InGene 2.0: a step towards the ICT-based diagnosis and monitoring of neuromuscular disorders

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***Abstract*— In the universe of neuromuscular disorders (NMD), a peculiar feature is represented by the amount of rare NMDs, singularly accounting for a relatively scarce number of individuals, but representing huge records when taken together. The main clinical problem with rare NMDs deals with their correct diagnosis, which is difficult due to their similar phenotypes, and with the correct choice towards their treatment, which is key to successfully improve the patients' health status. In this regard, it is essential to promote the collection of data in a structured, user-friendly manner for clinicians, at the same time keeping it usable for data scientists and researchers in the field. Information and Communication Technologies (ICT) are fundamental in this regard, making it possible to achieve this ambitious goal. The InGene 2.0 project is therefore aimed at setting up a safe, secure, GDPR-compliant, ICT-based software platform to collect multimodal, multiparametric data in this regard, entering the market of NMDs with useful tools for both the clinicians and data scientists.**

Keywords—healthcare, ICT, neuromuscular disorders, security, software.

I. INTRODUCTION

Rare neuromuscular diseases (NMDs) represent a broad group of conditions with various etiology, severity and clinical characteristics, presenting a significant heterogeneity when it comes to the modality of treatment, leading to notable unbalance in their successful/unsuccessful treatment. The only manner to treat the disease in a proper way, maximizing the clinical outcome and the health status of the patients, is necessarily related to the knowledge of the complex relationships between the genotype (i.e., the genetic background) and the clinical phenotype (i.e., the clinical characteristics) of such individuals or groups [1]. To unravel such complex relationships, it is necessary to adopt a multimodal, multiparametric approach that should ultimately apply the technological knowledge to a very important clinical question [2].

Under such considerations, the project InGene 2.0 was conceived and developed, starting from the prior knowledge achieved during a previous project action, named InGene. The project actually involves two technological partners (the National Research Council of Italy and the Sant'Anna School of Advanced Studies) and four clinical counterparts (IRCCS Stella Maris Foundation, Pisa University Hospital, Florence University Hospital and Siena University Hospital), the four most important clinical centers for the treatment of NMDs in the Italian region of Tuscany.

InGene 2.0 has the ambitious aim to merge together the experience and the expertise of the most important clinicians in this domain with the ability and technological knowledge of engineers, computer scientists, software developers and data scientists, to create an ICT-based environment to optimize the diagnosis and treatment of patients with rare NMDs.

The present document includes a brief overview of the InGene 2.0 ICT framework with its modules, ending with a wrap-up of what is presented in the report, overall.

II. THE INGENE 2.0 FRAMEWORK

A. Premises

In the modern era, data is considered "the new gold", as its ownership, access and related knowledge would drive to unprecedented advantage over the competitors in nearly all fields of investigation. In such a perspective, also the medical universe, historically quite conservative in their approach, have started a massive use of technology during everyday practice, with the role played by Electronic Health Records or similar tools being always more important in medicine [3], even more after the technological drift of the practice due to the COVID-19 pandemic [4, 5]. The application of such approaches in medicine have manifold importance, including the making data available for consultation, the possibility allowed to set up personalized treatments and protocols and the boost towards epidemiological studies making use of large-scale data to be successfully carried out [6, 7].

To do so, it is mandatory to have large amounts of data, with a certain structure, and being multimodal and multiparametric, in order to create a full perspective on a single patient (or a group of individuals) and their related condition [8], allowing the physician to carry out related clinical investigations, and the data scientist to work with the data collected.

B. Overall presentation

As said, InGene 2.0 involves a consortium made up of clinicians and technologists (computer scientists, engineers and data scientists), whose core product is represented by a modular platform, named "Health360", shaping up a patient's (or an individual's) health on a 360° perspective. Health360 integrates several external sources purposely developed for the InGene project with an excellent scalability, flexibility, and user-friendliness. It is therefore usable in nearly any framework within clinics and research fields, making the solution ideal for research projects, and eventually for small clinical centers. Its modules include: i) personal data, ii) anamnesis, iii) physiotherapy assessments, iv) neuromuscular evaluation, v) genetics, vi) muscular Magnetic Resonance Imaging (mMRI), vii) data analysis.

C. Architecture

Health360 was developed under the ReST, API-first principles, under a modular, web-based structure, capable of operating with mixed infrastructure. The platform is developed under the Software-as-a-Service (SaaS) principles, managing the tests through digital devices and enabling data collection, scores and session details directly on the Cloud.

Health360 is conceived on a two-level architecture, with a front-end implementing a web-based User Interface (UI), aimed to aggregate data, and a modular, distributed back-end, each module of which is in charge of a data subset through an own database. The core back-end in particular is able to adapt to the specific framework and integrates new modules developed with existing systems, as it is based on the NoSQL MongoDB database, whose configuration files, in YAML, are used to define the data model [2, 9].

D. Modules

Personal data are contained in a separate database within the core back-end. A mechanism of roles and privileges allows entering the personal information of a subset of patients only to clinicians of a given structure (e.g., the clinicians of an "A" institution can have access only to the patients of the "A" institution, unless otherwise stated with the approval of the other members of the consortium and with the authorization of the patient involved) [9].

Anamnestic information is managed in a dedicated module, where the patient is fully characterized in terms of their clinical features and therapies administered.

Physiotherapy assessment is performed through the "PhysioTest" module, featuring user interfaces dedicated to the Performance of Upper Limb (PUL), Six-Minute Walk Test (6MWT), Motor Function Measure (MFM), and North Star Ambulatory Assessment (NSAA), typical evaluation tools for NMDs. Among them, the interface for the 6MWT (Figure 1) is probably the most advanced one, allowing the clinician to monitor the overall assessment in terms of distance covered, events, including falls, breaks and so forth, commonly happening during the test administration [10].

Figure 1. The 6MWT user interface.

Neuromuscular assessment is performed through the "NeuroExam" module [11], allowing the clinician to include the Medical Research Council (MRC) Scale for each muscular district and featuring the opportunity to characterize muscular impairment through the inclusion of a Human Phenotype Ontology (HPO) code, a biomedical ontology allowing the user to define, in a coded manner, a patient's phenotype. This perspective is particularly useful to the data scientists to retrieve data included by the clinicians already coded, therefore not affected by subjectivity normally dealing with data entry.

Genetics is characterized by the module "GenoStore", storing the patient's genotype, making it available for subsequent analysis, also by the means of Machine Learning/Deep Learning.

Muscular MRI is faced in the module "MRIndex". The module integrates muscular MRI and, by applying a segmentation algorithm, it provides a score for the subcutaneous fat infiltration within the muscular tissue, as an indicator of the muscular involvement within the clinical condition [12].

The module "InGene" features data analysis. It includes Machine Learning models to highlight clusters of individuals based on the genotype–phenotype correlations. It represents a useful tool in clinical research, supporting diagnostic and care plan personalization.

III. CONCLUSIONS

The present document briefly outlines the idea and the main characteristics of the InGene 2.0 framework, conceived as an ICT-based tool for data collection and analysis. The framework is currently used in the InGene 2.0 project in the domain of rare NMDs but, thanks to its scalability and modularity, can be used in nearly any field of biomedical research and beyond that, representing a possible alternative to the Electronic Health Records developed by main international players, which in turn offer high reliability, however with poor customization and considerable costs, making them scarcely affordable for small clinical centers or for inclusion in research projects. Overall, the platform can be provided as a modular tool, or eventually its modules can

be used as a standalone solution. For example, the PhysioTest module, featuring the functionality for the execution of the 6MWT, is actually under development as a multi-platform mobile App, that will be distributed through App Store and Google Play Store for iOS and Android OS, respectively, on a "freemium" principle (i.e., basic functionalities can be distributed to everyone for free, while more advanced ones, including the possibility to store own data, can be distributed under the payment of a one-time or periodical subscription). In the meantime, the framework will be kept updated and new functionalities will be developed, upon the needs of clinicians and researchers eventually interested for their centers or research projects.

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