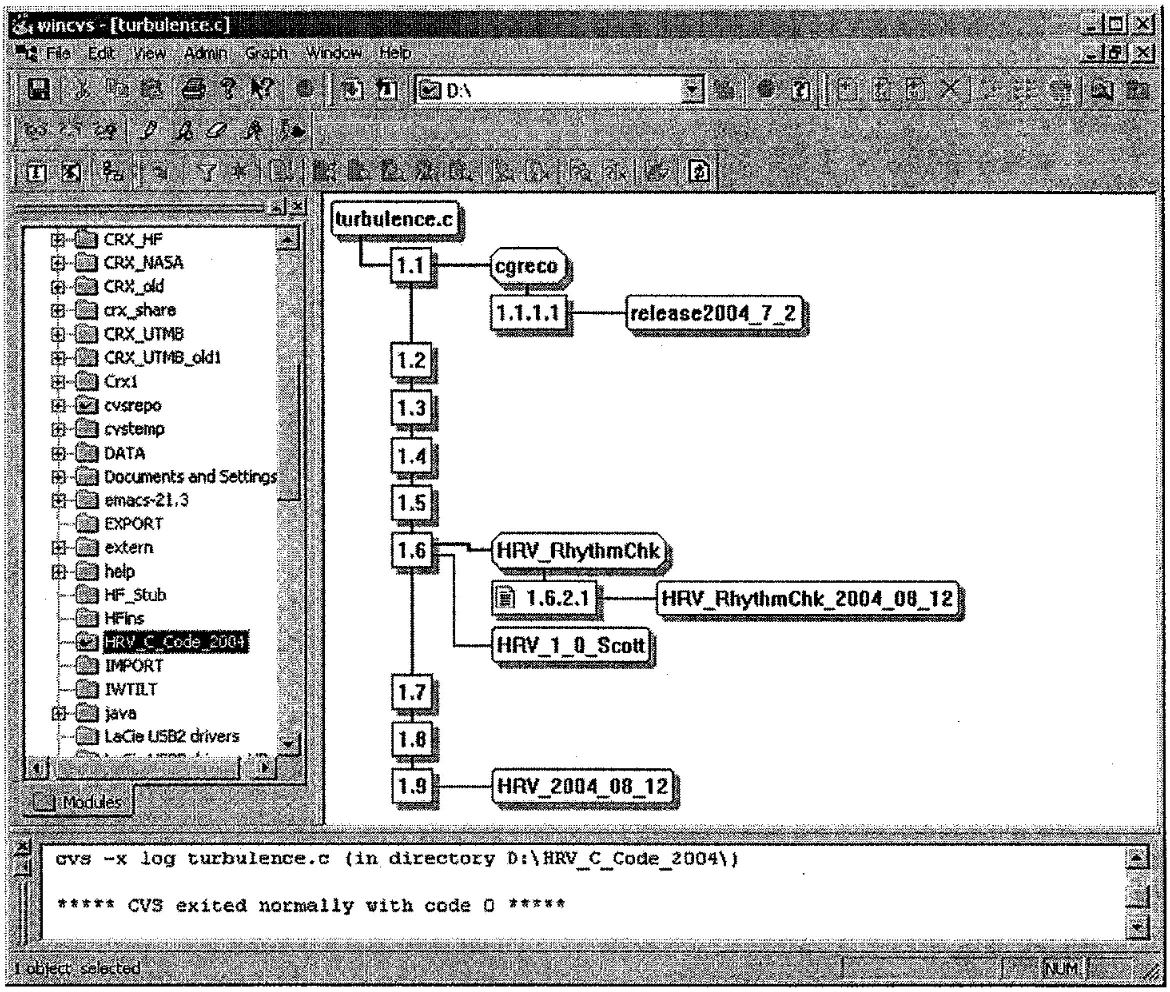

Figure 4: WinCvs client interface with graphical view of the revision history for turbulence.c. The HRV_2004_08_12 and HRV_RhythmChk_2004_08_12 tags correlate this module with the others at this revision level

The WinCvs provided the client side access to the code database required for daily updates (commits), updates and checkouts and yet was easy and straight forward to use.

The CVSNT server maintained the code database and provided network access for designated users. CVSNT supports several communication protocols. The Microsoft's Security Support Provide Interface (sspi) was selected for its support of domain name access and its encryption features. Two Groups were setup on the CVSNT server: CVSAdmins and CVSUsers, Figure 5 and 6. Users added to the CVSUsers group had access to the CVS code database to checkout, update and commit changes. The CVSAdmins group included users given additional administrative access not required by the general user. The CVS database was then assigned the necessary permissions for the

CVSUsers and CVSAdmins groups as stipulated in the installation CVSNT installation guide[8]. A command script, SetACL, was obtained from the CVSNT website and modified to facilitate this process.

The CVS database, or repository, contains the following packages: HRV_C_Code_2004, Beat_Class_Test, CBuf, dsp, and NamedPipeClient. Each package contains several modules, or files. Figure 4 displays the version history of the turbulence.c module from HRV_C_Code_2004 in graphical format. This turbulence.c module was initially checked in (committed) as version 1.1. It was revised five times, versions 1.1 – 1.6. Version 1.6 was tagged HRV_1_0_Scott along with all other modules in this package at the same level of development. A member of the CVSUsers group may then check out all modules associated with the HRV_1_0_Scott tag to obtain the package at this level of development. Also, at version 1.6 a branch was started and tagged HRV_RhythmChk. All additional modules included in this branch were similarly tagged. Again the user can checkout all modules associated with this branch by specifying the HRV_RhythmChk tag on checkout. The main branch was tagged HRV_2004_08_12 and the branch was tagged HRV_RhythmChk_2004_08_12 to identify and synchronize the modules at that development level.

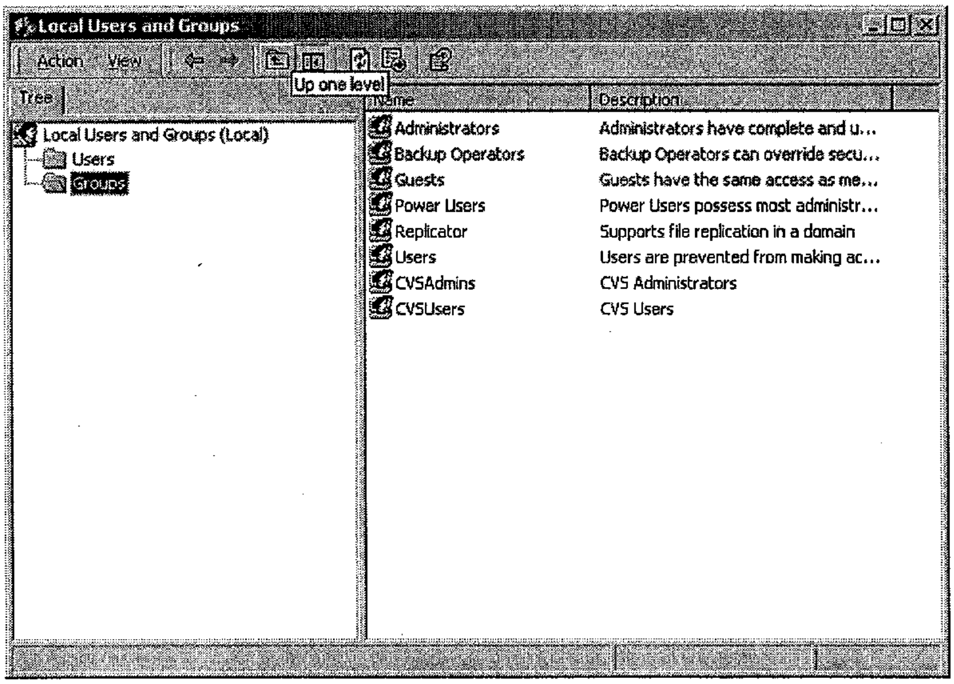

Figure 5: CVSNT Groups CVSAdmins and CVSUsers added to the CVSNT server

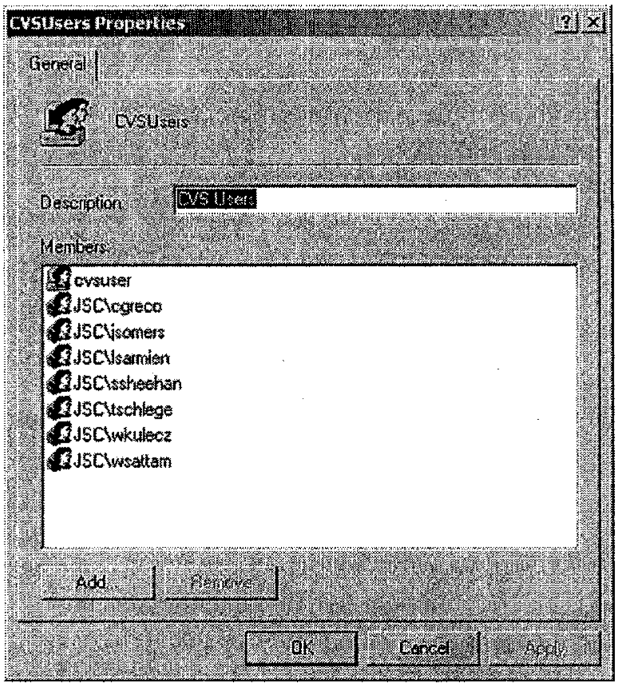

Figure 6: CVSUsers identified by their domain usernames

WORK COMPLETED THIS SUMMER

The work completed this summer included the development of the computer software to classify RR intervals based on the interval analyses noted above. A program was then written to identify PVCs to be included in the real-time HRT analysis as described in detail above. The code was integrated into a package of advanced electrocardiography software applications for heart rate variability analysis used in Dr. Schlegel's laboratory. The HRT software application described herein was written in the C computer language and was constructed in a LabWindows CVI (National Instruments, Austin, TX) programming environment, compatible with Microsoft Windows. Interested parties can view a demonstration of the HRT program by contacting Todd T. Schlegel, M.D. in the JSC Neurosciences Laboratory.

I worked with Scott Sheehan, a NSBRI student, to purge ectopic beats from several HRV parameters.

CONCLUSIONS

A series of tools were developed to facilitate the analysis of the electrocardiogram online in real time, and assist NASA flight surgeons and other physicians with cardiovascular diagnoses. The evaluation of HRT onset and slope following premature ventricular contractions might eventually allow for a non-invasive and unobtrusive way to assess both susceptibility to arrhythmia and changes in baroreflex sensitivity in astronauts during and after space flight. Both cardiac arrhythmias and reduced baroreflex responsiveness are known to occur during space flight. The HRT software developed this summer has therefore been designed to ultimately allow NASA flight surgeons to follow trends in baroreflex sensitivity and arrhythmic risk in astronauts who have premature ventricular contractions. Similarly, the software should eventually allow other physicians to monitor at-risk cardiac patients on the ground, particularly those who may have a propensity for cardiac arrhythmias.

REFERENCES

1. Schmidt G, Malik M, Barthel P, Schneider R, Ulm K, Rolnitzky L, Camm AJ, Bigger JT, Jr., Schomig A: Heart-rate turbulence after ventricular premature beats as a predictor of mortality after acute myocardial infarction. Lancet 353:1390-6, 1999
2. Heart Rate Turbulence, Technische Universitat Munchen, 2004, pp http://www.h-r-t.org
3. Diaz JO, Castellanos A, Moleiro F, Interian A, Myerburg RJ: Relation between sinus rates preceding and following ectopic beats occurring in isolation and as episodes of bigeminy in young healthy subjects. *In* Am J Cardiol. Vol 90, 2002, pp 332-5
4. Pino F, Schlegel T: HRV Online Analysis Program. In Preparation, 2004
5. Hamilton PS, Tompkins WJ: Quantitative investigation of QRS detection rules using the MIT/BIH arrhythmia database. IEEE Trans Biomed Eng 33:1157-65, 1986
6. Hamilton PS, Curley MG: OSEA: RhythmChk. Vol 2004, 2.1 edition, EP Limited, 2004, pp http://www.eplimited.com/software.htm
7. WinCvs, 1.3.17.2 edition, CvsGui, 2004, pp http://www.wincvs.org/
8. CVSNT Wiki. Vol 2004, 2.0.51c edition, March Hare Pty Ltd, 2004, pp http://www.cvsnt.org/wiki/FrontPage