# RETRAINER project: perspectives and lesson learnt on clinical trial in rehabilitation robotics to foster industrial exploitation

A. Pedrocchi, IEEE Senior Member and Maria Bulgheroni

***Abstract*—The RETRAINER (Reaching and grasping Training based on Robotic hybrid AssIstance for Neurological patients: End users Real life evaluation) project is an Innovation Action funded by the European Commission under the H2020 research framework programme. The project aims at a full technology transfer of the results of a previous FP7 project, MUNDUS, aimed at the development of upper limb assistive technologies, to a robotic system for upper limb and hand rehabilitation to be tested in a wide clinical trial with stroke survivors in two clinical centers. The final result of the project is the design of a validated system suitable to address the rehabilitation market. Along this project's path, several issues affecting both development and validation have been pointed out and are here summarized to serve as lesson learnt for prospective projects and challenges.**

## I. Introduction

Rehabilitation robotics plays a key role in reducing the personal and social burden of disability and it may represent an important contribution in coping with chronic disabilities. Its main advantages are: 1) intense controlled training with reduced supervision by clinical operators, 2) repetitive exercises management through gaming and immersive training to foster patient's involvement and engagement, 3) exercises execution in safe conditions, even in case of severe disability, 4) continuous monitoring of performances, 5) therapy personalization, scaling the required effort on current performances, 6) proper reward delivery [1]. All these aspects are extremely promising and represent a huge change with respect to conventional therapy, even though the supervision of the therapist encouraging and stimulating the patient remains a key point.

The diffusion of robotic devices in rehabilitation is however still minimal, partly because of initial costs, partly because of learning difficulties in the use of the systems and partly because of limited support of scientific evidence. The adoption of randomized controlled trials to gather proper scientific evidence of new treatments with respect to conventional therapy is not yet widely spread in rehabilitation. One of the major limitations is the personalization of therapies, that affects the comparability of treatments and patients. There is a clear need to improve the current limited evidence-based approach, to assess and promote the diffusion of robots in rehabilitation practice. Further, the relationship between functional rehabilitation and brain plasticity is still under investigation [2,3,4].

RETRAINER [5] is an Innovation Action funded by the European Commission (EC) under the H2020 research framework programme aimed at the technology transfer of the results of a previous EC funded FP7 project, MUNDUS [6], dealing with the development of upper limb assistive technologies, to upper limb and hand rehabilitation to be tested in a wide clinical trial with stroke survivors in two clinical centers. The project is now close to its end and it is time for summarizing main achievements and lessons learnt.

## II. What does "Moving a research prototype outside of the lab" mean?

Several issues need to be taken into account moving a system from research to clinics. The main ones are:

*Usability*: one of the major assets, often highly neglected by researchers, is usability in its multiple facets: easiness of donning and doffing, time to set up, time for calibration, clarity of instructions, but also user interface both for the operator and the patient. Definition of usability requirements must be accomplished in strict collaboration among patients, therapists, clinicians and technicians. User centered design is still encountering difficulties in entering robotic research, often still heavily technically driven, not equally involving all the actors of the entire value chain.

*Reproducibility*: Pre-series prototypes are to be used in the controlled trials with as many patients as those required to get scientific evidence of effectiveness. A suitable number of devices has to be properly produced and spare parts have to be promptly available. A parallel patients' recruitment using multiple devices and possibly multiple clinics to compensate the potential inter-operator biases is required.

*Pilot tests:* It is mandatory to move the device to clinical sites only after a thorough testing by system engineers. A continuous iterative process involving designers and system integrators is necessary not only to fix bugs, but to improve usability and reliability of the system before the transfer to clinics. Otherwise, with a direct transfer from developers to clinics, clinicians are frustrated by the burden of these preliminary tests and their engagement immediately fails.

*Full ethical clearance:* moving a new prototype to clinics for testing with patients implies an ethical approval by relevant local authorities. When the CE mark is missing, as in

This work was supported by the RETRAINER project (H2020 Research and Innovation Program, grant agreement No 644721).

M.B. is with Ab.Acus srl. Milano, Italy (M.B. is the corresponding author to provide e-mail: mariabulgheroni@ab-acus.com).

A.P. is with NEARLAB, Department of Electronics, Information and Bioengineering, Politecnico di Milano, Italy.

the case of a prototype, existing directives on medical devices require specific steps to ensure safety and performance. Devoted competences are required from early design phases to assure full compliance with the regulations.

*Therapists involvement:* The success of a clinical trial strongly bases on the conduction of the trials by clinical operators, not technicians. The relation between the therapist and the patient is different in conventional and robotic therapy, but it still plays an essential role. Therapists need to be committed in using the device and in supporting the patients during the exercises. The best way to assure positive commitment of the therapists is to make them completely confident in using the device. A strong and effortful training is essential as well as a continuous remote support, but engineers must not to be physically on-site.

*Faults managements:* The efficiency of the technical support in solving possible failures is crucial to sustain the engagement of clinicians, to compress the time of the trials and to avoid losing patients across the treatment.

## III. What are the main aspects of a proper clinical trial of rehabilitation treatments based on robots?

To make effective a clinical trial addressing robotic rehabilitation, given the fulfillment of the standard rules, such as randomization, lack of bias, proper sample sizes, etc., two additional aspects need to be properly considered:

*Clear design:* the design of the trial has always to choose the happy medium between a clear definition of the target population, which is the most promising one in getting the best statistical significance, and a larger view to assure proper recruitment and relevant potential market size.

*Trial homogeneity:* the compromise between comparability of the provided training and the essential tailoring of the treatment to the single user is a key point. Personalizing the treatments is one of the most important features of rehabilitation and the adoption of robotic devices opens a potentially huge possibility of adaptation to the single user. However, some common clear rules of the treatment need to be set equally for all patients and centers, in order to assure the comparability of outcomes.

## IV. What are the most important elements to evaluate the trial?

The effectiveness of the trial has to be assessed both by standardized clinical outcome measures as well as by indicators derived by the sensors embedded in the system.

*Outcome measures* need to be very well acknowledged and clearly focused on the primary and secondary expected outcome of the treatment as well as patients' quality of life.

On the other side, it is also important to investigate the use of the robotic device by each patient. One of the advantages of using robots in rehabilitation is that there are plenty of *sensors monitoring the performance during each session*. Unfortunately, most of these data are not yet exploited, but, at least in controlled clinical trials, the way the single user works with the device as well as the changes across sessions is a key information to understand the results, improve the personalization of treatment and learn more on the possible benefits and limitations of the device.

## V. And the industrial exploitation?

Once moved out of a research lab and validated in a clinical trial, a system is expected to be ready for industrial exploitation, but several aspects need to be addressed in order to prepare the process:

*The gap between research and market*: an Innovation Action is expected to run activities leading to innovation through development of new solutions rather than research. However, even when a project is building on already existing research prototypes, obsolescence of the components as well as new clinical requirements and scientific achievements have to be taken into account and, still, the prototypes used in the clinical trials are far from engineered solutions exploitable on the market or even ready for certification. Time constraints need to be clearly kept in mind and the release of a final product is not feasible in a project's time frame.

*The role of companies in research consortia:* cooperation of academies and companies is expected to lead to more industry-oriented projects. Indeed, this strongly depends on the maturity of the initial idea or prototype. Companies may play different roles: suppliers of modules, observers of the solution's potential, integrators of research results, all of them pointing out new issues to cope with. Technology transfer is not a straightforward process.

*The dissemination of the results*: scientific dissemination is only one component of a strategy aimed at the market exploitation of a project's results. Prototypes need to be made visible and demonstrations in congresses and exhibitions are also required to investigate any potential exploitation pathway.

*The property of the results*: a mandatory Consortium Agreement manages roles, rights and duties in H2020 funded projects. However, this agreement ceases at the end of the project's life. As soon as results come, existing as well as newly generated IPRs need to be carefully investigated to prepare any exploitation action. Shared agreements need to be put in place to foster future exploitation of the results. While the most suitable solution is expected to be a pre-commercial agreement with one partner planning to tackle the market (at the end of a successful project), also stand-alone modules are worth of consideration.

## References


[1] Marchal-Crespo L, Reinkensmeyer DJ. "Review of control strategies for robotic movement training after neurologic injury." *J Neuroeng Rehabil*. 2009 Jun 16;6:20

[2] Jaeger L et al. "On the Modulation of Brain Activation During Simulated Weight Bearing" in *Supine Gait-Like Stepping Brain Topogr* (2016) 29: 193

[3] Tacchino et al. EEG "Analysis During Active and Assisted Repetitive Movements: Evidence for Differences" in *Neural EngagementIEEE Trans Neural Syst Rehabil Eng*. 2017 Jun;25(6):761-771

[4] Gandolla M et al. "The Neural Correlates of Long-Term Carryover following Functional Electrical Stimulation for Stroke", *Neural Plasticity*, vol. 2016, Article ID 4192718, 13 pages, 2016

[5] Bulgheroni M et al, "Reaching and Grasping Training based on Robotic

Hybrid Assistance for Neurological Patients", 2016, TAT 2016 Proceedings, ActaPress
[6] A. Pedrocchi et al. "MUNDUS project : MUltimodal Neuroprosthesis for Daily Upper Limb Support", *J Neuroeng Rehabil*. 2013 Jul 3;10:66