Publishable Summary for 18RPT02 adOSSIG
Developing an infrastructure for improved and harmonised metrological checks of blood-pressure measurements in Europe

Overview

This project aimed to improve the reliability and accuracy of blood pressure (BP) measurements by developing an advanced oscillometric signal generator (aOSG) and by establishing new calibration procedures and services for blood pressure metrology. Meeting the technical objectives made in-depth accuracy assessment of sphygmomanometers easier, faster and it improved traceability chain for blood pressure measurements. Furthermore, the project established a competence centre for blood pressure metrology and created a network in this field consisting of NMIs, DIs, surveillance bodies and medical professionals. The competence centre and implementation of smart specialisation concept for blood pressure, representing the capacity building objectives, makes metrology for advanced blood pressure measurement accessible to a broader range of interested parties and provides support for blood pressure metrology even beyond the project lifetime.

Need

Hypertension affects almost half of the European population and is responsible for 13 % of all non-accidental deaths. Hypertension increases the probability of stroke, heart attack and kidney diseases, causing over 22 % of all heart attacks. Reliable and accurate BP measurements using sphygmomanometers (SMs) are indispensable in the diagnostic and treatment of hypertension as its detection is very sensitive to measurement errors. Studies show that even small deviations can have critical consequences.

While the European legislation requires lengthy and costly clinical trials before a new sphygmomanometer enters the market, such trials are not performed on every manufactured device, but on single, well-maintained specimens. In addition, despite the fact that periodical verifications of medical devices in use are recommended by the European Society of Hypertension, most EU countries ignore this recommendation. Only few countries adopt mandatory periodical checks for SMs in operation. Currently these checks are only performed at static pressure and check the accuracy of the pressure sensor. The algorithm used for the determination of the systolic and diastolic pressure is ignored and consequently the accuracy of the measurands themselves is never examined.

The challenges in the area of BP measurements are exacerbated by an insufficient metrology infrastructure at NMI level, where blood pressure metrology is considered of secondary importance to pressure metrology. Consequently, instead of establishing urgently needed true traceability for dynamic oscillometric instruments, only the surrogate of static pressure measurements is verified.

To rectify this situation, a new standard for suitable blood pressure measurements, capable of generating BP signals indistinguishable from real-life human signals was needed. As there were no aOSG on the market, this had to be developed and tested. As there were no procedures for testing sphygmomanometers with such a device available, corresponding procedures had to be defined as well. Using aOSGs for SM testing would solve the problem on the device level but the aOSGs must also be adequately calibrated. To exploit the full potential, the complete traceability chain for aOSGs had to be established as well

Objectives

The overall aim of the project was to develop sustainable metrological research capabilities to provide traceability for blood pressure measurement in Europe. This included the development of a new advanced blood pressure oscillometric signal generator and investigation of its possible role as an absolute blood pressure standard to carry out checks of the performance of sphygmomanometers.

The specific objectives were:

1. **To develop an advanced oscillometric signal generator device** with the capability of accurately reproducing pre-recorded real-life oscillometric blood pressure pulses.
2. **To define the necessary requirements and test procedures** for the newly developed advanced oscillometric signal generator to become a reference standard to establish traceability for automated sphygmomanometers.
3. **To develop a procedure for the periodic recalibration of the newly developed advanced oscillometric signal generator** at the NMI level, including defining acceptable uncertainty limits of ±1.5 mmHg or better.
4. **To engage closely with regional and European stakeholders**, including regulatory and governmental bodies, medical experts, professional medical societies, standards developing organisations, metrological committees and device manufacturers to ensure that all medical, legal and metrological requirements regarding blood pressure measuring devices are met.
5. **To develop and implement a concept for smart specialisation in the field of traceable blood pressure measurements and to integrate this concept with similar ones for other medical devices**. To establish a single joint research capacity and to develop a strategy for the perpetuation and sustainability of this new capability and a strategy for offering calibration and research services to national or international customers including NMIs/DIs. Additionally, for each internal partner, to develop an individual strategy for the long-term operation and transnational use of this joint research capacity, and for the access to its calibration and testing services from their respective countries. The individual strategies would be discussed within the consortium, to ensure that a coordinated and optimised approach to the development of traceability in this field is developed which is suitable for Europe as a whole.

Progress beyond the state of the art

The first three objectives of the project aimed to progress metrological testing of sphygmomanometers beyond the state of the art by creating an advanced test device, procedures and calibration methods.

To this end, an advanced oscillometric signal generator able to generate real life signals was developed and tested. Unlike its commercial counterparts, this generator is able to re-create real life oscillometric blood pressure signals to very high degree of accuracy.

In order to allow for calibration and in-depth performance checks of sphygmomanometers using the aOSG, procedures and guide had to be developed to amend state-of-the-art static pressure testing. This will allow the evaluation of performance of the whole sphygmomanometer rather than just the ability of pressure sensor to display static pressure correctly.

State of the art calibration for oscillometric signal generator were so far provided by static pressure. That, similarly to sphygmomanometer testing, only assures the ability of pressure sensor to correctly measure test pressure, but it doesn't evaluate the ability to correctly generate the oscillometric signals. As it is essential to evaluate the performance of aOSG in dynamic mode, new, dynamic pressure traceability chain had to be established. This will increase the trust in the proper operation of both the aOSG, and sphygmomanometers and as well the confidence in the measured blood pressure values.

Beyond the technical development, the project aimed at the implementation of smart specialisation concept for blood pressure measurements. To this end, the project partners established joint research capacity consisting of competence centre for blood pressure measurements, working group on blood pressure metrology and a laboratory capable of providing traceability to aOSG and similar devices, these will persist beyond the project lifetime and will support, promote and further develop advanced blood pressure metrology.

Results

To develop an advanced oscillometric signal generator device

An aOSG able to generate signals undistinguishable from real-life human signals has been developed, constructed and tested. The technical and metrological specifications for the aOSG were defined early in the project. The needed components for the device were identified based on literature research and prior experience in order to ensure a reliable performance of the device, while the requirements for the software concentrated on ensuring the complex processing of the recorded data while keeping the user interface friendly.

The aOSG and the corresponding software were developed together with the developed recording unit (RU) during the first quarter of the project. The RU is required for the in-depth assessment of the aOSG, allowing a quantitative comparison between the input data and the data generated by the aOSG. Tests using real-life signals collected from the patients of a cardiology clinic in the UK were performed using a protocol based on the requirements of ISO/TS 81060-5. These tests aimed at the thorough characterisation and evaluation of the repeatability and reproducibility of the aOSG.

The aOSG, its performance and experience with sphygmomanometer testing using the aOSG were presented to participants of stakeholder workshops in September 2021 and in September 2022. Particularly clinicians present at these events welcomed the developments of the project and underlined the importance of having access to trustworthy test devices designed to ensure a correct performance of BP measuring devices. Furthermore, the topic of oscillometric blood pressure simulators with focus on aOSG and progress and results were presented at several conferences and during meetings of standards development organisation and metrology committees.

With excellent performance of the aOSG and good results of testing, all defined criteria were achieved and thus this project objective was fully met.

To define the necessary requirements and test procedures

For the aOSG to be used for in-depth performance checks of oscillometric sphygmomanometers, test procedures for such testing of sphygmomanometers as well as technical and metrological requirements had to be developed. These were developed to amend the insufficient static pressure testing and will allow the evaluation of the performance of the entire components of the sphygmomanometer rather than just the pressure sensor. The test procedures and requirements are based on harmonised standard EN ISO 81060-2 and define simulated clinical trial and repeatability tests.

The applicability was of the procedures was evaluated by practical tests, i.e. testing of sphygmomanometers. In second quarter of 2022 these procedures were used during an example of early uptake, testing of sphygmomanometers as part of consumer test for Czech newspaper Mladá Fronta Dnes. The testing with aOSG and a sample of 85 signals fulfilling the criteria of EN ISO 81060-2 compared results of 11 sphygmomanometers available on the market. It also confirmed the applicability of the aOSG and developed test procedures.

This objective was fully met. Practical implication of the procedures published as one of project deliverables together with an excellent performance of the aOSG can be faster and easier in-depth testing of sphygmomanometers, easier clinical trials and faster development. Here, the aOSG could substitute some hard-to-be found or ethically sensitive human test subjects or make repeated testing easier.

To develop a procedure for the periodic recalibration of the newly developed advanced oscillometric signal generator

Introduction of the aOSG for the in-depth checks of SMs accuracy brought the need for valid traceability of the aOSG itself. Until recently, the only option for traceability of aOSG and similar devices was a static pressure calibration, although the devices measure and generate time-dependent, highly variable, i.e. dynamic pressure.

Although there were significant developments if for dynamic pressures in recent years, these usually focused on measurements suitable for internal combustion engines, turbines and similar devices, i.e. on high amplitude and milliseconds long pressure pulses. To provide valid traceability for aOSG and similar devices, the metrological challenges are related to measurement and evaluation of low amplitude, low frequency pressure pulses superimposed on semi-static pressure. Prior this project a valid calibration of such a aOSG was not possible at NMI level, hence the development of suitable dynamic calibration procedures was one of the necessary steps to allow the aOSG to work as intended.

Following thorough literature survey on available solutions for dynamic pressure with emphasis on range of the oscillometric signals and BP applications, the consortium continued research on the dynamic pressure traceability. Project partners investigated two alternative dynamic pressure traceability paths; classical fast pressure sampling measurement and novel acoustic measurement. While the calibration via acoustic path was considered a research study, the fast pressure measurement was decided to be used within the project.

Precision pressure transducer with fast response connected to fast sampling data acquisition system was used as the main component. Calibration procedure based on ISO/TS 81060-5 for calibration was defined with

calibration model for uncertainty evaluation being developed. The project had initially rather ambitious goal of reaching ± 1.5 mmHg uncertainty of measurement. By reaching lower-level of uncertainty of only ± 0.78 mmHg (k = 2), this project objective was fully met.

Concept for smart specialisation in the field of traceable blood pressure measurements

This project aimed at developing and implementing smart specialisation concept (SSC) and creating a network of NMIs, DIs and universities that will be able to support blood pressure metrology in Europe at all levels.

Through this concept, metrology for advanced blood pressure measurement is accessible to a broader range of countries. This was be achieved by condensing expertise and knowledge at one site, while simultaneously making it accessible to others.

To develop the framework of SSC, the project partners wrote and published the White Paper on the smart specialisation for blood pressure specialisation. The idea of smart specialisation concept for blood pressure metrology was also presented to the participants of both stakeholder workshop.

A centre of excellence for blood pressure measurement (competence centre) was created. The competence centre was established with the scope of ensuring the harmonisation of the metrological requirements at European level, by offering countries the possibility to work together, develop common requirements and provide all interested parties with access to an advanced level of expertise in the field of medical devices. The centre serves as a hub of future network for medical devices with measuring function (MDMF) metrology and consists of both, a physical and a virtual section.

The physical section is represented by the laboratory established at pressure department of CMI to provide traceability to aOSG and similar devices, while the virtual network was created in order to support the competence centre.

To support the competence centre, the project partners established the Working Group on blood pressure. The working group has a permanent core composed of active and experienced NMIs and DIs in the field and a temporary group of stakeholders which will change depending on the topics worked on by the group. In 2022 the working group started development of the draft for the future OIML Recommendation on the requirements for the evaluation of non-invasive blood pressure simulators used for the testing of automated non-invasive sphygmomanometers.

An important step in the development of the long-term operation use of the proposed joint research capacity has been achieved by developing a strategy for the long-term operation and transnational use of this joint research capacity by all internal partners. This document, published as Deliverable 8, summarises the needs of each internal partner and their respective countries. These individual strategies ensure a coordinated and optimised approach to the development of traceability in this field is developed which is suitable for Europe as a whole. With these steps made, the objective of SSC in the field of traceable blood pressure measurements was fully met.

Impact

This project brought together the most relevant international metrological and medical institutions, producers of sphygmomanometers and market surveillance bodies; which made the project known and accessible to the wider community. The consortium approached more than 50 potential stakeholders. Positive responses were received froms 33 institutions from 11 countries and 3 continents. The institutions that expressed their interest in project were continuously updated on the latest development within the project.

Majority of stakeholders, medical experts, notified body and NMI representatives attended both stakeholder workshops organised in 2021 and 2022 where the project, its objectives and progress were presented. In particular, the interaction with stakeholders from the clinical sector was highly valuable.

In addition to the presentation of the project at the annual conference of the Czech society for hypertension, the partners presented the project and its objectives and results at four more scientific conferences. Presentations were given at 30th International Electrotechnical and Computer Science Conference ERK 2021, 9th Congress of Alps Adria Acoustics and XXIII IMEKO World Congress where two presentations were given and a presentation was given at Joint IMEKO TC11 & TC24 hybrid conference 2022. Papers from XXIII IMEKO World Congress were subsequently published in peer-revied journal Measurement: Sensors.

Impact on industrial and other user communities

The development of the aOSG and corresponding advanced calibration procedures will allow easier and more affordable in-depth performance checks of automated sphygmomanometers. This will ease the development process of SMs for new and small manufacturers, offering them a chance to access the market at lower costs and thus encouraging the innovation.

The research and competence centre for blood pressure metrology established by the project creates a well-developed metrological infrastructure with advanced calibration services and will provide manufacturers with clear guidance, and hence legal certainty on how requirements can be met. Physicians and medical staff will be able to rely on the existing traceability chain, trust the measurement results are correct and methods are validated. Patients in clinics, practitioner offices, and home-care settings will have more confidence in the measured BP values, as the improved infrastructure will allow surveillance bodies and other legal entities to ensure adequate quality of the devices available on the market.

Impact on the metrology and scientific communities

Main impact on the metrology and scientific communities is achieved through knowledge and know-how concentration in one place. Until recently, all European countries and their NMIs had to face challenges of blood pressure traceability and specifics on their own, which ultimately led to many equally undeveloped NMIs facing similar problems.

The project has started correcting the situation in several steps. Early in the project, the network of interested organisations has been created by connecting the project consortium with stakeholders and organisations interested in reliable and traceable blood pressure measurements consisting of NMIs, DIs, surveillance bodies and medical professionals. This led to establishment of the Working Group on advanced blood pressure metrology which was established in the second half of the project. The group will meet regularly, even beyond the project lifetime, and work on different priority topics in the field of blood pressure metrology. The first tasks of the working group is the development of two drafts for two newly proposed and accepted OIML publications; the draft for the future OIML Recommendation on the requirements for the evaluation of non-invasive blood pressure simulators used for the testing of automated non-invasive sphygmomanometers and the draft for a new OIML guide for the evaluation of automated sphygmomanometers using oscillometric signal generators able to generate real-life oscillometric signals. While the draft of the OIML Recommendation was developed by the end of the project, its finalisation and development of draft of the OIML Guide remain to be done beyond the project-lifetime.

Simultaneously, project partners have started investigation on traceability for oscillometric blood pressure generators. During the initial stages of the project development, the partners estimated that the final uncertainty of measurement of the dynamic oscillometric pressure pulses could be ± 1.5 mmHg. The calibration procedures, selected test equipment and the developed uncertainty model allowed a much lower uncertainty of measurement of ± 0.78 mmHg to be reached. The establishment of dynamic pressure traceability allowed for the calibration laboratory at CMI to be established. This laboratory will serve as the physical part of the competence centre which will provide traceability for aOSG and similar devices and expertise on BP measurements to all interested parties.

By implementing the smart specialisation concept, providing traceability, creating a working group in this field and integrating interested organisation into one network and finally, by concentrating knowledge and know-how on one place, this project makes metrology for advanced blood pressure measurements accessible to a broader range of countries. This can be important to many smaller NMIs, particularly emerging NMIs and DIs, who are lacking the capabilities or the resources to provide the complete traceability chain for BP measurements. With the implementation of SSC and help of the competence centre they will be able to serve their national customers with less demanding metrological services, while relying on the competence centre for the higher-level ones.

Impact on relevant standards

The project is actively participating in key blood pressure monitoring equipment and pressure related standardisation committees as well as international and European legal metrology organisations (e.g. ISO/TC 121/ SC3/ JWG 7, OIML TC 18 and IMEKO TC 16). This participation builds on links already established by the consortium, which is highly influential in national and international metrology and standardisation committees and will be used to facilitate greater awareness of the benefits of the project.

In the period September 2019 – March 2020, PTB was strongly involved in the revision of the OIML Recommendations *OIML R 16-1 Non-invasive non automated sphygmomanometers* and *OIML R 16-2 Non-invasive automated sphygmomanometers*. R 16-2 includes details regarding testing procedures for the verification of automated sphygmomanometers using patient simulators. The two Recommendations are in the committee draft stages and awaiting the balloting results.

As the main proposer of the *ISO TS 81060-5:2020 Non-invasive sphygmomanometers - Part 5: Requirements for the repeatability and reproducibility of NIBP simulators for testing of automated non-invasive sphygmomanometers,* PTB was highly involved in the development of this new technical specification. The TS was published in February 2020. The TS was relevant for the establishment of traceability chain for aOSG in WP3.

To ensure a world-wide dissemination of the guidelines for the evaluation of automated sphygmomanometers developed during the project, the consortium successfully applied in 2021 for two projects within OIML. First project is a new OIML Guide for the evaluation of automated sphygmomanometers using oscillometric signal generators able to generate real-life oscillometric signals. The second project is a new OIML Recommendation covering the requirements for the evaluation of non-invasive blood pressure (commercial and non-commercial) simulators used for the testing of automated non-invasive sphygmomanometers. The work is being conducted by the Working Group on blood pressure within the OIML SC1 "*Blood pressure instruments*" of the TC18 "*Medical measuring instruments*". By the end of the project the draft of the OIML Recommendation was developed, however its finalisation as well the development of draft of the OIML Guide remain to be done beyond the project-lifetime. In the longer term, the outcomes may contribute to the revision of different normative documents (e.g. IEC 80601-2-30, ISO TS 81060-5:2020).

Longer-term economic, social and environmental impacts

The European healthcare industry will primarily benefit from this project in the long term. The prevalence of hypertension is approx. 25 % in EU's adult population. Thus, the importance of accurate and reliable blood pressure measurements is obvious. At the end of the project, an aOSG exists with uncertainty of better than ±1.5 mmHg and a dynamic traceability chain was established. Although this doesn't improve the accuracy of the sphygmomanometers per se, it will allow cheaper complex in-depth testing of sphygmomanometers; either existing or in development. It can thus be expected that the accuracy of a sphygmomanometer can be maintained without significant deterioration over the whole production and lifetime cycle of the device; a guarantee which cannot possibly be given today. Cautiously, assuming that for only 1 % of the patient misdiagnoses can be avoided in the future, the direct benefits of the project can be quantified as:

- 2 million EU citizens who will be spared a false positive or false negative diagnosis,
- 370 M€ per year which will be saved for the EU healthcare systems by avoiding the costs for unnecessary medication of healthy subjects and the even higher costs for undetected and untreated hypertension (estimated from 196 B€/a total costs for cardiovascular diseases in the EU in 2009, 53 % of which are treatment costs, and a ~36 % share for hypertension treatment).

List of publications

Gregor Geršak, Markus Schiebl, Michał Nawotka, Ehlimana Jugo, Maria do Céu Ferreira, Alan Duffy, Dana Maria Rosu, Peter Pavlásek, Václav Sedlák, Dominik Pražák, Physiology-based patient simulator for blood pressure meter testing, *Measurement: Sensors*, Volume 18, 2021, 100260, ISSN 2665-9174, https://doi.org/10.1016/j.measen.2021.100260.

Václav Sedlák, Dominik Pražák, Markus Schiebl, Michał Nawotka, Ehlimana Jugo, Maria do Céu Ferreira, Alan Duffy, Dana Maria Rosu, Peter Pavlásek, Gregor Geršak, Smart specialisation concept in metrology for blood and intraocular pressure measurements, *Measurement: Sensors*, Volume 18, 2021, 100283, ISSN 2665-9174, https://doi.org/10.1016/j.measen.2021.100283.

This list is also available here: https://www.euramet.org/repository/research-publications-repository-link/

Project start date and duration:		01 June 2019, 42 months
Coordinator: Václav Sedlák, CMI Tel: +420 607 029 211 E-mail: vsedlak@cmi.cz Project website address: www.adossig-empir.eu		
Internal Funded Partners: 1. CMI, Czech Republic 2. BEV-PTP, Austria 3. GUM, Poland 4. IMBiH, Bosnia and Herzegovina 5. IPQ, Portugal 6. NSAI, Ireland 7. PTB, Germany 8. SMU, Slovakia	External Funded Partners: 9. UL, Slovenia	
RMG: -		