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The Technology Transfer of Machine Learning Solutions in Healthcare 4.0: The Case of Neurodegenerative Diseases

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ABSTRACT
Along with the advancement of Machine Learning (ML) research, there is an increasing need for supporting the exploitation of ML-based solutions in a wide range of application fields of Industry 4.0. Healthcare 4.0 is one of the liveliest and interesting fields of Industry 4.0, due to the huge economic and social value of this domain. Therefore, nowadays the adoption of Technology Transfer strategies for supporting the enhancement of ML-solutions for Health 4.0 is a very relevant topic. This paper focuses some aspects related to Technology Transfer (TT) in the field of Healthcare 4.0. Artificial intelligence and machine learning are promising tools for the study of neurodegenerative diseases, which today represent a growing problem worldwide as millions of people are affected and life expectancy is increasing. The paper discusses about a pipeline implemented for neurodegenerative diseases using AI that should be valorized through a variety of complex channels in order to create value for the society and the population, by offering a new service in the field of Healthcare 4.0 based on the prediction of the most important and impactful neurodegenerative diseases, such as Alzheimer and Parkinson diseases.
Keywords: *Machine Learning, Healthcare 4.0, Industry 4.0, Big Data, Magnetic Resonance Imaging*

I. INTRODUCTION
The manufacturing and service worlds are undergoing a distinct transformation thanks to the key enabling information and communication technologies of Industry 4.0. This is particularly the case of the health domain, where the Internet of Things, Cloud and Fog Computing, and Big Data technologies are radically changing eHealth and its 'world' [1].
Given the rapid technological evolution, together with government efforts and by virtue of the fact that Healthcare is certainly one of the most attractive areas for the application of IoT [2], it is possible to say that the healthcare sector is already facing the impact of Industry 4.0, moving from eHealth to Healthcare 4.0 (from now on also "HC4.0") [1]. The final aim is the remodeling of modern healthcare, with promising technological, economic and social prospects [3].
The inherent multidisciplinary nature of HC4.0 makes it increasingly difficult for operators and stakeholders in this field to keep up with technological progress.
Therefore, precisely in HC4.0 area, the knowledge/technology transfer and the creation of networks are especially important in order to develop applied research and make it quickly "usable" innovation according to continuous open innovation schemes. In particular, the involvement of all the actors in the innovation chain, which in the health sector becomes even more important, represents the emblem of the quadruple helix model in which the citizen with his needs becomes the protagonist, together with the public, private and academic sectors, in the development of health, social and other related services.The specific addressed challenge is: the P4 Medicine [4], i.e. predictive, preventive, personalized and participatory, thanks to these I4.0 new technologies [1].

Many EU initiatives tend to support national protection of human health, to decrease inequalities in health status and encourage social inclusion [5].
Moreover, regarding the 17 SDGs of Agenda 2030, health is present in SDG 3 “Ensure healthy lives and promote well-being for all at all ages” but the truth is that health is a goal that crosses many other SDG targets [6,7].
Today, people are living longer and therefore a large percentage of the world's population is elderly. The WHO states that by 2050, the global population of people over the age of 60 will double and the health sector will be greatly impacted by this demographic change [8]. In this context, the initiative called "United Nations Decade of Healthy Aging (2021-2030)" represents an important occasion through which governments, civil society, international agencies, professionals, academia, media and the private sector begin to work together to improve the lives of older people, their families and the communities in which they live, ensure governments towards the improvement and possibilities for good health at all stages of life, rising the social and economic participation of older adults in society and thus lowering health care costs [9].
In this context, the role of Digital Health to support the achievement of this Sustainable Development Goal becomes more and more important.
Regarding neurodegenerative diseases, in recent years the strategic role that machine learning and deep learning approaches can play in accurately predicting age using brain magnetic resonance imaging (MRI) has been verified, in order to define novel biomarkers of brain pathologies [10, 11].
Starting from the important results emerged, this article addresses the issue of exploitation of research results both in terms of use of existing computing infrastructures and technology transfer activities. The figure 1 represents the different parts of the article:

Figure 1: Paper organization

Section II presents the works concerning brain age prediction exploiting deep learning, applied to neurodegenerative diseases. The main results achieved for age prediction, based on a complex network model, are also illustrated. Section III reports related works anc contributions while Section VI presents the Bari ReCaS DataCenter, the computational infrastructure of the Bari University Aldo Moro and the Italian Institute of Nuclear Physics, that provides the computational and storage resources for the research activities. In Section V some relevant strategies for the valorization of the research results and their transfer will be presented and discussed. The conclusion of the paper is summarized in Section VI.

II. DEEP LEARNING APPROACHES FOR NEURODEGENERATIVE DISEASES

Machine learning and natural language processing are the most commonly used classes of artificial intelligence in healthcare settings as they allow robust querying of datasets in order to identify previously unknown patterns and associations among several data features.
In the last few years great debate has opened in the scientific community about the application of machine learning algorithms to medicine.
In particular, neurodegenerative disease (Alzheimer's disease (AD), Parkinson's disease (PD), and motor neuron disease (MND)) is a research topic of great relevance since the number of cases is enormously increasing in development countries and even more in those emerging countries, where life expectancy is rapidly growing. Therefore, it is not surprising the scientific community is devoting extraordinary efforts to face the issue from several research perspectives.
Machine learning, through the efficient use of data, is able to give intuition into the mechanisms underlying diseases in order to make early diagnosis, prognosis, patient stratification and development of new therapies.
One of the most interesting approaches is related to the application of machine learning and deep learning to Magnetic Resonance Imaging (MRI) [10, 11]. Brain aging is, in fact, a lifelong process which continuously affects the structure, the organization and the functionality of our brain. Accordingly, the design and development of accurate models capturing aging processes and the possibility to detect early signs of anomalous patterns (i.e early markers of disease) becomes of paramount importance. For example, measuring the so-called “brain gap” [12, 13], how brain age differs from the actual one, can support the

detection of early signs of disease and novel markers.

Finally, machine learning approaches yield a significant advance especially when providing an interpretable assessment of the role played by each feature during the learning phase. Morphological changes of the brain have been widely associated to several diseases, nevertheless machine learning can provide further insight as it is able to “explain” how these changes interact and how they can reveal the onset of pathological conditions. In particular, in recent years what is called “explainable machine learning” has seen a widespread diffusion, so that it is no longer important to accurately predict (only) the disease onset, but it is (also) important to provide along with the machine learning framework a comprehensive overview of the role played by each feature and a robust understanding, both from clinical and algorithmic perspectives, of the interaction of such features with the disease [14].

III. RELATED WORKS AND CONTRIBUTIONS

With respect to neurodegenerative diseases, scientists, physicians and patients, thanks to machine learning, are succeeding in address some important challenges in the development of early diagnostic tools and effective treatments for these diseases, characterized by intricate molecular processes underlying neuronal degeneration and the diversity of the patient population [15].

in the last few years, machine learning and deep learning techniques have been suitably used to correctly predict the early onset of neurodegenerative diseases using brain MRI data [16].

In particular, many studies have investigated a novel brain connectivity [17, 18, 19] and the possibility to exploit such a framework to assess neurodegeneration and therefore reveal the early signs of pathological processes. However, the amount of information provided by such connectivity is so huge that it cannot fully exploited without the use of proper artificial intelligence strategies. In general, the adoption of machine learning and deep learning strategies can be used in these cases to manage the informative content provided by connectivity. As a consequence, the use and the role played by modern computer facilities has gained more and more relevance.

Alzheimer's disease has also been studied in relation to specific gene communities, i.e., groups of interacting genes that have been found to be relevant in the development of AD. The study combined the analysis of the co-expression network with the study of Shannon entropy of betweenness [20].

Similar studies have been conducted on Parkinson's disease, the second major disease after Alzheimer's dementia. Genetic research has allowed for demonstration of the complexity and multisystemicity of PD; therefore, the use of a complex network approach was most appropriate to capture the molecular complexity of this disease. The information entropy of the betweenness gene co-expression matrix was maximized to have a gene adjacency matrix; then a fast greedy algorithm was used to identify communities and subsequently a principal component analysis was performed on the identified gene communities with the goal of separating between PD patients and healthy controls using a random forest classifier [21].

VI. ReCaS DATACENTER

The ReCaS datacenter, the computational infrastructure of the University of Bari Aldo Moro and the Italian Institute of Nuclear Physics (INFN), completed in 2015, provides the computational and data storage resources necessary for the research activities illustrated in the previous section. The datacenter, created as part of the ReCaS project (http://www.pon-recas.it), funded by the Italian Ministry of Education, University and Research, had as objective the strengthening of the pre-existing IT infrastructures of Southern Italy (located in Catania, Cosenza, Naples and Bari) to create one of the largest Italian supercomputers publicly available.

The ReCaS datacenter offers 128 servers and today is able to offer an open source software platform whose objectives are (i) the empowerment and federation of the computing resources of the Middle Medium (in particular the convergence regions, according to community paradigms), (ii) the implementation of innovative cloud computing for eGovernment services, with a focus on Public Administration services and (iii) the creation of a distributed infrastructure based on both grid and cloud paradigms.

The ReCaS Farm today supports several life science communities and projects (Medical Phisycs, Project Elixir, LifeWatch, etc.) ReCaS is designed to manage and automate pools of computing resources and can work with widely available virtualization technologies, as well as bare metal and high performance computing (HPC) configurations [22].

V. VALORIZATION OF RESEARCH RESULTS

Knowledge transfer (KT) or technology transfer (TT) is an activity in which universities today have to necessarily engage and is also an essential source of innovation as well as a way to disseminate research results [23].

Nowadays, public and private research bodies are the seed capital for the creation of know-how and technologies that foster economic and social development [24].

KT or research results valorization promotes the dissemination and use of new technologies developed at the research organizations with the aim to increase the impact, economic and/or social, of the research for all the stakeholders and partners involved [25,26].

These issues are particularly true in the healthcare domain: the exploitation and transfer of excellent research results would empower researchers and practitioners to devise new solutions and products that can renovate some established healthcare practices or even be useful in addressing and mitigating long-standing healthcare problems.

When dealing with data-intensive applications, co-design approaches involving multiple stakeholders must be used to guide and solve service performance [1]

In this framework, the research results about the pipeline implemented for neurodegenerative diseases using AI, illustrated in Section II, could be valorized through a variety of complex channels including research conversion to IP and its patenting and licensing activity, creation of academic start-ups or externally-formed entrepreneurial entities, collaborative research with private sector firms or contract research consulting, etc. Figure 2 describes the flow of knowledge and technologies towards the creation of impact for a multitude of actors:

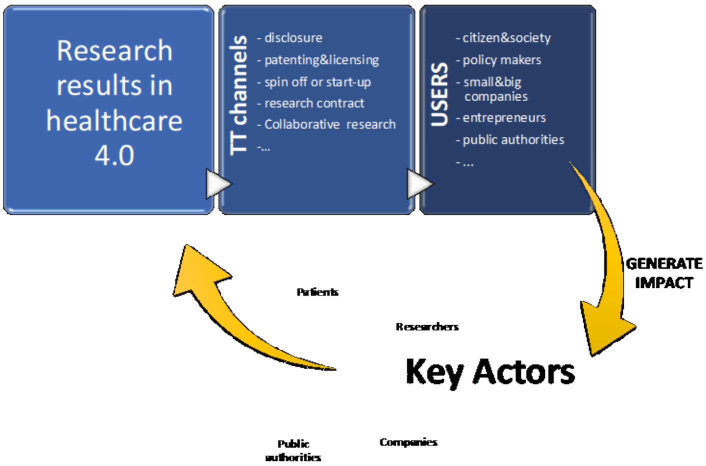

Figure 2: The flow of knowledge and technologies towards the creation of impact

Similar to the world's leading universities that are considered best practices in terms of valorization of research, technology development projects, entrepreneurial activities, collaborations with industry partners, and multidisciplinary technology innovations with a commercial focus (MIT, Stanford University, California Institute of Technology, Oxford University, Imperial College London etc), the authors, in collaboration with the Technology Transfer Office of their university, are implementing the most profitable strategy to create value for the society and the population, by offering a new service in the field of Healthcare 4.0 based on the prediction of the most important and impactful neurodegenerative diseases, such as Alzheimer and Parkinson diseases.

VI. CONCLUSION

In the context of Healthcare 4.0, TT is considered an essential mechanism for the dissemination of research results and a valuable source of innovation. In this paper, starting from the specific TT strategy used for the enhancement of new AI-based solutions for neurodegenerative disease analysis, some considerations on the most effective aspects of TT approaches for Healthcare 4.0 are discussed.

AI and Machine Learning have a unique opportunity to strongly triage populations, diagnose and offer treatment plans with the most up-to-date health data. The academic AI community, together with policy makers, entrepreneurs, citizens, patients and clinicians, have to co-design new solutions and/or improve solutions in heathcare domain.

According to the strategies of the world's leading universities, some valuable options that could be considered for supporting the enhancement of the new solutions are related to patenting and licensing activity, creation of academic start-ups or externally formed entrepreneurial entities, research consulting.

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