

## IMAGING IN MEDICAL REHABILITATION

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RFA: HD-98-006

P.T.

National Institute of Child Health and Human Development  
National Institute of Arthritis and Musculoskeletal and Skin Diseases

Letter of Intent Receipt Date: May 20, 1998

Application Receipt Date: July 24, 1998

### PURPOSE

The National Center for Medical Rehabilitation Research (NCMRR) of the National Institute of Child Health and Human Development (NICHD) and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invite applications for research that employs contemporary imaging methods to: (1) analyze mechanisms of soft tissue injury and repair in relation to the functioning of the extremities; (2) develop computer-based models to quantify the biomechanical environment and function of soft tissues of the extremities; or (3) document the outcomes of treatment interventions aimed at facilitating soft tissue repair and promoting functioning of the extremities. The major goal of this initiative is to better understand the recovery of soft tissue integrity and functioning of the extremities of individuals with disabling soft tissue impairments.

### HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Request for Applications (RFA), "Imaging in Medical Rehabilitation," is related to the priority area of chronic and disabling conditions and the goal to reduce health disparities among Americans. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing office, Washington, DC 20402-9325 (telephone 202-512-1800).

## ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Racial/ethnic minority individuals, women, and persons with disabilities are encouraged to apply as principal investigators.

## MECHANISM OF SUPPORT

This program will use the National Institutes of Health (NIH) individual research project grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total (direct and indirect) costs for any application in any one-year budget period may not exceed \$260,000. The anticipated award date is April 1, 1999.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all unsolicited investigator-initiated applications and will be reviewed according to the customary peer review procedures.

## FUNDS AVAILABLE

Approximately \$1,500,000 in total costs for FY 99 will be committed to fund applications that are submitted in response to this RFA. NICHD will allocate approximately \$1,000,000 in total costs for FY 99 to support four to six awards. NIAMS will allocate approximately \$500,000 in total costs for FY 99 to support two to three awards. The number of awards depends on the overall scientific merit of the applications, their relevance to the stated goals of this RFA, and the availability of funds.

## RESEARCH OBJECTIVES

### Background

Soft tissue injuries in the extremities are among the leading causes of activity limitations, restrictions during sports/recreational activities, and losses of time at work and school. The integrity of soft tissues such as muscles, tendons, ligaments, and cartilage is important for maintaining joint stability, decreasing susceptibility to other injuries, and preventing the development of degenerative joint disease. It is essential to have a better understanding of how

the structure and functioning of such tissues are affected by injury or degenerative conditions and how repair processes can be facilitated. These areas offer the potential for fruitful collaborations between clinicians and basic researchers.

On a daily basis, health care providers encounter clinical phenomena that are clearly important, but not well understood in biological terms. A large number of these soft tissue injuries involve the soft tissues of the hands, arms, feet, and legs. Limited capabilities of visualization and quantification have hampered the detailed study of repair processes and the recovery of functioning of impaired extremities. Modern imaging technology has much to contribute to elucidating these processes, developing more effective treatments, and evaluating their outcomes.

### Scope

Applications should focus on the soft tissue repair and functioning of the extremities, studied by means of contemporary imaging methods, e.g., x-ray projection imaging, x-ray computed tomography, magnetic resonance imaging, magnetic resonance spectroscopy, single photon tomography, positron emission tomography, ultrasound imaging, electrical source imaging, electrical impedance tomography, magnetic source imaging or medical optical imaging. Applications must address one or more of the following research themes.

#### I. Mechanisms of soft tissue repair

Research will be supported that analyzes repair mechanisms in the soft tissues of the extremities (e.g., muscles, tendons, ligaments, cartilage, bursae, and fasciae) of individuals with acute/chronic injuries. The research may focus on the relationship of soft tissue pathology to impairments (e.g., diminished range of motion or muscle strength) or to functional limitations (e.g., ambulation or self-care activities). Emphasis should be placed on understanding how pathophysiological changes in the structure and processes of soft tissues impact on the limbs' functional capabilities and on individuals' use of their limbs to perform activities of daily living or other desired activities.

Illustrative of appropriate research are studies that use imaging methods to document age or gender differences in the biochemistry of injury responses and soft tissue repair following trauma. Also relevant are studies that use imaging data to describe the effects of (a) limb disuse or soft tissue atrophy in people with conditions such as stroke, or (b) spasticity on the development of

contractures in people with congenital conditions such as cerebral palsy, or (c) imaging data to better understand the pathophysiology and repair of overuse syndromes.

## II. Model development

Detailed understanding is lacking of how the structure and functioning of the soft tissue of the extremities are affected by injury, or by degenerative conditions such as muscular dystrophy. The development of computer graphic models based on imaging data is promising for clarifying these issues and for illuminating how repair processes proceed in the functional recovery of the extremities. Modeling may also advance understanding of repair processes that are enhanced by treatment interventions such as physical therapy or surgery. For example, models might be developed to analyze the effects of tendon transfers to reduce the spasticity that is associated with cerebral palsy, or for investigating the effects of repetitive use of muscles, tendons, ligaments, and synovium.

## III. Interventions

Research is encouraged that explores the usefulness of contemporary imaging techniques to document the outcomes of treatment interventions such as surgery, physical therapy, drug therapy, or functional electrical stimulation on the recovery of limb function. For example, it is generally recognized that contractures can form in the immobilized or spastic limb that limit range of motion and function. Preventive or therapeutic treatments of contractures often use the application of forces, motions, or physical modalities such as heat and electrical stimulation on soft tissues. Notwithstanding their therapeutic potential, these interventions are also capable of interfering with healing or of producing secondary injury such as repetitive microtrauma. Studies are needed of how these interventions can be optimized in order to maintain tissue integrity, promote healing, and restore useful limb functioning. As another example, imaging techniques might be used to monitor the contribution of various growth factors promoting the healing or functional enhancement of soft tissues in the extremities.

Applicants are encouraged to communicate with program staff regarding the responsiveness of other topics to this RFA.

References:

National Institute of Child Health and Human Development (1993). Research Plan for the National Center for the National Center for Medical Rehabilitation Research. Bethesda, MD: DHHS, PHS, NIH, NICHD, Pub. No. 93-3509.

Research on Repetitive Motion Disorders" (PA-97-059), in the NIH Guide, Volume 26, Number 16, May, 1997.

#### INCLUSION OF WOMEN AND MINORITIES IN RESEARCH INVOLVING HUMAN SUBJECTS

It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43).

All investigators proposing research involving human subjects should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research," which have been published in the Federal Register of March 28, 1994 (59 FR 14508-14513) and the NIH Guide for Grants and Contracts, Volume 23, Number 11, March 18, 1994.

#### LETTER OF INTENT

Prospective applicants are asked to submit, by May 20, 1998, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the principal investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application is being submitted. Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows program and review staff to estimate the potential review workload and avoid conflict of interest in the review.

This letter of intent is to be sent to:

Louis A. Quatrano, Ph.D.  
National Center for Medical Rehabilitation Research  
National Institute of Child Health and Human Development  
Building 61E, Room 2A03

Bethesda, MD 20892-7510  
Telephone: (301) 402-2242  
FAX: (301) 402-0832  
Email: [quatranl@hd01.nichd.nih.gov](mailto:quatranl@hd01.nichd.nih.gov)

#### APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 5/95) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research; from the Division of Extramural Outreach and Information Resources, National Institutes of Health, 6701 Rockledge Drive, MSC 7910, Bethesda, MD 20892-7910, telephone 301/435-0714, Email: [asknih@od.nih.gov](mailto:asknih@od.nih.gov). The PHS 398 may also be downloaded over the Internet from <http://www.nih.gov/grants/funding/funding.htm>

The RFA label available in the PHS 398 (rev. 5/95) application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2 of the face page of the application form, and the YES box must be marked.

Submit a signed, typewritten original of the application, including the Checklist, and three signed photocopies, in one package to:

CENTER FOR SCIENTIFIC REVIEW  
NATIONAL INSTITUTES OF HEALTH  
6701 ROCKLEDGE DRIVE, ROOM 1040-MSC 7710  
BETHESDA, MD 20892-7710  
BETHESDA, MD 20817 (for express/courier services)

At the time of submission, two additional copies of the application must be sent to:

Scott F, Andres, Ph.D.  
Division of Scientific Review  
National Institute of Child Health and Human Development  
Building 6100, Room 5E03H  
6100 Executive Boulevard  
Bethesda, MD 20892-7510

Rockville, MD 20852 (for express/courier service)

Applications must be received by July 24, 1998. If an application is received after that date, it will be returned to the applicant without review. The Center for Scientific Review (CSR) will not accept any application in response to this RFA that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The CSR will not accept any application that is essentially the same as one previously reviewed.

This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

## REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by CSR and for responsiveness by staff at the NICHD and the NIAMS. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NICHD staff may contact the applicant to determine whether to return the application or submit it for review in competition with unsolicited applications at the next review cycle. Applications that are complete and responsive to the RFA will be evaluated for scientific and technical merit by an appropriate peer review group convened by the NICHD in accordance with the review criteria stated below.

As part of the initial merit review, a process may be used in which applications will be determined to be competitive or noncompetitive based on their scientific merit relative to other applications received in response to the RFA. Applications judged to be competitive will be discussed and assigned a priority score. Applications determined to be noncompetitive will be withdrawn from further consideration and the principal investigator will be sent a summary statement presenting the reviewers' comments.

### Review Criteria

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. The reviewers will comment on the following aspects of the application in their written critiques in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. Each of these criteria will be addressed and considered by the reviewers in assigning the overall score weighting them as appropriate for each application. Note that the application does not need to be strong in all categories to be judged likely to have a major scientific impact and thus deserve a

high priority score. For example, an investigator may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

(1) Significance: Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of these studies on the concepts or methods that drive this field?

(2) Approach: Are the conceptual framework, design, methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

(3) Innovation: Does the project employ novel concepts, approaches or method? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

(4) Investigator: Is the investigator appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers (if any)?

(5) Environment: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

In addition to the above criteria, in accordance with NIH policy, all applications will also be reviewed with respect to the following:

- o The adequacy of plans to include both genders, minorities, and their subgroups as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated.

- o The reasonableness of the proposed budget and duration in relation to the proposed research

- o The adequacy of the proposed protection for humans, animals or the environment, to the extent they may be adversely affected by the project proposed in the application.

## AWARD CRITERIA

Applications will be selected for funding based on scientific merit of the proposal, the availability of funds, and program priorities.

## INQUIRIES

Inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcomed. Additional information on the National Center for Medical Rehabilitation Research is available on the Web at <http://silk.nih.gov/silk/NCMRR/>

Direct inquiries regarding programmatic issues to:

Louis A. Quatrano, Ph.D.  
National Center for Medical Rehabilitation Research  
National Institute of Child Health and Human Development  
Building 61E, Room 2AO3  
Bethesda, MD 20892-7510  
Telephone: (301) 402-2242  
FAX: (301) 402-0832  
Email: [LQ2N@nih.gov](mailto:LQ2N@nih.gov)

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45 Center Drive, Room 5AS-37K, MSC 4500  
Bethesda, MD 20892-6500  
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Bethesda, MD 20892-6500  
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FAX: (301) 480-4543

Email: [rl28bnih.gov](mailto:rl28bnih.gov)

Direct inquiries regarding fiscal matters to:

Mary Ellen Colvin

Grants Management Branch

National Institute of Child Health and Human Development

Building 61E, Room 8A17

Bethesda, MD 20892-7510

Telephone: (301) 496-1303

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Ms. Sally A. Nichols

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#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.929 Medical Rehabilitation Research and No. 93.846 Arthritis, Musculoskeletal and Skin Diseases Research. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and promote the non-use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care or early childhood development

services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

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