Early Detection and Prevention of Diabetic Foot

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1 Social Need

Diabetes is an incurable metabolic disease characterized by high blood sugar levels and afflicts an estimated 285 million people worldwide, about 5.1% of the global population. According to International Diabetes Federation (IDF), diabetes accounted for 12% of global healthcare expenditures, where the indirect social and economic cost is estimated to be at least 5 times of the direct medical costs.

Sadly, the burden of diabetes are shifting to developing countries. Over 80% of the diabetes population now live in developing countries. Unlike in developed countries, where the diseased population are older and over 65 years of age, the majority in developing countries are at a working age (between 45 and 65 years of age), which leads to much more severe social and economic consequences.

Diabetes care is one of the most difficult medical, social and economic challenges facing developing countries. The main reason for the high cost associated with diabetes is its devastating complications. One such complication is a condition known as ***diabetic foot.*** A recent study carried out by the Department of Surgery, Boston Medical Center found that 33% of the direct medical costs attributed to diabetes are linked to diabetic foot. Generally speaking, diabetic foot is a consequence of the damage to blood vessel and nervous system from the high blood sugar levels. The damaged blood vessels inhibits blood circulation, reduces the amount of oxygen and nutrition supplied to the tissues, causing injuries to heal poorly. The damage to the nervous system causes loss of sensitivity, and minor injuries can go unnoticed and develop into ulceration, deformation and amputation. The lifetime risk of foot ulcers for people with diabetes is 25%, and 33% of which will result in *amputation.* For example, in India alone, 40,000 legs are amputated every year due to diabetic complication!

The key to the management of diabetic foot is *prevention, monitoring, and early detection*. Unfortunately, most developing countries are ill-equipped and lack the qualified medical staff for diabetic foot care. There are only 19 counties in the world that has podiatry schools (medical programs for training physicians specializing in foot care). Most developing countries simply don't have any licensed podiatrists. As for the nursing staff, a recent survey in Bangladesh involving nurses specializing in diabetes care at a well-established national institute found that the majority of the nurses (52.6%) have very low knowledge of the condition. Resulting from all of these is massive number of miss-diagnosis. For example, a study done in Egypt shows that physicians may miss the diagnosis of diabetic foot problems in 61% of the patients!

Figure 1: Diabetic foot ulcers and deformities.

According to the World Health Organization (WHO), the number of diabetes patients in developing countries will double in next 30 years! Training health care professionals to tackle this growth is infeasible when there is already a shortage of trained professionals in the developing world. Therefore, a *low cost*, *quantitative* and *fool-proof* screening system for the early detection is an urgent need of the developing countries to fight diabetic foot. Vodafone holds the largest share of the telecommunication market in the continent of Africa and India. Vodafone is increasingly investing in the emerging markets and shows strong commitment to help *humanity and environment*. Our project goal not only *aligns* with that of Vodafone Americas Foundation, but also builds upon technologies that Vodafone owns and operates in developing countries. Thus, partnering with Vodafone will provide with the largest impact of our proposed work.

Our proposal greatly benefits from the formatting and figures in a PDF. However we have not cheated by going over the proscribe word limit.

2 About the Project

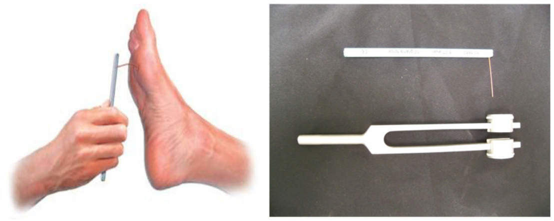

Figure 2: Sensory testing using monofilament and tuning fork.

Traditional techniques for diagnosing diabetic foot are mostly based on *sensory* examination, and aim to determine if a patient has lost sensation in the feet. Examples of these tests include Semmes-Weinstein monofilament testing, tuning fork, pinprick sensation, and vibration perception threshold. Many of these tests unfortunately present significant inter- and intra-observer variability. A reliable and quantitative means for evaluating capillary function for early (possibly pre-clinical) diagnosis of peripheral neuropathy (i.e. diabetic foot) and the risk of foot ulcers are still lacking.

We have developed a quantitative system for prevention and early detection of diabetic foot using *thermal imaging*. Our key idea is to use *infrared imaging* to measure the thermal response of the feet of diabetes patients following cold stress. *The rationale is that a diabetic foot has poor thermoregulation*, and should recover *slowly* compared to core body temperature after being cooled. The *recovery speed* can then be used to quantify the degree of diabetic foot problems. A small-scale patient study funded by the National Institute of Health has been carried out. The recovery of the foot to the core body temperature after cold stress was captured with a high-end FLIR Infrared Camera with a thermal sensitivity of ≤ 0.05°C. More than 40 subjects have been imaged in the study. Our studies show that the normal subject has good thermal regulation, while the diabetic subject has bad thermal regulation in the *diseased regions* of the foot. However, our current research is based on an expensive high-end camera and designed toward hospitals and clinics in the United States.

The aim of this research is to develop a similar type of system that is *inexpensive*, *accurate*, and *easy-to-use* for patients in the developing countries. The system that we propose will consist of a hardware and a software system. The *hardware system* mainly consists of a smart phone and a 2nd Generation FLIR One Thermal Imager. We chose to develop our system around smart phones because of their prevalence in developing countries as the most popular computing device. The FLIR One Thermal Imager is a low-cost thermal imaging system designed for cell phones. It has a thermal resolution of 160x120 and a sensitivity of 0.1 C, which is sufficient for our study. Our *software system* will be a mobile app capable of running on both iOS and Android platforms. The chief functionality of the app is to process infrared videos and extract temperature recovery rate and thermal regulation characteristics of diabetic foot.

Our system is designed for both clinical and in-home usages in developing countries. The primary process in quantifying neuropathy using our system is the following: (1) A *cold stimulus* (e.g., an ice pack) is first applied to the diabetic foot, which will trigger the *thermal autoregulation*. (2) The recovery of the foot to the core body temperature is then captured with the FLIR One Thermal Imager and *connected* to a mobile phone. (3) The thermal video is then analyzed by our app to produce a *quantitative measure* of the thermoregulation of the foot, which is used to identify regions on the foot that are at risk of diabetic foot problems. (4) The app will also keep track of repeated measurements of the foot as a time series and monitor the progression of the diabetic foot over years.

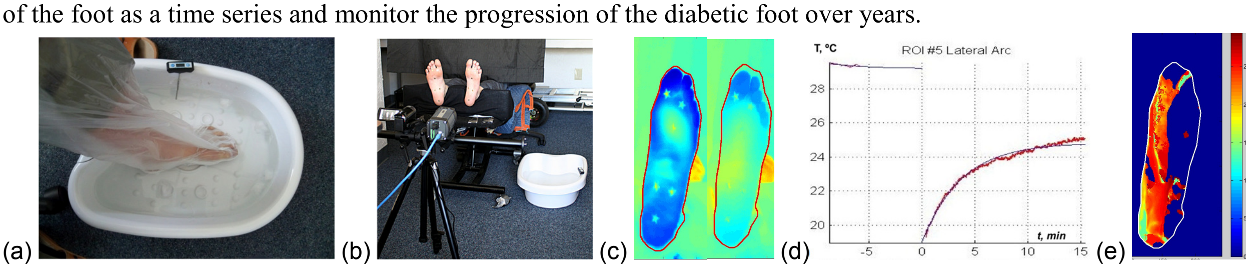

Figure 3: The workflow of our current screening system. (a) The diabetic foot is cooled down using ice water. (b) After the cold stress, the recovery of the foot is videotaped using a high-end FLIR thermal imager. (c) The thermal video is then segmented and registered. The images shown is the first and last frames of the thermal video. (d) The extracted temperature recovery curve fitted with our bioheat transfer model. (e) The calculated thermal regulation speed of every point on the foot plantar, indicating bad thermal regulations in blue.

This above mentioned process is the first *seed* to the ***grand vision*** of *personalized health care via accessible thermal imaging.* The proposed app will build upon digital image processing and machine learning techniques that can be applied to thermal images of other limbs, under different stresses, at different progression. The captured images can be transmitted over the wireless network to centralized management who can provide expert supervision over the tests performed at home or in rural hospitals. Although the research will be performed using a $250 camera, smartphones with integrated thermal camera will soon be in the market at the same price as other smartphones. Moreover, the average price of a smartphone is going down every year significantly, which suggests that thermal imaging based in-home diagnosis will be accessible to diabetic patients worldwide.

3. Stage of the Project

Our past research has successfully proved the concept of diagnosing diabetic foot problems using thermal imaging. Technically, we have already implemented the following system components:

(1) *Infrared video segmentation:* The recovery of the diabetic foot following cold stress is captured as an infrared video. In order to extract the temperature recovery for each point on the foot, the foot on each image frame of the video must be segmented and registered. We have developed a model based infrared video segmentation algorithm with perfect accuracy at a resolution of up to 1-2 pixels.

(2) *Bioheat Transfer Model:* The temperature data for each point on the foot are extremely noisy and the true signal must be obtained using our bio-heat transfer model. Our model was inspired by the Penne's Bio-heat Equation and control theory, and can extract thermal regulation speed of every point on the foot.

With the above strong proof of the concept, our project is in between prototype and field testing. Integrating our thermal image segmentation algorithm and bioheat transfer model in a mobile app with an inexpensive infrared camera will complete the prototype phase. We expect to build working prototypes in 6-9 months, and move on to field testing in developing countries in the later part of the first year of the project. More specifically, the ***proposed research activities*** include two key aspects: system software development and clinical studies.

System Software Development: We will develop a mobile app that will be capable of quantitatively measure the condition of a diabetic foot. We will develop the following pieces in order to achieve that. (1) We will develop a calibration tool that will calibrate the temperature profile of an unstressed foot. (2) We will develop active registration tools by exploiting the touch sensitivity of mobile devices. (3) We will develop resilient algorithms that allow us to achieve the same results as the high-end cameras produce. We expect the key challenge in software development will be developing algorithms for infrared video segmentation and registration for mobile devices.

Clinical Trials: For this research, we have chosen Bangladesh, a Southeast Asian developing country as our primary field testing site. Asia accounts for 60% of the world's diabetic population. In recent decades, the continent has seen rapid economic development, urbanizations and nutritional transitions, which unfortunately are accompanied with an explosive increase in diabetes. Southeast Asia is currently and will continue to be an epicenter of future diabetes population. Bangladesh has a large population of 168 Million with a per capita GDP of $3,581. The prevalence of diabetes in Bangladesh is 7.1%, much higher than the global average. We believe having our system tested at an epicenter of diabetes such as Bangladesh will allow us to (1) realistically quantify the potential impact of our system for the future of diabetes care, (2) understanding the scalability of our system in developing countries, and (3) fine tune our system toward the characteristics of future diabetes population.

Dr. Farzana Alam, attending physician and MD specialist in diabetes complications from Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh will act as our primary medical consultant. She will assist our team in carrying out the clinical trials of our newly developed screening system for diabetic foot. Dr. Alam will oversee the medical aspects of the trials such as IRB approvals, patient study consent forms, subjects recruiting, results analysis, and system improvement.

For this research, we will recruit at least 100 subjects between 50 to 60 years old. The distributions of the subjects are: 50 Male (25 with Diabetic Foot, and 25 Diabetes without Diabetic Foot) and 50 Female (25 with Diabetic Foot, and 25 Diabetes without Diabetic Foot). We plan to image each subject on a monthly basis for at least two years. Each subject will be reimbursed at $15 per study. We have also budgeted the cost for compensating the staff involved in the study.

4. Project Implementation

Tasks	Y1		Y2		Y3	
System Integration, App development, Adaptation of image processing algorithms						
Prototype testing in the U.S. with healthy subjects						
Clinical trials in Bangladesh on 100 patients for two years						
System refinement based on user feedback						
App release and data collection						

Table 1: Gantt chart of project timeline. The darkness of a cell denote intensity of the work.

5. Measuring Impact

The goodness of our screening system will be measured using the following metrics: single-patient tracking, cross-patient tracking. We will track the *progression* of diabetic neuropathy of individual patients over the duration of the project and validate that against known (from Dr. Alam) and published statistics. We will *cross-match* diabetic neuropathic patients with other diabetic patients without neuropathy. We will compare the rates of their developing foot problems against known and published statistics. These comparisons will allow us to quantify (1) our ability of *early detection* and *diagnosis* of the diabetic foot problems, and (2) *prevention* of developing diabetic foot disorders in new patients. The *ultimate impact* of our research will be measured once we release the app in the app stores and collect voluntarily shared user data in the forms of feedback, usage history and bug reports.

6. Scalability

Our mobile App is inherently scalable. Upon completion, we will freely distribute the App in popular stores such as Google Play, Amazon and App Store. Scaling to various population groups in different developing countries will require data collection from volunteers across the world to tune the algorithms for specific demographics.

The scalability of our system will depend on the availability of inexpensive mobile phones and infrared cameras. We believe within 10 years, both technologies will be widely accessible to people in developing countries. For example, as per a report from CNN Money, Ringing Bells, an Indian mobile phone company has just unveiled its Freedom 251 smartphone with features that included a 4-inch display, 1.3-GHz quad-core processor and 8GB of storage for only $3.65! As for Infrared technologies, the smartphones market is expected to be the main driving force behind inexpensive infrared cameras. Demand is expected to explode in the next decade, which in turn will drive the price down significantly. For example, just between 2014 and 2015 alone, prices of infrared cameras fell by 30% to $250. Considering that the first smartphone with built-in infrared camera is being released in 2016, we are optimistic that within the next 10 years, such phones will be inexpensive enough to scale this project's outcome to almost all diabetic foot patients in the world.

7. Vodafone Funds

The Vodafone Funds will be designated to our effort in developing an economical screening system for the prevention and diagnosis of diabetic foot disease in developing countries. We budget the following items:

Personnel: Principal Investigator, Prof. Abdullah Mueen, will be involved in all aspects of this research related to the statement of work. Co-Principal Investigator, Prof. Shuang Luan, will focus on the infrared video processing and thermal regulation speed calculation aspects of the project. For both PIs, funding is request for a 15% release time in the first year, and a summer month in the second and third years. This is because the team will focus on system development in the first year, and field testing in the second and third year. Co-Principal Investigator, Dr. Farzana Alam will act as our primary medical consultant. Funding is requested for supporting one graduate research assistant. The student will assist the PIs in developing the proposed screening system, and responsible for maintenance and fine tuning of the system during the field tests.

Research Costs: Funding is requested for patients' studies, which will cover both patient incentives and the cost of the studies. Incentives ($15 per visit) will be paid to the study subjects for the time and inconvenience of taking part in the study. Other research costs are for hospital-related charges for rooms and personnel costs for coordinators (charged hourly). *Travel:* Funding is requested for the project personnel to travel to Bangladesh for the clinical trials of the developed imaging system. *Indirect Costs:* Facilities and administration rate is set at 15%.

8. Other Sources of Funding

Our previous research was supported in part by a Phase I Clinical Trial Grant from NIH NIDDK (National Institute of Diabetes, Digestive and Kidney Diseases) and in part by a grant from NSF CBET (Chemical, Bioengineering, Engineering and Transportation). However, the research was targeting US Hospitals and clinics, and focused on high end infrared technologies.

9. Additional Information

Our webpage (www.cs.unm.edu/~mueen/diabeticfoot) contains more information about the project. We have the letter of collaboration from Dr. Alam uploaded in the webpage. More pictures of our prototype system and thermal videos are available in webpage. We have our initial results published in various venues and made available in our webpage.

1. Chekh V, **Luan S**, Burge M, Carranza C, Soliz P, Barriga S, and McGrew E. Quantitative Early Detection of Diabetic Foot. ACM Conference on Bioinformatics, Computational Biology, Biomedical Informatics (ACM BCB 2013).
2. Chekh V, Soliz P, **Luan S**, McGrew E, Barriga S, Burge M, and Luan S. Computer Aided Diagnosis of Diabetic Peripheral Neuropathy. SPIE Medical Imaging 2014
3. Iven G, Chekh V, **Luan S**, **Mueen A**, Soliz P, Xu W and Burge M. Non-contact Sensation Screening of Diabetic Foot using Low Cost Infrared Sensors. IEEE Computer Based Medical Systems (CBMS'2014).