ECRONICON OPEN ACCESS

EC PROTEOMICS AND BIOINFORMATICS
Editorial

Expansion of Advanced Computational Methods in Clinical Medicine: Body Surface Area Estimation for Drug Development

Grzegorz Redlarski*

Department of Mechatronics and High Voltage Engineering, Gdansk University of Technology, Gdansk, Poland

***Corresponding Author**: Grzegorz Redlarski, Department of Mechatronics and High Voltage Engineering, Gdansk University of Technology, Gdansk, Poland.

Received: October 25, 2017; **Published:** November 03, 2017

The current state of the art shows that the development of biological and computational sciences constantly intertwine. This is especially evident for the last years where progress of medicinal arts is based on current technology and understanding of human development. The occurring synergy provides more satisfying results than using the fields separately. Therefore, combining bioinformatics and proteomics will set the trends for future biological sciences.

One of the most notable examples of this process is inclusion of advanced modelling and machine learning methods in the development of drugs acting at the cellular level, e.g. chemotherapy drugs. However, there are fields where the development is based not only on analysing chemical processes or human genome, but also on the variability of human physique. An example of such a process is establishing medical procedures based on the human body surface area.

Body surface area (BSA), the measured or calculated surface area of a human body, is one of the major parameters used in medicine and physiology. Because of being unaffected by abnormal adipose mass, BSA is considered as a better indicator of metabolic mass than the body weight or body mass index. BSA is used as a basis for deciding the course of treatment in a number of medical fields, such as oncology, transplantology. BSA is an established parameter for the calculation of chemotherapy drugs dosage [1,2], [3,4], treatment of chronic hepatitis B [5], treatment of burns [6], or for establishing a dosing regimen for antimicrobials [7].

The scientific community points out several concerns related to the use of BSA in determining medications dosage or of its importance in indexing hemodynamic parameters [8-10]. Most of the concerns raised are due to the inaccuracy of methods used in obtaining BSA, especially for the extremes of human physique. Most importantly, relying on an erroneous value of BSA often leads to serious consequences, with under dosing of BSA-based chemotherapy doses, accounting for up to 30% of patients, being particularly adverse [11]. However, these weaknesses lose their importance given the current trends towards personalising the medical care and the usage of advanced computational methods for a precise evaluation of anthropometric parameters.

Based on the analysis of popular BSA formulae alone, one can see ambiguity concerning their effect [12]. Irinotecan, a known drug used for the treatment of cancer, can be administered (often in combination with cisplatin) as a 90-minutes continuous intravenous infusion at a dose level between 175 and 350 mg/m^2 [13]. For an extreme case of a very severely obese average height male adult (weight: 350 kg; height: 175 cm) the maximum irinotecan dose spans from 1,128.05 to 1,888.25 mg. The difference is higher that the recommended average fixed dose for irinotecan treatment. A less extreme example shows significant differences as well. For an average weight and height male adult (weight: 80 kg; height: 180 cm) the maximum irinotecan dose spans from 668.85 to 793.01 mg.

Therefore, the exact BSA calculation is one of the most important issues in the processes that support the effectiveness of the treatment of numerous diseases, primarily those that, if untreated or treated incorrectly, lead to the death of patients. The currently used formulae for the determination of the BSA, including the latest ones, not only do not allow for the precise determination of the body surface area but also provide no information concerning which one, in relation to the individual variability of patients, leads to the most accurate results.

One of the potential solutions to this problem is redefinition of the BSA model that is used to this day, i.e. replacement of simple power models, which are based only on weight and height of a patient, with models that take into account more anthropometric parameters. We can consider power models of the form $s(x)=a_0 \times x_1^{a_1} \cdots x_k^{a_k}$, using various number of k anthropometric variables x_i and their coefficients a_i. A fundamental issue is appropriate selection of the anthropometric parameters to be utilised in the model. These parameters can be selected by interleaving model identification and adding parameter as follows. At the k-th iteration of the procedure, all parameters are added (one at a time) and the model is extracted. Statistical analysis of the model errors can be used to find the parameter that is the most beneficial in terms of improving the predictive power of the model. The procedure continues by adding subsequent anthropometric parameters. At each stage of the model development process, cross-validation should be used to ensure that model generalisation is not degraded due to potentially too large number of degrees of freedom.

It is clear that medicine needs the inclusion of numerous mathematical methods, e.g. advanced modelling, optimisation or machine learning techniques, even on a macro scale. Methods used in bioinformatics provide ways to understand specifics of human development and to apply this knowledge to improve the quality of medical treatment. In the upcoming age of personalised medicine those methods should be constantly expanding and new ways to apply them researched.

Bibliography

1. Kouno T., *et al*. "Standardization of the Body Surface Area (BSA) Formula to Calculate the Dose of Anticancer Agents in Japan". *Japanese Journal of Clinical Oncology* 33.6 (2003): 309-313.

2. Gerina-Berzina A., *et al*. "Anthropometric measurements of the body composition of cancer patients determine the precise role of the body surface area and the calculation of the dose of chemotherapy". *Paper on Anthropology* 21 (2012): 56-71.

3. Baker SD., *et al*. "Role of Body Surface Area in Dosing of Investigational Anticancer Agents in Adults, 1991-2001". *Journal of the National Cancer Institute* 94.24 (2002): 1883-1888.

4. Sacco JJ., *et al*. "The Average Body Surface Area of Adult Cancer Patients in the UK: A Multicentre Retrospective Study". *PLoS One* 5 (2010): e8933.

5. Nakamuta M., *et al*. "Relationship between body surface area and ALT normalization after long-term lamivudine treatment". *World Journal of Gastroenterology* 11.44 (2005): 6948-6953.

6. Reading BD and Freeman B. "Simple formula for the surface area of the body and a simple model for anthropometry". *Clinical Anatomy* 18.2 (2005): 126-130.

7. Pai MP. "Drug Dosing Based on Weight and Body Surface Area: Mathematical Assumptions and Limitations in Obese Adults". *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy* 32.9 (2012): 856-868.

8. Beumer JH., *et al*. "Body-Surface Area-Based Chemotherapy Dosing: Appropriate in the 21st Century?" *Journal of Clinical Oncology* 30.31 (2012): 3896-3897.

9. Faisal W., *et al*. "Not All Body Surface Area Formulas Are the Same, but Does It Matter?" *Journal of Global Oncology* 2.6 (2016): 436-437.

10. Adler AC., *et al*. "Misleading indexed hemodynamic parameters: the clinical importance of discordant BMI and BSA at extremes of weight". *Critical Care* 16.6 (2012): 471.

11. Gurney H. "How to calculate the dose of chemotherapy". *British Journal of Cancer* 86.8 (2002): 1297-1302.

12. Redlarski G., *et al*. "Body surface area formulae: an alarming ambiguity". *Scientific Reports* 6 (2016): 27966.

13. Chatelut E., *et al*. "Dose banding as an alternative to body surface area-based dosing of chemotherapeutic agents". *British Journal of Cancer* 107.7 (2012): 1100-1106.

Volume 2 Issue 2 November 2017