Doctoral Program in Metrology (35th Cycle)

Impedance spectroscopy: non-invasive measurements for human tissues characterization

By

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Summary

Impedance spectroscopy is considered a powerful, painless, and harmless measurement technique in many medical fields. This dissertation focuses on the application of impedance spectroscopy in medicine, by paying particular attention to drug bioavailability assessment and tissue characterization.

Diabetes is one of the most widely spread non-communicable chronic diseases worldwide, thus a full control of blood glucose concentration is a challenge with a relevant clinical, social, and economic impact. To date, instruments capable to measure in-vivo the delivered amount of insulin immediately after administration have not been developed. The most popular methods for assessing insulin bioavailability are often invasive or have high latency. Thus, the demand for painless and non-invasive analytical methods to achieve effective glucose monitoring in diabetics is significantly increasing.

An insulin meter, based on an on-chip transducer, for real-time non-invasive monitoring of insulin absorption is presented. The instrument, prototyped by using off-the-shelf components, analyses the electrical impedance in the frequency domain and its variations over time in order to monitor the diffusion of insulin from the administration site. The instrument was metrologically characterized in laboratory, in-vitro, and ex-vivo. The insulin bioavailability is assessed non-invasively and in real-time, after the administration in a specific injection site, of a known amount of drug, as in common diabetic therapy. The Insulin Meter implements a personalized model identification by measuring step by step the impedance variation corresponding to the injection of a known amount of insulin, improving thus the inter-and intra-individual reproducibility.

Then, with the aim to improve the sensitivity of the measurement method, a numerical model of the tissue based on “Finite Element Method” is proposed for the measurement of insulin transdermal delivery. In order to improve the accuracy of the insulin absorption assessment, an experimental campaign was carried out to assess the impact of mechanical stresses acting on the human abdomen on the impedance spectroscopy, in particular due to the pressure exerted during the injecting phase and the tissue defamation because of breathing.

Furthermore, tissue characterisation by impedance spectroscopy has been applied to dental diseases assessment. In particular, a simple automatic approach for the assessment of the tooth demineralization, which represents the earlier stage of the dynamic carious process, was developed.

The proposed approach based on impedance measurements and classification algorithms was tested and validated in-vitro. The possibility to use of impedance spectroscopy measurements in caries detection is based on the typical loss of mineral due to the caries process, resulting in an increased porosity of the tooth structure, which entails a higher liquid content than healthy tissue.

In parallel, a dental tissue characterisation by scanning electron microscopy and Raman spectroscopy to assess demineralized and sound teeth was performed.

This work proved possibility to discriminate between sound and demineralized teeth, and thus the carious lesion, by using impedance spectroscopy measurements.

Therefore, impedance measurement can be considered as additional diagnostic method in dental practice thanks to its safety, reliability, simplicity, rapid response, cost-effective, robust, and adequate detection limit. Further work will include the development of a low-cost device for in-vivo application in dental practices.

Thus, the objective of the research work presented in this dissertation is to propose impedance spectroscopy measurement as additional tool in different medical applications. It has been pursued, in diabetology, by developing a new instrument able to detect the non-invasively the amount of insulin absorbed by the tissue. In dentistry, a non-invasive and fast approach for assessing dental caries has been proposed.