PRoF Award abstract – Call 2018

Deadline for submission: Thursday March 1st 2018 (12 o'clock noon)
Please send to: PRoF-Award@uzgent.be.

<Project acronym and name>

1. Research Outline

Acronym	
Project name in English	Non-invasive detection and monitoring of diabetes mellitus based on finger nail glycation.
Pitch (1 sentence)	By illumination finger nails during 10 milliseconds, quick non-invasive detection of diabetes mellitus is possible at a very low cost.
Executive summary (max. 10 lines)	
Diabetes mellitus is a growing threat in global public health. In 10 years from now, most diabetics will live in low-income countries. Classical diagnosis of diabetes in Africa is hampered by transport issues (glucose), interpretation problems (HbA1c), price and psychological thresholds (blood sampling). We present an innovative system based on the detection of finger nail glycation with infrared spectroscopy. Nails contain proteins (keratins), which are in close contact with underlying blood vessels (Fig. 1). Blood glucose diffuses from the deep part to the superficial part of the nail. By applying near-infrared spectroscopy, nail protein glycation can be assessed and analyzed. Nail protein glycation is representative for glycation of target organs. By applying cheap telecom electronic components, a commercial product can be developed.	

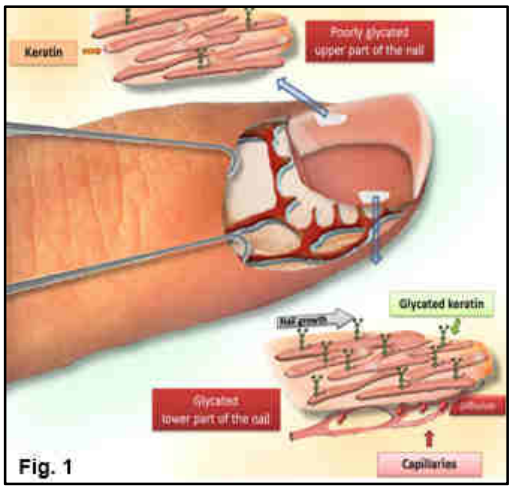

Fig. 1

Cause and context of the research

In the 21st century, the world is confronted with a huge increase in prevalence of diabetes mellitus, in particular in developing countries. Conventional diagnosis of diabetes relies on glucose determination and HbA1c assays. Unfortunately, pre-analytical problems (due to poor conditions of the road network) hamper the use of glycaemia as a diagnostic marker for diabetes mellitus in many third world countries. In Africa, the number of diabetics will increase from 14.2 million (2015) to 34.2 million in 2040. According to the International Federation of Diabetes (2015 report), about half of the 192.8 million diabetics in the world were undiagnosed. Point of care assays for glucose are characterized by a large error and therefore unreliable and explicitly not allowed by the World Health Organization for diagnosing diabetes. As the lion share of donor money for health care projects still goes to infectious diseases, the Third World is ill-prepared to tackle the ungoing transition from communicable to non-communicable diseases. The determination of HbA1c is quite expensive and unsuited in areas affected by high prevalence of haemoglobinopathies, malaria, … There is a clear need for an affordable diagnostic tool for diabetes mellitus.


Fig. 2

Near-infrared spectroscopy is an alternative, non-invasive and fast tool to assess glycation. The infrared spectrometer emits the radiation onto the intact nail surface and then receives it again. Depending on the molecular structure of the material at atomic and molecular level, there is a reflection of this infrared radiation. The intensity of this reflection depends on the underlying molecular structure of the tissue. This gives an infrared spectrum of the fingernail that shows a difference between diabetic patients and healthy individuals. On this basis, it is possible to distinguish diabetic patients from healthy persons. Our results suggest that the determination of glycated nail proteins by near infrared spectroscopy may have the potential to serve as a diagnostic marker of diabetes mellitus in

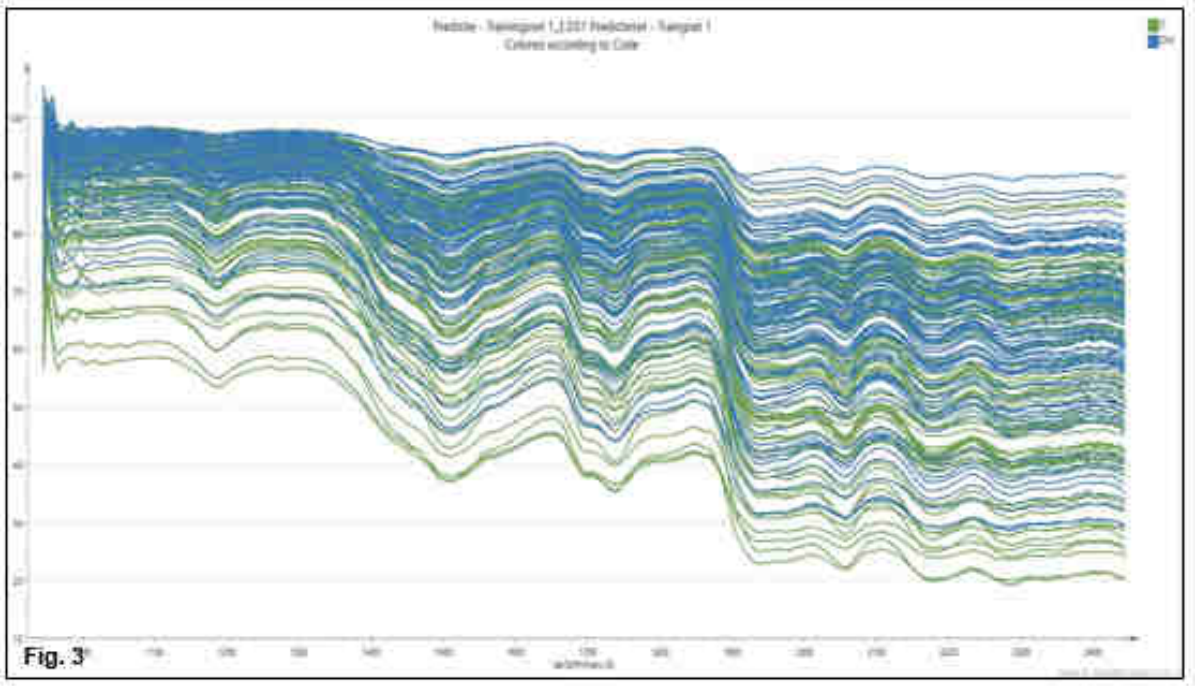
Fig. 3

situations where blood sample analysis is not possible. A prototype is shown on Fig. 2, whereas Fig. 3 shows the raw near-infrared spectrum of human finger nails. The complex near-infrared spectrum cannot be analyzed without mathematical processing. Chemometric analysis is therefore required. Fig. 4 shows the positioning of the dots following chemometric analysis. Each dot represents an individual. The green dots (healthy persons) and blue dots (diabetics) can easily be distinguished.

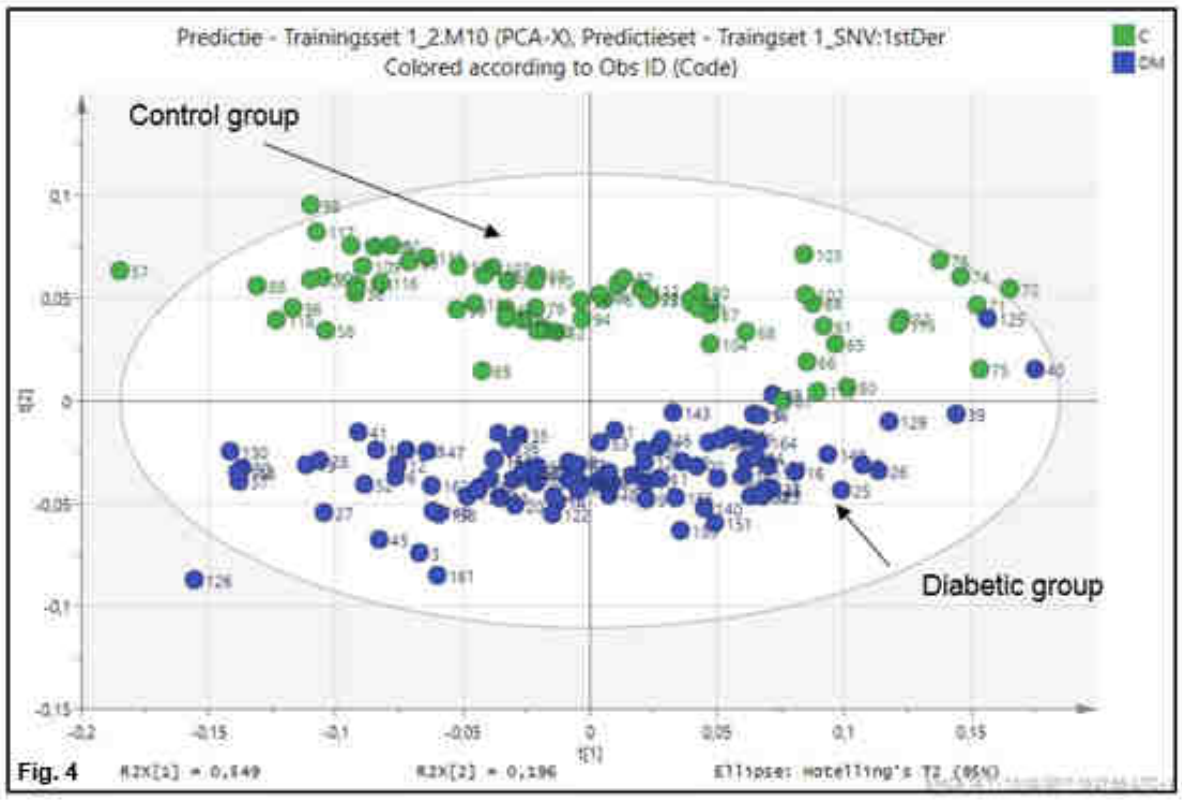

Fig. 4

2. Innovation results achieved

The project is the final product of five years of research. Starting from cumbersome chemical analysis of nails (Kishabongo AS et al. Trop Med & Int Health 2014;19:58-64), our attention switched to swifter mid-infrared spectroscopic analysis of nail clippings (Coopman R et al. Clin Biochem 2017;50: 62-67). In the meantime, the practicability and the acceptance of the early versions of the chemical method were assessed in an African context and well received by African diabetes patients (Katchunga PB et al. Biochemia Medica 2015;25:469-473). Finally, non-invasive near-infrared spectroscopy of finger nails was developed in 2016. This lead to the filing of a patent at the European Patent Office in March 2016. In an IOF project (supported by Ghent University Oct 2016 - Oct 2017), we have further elaborated the technique in order to simplify the electronic design of the instrument and to collect additional clinical data. The methodology was demonstrated to the general public during the Festival of Light in Ghent (Jan

31-Feb 4, 2018). Our latest data on NIR have been submitted for publication to the journal Clinical Chemistry and Laboratory Medicine.

The infrared spectrum needed for glycation analysis can be significantly narrowed, which opens perspectives for developing affordable hand-held instruments for diabetes screening. Depending on the production size, the manufacturing cost of the hand-held instrument could be as low a few hundreds euro per instrument. The described method does not consume any reagents at all and therefore has an extremely low operational cost. Furthermore, the solid state electronics warrant an extremely long functioning of the equipment. At the time being, negotiations with an industrial partner are in an advanced stage.

BASIC CHARACTERISTICS OF THE INSTRUMENT:

Principle	NIR spectroscopy followed by chemometric analysis
Key analyte	Glycated nail keratins
Data readout	Via app
Duration of analysis	Illumination of the nail during 10 milliseconds, followed by mathematical processing
Key electronic components	Affordable NIR LEDs mass produced for telecom applications
Power supply	Battery powered (or lighter of a car)
Assembly cost	500 - 1000 euro/instrument (depending on production size)
Maintenance	Not needed (solid state electronics)
Operational cost	(<0.01 euro/test) (occasionaly some calibrator material would be necessary, power cost negligible)

What is aimed by this project?

A. **In poor resources countries**: Affordable diagnosis of diabetes mellitus will be achieved. In these countries, conditions of the roads are often terrible. In consequence, often no reliable diagnosis of diabetes mellitus can be made because of quality loss of the blood specimen during transport. The World Health Organization Guidelines explicitly do not allow the use of portable glucometers for diagnosis because of measurement uncertainty. However, our method has the potential to become a valuable alternative screening tool to diagnose diabetes mellitus in developing countries. The **potential economic benefits are important**: for comparison, in the DR Congo, 1 glucose test strip costs ± 1 US Dollar, 1 HbA1c test costs ± 15 dollar; in

contrast the present NIR test costs less than 0.01 US Dollar (a significant difference in a country where the median income is only 1 US Dollar/day).

B. **In rich countries**: The test provides reliable information about glycation and allows to better assess target organ damage caused by diabetes mellitus. In contrast to the commonly used HbA1c, which is a very atypical (valine based) glycation product, glycated nail keratins are representative for what is happening in the body (e.g. the eye lens; Kishabongo AS et al. Plos One 2015;10:e01201124). Target organ damage (kidney damage, blindness, vascular damage) will be better monitored by our method.

If the award is wun, how will the money be spent?
The money will be invested in further miniaturization of the equipment and in industrial production of affordable hand-held instruments.

3. Link to the PRoF values

- **Minimal comfort:** As the technique is totally non-invasive, the analysis can be carried out near the patient and the applied near-infrared light source is totally harmless. Patients' comfort is a key element in the proposed application. The time needed for an analysis is less than a minute.
- **Privacy:** The complex raw infrared spectra results cannot be interpreted manually and require a computer algorithm app for reading. It is impossible for non-experts to analyse the raw data. The data are protected. The stand-alone character of the hand-held device further warrants the privacy of the data.
- **Security:** Since the technology does not require any sampling of body fluids and there is no direct contact with the body during the analysis, there is no contamination risk.
- **Anti-loneliness:** By avoiding target organ damage, preservation of the patient's capacities can be maximally preserved: retinopathy and neuropathy are essential in fighting loneliness in diabetic patients. Nail glycation is correlating very well with glycation of the eye lens (Kishabongo AS, et al. Plos One 2015;10(3):e0120112), which makes the test results representative for the status of important target organ damage (eye, kidney, nerves). So evolution towards blindness (a major cause of loneliness) and neuropathy can be better monitored and better prevented and treated.
- **Non-stigmatising solutions:** The method is totally harmless (illumination of a finger nail with a weak light source during 10 milliseconds). During the procedure, the patient's body is not even touched.
- **Intergenerational:** There are no age limits for the application of the technique. The entire age spectrum from neonates to geriatric populations may profit from the developed technology.
- **Respect:** By avoiding the need for blood or urine sampling, respect for the patient is fully warranted. In countries where blood sampling is associated with an important psychological threshold (e.g. Central Africa), the method has been well received by the local population (Katchunga PB et al. Biochemia Medica 2015;25:469-473).

- **Flexibility:** Reference values can be adapted for every reference population (age, gender, ethnicity, …). Analysis can be carried out both on nail clippings (not requiring the presence of the patient during the analysis) and on intact finger nails (e.g. during a medical consultation).

4. Applicable IPR rules

Priority claim has been filed; Title: “DIRECT INFRARED ANALYSIS OF KERATIN GLYCATION” (UGent ref: P2015/073-Nail proteins). The patent has been filed at the European Patent Office as EP priority request. The EPO has confirmed receipt on March 06 2016 (= priority date, file number EP16158854.6) .

5. Information on the partners

Prof Joris Delanghe, MD, PhD is an ordinary professor in clinical chemistry at Ghent University and has more than 35 years of experience in research on human diagnostics. His particular research interests are plasma protein chemistry and affordable laboratory medicine for third world countries. Since 2001, he has been involved in university development programs in various Third World countries (Zimbabwe, PR China, Rwanda, D.R. Congo).

Prof Marijn Speeckaert, MD, PhD, Dept of Internal Medicine, Ghent University is a clinical nephrologist with a particular interest in clinical biochemistry. He has a long standing research collaboration with prof. J. Delanghe.

Prof Thomas De Beer, PhD, Faculty of Pharmacy, Ghent University is a professor in pharmaceutical technology and is an expert in (near)-infrared spectroscopy and chemometrics.

Note:

If your project is selected as laureate for the Award Symposium, a powerpoint presentation that reflects the project as suggested will be required (in advance), including a future plan how the funding will be used.

If your project is selected as the winner of the Award, you will be invited to present the results achieved thanks to the award during the Award Symposium of the next year.

Addendum: Contact information

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