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SPECIAL REPORT

NHLBI Working Group on Cardiovascular Magnetic Resonance

Magnetic Resonance Imaging of the Cardiovascular System*

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INTRODUCTION

Dramatic progress has been made over the past several years in the research and development of magnetic resonance (MR) techniques for imaging biologic structure and function, and much of this has been supported by the National Institutes of Health (NIH). MR imaging has capabilities that are unique compared with other imaging modalities for measurement and monitoring of biologic processes in vivo. Despite these capabilities, the use of MR by cardiovascular and cardiopulmonary clinicians remains limited; in many institutions, clinicians hardly ever refer patients for MR examinations. The principal reasons for this include long scan times with associated patient discomfort, low postprocessing speeds, inadequate access to patients during scanning, and lack of understanding of MR processes and benefits by clinicians and their associates.

On October 28 and 29, 1996, the National Heart, Lung, and Blood Institute (NHLBI) sponsored a Working Group to explore the potentials of MR for imaging the heart, lung, and vasculature and to recommend areas of research and development that could lead to more extensive clinical use of MR methods to improve the diagnosis and management of patients with cardiovascular and cardiopulmonary disorders. Approximately 50 scientists, bioengineers, and clinicians from academia, industry, and government convened at the NIH Natcher Conference Center.

OVERVIEW OF PRESENTATIONS

Several sessions were organized to allow cardiologists to present their views of needs in patient diagnosis and care. There is a changing paradigm for cardiovascular

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medicine that focuses on the features of outpatient examinations that are noninvasive and patient friendly, with the consideration of atherosclerosis and its sequelae as a chronic disease requiring a long-term approach. The consolidation of many tests into one to produce an examination that requires 1 hr or less for complete diagnosis, allowing triage decisions to medical versus interventional therapy, must be demonstrated to be cost effective relative to other standard examinations. The principal capabilities that influence diagnosis and patient management that can be currently accomplished by MR imaging of the heart are in the anatomic and functional assessments, including volumetric and deformation evaluation and assessment of myocardial perfusion and viability.

Visualization of Coronary Arteries

Imaging of the coronary arteries at a resolution equivalent to that of conventional angiography remains a crucial goal that has not yet been achieved. MR angiography is continually progressing, but considerable additional research is required before it can replace conventional x-ray angiography for both clinical and epidemiologic applications. Clinical acceptance of MR cardiac imaging will not occur until diagnostic quality images are achieved in a cost-effective manner for most of the coronary tree. Development of suitable intravascular contrast agents may be essential for accomplishing this. Success in this area will allow repeat examinations at reduced costs with no additional risk to patients.

Functional Assessment of the Ventricles

MR imaging of structure and function should provide optimal ability to assess

- Detection of ischemia through stress testing;
- Risk stratification in coronary artery disease;
- Remodeling;
- Right ventricular disease and the response of the right ventricle to pulmonary hypertension;
- Chemotherapy cardiotoxicity;
- Allograft rejection;
- Risk stratification in valvular and congenital volume overload states.

Although ventricular evaluation with MR has been predominantly aimed at the left ventricle, MR also allows evaluation of the right ventricle. Assessment of its function in response to diseases such as chronic obstructive pulmonary disease, relevant congenital heart disease, and primary pulmonary hypertension is currently receiving more attention.

Myocardial Flow, Perfusion, and Viability

Ischemic heart disease leads to greater mortality than any other single cardiovascular disease. MR methods currently exist for blood flow measurements, but there is a clinical need for improvements in quantitation and volume coverage, especially for low flow. MR methods are potentially capable of assessing the distribution of myocardial perfusion with high resolution. Innovations in contrast agents are helping to achieve this potential. Several MR approaches have the potential to assess viability. One approach is the use of cine MR imaging before and during the infusion of a myocardial stimulant such as dobutamine in low doses. Another approach makes use of the ability of MR spectroscopy to assess high-energy phosphate metabolism. Viability studies by metabolite spectroscopy require improvements in hardware and collaborations between researchers and manufacturers. Basic research in chemistry, physics, and bioengineering are needed to accomplish this.

Vascular Disease and Tissue Characterization

Major clinical applications of MR imaging are in the evaluation of the carotids and the iliofemoral systems. Imaging of these structures with MR is now possible with high resolution. Atherosclerotic plaque, particularly the unstable plaque, is now understood to greatly influence coronary events and/or stroke. The evaluation of plaque constituents and the characterization of tissue within and around the plaque using MR imaging and spectroscopy techniques may allow investigators to differentiate between stable and unstable plaque. This is an important research area that has high risks in terms of its clinical success but also has potentially high payoffs.

The perspectives of physicists, physiologists, radiologists, bioengineers, and computer scientists were provided in several other sessions, reviewed below.

Myocardial Dynamics and Fiber Architecture

Evaluation of myocardial function is fraught with uncertainties and errors that include the inability to track the same volume because of through-plane and in-plane motion, nonobjective measures of wall function, the transmural variation of motion, and limited views of the heart. Wall motion MR techniques of tagging and velocity tracking offer ways to solve these problems. This is a research area that holds great promise and is near the stage of validating its accuracy and efficacy. Well-characterized multicenter clinical studies should be undertaken to assess sensitivity and specificity compared with coronary catheterization.

The unique capabilities of MR to visualize and quantify muscle microstructure with diffusion imaging have been reported in preliminary studies. The ability to measure and monitor muscle microstructure over time is still under development but may open doors into basic physiology of muscle during phases of myocardial development and progression and regression of disease.

A database of normal hearts can now be obtained for the construction of the "normal human heart model." Additionally, a cohort of heart failure patients can be tracked in a longitudinal study from the preclinical condition to full heart failure. These data can be used to increase our understanding of this disease and manage dose levels of drugs with an objective measurement of response and disease progress.

Hardware and Software

The major limitations of current MR imaging systems are associated with efficiency, safety, patient comfort, and cost effectiveness. MR systems should incorporate integrated continuous patient modular monitoring of functions such as Po_2, electrocardiogram, and blood pressure. Needed improvements that should make cardiac and vascular MR imaging more accurate and acceptable are in electrocardiographic and respiratory gating techniques and in the standardization of imaging protocols.

The inability to have data presentation during or immediately after scanning is a serious impediment to clinical acceptance. It is crucial that results are presented in near real time. This would include standard sets of views as a basis set and convenient provision of images for referring physicians to facilitate rapid decision making. Methods should be standardized and automated to the extent possible for clinical applications in both resting and stress conditions (e.g., radiofrequency tagging, phase contrast to assess ventricular function, perfusion, and viability). Efficiency and patient friendliness will profit from more comfortable and accessible magnet configurations, reduced scanning times, noise abatement, and faster post-processing of data. Patient safety needs to be enhanced by monitoring patients in real time during the scanning procedure.

Substantial gains in signal-to-noise ratio can be achieved through optimal coil design. Phased arrays have been developed for cardiac imaging, but more efficient arrays will contribute importantly to the improved spatial resolution and patient comfort demanded by clinical cardiologists. MR-compatible implants, stents, sutures, clips, and pacemakers are important so that the ever increasing number of patients with these devices can be considered for MR studies.

The following principal achievable technical specifications are essential for advancements in cardiac MR imaging:

- The optimum range for magnets designed for cardiovascular MR imaging is 0.5- to 2-T field strength, homogeneity of at least 2.5 parts per million across a 45- to 50-cm diameter, with 0.65 m diameter free access to bore.
- Gradients of 2–5 G/cm are acceptable for most imaging applications. Some velocity encoding techniques may require higher than 2 G/cm; diffusion encoding gradients should be as high as possible.
- Switching should take into account physiologic limits by minimizing dB/dt in nonimaged regions of the patient.
- The magnet configuration should take into account patient comfort for a 1-hr examination and allow easy access to the patient by the physician.
- Audio noise should be minimized to allow communications with the patient and for patient comfort.
- Image reconstruction should be performed at rates up to 30 frames/sec.

Outside of the above research and technical areas, the Working Group considered two issues that need to be addressed because they importantly affect the acceptance of MR methods into clinical cardiology, as follows.

Cost Effectiveness

Appropriate clinical studies must be designed to demonstrate improvement in outcome and in physician acceptance for selected diagnostic problems. Questions of the value of MR methods to replace other methods in a cost-effective way must be resolved. Models of cost effectiveness using preliminary data may begin this effort for specific disease entities, such as ischemic heart disease and heart failure. These modeling strategies can provide an initial estimate of the cost effectiveness of MR methods.

The Working Group discussed a model for research wherein the NIH would take a leadership role for the strategy and development of research followed by the initiation of carefully designed clinical trials. The problem is that a protocol for MR cardiac studies could become obsolete during the course of the clinical trial. It is important that the trials not prematurely test applications that require more sophisticated capabilities than are widely available, that they include a mechanism for recognizing and incorporating technologic advances as they occur, and that by a concurrent analysis strategy they point to directions required to achieve or improve the desired results. This is different from the conventional clinical trial, and the strategy development should receive careful attention by NIH. The trial design must take into account the fact that the MR technology is rapidly improving.

Training

Training must be available for researchers and clinicians who specialize in cardiovascular MR studies. In contrast to many other imaging modalities, MR imaging has greater versatility but at the same time is more complex in the underlying physics and engineering. Trainees must be made aware of cardiovascular physiology, of the risks in cardiac patients, of other cardiovascular procedures, and of the contraindications for MR studies. Training must include basic physics, an understanding of the variety of MR imaging and spectroscopic methods, the cost effectiveness of MR methods, and a firm grounding in the other noninvasive imaging modalities. The initiative for training programs is a shared responsibility of NIH and the professional cardiology and radiology societies.

WORKING GROUP RECOMMENDATIONS

The Working Group recommends that the scientific and engineering communities of academia and industry vigorously continue these tasks of enhancing the value of MR imaging for clinical decision making:

- Efficiency: Systems must be optimized for high-speed imaging to complete a cardiac examination of anatomy and function within 1 hr, including patient preparation time.
- Monitoring and Patient Safety: Electrocardiogram and respiratory gating techniques that can be applied during the scanning procedure without the need for breathholding must be developed, including real-time monitoring during stress testing. The MR system should also be designed for integrated patient monitoring of such functions as Po_2 and blood pressure during scanning.
- Display of Results: Processing time of image data must be significantly reduced to provide images in near real time, and readily comprehended image displays must be available nearly as fast as the data are acquired. Fast and interactive scanning is critically necessary. Additionally, standardization of imaging protocols is needed to facilitate clinical testing and comparison among laboratories.

These activities are recommended for immediate implementation:

- Cost Effectiveness: Under the NIH, models for estimating the cost effectiveness should be developed in anticipation of a method of clinical evaluation of a rapidly developing technology. Trials should begin to establish those applications that have the potential for cost effectiveness.
- Training: The NIH should initiate training opportunities for researchers and clinicians in MR imaging.
- Magnet Configuration: Diagnosis and patient management are hampered by the inability to have access to patients during scanning. Industry designers must concentrate on changing the magnet architecture to resolve this problem. At the same time, this will address the issue of patient acceptance.

These high risk-to-high benefit activities are recommended as foci for academic researchers and as special areas of emphasis for the NIH:

- Coronary Artery Visualization and Flow Quantitation: Replacing conventional coronary angiography by MR could lead to considerable cost savings with the ability to perform repeat examinations with no risk to patients. The potential has been realized for visualizing the proximal major coronary arteries with near diagnostic quality. Continued efforts are needed to improve spatial resolution and motion compensation so as to image most of the coronary tree with a resolution approaching that of conventional x-ray angiography. Fast imaging methods and effective intravascular contrast agents will be needed to accomplish this. Evaluation of the coronaries should ideally include the quantitation of coronary blood flow. The clinical significance of this is very high, and the potential for MRI to accomplish this with high accuracy should be a specific focus.

- Plaque Characterization: The potential for characterizing important compositional components of atherosclerotic plaque with MR methods should lead to vastly improved predictive capability in identifying unstable plaque. Several preliminary studies have been reported that suggest that MR imaging and/or spectroscopy could be successful, including use of intraluminal coils. The goal should be to obtain compositional information of plaque in vivo that is comparable with measurements of excised tissue in the pathology laboratory. This is an ambitious goal with considerable risk for success, but the impact would be extremely high.
- Cardiac Wall Strain: Myocardial dynamics may be an important marker of physiology associated with heart failure and ischemic heart disease. Quantitation of cardiac wall strain in vivo is a unique capability of MR that has been demonstrated in preliminary studies. It is timely to conduct additional research, including human studies to validate the accuracy and clinical utility of these techniques.
- Heart Muscle Function and Orientation: Preliminary research in high-resolution MR imaging of heart muscle demonstrates that it may be possible to quantitate myocyte fiber architecture and that structural aberrations may be an early manifestation of ineffectual heart contractile activity. The in vivo assessment of fiber architecture is one of the several unique potential capabilities of MR imaging techniques.
- Contrast Imaging Agents: Although a principal advantage of MR imaging is its relative noninvasiveness, significant image improvement may be obtained with the use of appropriate intravenously administered intravascular blood pool agents. Such agents offer the promise for visualizing the entire vascular system, including coronary arteries, in a cost-effective way.

Summary of Scientific Priorities and Implementation Strategies

If MR imaging is to achieve greater credibility among cardiovascular and cardiopulmonary clinicians, academic and industry researchers must continue to address the issues of reduced scanning time, higher postprocessing speeds, more friendly and accessible magnet configurations, standardized protocols for image processing and display, real-time display, and improved gating and monitoring during scanning. Some of these activities are supported by the NIH through regular and small business research grants, and this will no doubt continue. Industry efforts should be much more aggressive, responding to the priorities and needs of the practitioners responsible for cost-effective patient care.

Scientific priorities that require specific government support relate to the cost effectiveness and accuracy of MR imaging methods and to the training of researchers involved in cardiovascular imaging. It is now timely to develop models to evaluate cost effectiveness and to show the potential sensitivity, specificity, and outcomes of imaging structure and function in specific patient groups with those MR technologies, taking into account the continuing rapid advances.

Long-term research support by the NIH can ensure that several high risk and high benefit potentials of MR imaging are pursued to determine whether or not they can be clinically useful and cost effective. Some areas worthy of special attention are coronary artery imaging, plaque characterization, cardiac wall strain, heart muscle microstructure, and intravascular contrast agents.

Five recommendations are offered by the Working Group that require actions by the NIH, academic researchers, and industry researchers and developers:

1. The NIH must initiate trials to establish the cost effectiveness of dynamic functional MR imaging of the heart, imaging of the coronary artery tree, and perfusion imaging and to evaluate the clinical utility for important disease entities such as ischemic heart disease and heart failure.
2. The NIH must initiate training opportunities in MR imaging for researchers and clinicians within the next 3 yr.
3. The NIH must maintain its leadership in this field by continuing its support of research. There is a high likelihood that advances will occur in the near future in coronary artery imaging and in the development and use of contrast agents that will have great impact on clinical acceptance of MR functional and perfusion imaging. In coronary artery imaging, improved resolution is necessary to allow visualization of most of the coronary artery tree so that MR may replace conventional angiography in a cost-effective manner for many applications. Contrast agents for enhancing images may be necessary to achieve clinically acceptable structural and functional images. Research is expected to continue in quantitation of perfusion imaging of the entire myocardium.
4. Because MR offers a unique technique for discov-

eries through the measurement and monitoring of physical and biochemical data in vivo and noninvasively, several high risk and high benefit research areas should be considered for special NIH emphasis: imaging of cardiac wall strain, delineation and quantitation of muscle fiber orientation, characterization of atherosclerotic plaque, imaging of myocardial metabolites, and multinuclear selected region spectroscopy. Each of these applications is critically important for advancing our knowledge of the physiology and pathophysiology of the heart and vascular system.

5. There is an urgent need for close industry and academic research cooperation and collaboration in developing solutions to several important problems that currently limit the usefulness of MR imaging. Industry in particular must respond aggressively to the needs for cost-effective patient care. These problems include system architecture to address patient comfort and accessibility; scanning protocols to allow complete cardiac examinations within 60 min; postprocessing of data to access images in near real time; monitoring of physiologic parameters such as Po_2, electrocardiogram, and blood pressure during scanning; and development of MR-compatible materials for improved safety and acceptance of patients with implants (e.g., catheters, stent materials, pacemakers).

The Working Group participants shared the NIH's interest and optimism in the challenges and opportunities that exist in this exciting area of science and medicine. Implementing the recommendations will lead to important and significant benefits for patients through improved and earlier diagnosis and improved patient management and cost-effective strategies. Additionally, it will advance scientific knowledge of heart and vascular physiology and pathophysiology.

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