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A FINITE ELEMENT MODEL OF ABDOMINAL HUMAN TISSUE FOR IMPROVING THE ACCURACY IN INSULIN ABSORPTION ASSESSMENT: A FEASIBILITY STUDY

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Abstract – A Finite Element Model of the human abdomen biomechanics for patients undergoing diabetes therapies was developed. In particular, FEM was used to improve a previous insulin absorption measurement method based on bioimpedance spectroscopy (BIS). As a matter of facts, the noise introduced during the insulin injection phase significantly affects the BIS measurements. The noise, due to the pressure exerted on the abdomen tissue, arises sensibility issues on the signal correlated to the drug presence under the skin. In this study, the abdomen is modeled with three layers (skin, fat and muscle). A feasibility study about the decoupling of the mechanical deformation and the electrical dynamics is presented in order to model the effect of mechanical uncertainty sources (e.g., pressure exerted during the injection phase and/or breathing) on the impedance measurements. The proposed simplified model is realised by referring to the average values of skin, fat and muscle thickness, along with mechanical abdomen parameters already presented and validated in scientific literature. The obtained results confirm the possibility to decouple mechanical and electrical analyses when the excitation voltage is characterized by a frequency higher than 1 kHz. The results will be used to improve the accuracy of an exhaustive approach, already developed by the authors, for real-time insulin absorption measurement.

Keywords: insulin, uncertainty sources, absorption measurement, FEM, biological system modeling, natural frequency, multilayered structure,

1. INTRODUCTION

According to International Diabetes Federation (IDF), the number of world-wide people living with diabetes is approximately 463 million and it is expected to rise to 700 million by 2045. This points out that a full and non-invasive control of the Blood Glucose Concentration (BGC) would be an optimal solution for diabetic patients, which is currently carried out with daily insulin injections by means of syringes, insulin pens, insulin pumps, and jet injectors. The BGC control, performed by glucose sensors, aims at evaluating the individual insulin requirement. The artificial pancreas (AP), on the base of this information, regulates the insulin dosage for each administration

(closed loop) [1]. Thus, novel methods and techniques to treat diabetes, as well as the development of more efficient automatic control systems, are becoming increasingly important. To date, the major issues in automated system arise during meals, due to system inefficiency to adapt itself to the fast glucose increase following food ingestion. Therefore, an efficient control system requires additional information (external control inputs) in order to adapt the system to the relevant variations related to insulin absorption kinetics. Moreover, skin alterations (e.g., lipodystrophy) interfere with insulin absorption and lead to considerable intra-individual glycaemic instability [2].

In a recent article, an exhausting measuring method of insulin absorption, based on bioimpedance spectroscopy (BIS), was validated [3]. The referred method was proposed to perform a customized insulin model identification, starting from a real-time evaluation of the impedance variation at injection site [4]. Indeed, the administration of note pharmacological doses, through an insulin pump, allows the identification of a specific personalized impedance model for each tissue physiological condition. Then, the model was used during the absorption measurement to assess the bioavailable insulin. This method improves effectively both intra- and inter-subjects reproducibility. Nevertheless, experimental evidences showed that any pressure exerted during the procedure (e.g., injection and breathing), and the subsequent tissues deformation, affect the bioimpedance measurement, generating sensibility issues on the signal referable to the drug presence under skin [3]. In a previous work, a Finite Element Model (FEM) was implemented to model the electrical behaviour of human tissues and, thus, to manage intra-individual reproducibility uncertainty. In particular, the skin, fat and muscle electrical characteristics for each subject were identified by a preliminary impedance spectroscopy measurement [5]. In this work, a FEM approach introduces a numerical mechanical analysis aiming to estimate tissues deformation contribution to bioimpedance measurements, in order to improve the accuracy in insulin absorption assessment. In this regard, it would be necessary to set-up a multiphysics time-dependent study: a mechanical deformation dynamics, coupled with an electrical analysis, will allow to simulate the bioimpedance mea-

surement at the BIS device's terminals. Tissues deformation dynamics is provided by the superposition of the injection/breathing pressure effect, and a number of vibrational modes, both affecting the bio-impedance measurement. When the characteristic time of the mechanical dynamic and the period of the sinusoidal electrical excitation of the tissues are comparable, the analysis complexity and the computational burden are very high. However, this can be significantly reduced when the electrical excitation frequency is much higher than the natural mechanical oscillation frequencies. In this case, it is possible to decouple the mechanical deformation dynamics and the electrical dynamics. This allows to study the electrical field and current density distribution into the tissues, assuming a sequence of quasi-AC regime states, where the deformation is negligible over the period of the excitation voltage. Therefore, the same procedure to simulate the bioimpedance measurement, as shown in [5], can be used.

Hence, this paper is focused on a mechanical analysis aimed at evaluating the natural frequencies of the portion of human body under test. The main aim is to provide indications about the minimum frequency applicable across the BIS' terminals in order to meet the above-mentioned conditions. The preferred site for insulin injection is the abdomen thanks to its easy access and faster insulin absorption. Moreover, the choice of the preferred injection site is based on the following considerations: the patient should rotate the injection site and (ii) insulin should be injected into the subcutaneous tissue. Insulin injection into the abdomen subcutaneous tissue is required, since an intramuscular injection leads to a faster absorption than the desirable rate, higher frequencies of unexpected hypoglycemia, and glucose variability. On the other hand, intradermal injection provokes insulin leakage and pain [6]. Therefore, the selected area for the mechanical analysis is located between the bottom of the ribs and the pubic area, about 10 cm the area surrounding the navel.

The paper is structured as follows: Section 2 reports the theoretical background of the model, the equations physics, and the boundary conditions. Section 3 describes the human abdomen model in terms of anatomical, geometrical, and mechanical characteristics. Then, Section 4 reports the investigation about the natural vibrational frequencies of the system, and in Section 5 the main conclusions and future developments of the work are finally presented.

2. THEORETICAL BACKGROUND

Numerical models and experiments are essential to study the behaviour of human tissues. Since the human tissues are non-homogeneous and characterized by a complex biological structure, many approaches, usually based on a multi-layered structure modeling, were developed: for instance, in [7], Flynn developed a finite element model of the skin to study the formation of wrinkles around healing scars. From a mechanical point of view, it is usual to consider human tissues of the abdomen (skin, fat and muscle) as viscoelastic materials, characterized by stress relax-

ation, creep and hysteresis. Their rheological properties determine the stress-strain characteristic when subjected to different external loads. Since elastic and viscous behaviour of human tissues depend upon their Young's modulus, Poisson's ratio and density, they could also be used for diagnostic purposes, to retrieve information about disease and treatment progressions from their variations over time [8]. Many techniques have been developed over the years to determine the mechanical parameters: wave propagation methods were adopted to determine the thickness and mechanical properties of the skin; in vivo and in vitro indentation tests were conducted to define the characteristic stress-strain curve of human tissues, and imaging techniques were implemented to improve the accuracy in defining mechanical properties.

Mechanical parameters, once identified, are used into partial differential equations standing the indefinite equilibrium of the tissue, which calculate their stress condition. To calculate the natural vibrational frequencies of the human tissue under test, such equations are solved into the frequency domain with no external loads as stated in 1:

$$-\rho\omega^2\mathbf{u} = \nabla \cdot \mathbf{S} \quad (1)$$

where ρ is the density, ω the angular frequency, \mathbf{u} the displacement field, and \mathbf{S} the stress tensor.

Equation 1 needs to be solved with a proper set of boundary conditions, taking also into account the presence of the remaining part of abdomen not modeled in our study. Panchal et al. developed a FEM model to estimate the natural frequencies of human skin of the forearm. Symmetry conditions, applied to the model, allow to exclude the edge effects of the section in the results, and to connect each layer to the underlying one by using tie constraints. [9].

3. NUMERICAL MODEL

Modeling human tissues is challenging due to the intrinsic complexity of biological structures. Despite human tissues behave as viscoelastic and anisotropic materials whose characteristics change with ageing, gender and, location, a linear isotropic behaviour can be adopted in a definite range of vibration analysis constant parameters [10]. The mechanical parameters used for the abdominal model are the tissues density, elastic modulus, namely Young's modulus [11], and the Poisson's ratio. The proposed simplified abdomen model consists of 3 layers, namely skin (including epidermis and dermis), fat and muscle, whose thickness are reported in Tab. 1. The average skin thickness is defined as the total epidermis and dermis thickness, it is chosen equal to 2.29 ± 0.37 mm considering both male and female abdomens, according to studies reported in [12]. These values were measured by ultrasound technique and collected on 156 Korean adults with diabetes, and they are consistent with those reported in scientific literature [13] [12]. The subcutaneous fat tissue thickness depends on many parameters, such as Body Mass Index (BMI), age and gender; therefore, the average value of 10.15 ± 6.45 mm was chosen, considering 7.75 mm \pm

5.03 for men and 13.07 ± 7.03 mm for women. Such values are compatible with the values proposed in a study on American diabetic patients [14]. Finally, considering the injection site, the abdominal muscle selected is the Rectus Abdominis (RA) whose size was measured by ultrasound imaging on a total of 123 subjects, 55 men (mean age 40.0 ± 14.1) and 68 women (mean age 33.8 ± 12.7) in [15]. Men showed to have significantly larger muscles than women, nonetheless a significant correlation between thickness of RA, weight and BMI was seen in both genders. The RA thickness was 1.25 ± 0.22 cm and 1.02 ± 0.16 cm for men and women respectively.

As regards tissues density, abdomen skin density, fat and muscle density we estimated to be 1.1 g/cm^3 in [16], 0.90 g/cm^3 in [17] 1.0597 g/cm^3 in [18], respectively.

Skin, fat and muscle Young's modulus are 2.1 MPa, 3.25 kPa and 110 kPa respectively. At last, the Poisson's ratio has been chosen equal to 0.30 for all the tissues, according to [10]. All values are reported in Tab.1.

These values are used to build a simplified finite element

Table 1. Mechanical and Anatomical parameters

	Skin	Fat	Muscle
Young's Modulus [kPa]	2.10×10^3	3.25	110.00
Poisson's Ratio	0.30	0.30	0.30
Density [g/cm^3]	1.10	0.90	1.06
Thickness [mm]	2.29	10.15	12.50

model to evaluate the human abdomen natural frequencies. A generic abdominal surface $100 \times 50 \text{ mm}^2$ centered in the navel was chosen for this analysis. The chosen surface size depends on the futures needed to evaluate macroscopic effects, such as the pressure exerted by the syringe or the injection of the drug, which are not appreciable on infinitesimal areas.

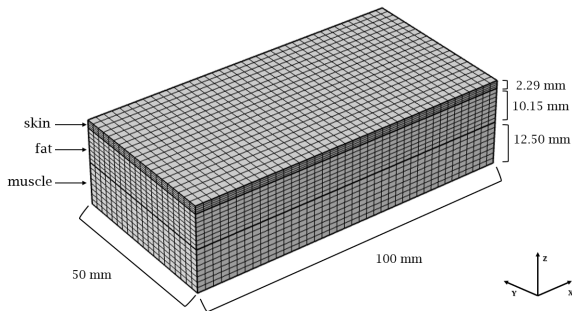


Fig. 1. The FE model of abdominal portion

The geometrical model is shown in Fig.1 with indications of the different layers. Equation 1 is solved in this volume with constraints fixed according to [9]. Symmetrical boundary conditions were chosen for all tissues lateral surfaces in order to prevent edge reflection effects. Due to the high difference in skin thickness w.r.t. fat and muscle's, the former was treated as a shell and shell-solid connection

that was added at the skin-fat interface model the tie constraint set as reported in [9]. Thanks to the geometry of the system, a mapped mesh was generated on the skin external surface and then extruded along the depth direction, resulting into the hexahedral mesh shown in Fig. 1.

4. SIMULATION RESULTS

Natural frequencies of the multi-layer tissue were calculated by solving equation 1 with proper boundary conditions by means of a finite element analysis. Results are reported in Table 2.

Table 2. First Natural Frequencies of human abdomen tissues

Natural frequency [Hz]
19.76
27.32
56.87
57.59
58.72
59.79

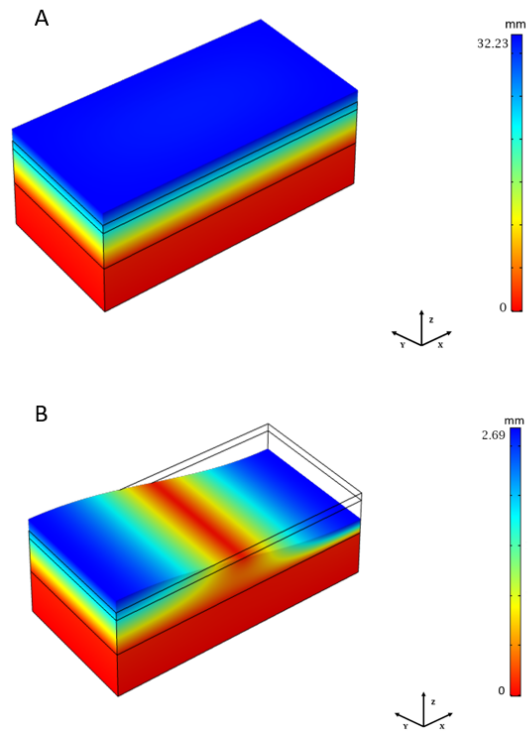


Fig. 2. A) Total displacement of abdominal portion at frequency= 19.76 Hz B) Total displacement of abdominal portion at frequency= 27.32 Hz

Table 2 shows that natural frequency of vibrating modes of the multilayered human abdomen falls into the range 19-60 Hz. This results provide information regarding the

excitation voltage to be applied at the BIS' terminals. Considering that the abdomen deformation generated by the exerted pressure of the insulin injector is slow enough (up to one second), the excitation voltage frequency should be higher than 1 kHz to decouple the electrical analysis, in the frequency domain, from the mechanical transient analysis.

5. CONCLUSIONS

In this paper, a contribution to improve the assessment of the injected insulin absorbed by the subcutaneous tissue, based on bioimpedance measurement, is proposed. In particular, a feasibility study about the possibility to decouple the mechanical deformation and the electrical dynamics is presented to model the effect of the mechanical uncertainty sources (e.g., pressure exerted during the injection phase and/or breathing) on the impedance measurement. The proposed simplified model is realised by referring to the average values of skin, fat and muscle thickness and mechanical abdomen parameters, already present and validated in scientific literature. The calculated natural frequencies fall into the range 19-59 Hz, highlighting the possibility to decouple mechanical and electrical analyses when the excitation voltage is characterized by a frequency higher than 1 kHz. Future developments foresee the study of the deformation dynamics, the subsequent evolution over time of the bioimpedance measured at the BIS' terminals, and the experimental validation of the decoupled model.

REFERENCES

- [1] C. Cobelli, E. Renard, and B. Kovatchev, "Artificial pancreas: past, present, future," *Diabetes*, vol. 60, no. 11, pp. 2672–2682, 2011.
- [2] R. J. Young, W. J. Hannan, B. M. Frier, J. M. Steel, and L. J. Duncan, "Diabetic lipohypertrophy delays insulin absorption," *Diabetes Care*, vol. 7, no. 5, pp. 479–480, 1984.
- [3] P. Arpaia, U. Cesaro, M. Frosolone, N. Moccaldi, and M. Tagliatela, "A micro-bioimpedance meter for monitoring insulin bioavailability in personalized diabetes therapy," *Scientific Reports*, vol. 10, no. 1, pp. 1–11, 2020.
- [4] G. Annuzzi, P. Arpaia, U. Cesaro, O. Cuomo, M. Frosolone, S. Grassini, N. Moccaldi, and I. Sannino, "A customized bioimpedance meter for monitoring insulin bioavailability," in *2020 IEEE International Instrumentation and Measurement Technology Conference (I2MTC)*. IEEE, 2020, pp. 1–5.
- [5] P. Arpaia, F. Crauso, S. Grassini, S. Minucci, N. Moccaldi, and I. Sannino, "Preliminary experimental identification of a fem human knee model," in *2020 IEEE International Symposium on Medical Measurements and Applications (MeMeA)*. IEEE, 2020, pp. 1–6.
- [6] R. S. Poudel, S. Shrestha, R. M. Piryani, B. Basyal, K. Kaucha, and S. Adhikari, "Assessment of insulin injection practice among diabetes patients in a tertiary healthcare centre in nepal: a preliminary study," *Journal of diabetes research*, vol. 2017, 2017.
- [7] C. Flynn, "The design and validation of a multi-layer model of human skin," *PhD Thesis*, 2007.
- [8] A. Dyachenko, M. Veremyeva, and E. Fomina, "Elasticity and viscosity of surface tissues of the human chest wall," *Russian Journal of Biomechanics*, vol. 21, pp. 164–174, 01 2017.
- [9] R. Panchal, L. Horton, P. Poozesh, J. Baqersad, and M. Nasiriavanaki, "Vibration analysis of healthy skin: toward a noninvasive skin diagnosis methodology," *Journal of biomedical optics*, vol. 24, no. 1, p. 015001, 2019.
- [10] M. Halabian, B. Beigzadeh, A. Karimi, H. A. Shirazi, and M. H. Shaali, "A combination of experimental and finite element analyses of needle–tissue interaction to compute the stresses and deformations during injection at different angles," *Journal of clinical monitoring and computing*, vol. 30, no. 6, pp. 965–975, 2016.
- [11] A. Samani, J. Zubovits, and D. Plewes, "Elastic moduli of normal and pathological human breast tissues: an inversion-technique-based investigation of 169 samples," *Physics in medicine & biology*, vol. 52, no. 6, p. 1565, 2007.
- [12] K. H. Sim, M. S. Hwang, S. Y. Kim, H. M. Lee, J. Y. Chang, and M. K. Lee, "The appropriateness of the length of insulin needles based on determination of skin and subcutaneous fat thickness in the abdomen and upper arm in patients with type 2 diabetes," *Diabetes & metabolism journal*, vol. 38, no. 2, p. 120, 2014.
- [13] D. Lo Presti, C. Ingegnosi, and K. Strauss, "Skin and subcutaneous thickness at injecting sites in children with diabetes: ultrasound findings and recommendations for giving injection," *Pediatric diabetes*, vol. 13, no. 7, pp. 525–533, 2012.
- [14] M. A. Gibney, C. H. Arce, K. J. Byron, and L. J. Hirsch, "Skin and subcutaneous adipose layer thickness in adults with diabetes at sites used for insulin injections: implications for needle length recommendations," *Current medical research and opinion*, vol. 26, no. 6, pp. 1519–1530, 2010.
- [15] G. Rankin, M. Stokes, and D. J. Newham, "Abdominal muscle size and symmetry in normal subjects," *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine*, vol. 34, no. 3, pp. 320–326, 2006.
- [16] A. Chawla, S. Mukherjee, and B. Karthikeyan, "Mechanical properties of soft tissues in the human chest, abdomen and upper extremities," *Institution of Engineers, J. Mechanical Engineering*, 2006.
- [17] F. Fidanza, A. Keys, and J. T. Anderson, "Density of body fat in man and other mammals," *Journal of Applied Physiology*, vol. 6, no. 4, pp. 252–256, 1953.
- [18] S. R. Ward and R. L. Lieber, "Density and hydration of fresh and fixed human skeletal muscle," *Journal of biomechanics*, vol. 38, no. 11, pp. 2317–2320, 2005.