Sample Application for Small Business Funding

Through the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs, NIA aims to help small businesses develop effective treatments and interventions for healthy aging. NIH small business funding is competitive, and resubmissions are a common and important part of the award process.

Find more NIA sample applications and information about SBIR/STTR funding:
https://www.nia.nih.gov/research/sbir/nia-small-business-sample-applications

SUMMARY STATEMENT

PROGRAM CONTACT: **(Privileged Communication)** ***Release Date:*** **07/25/2018**
BRADLEY WISE ***Revised Date:***
[redacted]

Application Number: **1 R42 AG062026-01**

Principal Investigators (Listed Alphabetically):

FISCHL, BRUCE
WIGHTON, PAUL (Contact)

Applicant Organization: CORTICOMETRICS, LLC

Review Group: **ZRG1 SBIB-T (10)**
Center for Scientific Review Special Emphasis Panel
Small Business: Medical Imaging

Meeting Date: **06/28/2018** ***RFA/PA:*** **PAS18-188**
Council: **AUG 2018** ***PCC:*** **3BFBRBW**
Requested Start: **12/03/2018**

Project Title: **Unbiased longitudinal neuromorphometry for clinical decision support**

SRG Action: **++**
Next Steps: **Visit https://grants.nih.gov/grants/next_steps.htm**
Human Subjects: **10-No human subjects involved**
Animal Subjects: **10-No live vertebrate animals involved for competing appl.**

Project Year	Direct Costs Requested
1	[redacted]
2	
3	
TOTAL	[redacted]

++NOTE TO APPLICANT: Members of the Scientific Review Group (SRG) were asked to identify those applications with the highest scientific merit, generally the top half. Written comments, criterion scores, and preliminary impact scores were submitted by the assigned reviewers prior to the SRG meeting. At the meeting, the more meritorious applications were discussed and given final impact scores; by concurrence of the full SRG, the remaining applications, including this application, were not discussed or scored. The reviewers' comments (largely unedited by NIH staff) and criterion scores for this application are provided below. Because applications deemed by the SRG to have the highest scientific merit generally are considered for funding first, it is highly unlikely that an application with an ND recommendation will be funded. Each applicant should read the written critiques carefully and, if there are questions about the review or future options for the project, discuss them with the Program Contact listed above.

1R42AG062026-01 Wighton, Paul

DESCRIPTION (provided by applicant): Normal human neuroanatomy is incredibly variable, and increases with age. This impedes the ability of neuroimaging to detect effects in neurological conditions such as Alzheimer's disease (AD), Huntington's disease (HD), multiple sclerosis (MS) and schizophrenia. Most of the recently available state-of-the-art quantitative imaging tools still use cross-sectional methods to analyze repeated scans. These tools lack the sensitivity to monitor subtle progressive changes because such approaches do not account for the large intrinsic variability of normal neuroanatomy. The goal of this project is to commercialize a longitudinal, neuro-morphometric image processing pipeline for use in radiology, neurology and related clinical fields. The successful completion of this project will result in a clinically useful neuro-morphometric longitudinal analysis stream with more statistical power than is currently available commercially. This increase in power will directly translate into an enhanced ability to detect and assess progression at both the individual and group levels. It will also alleviate a major pain point in current longitudinal neuroradiology reading workflows, reducing radiology report turnaround times (RTAT).

PUBLIC HEALTH RELEVANCE: The proposed project will develop software to help clinicians quantitatively assess and interpret changes in brain MRI data in a way that integrates seamlessly into an existing clinical workflow. It will help radiologists detect changes to brain structures earlier and more accurately, in neurological conditions such as Alzheimer's disease (AD), Huntington's disease (HD), multiple sclerosis (MS) and schizophrenia. The resulting efforts will translate into an enhanced ability to detect and assess disease progression, and reduce radiology report turnaround time.

CRITIQUE 1

Significance: 3
Investigator(s): 2
Innovation: 3
Approach: 3
Environment: 2

Overall Impact: This is a Fast Track application. The goal for this grant proposal is to commercialize a longitudinal, neuro-morphometric image processing pipeline. It can be used to detect patient-specific neurological changes from brain imaging and will have implications for neural disorders such as Alzheimer's disease. Such a tool, if successful, can have significant impact on the diagnosis, prognosis and management of such neural diseases. This proposal is built on the premise that longitudinal change in hippocampal volume, as measured by structural MRI, is the best performing biomarker as an outcome measure. While there is literature supporting this premise, it is not clear if imaging and imaging alone is sufficient. That said, it is still worthwhile to investigate image-based markers. The company, CorticoMetrics has developed software called FreeSurfer has been widely used by the researchers and clinicians. The goal of this grant application is to do the necessary work to bring the software to market. This include migrating the FreeSurfer to formal compute and execution environment, improve computational efficiency and seek (along with AutoRegistration) FDA approval, so the focus is on validation and optimization. As for as commercialization is concerned, the approach is well defined and thus rigorous. The team is well qualified and experienced.

1. Significance:

Strengths

- An effective treatment neural-degenerative diseases such as Alzheimer’s and Parkinson’s is still elusive.

- A method that can detect longitudinal neuro-morphometric changes that can serve as disease biomarkers will have significant impact on health and health care.

Weaknesses

- It is not clear if imaging and imaging alone can provide such a biomarker.

2. Investigator(s):

Strengths

- The PI, Dr. Wighton, has training in engineering, computer science and MRI physics, and is experienced with the proposed work.
- The rest of the team are well qualified to carry out the work.

Weaknesses

- Not noted.

3. Innovation:

Strengths

- FreeSurfer has novel algorithmic components built in, such as inverse consistency and novel image registration with content distortion, resulting in more accurate and robust image analysis.

Weaknesses

- Not noted.

4. Approach:

Strengths

- The aims are well thought out and the overall development plan logical.

Weaknesses

- Clearly defined pass-fail metric would have strengthened the rigor.

5. Environment:

Strengths

- Appropriate.

Weaknesses

- No concerns.

Fast Track (Type 1 R42 and Type 1 R44 applications):

Protections for Human Subjects:

Not Applicable (No Human Subjects)

Inclusion of Women, Minorities and Children:

Not Applicable (No Human Subjects)

Vertebrate Animals:

Not Applicable (No Vertebrate Animals)

Biohazards:

Not Applicable (No Biohazards)

Resource Sharing Plans:

Acceptable

Authentication of Key Biological and/or Chemical Resources:

Not Applicable (No Relevant Resources)

Budget and Period of Support:

Recommend as Requested

CRITIQUE 2

Significance: 2
Investigator(s): 1
Innovation: 3
Approach: 2
Environment: 1

Overall Impact: In this Fast-Track STTR application, the investigators seek to optimize FreeSurfer for longitudinal analysis. The software will be hardened with modern software practices such as docker and common workflow language (CWL). The software will allow radiologists to more conveniently leverage the benefits of longitudinal imaging. Scientific premise is solid, building upon the team's extensive experience and expertise in this area. The project is scientifically rigorous with carefully worked out details on how the aims are going to be achieved. The team is very competent to carry out the research.

1. Significance:

Strengths

- Most quantitative imaging tools are still cross-sectional not longitudinal.
- Cross-sectional studies confounded by large inter-subject variability in neuroanatomy.
- Technology will increase sensitivity in detecting subtle disease progression.
- Technology will increase report turnaround times (RTAT).
- Help radiologists avoid having to find comparable slices for longitudinal follow-up scans.

Weaknesses

- Nothing significant.

2. Investigator(s):

Strengths

- The investigators are very strong and have the relevant expertise and experience to carry out the proposed research.

Weaknesses

- Nothing significant.

3. Innovation:

Strengths

- Longitudinal analysis pipeline.
- Modern software deployment using docker.
- Integration with AutoRegister.
- Midspace registration.

Weaknesses

- Some of these techniques were developed quite some time ago.

4. Approach:

Strengths

- The research plan is scientifically rigorous with carefully worked out experimental plans.
- Use of state-of-the-art software deployment techniques (docker, CWL, etc.).
- Solid software development practices.
- Speed optimization for clinical use, aiming 15 minutes total execution time.
- Integration of the longitudinal pipeline with slice prescription tool using the AutoRegister, which is developed by the same company (CortioMetrics).

Weaknesses

- Nothing significant.

5. Environment:

Strengths

- Excellent.

Weaknesses

- Nothing significant.

Fast Track (Type 1 R42 and Type 1 R44 applications):

Protections for Human Subjects:

Not Applicable (No Human Subjects)

Inclusion of Women, Minorities and Children:

Not Applicable (No Human Subjects)

Vertebrate Animals:

Not Applicable (No Vertebrate Animals)

Biohazards:

Not Applicable (No Biohazards)

Resource Sharing Plans:

Acceptable

Authentication of Key Biological and/or Chemical Resources:

Not Applicable (No Relevant Resources)

Budget and Period of Support:

Recommend as Requested

CRITIQUE 3

Significance: 2
Investigator(s): 1
Innovation: 5
Approach: 5
Environment: 1

Overall Impact: The development of a longitudinal, neuro-morphometric image processing pipeline with widespread application in neurological conditions of Alzheimer's Disease, Huntington's Disease, Multiple Sclerosis, and others through neuroimaging is of high significance. The goal of this proposal is to integrate longitudinal neuroimaging algorithms within a widely used and well established open source software called FreeSurfer into an image processing pipeline and commercialize it for use in the clinical environment. The Phase I aims are to port code over to the image processing pipeline and test, validate, and develop documentation. Phase II of the fast track is to streamline the pipeline and improve the overall speed of processing for clinical acceptance. Then, integrate with another developed program called AutoRegister and finally prepare for FDA acceptance. Although the aims are well thought out, the timeline of such a developmental process seems excessive. In addition, the innovation is limited to the propose image processing pipeline which is not innovative in the image processing software development community. These concerns limit the overall scientific premise as well as overall enthusiasm for this proposal.

Fast Track (Type 1 R42 and Type 1 R44 applications):

Protections for Human Subjects:

Not Applicable (No Human Subjects)

Inclusion of Women, Minorities and Children:

Not Applicable (No Human Subjects)

Vertebrate Animals:

Not Applicable (No Vertebrate Animals)

Biohazards:

Not Applicable (No Biohazards)

Resource Sharing Plans:

Acceptable

Authentication of Key Biological and/or Chemical Resources:

Not Applicable (No Relevant Resources)

Budget and Period of Support:

Recommend as Requested

Footnotes for 1 R42 AG062026-01; PI Name: Wighton, Paul

NIH has modified its policy regarding the receipt of resubmissions (amended applications). See Guide Notice NOT-OD-14-074 at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-074.html. The impact/priority score is calculated after discussion of an application by averaging the overall scores (1-9) given by all voting reviewers on the committee and multiplying by 10. The criterion scores are submitted prior to the meeting by the individual reviewers assigned to an application, and are not discussed specifically at the review meeting or calculated into the overall impact score. Some applications also receive a percentile ranking. For details on the review process, see http://grants.nih.gov/grants/peer_review_process.htm#scoring.

MEETING ROSTER

Center for Scientific Review Special Emphasis Panel
CENTER FOR SCIENTIFIC REVIEW
Small Business: Medical Imaging
ZRG1 SBIB-T (10)
06/28/2018 - 06/29/2018

Notice of NIH Policy to All Applicants: Meeting rosters are provided for information purposes only. Applicant investigators and institutional officials must not communicate directly with study section members about an application before or after the review. Failure to observe this policy will create a serious breach of integrity in the peer review process, and may lead to actions outlined in NOT-OD-14-073 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-073.html and NOT-OD-15-106 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-106.html, including removal of the application from immediate review.

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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.