**Please refer to new guidelines BEFORE completing application.**

**Application Checklist:**

**COMPLETED AND SIGNED APPLICATION FORM**

* + **CHIEF OF YOUR CLINICAL DEPARTMENT AT LHSC OR ST. JOSEPH’S**
  + **PRINCIPAL INVESTIGATOR**
  + **CO-INVESTIGATORS**

**APPENDIX A – NAMES OF THREE EXTERNAL REVIEWERS**

**APPENDIX B - REFERENCES (MAXIMUM 20)**

**APPENDIX C – MAXIMUM OF 3 PAGES OF SUPPORTING DOCUMENTATION (PHOTOGRAPHS, CHARTS, DIAGRAMS, OR OTHER RELEVANT INFORMATION)**

**APPENDIX D – NOTICE OF DECISION AND ABSTRACT FROM UNSUCCESSFUL GRANT APPLICATION TO EXTERNAL FUNDING AGENCY. ONLY REQUIRED IF THIS APPLICATION IS TO SUPPORT “BRIDGE FUNDING”**

**APPENDIX E – LETTERS OF COLLABORATION FROM EACH COLLABORATOR MENTIONED IN THE PROPOSAL**

**Please be sure to answer ALL questions on this page.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Principal Investigator:**  Tarek Loubani | | **Campus Mailing Address:**  800 Commissioners Rd E, London, ON, N6A 5W9 | |
| **Email:** tarek@tarek.org | | | |
| **Lawson Scientist Status (Scientist or Associate):** Scientist | | | |
| **Date of First Academic Appointment:** 2010-06 | | **Clinical Department Appointed to:**  Emergency medicine | |
| **Previously Received an IRF:**  Yes  No | |
| **Project Title:**  Laboratory validation of a novel low-cost high-quality open-source electrocardiogram | | | |
| **Is this a resubmission:**  Yes  No | | **Primary location where research will be conducted:**  LHSC  St. Joseph’s  Off-site | |
| **Co-Investigators (Name and Department):**  **1.**  **2.**  **3.** | | | |
| **Application for (choose one):**  New Investigator  “Bridge” Funding  Competition Name:  Novel Research Direction  Post-Doctoral Support  Name of Post-Doctoral Trainee: | | | |
| **Period of Support:**  1 year  2 years | | **Start Date: July 1, 2018**  All projects will have a July 1, 2018 start date and a June 30 end date. | |
| **Total Amount Requested (maximum $15,000): $14,683** | | | |
| **Has this project been submitted for review by Western’s Health Sciences Research Ethics Board?**  No, not applicable  Yes, approved (Attach copy of approval notice)  Yes, approval pending  Not yet submitted | | | |
| **Has this project been submitted for review by Western’s Animal Use Subcommittee?**  No, not applicable  Yes, approved (Attach copy of approval notice)  Yes, approval pending  Not yet submitted | | | |
| Note: If ethics approval has not been received within 6 months of award notification, the award is subject to withdrawal.  SIGNATURE PAGE  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_2018 April 25\_\_\_\_\_\_\_\_\_ Signature of Principal Investigator Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Signature of Post-Doctoral Trainee (if applicable) Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Signature of Co-Investigator 1 Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Signature of Co-Investigator 2 Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Signature of Co-Investigator 3 Date ***Co-Investigator signatures mean that they have read and approved the submitted version of the application.***  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Signature, Chief of Clinical Department Date \_\_Dr. Adam Dukelow \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_Emergency Medicine \_\_\_\_\_\_\_\_\_\_  **Please Print Name of Chief of Department Print Name of Clinical Department**  *Clinical Department approval attests to the following: they are aware of the clinical research being proposed and the availability of appropriate facilities (laboratory, office, research space, other support) for this project to be carried out.*  ***Submission Instructions: Print this page, obtain signatures, scan into final PDF file***  ***to be e-mailed along with completed application to*** [***internalresearchfund@lawsonresearch.com***](mailto:internalresearchfund@lawsonresearch.com) | | | |
| **1.** Please provide a brief **Lay Summary (250 words maximum)** of your project in simple, non-scientific language that can be used beyond the scientific awards committee, e.g., for donors’ publicity purposes. Please conform to the structure provided below.   1. **Background** 2. **Hypothesis** 3. **Methods** 4. **Expected Results and Significance**   **A) Background**  Electrocardiograms (ECGs) are the standard of care for detecting cardiac pathologies such as arrhythmias, ischemia and hypertrophy with high sensitivity. Although vital in hospitals, many rural and solo Canadian clinics cannot access electrocardiography. In low- and middle-income countries, ECGs are also unattainable due to high costs and the complex nature of ECG interpretation.  **B) Hypothesis**  Our hypothesis is that low cost, 3D printed ECG devices will not be inferior to currently available premium brand ECG devices at detecting electrical cardiac signals.  **C) Methods**  ***Hardware and Software.*** Preliminary engineering work is underway for the electrocardiogram by a not-for-profit in Slovenia that specializes in creating effective and affordable systems using an open-source model.  ***Laboratory calibration.*** Calibration will involve devices simulating electrical heart activity. A spectrum of electrical activity will be transmitted through the prototype device. The prototype electrocardiogram output will be compared against input from the electrical simulator to determine signal loss and quality.  ***Laboratory validation.*** A heart activity simulator will be used to transmit electrical signals through both the prototype ECG device and a gold standard premium ECG device. Data will be collected from both electrocardiograms and compared statistically to determine if the prototype device is non-inferior to the gold-standard premium ECG device.  **D) Expected Results and Significance**  This project will act as a proof-of-concept that 3D printing and other technologies can create low-cost, effective electrocardiograms. The goal is to design, calibrate and validate low-cost ECG devices released under the Open Hardware License. This allows widespread access in underserved communities.  **2. Research Proposal:** Please provide an outline of the research you are proposing, using up to a maximum of 3 pages (12-point and Times New Roman font, with 3/4” margins (2 cm), 6 lines per inch).  The 3 pages allotted to your outline must include the following sections:   * Background (information describing why this research is important, and how this research aligns with [Lawson’s Strategic Plan](https://intra.lawsonresearch.ca/about-lawson/strategic-plan-2014-2018)) * Hypothesis and Objective(s) * Project Plan (experimental design, sample size calculation, etc.) * Data Analysis * Expected Results and Significance * Limitations (possible pitfalls and alternative approaches)   In addition, you may include up to a maximum of four appendices: Appendix B, References (max. 20); Appendix C, 3 pages maximum for preliminary data, charts, diagrams, or other relevant information; Appendix D, (for bridge funding applications only) letter of decision and abstract from a previous application to an external funding agency; and Appendix E, Letters of Collaboration. Manuscripts will not be accepted.  **Background**  The Electrocardiogram (ECG) is a medical device that is the standard of care in the developed world for detecting cardiac pathologies such as arrhythmias, ischemia, and hypertrophy with high sensitivity. Although a vital tool in the emergency department, operating room and ward settings, many rural hospitals and solo clinics do not have access to this piece of equipment. In low-and middle-income countries, ECG’s are unattainable due to high costs and the complex nature of ECG interpretation. The initial investment of a premium brand ECG is several thousand dollars. However, following the initial purchase, tests are inexpensive and non-invasive.Using current rapid prototyping technologies such as 3D printing, it is possible to create an inexpensive electrocardiogram that meets or exceeds the gold standard. The goal of this project is to design, calibrate and validate an ECG device that costs less than USD$500 to build. The completed device will be released under Open Hardware License (OHL), such that hospitals and ministries of health in rural and impoverished communities in Canada and internationally would have easy access to these devices.  **Hypothesis and Objectives**  This project relies on two pillars: the use of 3D printers and other rapid prototyping technology; and leveraging Open Access and Open Source principles and devices to decrease development costs and disseminate results to stakeholders. This model has been proved with a simple medical device (the stethoscope) and a more complex device (pulse oximeter). The main question of our research is: Can the successful model that developed, validated and deployed a low-cost stethoscope also be used to develop more complex devices such as an electrocardiogram?  Our hypothesis is that laboratory studies with an electrical heart rhythm simulator will demonstrate that our low-cost 3D printed ECG device is non-inferior to a gold standard premium ECG device.  **Project Plan**  ***Hardware****.* Design considerations include: cost, availability of parts, ease of construction, quality, ease of maintenance, and ease of use. Preliminary engineering work has been carried out for the electrocardiogram by Institute for Development of Advanced Applied Systems Rače (IRNAS), an engineering firm located in Slovenia that specializes in creating effective and affordable systems using an open-source model. Diagnostic electrical medical devices need to be covered by strict compliance standards and essential performance guidelines according to standards published by from the International Electrotechnical Commission (IEC), with the relevant standards concerning ECG machines being IEC 60601-1-2, 60601-2-25, and 60601-2-27. Our ECG device is designed to comply with these standards.  ***Software***. Software is also an important piece of the overall functioning of the electrocardiogram. The software involved in the electrocardiogram involves three aspects: Firmware, descriptive calculations, and interpretation algorithms. Firmware is the software necessary for the device to function and display the electrical signals of the heart. Descriptive calculations are those calculations of parts of the waveform such as heartrate, PR intervals, QT intervals, etc. Interpretation algorithms are those algorithms that give a clinical prediction of the patient's state based on electrical signals (e.g., ST-elevation MI).  ***Laboratory calibration.***  *Experimental Design*. Calibration study.  *Procedure.* A spectrum of electrical activity will be transmitted through the prototype device via devices that are simulators of electrical heart activity. The prototype electrocardiogram output will be compared against the source signal to determine accuracy of transmission of the electrical activity spectrum. PhysioNet is home to an open-source algorithm ECGSYN which can be used to calibrate biosignal acquisition devices. It serves as an open source database and software toolkit which will be used to acquire, test, and validate known signals for our manufactured ECG machine. By testing the model over multiple different heart rates, leads, and rhythms, it is possible to rapidly determine if the acquisition hardware causes significant distortions in the clinical parameters measured from the ECG. A set of electrical signals with varying characteristics will be used.  According to IEC standards, multiple different electrical signals will be used for calibration including electrical signals to test gain factors and linearity, to test varying heart rates, to test response to high frequency signal components and to test response to low frequency signal components (ST elevation/ depression). 100 real test ECGS signals obtained from the Common Standards for Quantitative Electrocardiography (CSE) Database will be transmitted through the ECG device under specified testing conditions, the ECG device prototype will read these calibration signals and output analysis measurements. The differences between the ECG measurements and the reference values will be determined. These output results will be analyzed to ensure that the prototype ECG performs within the allowable range of deviation outlined by the IEC.  ***Laboratory validation.***  *Experimental Design*. Non-inferiority study.  *Procedure.* A spectrum of electrical activity will be transmitted from a simulator of electrical heart activity through both the prototype device and the gold standard premium device. Data will be collected from both electrocardiograms and compared statistically against the source signal to determine accuracy of transmission of the electrical activity spectrum. A non-inferiority study will be conducted comparing the accuracy in performance of the prototypical 3D printed ECG device against the gold standard ECG device.  PhysioNet is an online resource that contains a large cache of clinically validated ECG signals, and also houses open-source software programs that can be used to view, process, and analyse these complex signals. Once the ECG device is designed and tested for basic safety and functionality, the next stage is to validate the prototype over a wide range of representative signals. The use of stored ECG signal databases provides a realistic range of data from actual patients, along with validated annotations from cardiologists. The accuracy of performance in various parameters including amplitude measurements and interval measurements will be compared between the prototypical 3D printed ECG device and the gold standard ECG device.  **Data Analysis**  ***Laboratory calibration.*** Statistical analysis of ECG prototype output results will be undertaken according to standards published by the IEC.  ***Laboratory validation.*** To compare the accuracy of performance in various parameters including amplitude measurements and interval measurements between the prototypical 3D printed ECG device and the gold standard ECG device, a non-inferiority statistical analysis will be conducted. Data will be analyzed for each parameter using a one-side 95% confidence interval. Noninferiority of the 3D printed ECG device would be established if the lower confidence limit lies above the noninferiority margin for a given parameter.  **Expected Results and Significance**  The Glia Academic Collaboration is a medical research project whose goal is to develop, validate, certify and disseminate high-quality, low-cost, open-access medical equipment that has been approved by Health Canada. These open source devices will be available for wide use in Ontario, especially at low-volume hospitals and low-income communities.  This project will act as a proof-of-concept study to show that 3D printers and other rapid prototyping technologies can be used to develop a low-cost and effective electrocardiogram. Given the success of this project, further validation studies will be carried out in humans and approval from Health Canada will be sought. The completed device will then be released under Open Hardware License (OHL), such that hospitals and ministries of health in rural and impoverished communities in Canada and internationally would have easy access to these devices.  Glia's stethoscope has already made a significant impact. Replicating this success with electrocardiograms will lead to the wide availability of essential medical devices. The availability of specifications for generic manufacturers to manufacture devices and the subsequent downward price pressure on premium brand manufacturers will increase the standard of care for all patients in Ontario. It will also allow LHINs to save costs while maintaining equivalent quality of care. In the developing world, availability of a low-cost electrocardiogram will allow ministries of health and hospitals to forgo rationing of ECG devices and provide them to hospitals and clinics, multiplying the availability dramatically.  **Limitations**        **3.** Outline your role as Principal Investigator.   **50 words maximum**  **4.** Outline the role of the Post-Doctoral Trainee (if applicable).   **50 words maximum**  **5.** Outline therole and area of expertise of each of the Co-Investigators.   **100 words maximum for each co-investigator**  **6.** If the proposed research activity will take place off-site (somewhere other than LHSC or SJHC) please explain why it cannot be completed at a Lawson location.  **200 words maximum**  **7**. Please state the reason(s) for applying to the IRF and explain why research funding cannot be obtained from other sources. Indicate clearly how the research in the application is novel or new and how it is/or is not related to other funded projects. **300 words maximum. \*If this application is for Bridge Funding, skip this section and go to section 8.**  **8.** If this application is for “Bridge Funding”, please list the most important comments from the reviewers and explain how IRF funds will help in responding to the comments and in improving the likelihood of funding from the external agency. **300 words maximum**  **9. Budget:**   |  |  |  | | --- | --- | --- | | **Item** | **Amount requested from IRF** | **Amount coming from another source** | | Personnel Support  # of hours total required for this project |  |  | | Salary – Post-doctoral Trainee |  |  | | Lab Supplies |  |  | | Research Equipment |  |  | | Animals (if appropriate) |  |  | | Other expenses |  |  | | **Total** |  |  |   **Budget Notes**:  **Salary Costs:** Contact Lawson HR to obtain salary costs. Hourly rates and benefits will apply and therefore should be stated within the project budget.  Post-Doctoral Trainees can be hired through Western University (as Post-Doctoral Associates) or through Lawson (as Research Assistants), and their salaries must include mandatory benefits, CPP, and EI.  **Research Equipment:** Funding for equipment, up to a **maximum of $1,500**, may be requested. Definition of Equipment: Any item (or interrelated collection of items comprising a system) of non-consumable tangible property, having a useful life of more than 1 year, which is used wholly or in part for research.  **Travel:** The IRF does not provide funds for travel or related expenses for Principal Investigators, Co-Investigators, Collaborators, or trainees.  **10. Budget Justification –** Each budget item should be listed, and a brief explanation should be provided for each item, explaining the importance of the costs for the proposed research (one page maximum).   1. **For Principal Investigator ONLY*: List current research funding held (F), or those applied (A) for (state date when a decision will be announced).*** *Include all funds received from internal and external sources, including industry. Please also include any funding received as a Co-Investigator.* Please use the format below.  |  |  |  |  |  | | --- | --- | --- | --- | --- | | **(F) or (A)**  *Indicate in this column* | **Title of project**  (State percentage overlap with current IRF application if it exists) | **Year(s) funded** | **Agency** | **Award total or date to be announced** | |  |  |  |  |  | |  |  |  |  |  | |  |  |  |  |  | |  |  |  |  |  | |  |  |  |  |  | | | | |
| 1. If this IRF application is a **resubmission,** applicants must respond directly to the comments received from the IRF reviewers regarding the previous application. **350 words maximum** 2. If you have received prior funding (as a Principal Investigator) for a pilot study from Lawson’s IRF, please explain if the prior IRF funding leveraged further funding for your research program. **250 words maximum** 3. Describe the possible translational outcomes in terms of enhanced clinical care, improved health outcomes or systems, and/or commercialization/patenting of a technology. Provide a clear description of who will benefit from the project outcomes. Only if applicable. **250 words maximum.** 4. Describe the potential of the project to lead to external funding opportunities (CIHR, CFI, ORF-RE, etc). **250 words maximum** | | | |
|  | |  |  |  |  |  | | --- | --- | --- | --- | --- | | BIOGRAPHICAL SKETCH – 2 PAGE MAXIMUM ***ONLY REQUIRED FOR: PRINCIPAL INVESTIGATOR, POST-DOCTORAL TRAINEE (if applicable)***  IOP | | | | | |  | | | | | | **NAME** | | **POSITION TITLE** | | | | **EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include post-doctoral training and residency training if applicable.)*** | | | | | | **INSTITUTION AND LOCATION** | **DEGREE**  ***(if applicable)*** | | **MM/YY** | **FIELD OF STUDY** | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  |   A. Personal Statement  Briefly describe why your experience and qualifications make you particularly well-suited for your role in the proposed project.  B. Positions and Honors  List in chronological order previous positions, concluding with the present position. List any honors. Include present committee memberships.  C. Selected Peer-Reviewed Abstracts/Publications  You may include selected publications based on relevance to the proposed research. **Please also highlight articles that have been published as a result of IRF Funding.**  D. Research Support  List both selected ongoing and completed research projects for the past three years. *Begin with the projects that are most relevant to the research proposed in the application.* Briefly indicate the overall goals of the projects and responsibilities of the person identified in the Biographical Sketch. Do not include number of person months or direct costs.    Biographical sketch Page 2  **APPENDIX A – THREE EXTERNAL REVIEWERS**  *Suggest* ***three*** *external reviewers (Canadian or international) that you feel have the expertise to review your application. IRF reserves the right to make the final selection of external reviewers. You should not suggest reviewers in conflict of interest, such as personal friends, co-applicants on currently funded grants, or co-authors on a manuscript published within the past 3 years.*  ***External Reviewer 1:***   |  |  | | --- | --- | | ***Name*** |  | | ***Institution*** |  | | ***Title*** |  | | ***Department/Area of Expertise*** |  | | ***Email*** |  |   ***External Reviewer 2:***   |  |  | | --- | --- | | ***Name*** |  | | ***Institution*** |  | | ***Title*** |  | | ***Department/Area of Expertise*** |  | | ***Email*** |  |   ***External Reviewer 3:***   |  |  | | --- | --- | | ***Name*** |  | | ***Institution*** |  | | ***Title*** |  | | ***Department/Area of Expertise*** |  | | ***Email*** |  |   **APPENDIX B – REFERENCES (MAXIMUM 20)**  Costa M, Moody GB, Henry I, Goldberger AL. PhysioNet: an NIH research resource for complex signals. J Electrocardiol [Internet]. 2003 Dec;36(SUPPL.):139–44. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0022073603001262  Silva I, Moody GB. An Open-source Toolbox for Analysing and Processing PhysioNet Databases in MATLAB and Octave. J Open Res Softw [Internet]. 2014 Sep 24;2:2–5. Available from: http://openresearchsoftware.metajnl.com/articles/10.5334/jors.bi/  Varma N. Role of the surface electrocardiogram in developing countries. J Electrocardiol [Internet]. 2010 Nov;43(6):612–4. Available from: http://dx.doi.org/10.1016/j.jelectrocard.2010.07.017  Goldberger AL, Amaral LAN, Glass L, Hausdorff JM, Ivanov PC, Mark RG, et al. PhysioBank, PhysioToolkit, and PhysioNet : Components of a New Research Resource for Complex Physiologic Signals. Circulation [Internet]. 2000 Jun 13;101(23):e215–20. Available from: <http://circ.ahajournals.org/cgi/doi/10.1161/01.CIR.101.23.e215>  IEC 60601-1-2, Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances - Requirements and tests  IEC 60601-2-25:2011, Particular requirements for the basic safety and essential performance of electrocardiographs  IEC 60601-2-27:2011, Particular requirements for the basic safety and essential performance of electrocardiographic monitoring equipment  **APPENDIX C - 3 PAGE LIMIT – ADDITIONAL INFORMATION (Note: No manuscripts)**  **APPENDIX D (FOR BRIDGE FUNDING APPLICATIONS ONLY)**   1. **Copy of the decision letter from external granting agency, showing the grant panel’s comments and numerical score/ranking, if applicable.** 2. **The abstract/summary page from the external application.**   **APPENDIX E – LETTERS OF COLLABORATION** | |  |