SUMMARY STATEMENT
(Privileged Communication)

Application Number: 1 R01 HL27459-01
Dual Review:

Review Group: SURGERY AND BICENGINEERING STUDY SECTION
Meeting Date: FEB/MARCH 1981

Investigator: CRAIGE, ERNEST Degree: MD
Position:

Organization: UNIVERSITY OF NORTH CAROLINA
City, State: CHAPEL HILL, N C Requested Start Date: 07/01/81

Project Title: PHYSIOLOGIC DETERMINANTS OF THE THIRD SOUND GALLOP

Recommendation: APPROVAL Priority Score: 134
Special Notes:

HUMAN SUBJECTS - PROTECTION ADEQUATE

	DIRECT COSTS REQUESTED	DIRECT COSTS RECOMMENDED	PREVIOUS RECOMMENDED	GRANT PERIOD
01	49,684	49,684		
02	54,597	54,597		
03	59,997	59,997		

RESUME: The objectives are: (1) To establish the physiologic basis of the third heart sound (S_3); (2) to determine the utility of a new transducer (Surface Velocity Analyzer or SVA) to record velocity of chest wall movements over the precordium as a more sensitive indicator of the disturbed physiology responsible for the S_3; and (3) to apply the transducer in a clinical setting such as the coronary care unit in order to monitor the course of critically ill cardiac patients and the effects of pharmacologic and hemodynamic interventions. This is a proposal with well posed objectives and reasonable methods. In view of the proven scientific competence of the investigators, progress towards definite answers can be anticipated.

DESCRIPTION: Preliminary studies using measurements from angiocardiograms have shown that in diastolic overload conditions such as mitral and aortic regurgitation in contrast to normals, the ventricle reaches its maximal velocity of filling in the long axis after it does in the short axis. The S_3 in such patients coincides with long axis filling. In the studies now proposed, the investigators will attempt to achieve the following steps: (1) Determine the pattern of ventricular filling velocity in patients with and without S_3 by means of range-gated Doppler studies in conjunction with two-dimensional (2-D) echo for accurate localization of the intracardiac Doppler observations; (2) establish the relationship between the filling patterns that are conducive to S_3 generation and velocity of precordial chest wall movements as perceived via the SVA; (3) study patterns of ventricular filling in dyskinetic ventricles by means of frame-by-frame analysis of angiocardiograms--a topographical map illustrating contrasts in velocity of filling in various parts of the ventricle will be constructed with computer assistance in order to establish temporal relationships between S_3 production and velocity of ventricular wall movements in areas of myocardium that retain their expansile capability in early diastole; and (4) apply the SVA in clinical situations such as in the coronary care unit in order to detect alterations in velocity of precordial movement which constitute S_3 equivalents so that therapeutic interventions may be introduced at a propitious time and their effect monitored to the end that the patient's vulnerability to sudden death might be altered in a favorable manner.

(continued)

CRITIQUE: Although some controversy persists regarding the genesis of the third heart sound, it is agreed that its presence is ominous. The applicants have posed an interesting hypothesis which has resulted from their preliminary work. The determination of the origin of the third heart sound would be an important contribution to the understanding of myocardial dynamics and may point the direction to simpler, more accurate noninvasive assessments of ventricular changes. The proposed methods are well considered and definite answers, particularly for nonischemic ventricles, can be anticipated.

Proposed studies of dyskinetic ventricles will be fraught with greater problems, since one view of the left ventricle (LV) may not show all dyskinetic LV segments. In such instances, correlations of the velocity contours with the phonocardiographic records would be meaningless. Nevertheless, this avenue should be explored and the experience and expertise of the principal investigator will be important assets in this difficult task.

The surface wave analyzer developed by the investigators is potentially a very sensitive noninvasive instrument which could have great clinical applicability. At this stage it is difficult to assess its accuracy. For example, it is not clear how involuntary chest muscle contractions, respiratory rate or patient movement will influence the output signal, and methods for calibration of this device are not suggested.

Overall, this is an excellent proposal to clearly define the hemodynamic basis for the third heart sound and to validate a new transducer for providing a reliable correlate of it. The experimental design is logical and systematic, and should provide valuable information.

INVESTIGATORS: Dr. Ernest Craige, Professor of Medicine, holds the Henry A. Foscue Distinguished Professor Chair of Cardiology at the University of North Carolina. He has served as Chief of Cardiology at this institution, and enjoys both a national and international reputation for his work on the physiological origins of heart sounds. Moreover, he has published extensively on noninvasive determinants of cardiac function. Yukio Ozawa, M.D., is a research associate who is on leave from the position of Chief of Cardiovascular Section, Nihon University School of Medicine. He has a variety of publications on various topics in cardiology. Damon Smith, B.S., is a mechanical engineer who will assist in the project. In view of the competence of the principal investigator, this team should be equal to the proposed task.

RESOURCES AND BUDGET: The research facilities and environment in the university center are appropriate for this project. Clinical material is abundant; the computerized files of 12,000 well studied patients are available, and the phonocardiographic equipment is in place and in use. The budget is both modest and appropriately allocated.

(Annual increments of 10 percent are requested in the personnel category.)

SURGERY AND BIOENGINEERING STUDY SECTION

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Consultants are required to absent themselves from the room during the review of any application if their presence would constitute or appear to constitute a conflict of interest.