Grant No. RR00311-02

Section III-B

INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT	INSTITUTION:
Emmanuel Mesel, M. D.	Pediatric Cardiology	Stanford Computation Center Stanford Medical School

FIELD OF INVESTIGATION	PROJECT TITLE:
Direct Measurement of Intracardiac Blood Flow	V S D

AMOUNT OF RESOURCE USAGE

45,523

PROJECT DESCRIPTION

(Approximately 300 words)

Project VSD is concerned with blood flow through ventricular septal defects (VSD) surgically produced in dogs. Two major sets of comparisons are made: the pattern of flow through the VSD is compared with the pattern of differential pressure between the left and right ventricles and with the electrocardiogram (ecg); and flow measured by an electromagnetic flow probe (which we consider a primary standard) is compared with flow measured by other techniques used on people (Flick, dye dilution).

During the experiment, VSD flow, left and right ventricular pressures, and the ecg are recorded on tape. The more interesting data are selected for A to D conversion and for computation of the differential pressure by program WORKHORSE. Program LISTING lists digitized data, which, when graphed, permits comparison of the pattern of flow with the pattern of differential pressure. As might be expected, we have found that these patterns are very similar even under varying conditions (eg, ectopic beats), with flow slightly delayed with respect to pressure. Program cathlog produces a file which summarizes all our VSD experiments.

Future effort will be directed towards the incorporation and use of programs developed in project carcat for pattern recognition of pressure and flow contours.

Grant No. FR 00311-02

Section III-B

INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT	INSTITUTION:
Emmanuel Mesel	Pediatrics	Stanford Medical School Stanford Computation Center

FIELD OF INVESTIGATION	PROJECT TITLE:
Medical Diagnosis	WFR

AMOUNT OF RESOURCE USAGE:

49,504

PROJECT DESCRIPTION

(Approximately 300 words)

The project is an investigation of mathematical modeling techniques applicable to medical diagrams. The plan is ultimately to apply the cause-effect modeling techniques developed in reference 1 in an environment that allows online interaction between physician and computer model.

Currently programmed is the congenital heart disease model of Warner and his collaborators[2]. Also programmed are text editor routines that are being used to speed the preparation of reference 1.

Though a program has been written to implement the cause-effect modeling techniques of reference 1 using a Burroughs B5500 computer, adapting even that program to ACME will require considerable effect as the program depends heavily on the nearly unique ability of the B5500 to efficiently handle recursion and treat overlay automatically. It is felt that the ability to experiment with the models constructed in a way available only in an online system and that the increased interest and criticism that will result from testing the models produced in a clinical environment justify the effort.

1. W.F. Rousseau, A Method for Computing Probabilities in Complex Situations, Doctoral Dissertation, Stanford University (in preparation).

2. H.R. Warner, A.F. Toronto, L.G. Veasy, R. Stephenson, "A Mathematical Approach to Medical Diagnosis," JAMA , Vol. 177, July 22, 1961, pp 177-183.

Grant No. RR 00711-02

Section III-B

INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT:	INSTITUTION:
Emmanuel Mesel, M.D.	Pediatrics	Stanford Medical Center Stanford Computation Center

FIELD OF INVESTIGATION	PROJECT TITLE:
On-line analysis of cardiac catheterization data.	Carcat

AMOUNT OF RESOURCE USAGE

186,106

PROJECT DESCRIPTION

(Approximately 300 words)

Project "carcat" analyzes cardiac catheterization pressure tracings in children. From catheters in the right and left heart, pressure tracings are transmitted to the ACME computer, converted to digital data, and analyzed to determine atrial, ventricular, arterial, venous and wedge pressures. Currently the values in millimeter of mercury are calculated for the a and u waves, x and y troughs, and mean pressures in the artia and great veins, for systolic and end-diastolic pressures in the ventricles, for systolic, diastolic and mean pressures in the great arteries, and for mean pressures for the wedge positions. These values are calculated immediately and printed out on the computer terminal in the catheterization room.

At this time, efforts are under way to improve and ascertain the accuracy of the algorithms used in pattern recognition for atrial and ventricular pressure tracings.

The basic data acquisition and analysis system that has been set up will also be used to store data acquisition and analysis sytem that has been set up will also be used to store data for additional calculations and for the preparation of reports. As data is accumulated in storage from cardiac catheterizations and from other sources of clinical information, it will be possible to analyze large amounts in clinical data rapidly using eh ACME computer. Research into methods of storing and recalling data for analysis of clinical information will be an important part of our future efforts.

Grant No. FR 00311-02

Section III-B

INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT:	INSTITUTION:
Emanuel Mesel	Pediatrics	Stanford Medical School Stanford Computation Center

FIELD OF INVESTIGATION:	PROJECT TITLE:
Indicator Dilution Measurements of Pulmonary Blood Flow	[illegible]

AMOUNT OF RESOURCE USAGE:

27,923

PROJECT DESCRIPTION
(Approximately 300 words)

One of the parameters to be derived from indicator dilution measurements of pulmonary blood flow is the "impulse response", which is essentially the distribution of transit times of particles through the lungs. If Ci(t) represents the dye concentrations in the right heart following injection of a bolus of dye at t=0 and Co(t) represents the concentration in the left heart, then the impulse response h(t) is described by the equation:

$$Co(t)=\int_{s=0}^{s=t} h(s)Ci(t-s)ds$$

Replacing the integral with a summation over equally spaced intervals of time:

$$Co(n)=\sum_{i=0}^{[illegible]} h(i)Ci(n-i)$$

Thus a program can be written for a digital computer which solves for the function h(t) when given the values for Ci(t) and Co(t).

However, a simple straightforward solution yields an impulse response which is hopelessly disrupted by artifacts in the collected data. A technique must be employed which somehow filters the data. Several possible methods are known; one has in fact been successfully used. The program was executed on the Burroughs 5500, a machine which has twelve significant figures in regular precision and twenty-four with double precision. [illegible] in [illegible] accumulated so much error during execution [illegible]. Thus [illegible] achieve our goal using [illegible] precision than is now available. Our current efforts are directed at the this problem of insufficient precision.

Grant No. FR 00311-02

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INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT:	INSTITUTION:
STEPHEN, JON MORRIS	GENETICS	Stanford Medical School Stanford Computation Center

FIELD OF INVESTIGATION:	PROJECT TITLE:
BRAIN PROTEIN BIOCHEMISTRY	EXPT4

AMOUNT OF RESOURCE USAGE:

123,74

PROJECT DESCRIPTION

(Approximately 300 words)

An inexpensive, easy to realize interface for a Packard # 3314 liquid scintillation counter - IBM 1800 was built and tested. Several support programs written in 1800 Assembly Language and PL/1 complete the interface. (A full description is available in ACME Note #TRA-1). The interface makes possible direct reading of data into ACME data files from the counter output.

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INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT	INSTITUTION:
W. Nye	Medical Microbiology	Stanford Medical School Stanford Computation Center

FIELD OF INVESTIGATION	PROJECT TITLE
see below	see below

AMOUNT OF RESOURCE USAGE:

31529

PROJECT DESCRIPTION

(Approximately 300 words)

The usage of this terminal under this name actually represents usage by several investigators in this department. Mr. Nye has written most of the programs and his field of usage has been calculation of equilibrium constants of antibody-hapten reactions and structural studies. Dr. Rosenberg has used it for genetic studies of complement in mice. Dr. Stocker has used it for genetic studies in bacteria, and Dr. Amkraut for statistical studies of the immunologlobulins in man. It has also been used in a pedagogic sense by students of these men as well as for manuscript editing. As the advantages of time sharing and data files become more evident, and directly connected instrumentation becomes more commonplace, it is expected that there will be considerably more usage by this department.

Grant No. FR 00311-02

Section III-B

INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT:	INSTITUTION:
Dr. Petralli	Infectious Diseases	Stanford Medical School Stanford Computation Center

FIELD OF INVESTIGATION:	PROJECT TITLE:
	Med-Data

AMOUNT OF RESOURCE USAGE:

43,922

PROJECT DESCRIPTION

(Approximately 300 words)

This project deals with the data collected in the Hospital Bacteriology Laboratory, quality control of the input as well as storage in a form suitable for later analysis.

As conceived the project will proceed as follows: the secretaries will type the information at the terminal. The data will be placed in a temporary file from which it will be analyzed for quality control. Data not consistent with previous data will be questioned and perhaps the laboratory test repeated. The data will then be placed in a complete file and a sorted file, each of which may be used for later analysis. The temporary file will be used to put out the daily laboratory reports. This step will include some calculations such as conversion of sensitivity zone size to "sensitive" or "resistant".

Using the computer to put on daily reports allows the project to proceed without addition of personnel to type in information. The input time of the secretary will be less than the time usually required to type reports.

The data analysis will give us information about the sensitivities of various bacteria to antibiotics. This information will help us to decide which treatment to use in certain cases. We will also be able to detect significant changes in sensitivity as well as major trends.

Grant No. FR 00311-02

Section III-B

INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT:	INSTITUTION:
Robert W. Porter	Biochemistry	Stanford Computation Center Stanford Medical School

FIELD OF INVESTIGATION:	PROJECT TITLE:
Kinetics of Aspartate Transcarbamylase	ATC_KIN

AMOUNT OF RESOURCE USAGE:

38,012

PROJECT DESCRIPTION

(Approximately 300 words)

ATC_KIN contains six programs used for the study of the reaction catalyzed by the enzyme, aspartate transcarbamylase. Program LstSq simply calculates a least-squares linear fit and standard deviation. Program DataFit calculates initial rates of reaction from experimental data. These data are time points and counts per minute of product at each time point. Initial rates are calculated by a least-squares linear fit; rates are taken from the fitted slopes, converted to molar values using a value for specific radio-activity, and also corrected for enzyme concentration. This program, like the others in Project ATC_KIN, has been written so that it can be operated easily by other workers in the research group without experience in using computers.

Other programs are used to fit the various kinetic equations which describe the relation of initial rate to substrate concentration. Program HyperFit fits the simple hyperbolic equation, called the Michaelis-Menten equation. The curve fitting procedure is very crude. For the two constant parameters in this function, initial estimates are provided, with ranges to be tested for both. In a first step, a coarse fit is obtained by testing all the combinations of the trial values for the two parameters, in coarse steps covering the two ranges. In succeeding steps, the operator provides new, smaller ranges to be tested, repeating this procedure until achieving a sufficiently defined pair of values. Next the data points are scanned for deviations from this fitted curve, and the point with the largest deviation may be rejected, at the option of the operator. If the point is rejected, the fitting process is repeated, giving new values of the two parameters for the best curve.

Program DataFit 2 simply gives a least-squares linear fit for the linear equation obtained from the reciprocal form of the Michaelis-Menten equation, first calculating reciprocal values of the data points, and also calculating the kinetic parameters from the fitted slope and intercept. These values are then used as the initial estimates for use in Program HyperFit.

Program DataFit 1 fits the much more complicated equation which describes the kinetics of the two substrate reaction, or the similar equation for the kinetics in the presence of inhibitor. The equation fitted is in the simpler reciprocal form, which predicts a family of straight lines having a common intersection. The program is designed to select the values for the coordinates of the common intersection point which gives the lowest value for the deviations of all the experimental points from their corresponding best lines. The fitting procedure is similar to the crude trial-and-error method described for program HyperFit. It should be noted that this curve-fitting procedure requires the use of an on-line communication system.

Finally, Program ATCase 11 is a manuscript in preparation for publication of these kinetic studies.

INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT:	INSTITUTION:
Walter E. Reynolds	Genetics - Instrumentation Research Lab	Stanford Medical School Stanford Computation Center

FIELD OF INVESTIGATION:	PROJECT TITLE:
Computer instrumentation of basic research instrumentation	S007

AMOUNT OF RESOURCE USAGE:

23,650

PROJECT DESCRIPTION

(Approximately 300 words)

The "S007" project is a subset of the general work of the Instrumentation Research Laboratory, Genetics Department, in the field of instrumentation research conceived to answer the question, "What kind of automated basic biological instrumentation would be suitable for interplanetary probes of exobiological life forms?" Actual accomplishments of this laboratory have shed light upon that area and have immediate here and now applications in conventional biological and medical research. An example is the computer-directed mass spectrometer implemented by this laboratory and reported in this laboratory's Technical Report No. IRL 1062. A quadrupole mass spectrometer was uniquely controlled by a computer to achieve a high order of instrument efficiency.

The "S007" account supports technical and engineering development. Programs to help in engineering design have been written and used. Two such programs are "RCs" and "Dblfocus." The first of these examples was a straightforward electrical engineering circuit analysis aid and the second was an evaluation of the accuracy and complexity of instrumentation needed for a contemplated mass spectrometer purchase. Other "S007" files have experimental data useful in the development of algorithims to be used in the control or data acquisition modes of ACME. "TRACE" and "PICKER" are examples of this type.

This investigator's prime interest is in the time-shared instrumentation capability that ACME is to develop. This is the direct digital connection of the ACME computer to laboratory instruments. All of this investigator's usage of ACME

has been directly or indirectly in pursuit of this goal. To this date usage has been in anticipation of ACME's ability to serve these direct instrumentation needs of this laboratory, primarily in the field of mass spectrometers.

Once principal goal is the integration of an Associated Electronic Industries (AEI) model MS-9 mass spectrometer into the ACME data system. This work is being supported by NIH grant 5 RO1 AM 04257-07.

Grant No. RR 00511-02

Section III-B

INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT:	INSTITUTION:
A.M. SAUNDERS M.D.	PATHOLOGY	Stanford Medical School Stanford Computation Center

FIELD OF INVESTIGATION:	PROJECT TITLE:
QUANTITATIVE CYTOLOGY	MAST CELL

AMOUNT OF RESOURCE USAGE:

25,456

PROJECT DESCRIPTION

(Approximately 300 words)

Individual objects, cells or standard spheres, are measured at a magniffication of 1000-3200x in a microscope for size and flourescence intensity at a specified wave length. Data thus tabulated forms the basis for statistical analysis by computer. The computer is used similarly in calculating corrections when the microscope is used as a spectroflourimeter. Two manuscripts have been accepted and two are in preparation using these facilities.

The computer is also used to write the text of the MS.

INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT	INSTITUTION:
F. M. Scudo	Genetics	Stanford Medical School Stanford Computation Center

FIELD OF INVESTIGATION:	PROJECT TITLE:
Population Genetics	Migra

AMOUNT OF RESOURCE USAGE:

14,655

PROJECT DESCRIPTION

(Approximately 300 words)

The program tabulates the results of models for the genetical variability among populations in a linear array, with migration between adjacent colonies.

The basic quantity is given by the symmetric recursion

$$\alpha(F_{d+2} + F_{d-2}) + \beta(F_{d-1} + F_{d+1}) + \gamma F_d = 0;$$

its proper, special solution has the form

$$F_d = A_1\alpha_1^d + A_2\alpha_i^d$$

where A_1, A_2 are very complicated algebraic functions of the parameters. The final quantity is a linear combination of F_d's, d up to a few hundred. Thus, with the precision of this computer, a too large error would result from its direct application.

To avoid this an equivalent direct procedure has been applied to the vector $F_0, F_1, \cdots, F_d$, making use of the asymptotic property $F_{d+1} \approx X_1 F_d$. Initial vectors were calculated by an approximate formula and iterated to determine if they were increasing or decreasing. The two nearest ones of each kind were stored and, as new trial vectors, their average was used. The process was repeated till oscillations of the last digit, due to truncation, were observed. Thus final precisions of the order of 10^{-5}, determined by perturbation of the parameters, were obtained. Time required for each calculation varied from a few minutes to more than one hour, according to the value of the parameters.

Grant No. FR 00311-02

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INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT:	INSTITUTION:
Abraham Silvers, Ph.D.	Medicine	Stanford Medical School Stanford Computation Center

FIELD OF INVESTIGATION:	PROJECT TITLE:
Metabolism	Lipid Research (PAT_DATA)

AMOUNT OF RESOURCE USAGE:

41,522

PROJECT DESCRIPTION

(Approximately 300 words)

Our laboratory has used extensively the ACME computer. We used the computor for two major purposes:

A. ACME is used for considerable statistical computations and for the processing of laboratory data. We have been able to improve our insulin assay significantly, and have obtained calculated values in a fraction of the time ordinarily spent on these computations in the past. The ACME statistical library has given us many programs which have proven to be very useful.

B. The ACME system has been helpful in the investigation of problems of glucose, insulin and triglyceride metabolism.

1. It has enabled us to obtain an initial mathematical formulation for the transport mechanism of glucose across the cell membrane when modified by insulin.

2. We have been able to obtain approximate answers for the kinetic constants describing 2 and 3 pool models.

3. It has been helpful for obtaining simulations of theoretical curves and therefore has given us insights into the possible mechanism operating in a particular metabolic situation.

We expect in the near future to utilize the analog digital conversion abilities of ACME and to expand our use of ACME considerably.

Grant No. FR 00311-02

Section III-B

INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT	INSTITUTION:
R. Smallwood	Dean's Office	Stanford Computation Center Stanford Medical School

FIELD OF INVESTIGATION	PROJECT TITLE
Medical Facility Planning	MEDIPLAN

AMOUNT OF RESOURCE USAGE:

101,849

PROJECT DESCRIPTION
(Approximately 300 words)

The Stanford Medical Facilities Planning Group is carrying out a system planning study for the design of the new Stanford Medical Care Facilities. The project is dependent upon the services of ACME for two important functions. The first of these is as a data gathering vehicle for acquiring medical information from the Medical School faculty and community physicians. In the evaluation of alternative design strategies for the Medical Care Facilities it is important that the medical care demands of the patients be known. To acquire this information a computer dialogue system has been programmed on ACME for interviewing doctors and encoding their standards of high quality medical care. This dialogue system has been completed and an extensive data gathering experiment is currently getting under way.

The second important use of ACME to the Medical Planning project will be in the evaluation via simulations of alternative macro organization strategies for the facility design. These simulation programs will use the data gathered via the dialogue system plus some estimate of patient mix to simulate the total patient care demands that will be made on the major units of a particular design. In this way estimates of the relative efficacy of particular designs can be obtained. Some preliminary programs toward this end are in the process of development. Later work under this project will very likely involve a much more extensive development of these simulation programs.

Grant No. FR 00311-02

Section III-B

INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT:	INSTITUTION:
Robert Stenson, M.D.	Cardiology Division Dept. of Medicine	Stanford Medical School Stanford Computation Center

FIELD OF INVESTIGATION:	PROJECT TITLE:
Cardiac catheterization	Cath Lab

AMOUNT OF RESOURCE USAGE:

233,453

PROJECT DESCRIPTION

(Approximately 300 words)

The Cardiology Division is currently employing the Acme computer system to develop a reliable, on-line method for analysis of cardiac catheterization data. At present four lines of analog data are being transmitted from transducers and a dye densitometer located in the catheterization laboratory to the IBM 1800 process control computer where the information is digitized at a rate of 100 samples per second. After completion of the sampling the information is transferred to the IBM 360/50 digital computer where analysis of atrial, ventricular, pulmonary artery, aortic, wedge and brachial artery pressures and cardiac output are performed. The results of the analysis permits of computation of various points of interest in the ventricular and arterial pressure waveforms such as end diastolic and maximum systolic pressures, diastolic and systolic time intervals, and A-V and semilunar valve gradients and areas. A preliminary description of the system and methods of analysis is contained in the articles entitled Computer Analysis of Cardiac Catheterization Data which has been accepted for publication in the American Journal of Cardiology and A Time-Shared Digital Computer System for On-Line Analysis of Cardiac Catheterization Data which has been submitted for publication to Computers in Biomedicine.

The ultimate design aims of the program are:

1. Rapid computer-cardiologist interaction
2. Capabilities of performing more detailed analysis of pressure waveforms and transient phenomena than can be conveniently accomplished at present
3. Computer service for peripheral catheterization laboratories
4. Centralized data files containing catheterization data and various important clinical features of patient records for correlation studies.

Grant No. FR 00541-02

Section III-B

INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT:	INSTITUTION:
Robert B. Tucker	Genetics (IRL)	Stanford Computation Center Stanford Medical School

FIELD OF INVESTIGATION:	PROJECT TITLE:
Computer -- Instrument Interaction	Computer Control of Mass Spectrometers

AMOUNT OF RESOURCE USAGE:

14449

PROJECT DESCRIPTION

(Approximately 300 words)

The ACME facilities are being used in the development of computer controlled instrumentation. This involves using the 360/50 either to communicate with a small laboratory computer or communicate directly with the instruments in the laboratory.

Data collected by a LINC computer (a small bio-medical computer) from mass spectrometers is being sent to the 360 where calculations are performed on it. The output is then returned to the LINC where it is displayed on a CRT display unit. Utilizing the 360 in this operation increases the speed at which the calculation can be done and provides the opportunity to program for them in a higher level language (PL/1). The communication is done via the 270X-270Y general purpose digital interface.

The 270X-270Y system also provides the ability to communicate directly with laboratory instruments and other devices (for example digital plotters). Programs have been written for testing the capabilities of this equipment and the 1800 Process Controller to compare their capabilities to those of the LINC for instrumentation control. In this instance the instrumentation involved is a GLC/mass spectrometer system. It is intended that with the ACME time sharing system we will have the flexibility and accessibility of the small computer combined with the capacity for data storage and computing of the large computer.

ACME is also being used in a rather conventional sense for time shared data storage and retrieval.

INDIVIDUAL USER PROJECT DESCRIPTION

INVESTIGATOR:	DEPARTMENT:	INSTITUTION:
Jobst von der Groeben, M.D.	Anesthesia	Stanford Computation Center Stanford Medical School

FIELD OF INVESTIGATION:	PROJECT TITLE:
Vector-electrocardiology	Larry[1]

AMOUNT OF RESOURCE USAGE:

79,932

PROJECT DESCRIPTION
(Approximately 300 words)

The programs separate basically into two categories: (1) PDP-8/ACME interfacing and utility routines, and (2) ACME data processing routines.

The PDP-8/ACME programs consist of generalized inter-computer communications, 2-way data transmission and 2-way storage routines which operate with the PDP-8 slaved to ACME. Utility programs provide some PDP-8 capabilities on ACME (e.g. PDP-8 assembly language program listings.)

Some of the major data processing programs are:-

(1) An adaptive digital filtering program for removing muscle tremor in the ECG waveform.

(2) A sorting program which allows re-grouping and listing of patient data stored on disk files by age, sex, diagnostics, etc.

(3) A processing program which given output from the sorting program computes various parameters for any time increment over the ECG waveform (e.g. mean, variance, conversion of rectangular to polar coordinates).

(4) Non-parametric pattern recognition algorithms to dichotomize disease entities collected and pre-processed by the PDP-8. The work is in early stages of development, thus it is premature to predict the eventual power of such procedures applied to the diagnosis of ECG waveforms.

(5) An adaptive classification program is in progress which forms a pattern vector from samples of the P-wave and QRS-wave. The vector is multiplied by a matrix to remove statistically insignificant elements, and the euclidean distance between the vector being classified and a set of vectors with known classification is measured. Using a massive amount of data soon to be collected and transferred from the PDP-8 to the ACME system, it is expected that the program will provide a significant improvement in current diagnostic techniques.