PoCOsteo (Point-of-care in-office device for identifying individuals at high risk of osteoporosis and osteoporotic fracture)

Summary

Hans Peter Dimai, Division of Endocrinology and Diabetology, Department of Internal Medicine, Medical University of Graz

Supervisor:	Prof. Dr. Hans Peter Dimai
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between August 02, 2017 00:00 and September 17, 2017 23:59 (CEST)

Description

Background:

As a consequence of the ageing population, osteoporosis has become a major health priority in many countries. The significance of osteoporosis lies in the fractures which occur after only a low, or sometimes even without any trauma, typically at skeletal sites such as the thoracic and the lumbar spine, the hip, the proximal humerus and the distal forearm. All osteoporotic fractures are associated with significant morbidity, and both hip and vertebral fractures are also associated with excess mortality[1]. Although useful non-invasive tools, aside from bone-mineral density (BMD) measurement, have been developed recently to estimate an individual's absolute fracture probability for a future period of up to ten years, only little of such information can be obtained from blood biochemical markers[2,3]. Furthermore, and irrespective of the fact that currently available biochemical markers may provide information on treatment response and also to some extent on an individual's future fracture risk, such markers are not available for routine use in health care facilites other than highly specialized institutions such as research facilities or tertiary hospitals.

Objectives:

The overall objective of the PoCOsteo project is the development, clinical validation and preparation for commercialisation of a whole-blood point-of-care tool for metabolic bone diesases, particularly osteoporosis. T o realize this objective, two Technology-Readyness-Level 3 (TRL3) devices for individual proteomic and genomic electrochemical sensors will form the base of the further development. These sensors have been developed / are being developed by two project partners; a) University of Gent (Belgium), who developed and characterised an electrochemical proteomic sensor for two types of bone-turnover markers, i.e. proteins reflecting bone formation and/or bone loss, and b) Universitat Rovira I Virgili (Spain), who is highly specialised in genomic electrochemical sensors which involve cost effective Printed Circuit Board (PCB) based DNA electrodes[4-7]. The sensors will be further optimised, combined in a single portable microfluidic cartridge and integrated into a complete and independent whole-blood point-of-care bone health assessment tool. The tool will then be clinically validated in two large tertiary hospitals (one in Austria, one in the Iran), involving a validation cohort of ~1,500 patients at the Austrian study center. The aim is to reach TRL6 / TRL7 for the combined microfluidic cartridges and the complete tool. Furthermore, depending on the proteomic and/or genomic sensors available at year three of the project, a fracture risk assessment model will be developed within the framework of the validation cohort recruited in the course of the first 18 months of the project. The risk model will be based on the incidence of vertebral fractures, hip fractures, proximal humeral fractures, and distal forearm fractures occurring during a pre-specified period of the project.

Methods:

The PhD candidate will be carrying out the following activities: a) recruitment of patients eligible to be integrated into the validation cohort (n~1.500), b) supervision of (pre-analytical) sample processing under involvement of the Biobank Graz, one of Europe's largest biobanks c) history taking in patients assigned to the validation cohort, d) data aquisition and data management e) assessment of the patients' absolute fracture probability by using online fracture risk assessment tools, including BMD as obtained by the current gold-standard method dual-x-ray absorptiometry (DXA), f) supervision (and also performing) of BTM (and if available at that time, also genomic) measurement in

whole blood samples, using the first available prototypes of the microfluidic cartridge containing point-of-care bone health assessment tool, g) validating BTM results against “gold-standard” methods such as ELISA/ECLIA a.o., and if available at that time, validating results of genomic measurements against high throughput DNA sequencing h) assessment of vertebral fractures (based on follow-up radiographs) and non-veretebral fractures (based on interviews / questionnaires), and i) development of a fracture risk assessment model/tool (depending on the proteomic and/or genomic sensors developed and available so far).

References:

1. Cooper C, Cole ZA, Holroyd CR, Earl SC, Harvey NC, Dennison EM, Melton LJ, Cummings SR, Kanis JA; IOF CSA Working Group on Fracture Epidemiology. Secular trends in the incidence of hip and other osteoporotic fractures. Osteoporos Int. 2011 May;22(5):1277-88. doi: 10.1007/s00198-011-1601-6.
2. Marques A, Ferreira RJ, Santos E, Loza E, Carmona L, da Silva JA. The accuracy of osteoporotic fracture risk prediction tools: a systematic review and meta-analysis. Ann Rheum Dis. 2015 Nov;74(11):1958-67. doi: 10.1136/annrheumdis-2015- 207907. Epub 2015 Aug 6. Review.
3. Dimai HP. Use of dual-energy X-ray absorptiometry (DXA) for diagnosis and fracture risk assessment; WHO-criteria, T- and Z-score, and reference databases. Bone. 2016 Dec 29. pii: S8756-3282(16)30386-6. doi: 10.1016/j.bone.2016.12.016. [Epub ahead of print]
4. Khashayar P, Amoabediny Gh, Larijani B, Hosseini M, Verplancke R, Schaubroek D, De Keersmaecker M, Adriaens A, Vanfleteren J. Characterization of gold nanoparticle layer deposited on gold electrode by various techniques for improved sensing abilities. Biointerface Research in Applied Chemistry. 2016; 6(4): 1380-90
5. Khashayar P, Amoabediny G, Larijani B, Vanfleteren J. Bone biosensors: knowing the present and predicting the future. Journal of Micromechanics and Microengineering 2016; 26(2)
6. Salvo P, Henry OY, Dhaenens K, Acero Sanchez JL, Gielen A, Werne Solnestam B, Lundeberg J, O'Sullivan CK, Vanfleteren J.Fabrication and functionalization of PCB gold electrodes suitable for DNA-based electrochemical sensing. Biomed Mater Eng. 2014;24(4):1705-14.
7. Sánchez JL, Henry OY, Joda H, Solnestam BW, Kvastad L, Johansson E, Akan P, Lundeberg J, Lladach N, Ramakrishnan D, Riley I, O'Sullivan CK. Multiplex PCB-based electrochemical detection of cancer biomarkers using MLPA-barcode approach. Biosens Bioelectron. 2016 Aug 15;82:224-32

To get more information or to apply online, visit https://mug.glowbase.com/positions/82 or scan the the code on the left with your smartphone.