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Summary of the REMPARK Project Findings: Innovative Steps

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Abstract

Considering that STAT-ON™ is the final result of some part of the research done in the REMPARK project, this chapter summarizes the contents of the book "*Parkinson's Disease Management through ICT: The REMPARK Approach*," published by River Publishers in 2017, where the research and innovation performed and achieved in this project is described.

Here, an analysis is done about the opportunity associated to the different obtained and reported results. It is explained how a decision was taken on the redesign and additional work done on a wearable sensor for the measurement and detection of movement symptoms related to Parkinson's disease.

The chapter ends with a concrete reference to the initiative for organizing the proposal of an SME Instrument (phases I and II) action project that provided the convenient framework for the development and subsequent launching to the market of a new medical device, commercialized by Sense4Care, with the name STAT-ON™.

2.1 Summary of the REMPARK Project: Objectives, Development, and Findings

It is very well known that Parkinson's disease (PD) is a progressive neurological condition with no cure and only treatments addressed to the management and mitigation of the different symptoms are available to the patients.

In order to contribute to helping patients, the REMPARK project [1] was organized as a challenging initiative with four concrete objectives:

1. The identification of the motor status in real-time conditions. This was supposed to be the identification of the associated relevant parameters and types of motor disorders, and the development of the minimum necessary system, mainly based on wearable inertial sensors and embedded intelligent algorithms.
2. The development of a system for gait improvement, when necessary, based on auditory cueing.
3. The design and implementation of a specific and adapted user interface in order to obtain feedback from the patient using a Smartphone. The application was mainly focused on the interaction with affected people for satisfactory answers to surveys, questionaries, and prompts generated by the system.
4. The specification and design of a service for the remote management of the disease. The service was planned and based on a server acting as the repository of the whole obtained ambulatory data, in combination with the Electronic Health Record of the patient and making easy the intercommunication between the professionals involved in the caring process and the patients and their relatives when required.

REMPARK was a huge and complex project, with an intensive activity developed from 2011 until 2015, the participation of 11 partners, a well-organized management process, and the involvement of medical institutions and PD patients from four different countries (Spain, Ireland, Italy, and Israel). This was a crucial point for the obtention and construction of the necessary database for the implementation of the machine learning-based algorithms, embedded in the developed sensors for the positive consecution of Objective 1 (the ambulatory evaluation of the critical motor symptoms associated with the disease).

REMPARK project, as can be seen in reference [1], obtained very good results and findings at the end of its execution (see a summary in Table 2.1). A short list of these results is the following:

- A huge and very complete database was obtained. This database was designed according to the objectives of the project and the main interest was to obtain a specific labeled collection of data for the implementation of a supervised learning process in order to get a set of intelligent algorithms to be embedded into the specified sensor prototype (see reference [1], Chapter 4).

The database contains data from 92 patients, obtained from a free activity period at patients' homes, where video recording and annotations were done according to the approved protocol by the Ethical Committees at the participating hospitals from the above-mentioned countries. This activity was covered and done during the first year of the project. At the end of this first experience, REMPARK database contained more than 30 hours of video recording and more than 140 hours of manual annotations of different motor disease symptoms (Dyskinesia, Bradykinesia, Freezing of Gait – FoG), synchronized and correlated to the corresponding tri-axial accelerometers' raw signals obtained from the movement sensor worn by the participating patients.

- A set of algorithmic developments, based on supervised learning methodology using the constructed database and able to identify the specified disease symptoms: Dyskinesia, Bradykinesia, FoG, ON and OFF state estimation, Gait parameters, and fall detection. This algorithmic set (see reference [1], Chapter 4) was designed to be embedded into the sensor prototype (see reference [1], Chapter 5).

- A sensor subsystem prototype able to embed the developed set of intelligent algorithms and to operate in an autonomous way, in order to be used for the implementation of a pilot verification activity, during the last year of the project activity.

- A very important piece for the REMPARK activity development was the patient's Smartphone. The Smartphone was used for interaction with the patients, covering a major part of the communication requirements. It is obvious that the design of an improved and well-adapted user interface was an important task (see reference [1], Chapter 6).

  Apart from other interesting functionalities, the most interesting characteristics for REMPARK purposes were the auditory cueing system controller and the medical questionnaires administration. These questionnaires were automatically sent to the patients, when necessary, after some condition detection not directly related to motor problems.

- The auditory cueing was an actuator REMPARK subsystem able to generate a rhythmic auditory stimulus when some specific condition is detected (gait disturbances, FoG, or Bradykinesia). The details and fundamentals are explained in Reference [1], in Chapter 7.

  In this case, when the condition is correctly detected by the sensor, embedding the developed algorithms, activation of the application implemented on the Smartphone is done. This application is generating

a set of rhythmic sounds (auditory cueing) that are sent to an earphone pair worn by the patient.

- A disease management system (DMS) adapted to the specific Parkinson's disease management needs and constraints. Details of this implementation can be found in reference [1], in Chapter 8, where a description of the main organization of the system and its different modules' inter-relationship is done.

  In fact, the DMS system developed for the REMPARK project was an adaptation of an already existing, at that time, generic platform in the Maccabi hospital, in Tel-Aviv (Israel) for the management of other diseases, but with many equivalent needs (storage of data, easy management of the disease, making easy and effective the inter-relationship of the involved professionals, etc.). An important part of this platform was the included Rule Engine module, where knowledge, procedures, and generation of alarms, etc., were included.

During the last year of the project, a validation pilot was organized and completely executed, with the participation of 41 volunteers. The description of the pilot and the main obtained results are presented in Chapter 9 of reference [1]. Remarkable results that must be mentioned are related to the detection of ON and OFF states, as a combination of the also detected movement symptoms. The obtained specificity was 89% and the sensitivity was 98%. The efficacy and effectiveness of the developed cueing system were also measured. Table 2.1 presents a summary of the achieved results in the project, with some annotations and comments on their usefulness for further development and the obtained degree of satisfaction.

2.2 Innovative Technology: Analysis of the Opportunity and Related Challenges

The REMPARK consortium was very happy with the obtained results and findings since the project frame was the opportunity to put in value and take profit of the available technology for more advanced and close care of Parkinson's disease, with the objective of improving the patients' quality of life. Some relevant advances, as indicated in the precedent text, were:

- A version of a wearable prototype able to measure and identify gait and related movement symptoms characterizing Parkinson's disease. Some of the related main advantages are:
  - Only one unique sensor is needed for the detection of all the collection of symptoms.

Table 2.1 Summary of the main REMPARK project results.

Results	Completeness	Satisfaction with the results	Usefulness for further development	Comments
Labeled database	100% according project specification	√√√	Good	To be used for algorithmic refinement and new learning processes
Algorithmic set for motor-related symptoms detection	100% according project specification	√√√	Good	Should be embedded in future developments
Sensor prototype	A version was generated for its use in the validation pilot	√√	Good	Obtained version arrived at RTL7, and it is able to evolve toward a competitive product
ON and OFF states identification	100% according project specification	√√√	Good	Should be embedded in future developments
Cueing system generation	Advanced state	√	Medium	Ideas should be used for future development and experience would be useful for further implementation
Disease management system – DMS	Medium state	√	To be discussed	Not implemented after the project for several reasons

  - The wearable is worn at the waist since this is the most appropriate location for correct detection of all the movement-related characteristics in a person.
  - The wearable has a large autonomy for continuous use for several days.
  - The wearable integrates advanced sensor technology, mainly based on tri-axial accelerometry for gait characteristics measurement.
  - The embedded processing capability of the wearable is designed for the complete integration of the developed set of algorithms, converting the device into a really autonomous one with a real-time and on-place processing capacity of the captured data.

- A very complete set of dedicated algorithms, based on AI and learning techniques, for the detection and identification of PD-related movement symptoms (mainly Bradykinesia, Dyskinesia, FoG, and ON/OFF states).
- A very complete system based on a platform for the storage of the captured and processed data, together with a recommender system (the DMS – disease management system) for the implementation of an efficient relationship between the different professionals taking care of the patient. This system was divided into several operative subsystems (the generation of auditive cueing when necessary, sending messages and interaction with the patients and caregivers, through a web-based application) and the most important part was the development of specific applications and interfaces adapted to persons suffering PD on a personal Smartphone.

A very interesting idea and concept was developed during the execution of REMPARK: **the establishment of a double loop of interaction for the enhancement of the quality of life of persons with Parkinson [2]**. A first level was considered and based on a set of wearables and actuators placed at the body's patient level (the worn sensor for the movement analysis and the auditory cueing system), with a high level of autonomy for processing and storing data. A Smartphone was integrated into this patient-level loop in order to facilitate interaction with the patient when necessary and to communicate with the established second-level loop (sending or receiving information).

The second-level loop was considered around a server where data was stored and processed. The core part of this loop is the disease management system module, which should be able to generate recommendations and alerts when necessary, according to the stored and processed information.

A secondary functionality of the second loop of the system was planned as a communication tool between the different professionals taking care of the patients and with the patients or caregivers, when necessary. In fact, the established system is a precursor solution of some actual telehealth initiatives for PD management.

2.2.1 Analysis of the opportunity

REMPARK was a RIA (Research and Innovation Action) in the frame of the EU-WP7 and this means that results, in an optimum case, should arrive at a TRL 7, suggesting that, for real use and transfer of these results, some additional actions are required. Within this context, an exercise of analysis was done, trying to identify which of the findings and results should be good candidates for real development and starting away to the real applicability world and market, if appropriate.

The results and final conclusions of the REMPARK Project were presented in 2015. The incredible evolution of the necessary electronic and sensors' technology, together with the evolving ICT deployment was a good scenario for this analysis, opening the door to a very necessary application in the domain of PD treatment.

As a good exercise, it is possible to follow some published references at that time, in connection with the needs of Parkinson's disease management context and medicine and care, in general [3–5]. An excellent review, published in 2017, can be found in reference [6], giving an overview of the status of the research and the associated challenges in reference to the different symptoms and problems of PD.

Principal ideas and thoughts considered at that moment are the following:

- The wearable prototype developed for the project works and the final pilot deployment and activity was a good example of useful technology for Parkinson's disease management when used for the detection and measurement of the associated disease motor symptoms. The main characteristics of the prototype were:
    - Only one wearable, worn at the waist, is necessary for the detection of movement-associated symptoms.
    - The wearable integrates the whole set of developed algorithms for this detection and measurement of symptoms when processing the related signals generated by the integrated tri-axial accelerometers.

- The processing of this information is done locally, and in real time, and no external connection with a server is necessary.
- The wearable prototype was specially designed for its use at home, and in ambulatory conditions, and for this reason, the autonomy of the integrated batteries is enough for several days.
- The prototype was able to determine the presence and duration of the main motor symptoms associated with the disease, except tremors: Dyskinesia, Bradykinesia, Freezing of Gait, ON and OFF states, gait characteristics, and falls.

In conclusion, **the wearable was considered as a main objective for further development activity and its transformation to a usable and, maybe, commercial medical device.**

- The auditory cueing generation subsystem developed for REMPARK, as an actuator, applicable when gait problems and disturbances are detected, is another example of useful technology considered in this analysis context. The main characteristics of the developed subsystem are:
  - Auditory cueing is generated by an internal application of the associated user's Smartphone.
  - There is a variety of sounds and frequencies available.
  - The application of the cueing can be automatic and decided by the system when gait problems are detected by the worn wearable.
  - Cueing associated sounds are received by the patient using Bluetooth earphones.

  The advantages and associated problems to the auditory cueing administration and use for gait problems mitigation in PD are quite well known [7, 8] and are very interesting for further study and applicability problems consideration. Some of the important known and existing problems are:
  - The administration of cueing under voluntary activation by the patient could be not as efficient as necessary.
  - The most effective type of cueing greatly depends on the specific patient. Not all people are sensitive to the same sounds or frequencies.
  - An automatic generation of auditory cueing is complicated since the online and on-time detection of the associated gait problems is not

completely solved. The sensor developed in REMPARK could be a perfect first step, but the management of the cueing through the Smartphone can suppose a problem, due to the associated delays in the synchronization and application activation processes.

In conclusion, the REMPARK subsystem is a good basis for looking for a correct context in order to advance and obtain further developments and improvements in auditory cueing generation.

- According to Table 2.1, the third relevant result to be considered is the implementation of the disease management system – DMS, adapted to Parkinson's disease needs on a related server. This system is able to store all the information generated during the care process and facilitates a loop of interaction between the different professionals, caregivers, and patients (when necessary). The DMS module, as described in Chapter 8 of reference [1], is able to relate personal data with the Electronic Health Record and to generate alarms, messages, and automatic appointments.

  The system, operated through a web interface application, could be considered a good initiative for the implementation of a convenient telehealth system, adapted to the requirements of PD.

  A telehealth system, including the necessary technology, can be a very good initiative to improve the quality of life of the patients affected by Parkinson. This kind of system can provide an adapted way to conveniently follow the evolution of the patients at home when developing their current activities. It must be seen as a complementary tool to the more traditional visits to the hospital and doctor's office. An interesting presentation of the real possibilities and discussion on the patients' satisfaction is included in the reference [9]. A complementary actual view on that topic, considering the perspectives and advantages, but also the barriers and related problems, can be found in [10]. It is very clear that the implantation of the telehealth service is feasible from the technological point of view, but real barriers still exist, in relation to the required skills for patients and doctors, some existing privacy concerns, the restrictive regulations that are implanted in many countries, and the lack of reimbursement.

Table 2.2 shows a summary of the conclusions obtained during the analysis of opportunities and their related problems.

According to the above-presented text and the Table 2.2 conclusions, a very good opportunity, at the moment when the REMPARK project finished,

Table 2.2 Conclusions of the analysis of opportunity after REMPARK.

Technology	Opportunity – advantages	Related problems	Comments	Feasibility
Sensor	• A good and already working prototype is available. • A complete algorithmic set is embedded in the sensor.	• The sensor autonomy must be increased. • User experience must be improved.	• For its commercialization, the sensor must obtain the qualification of "medical device" and the CE label, according to the European regulations. • Clinical evidence is necessary.	High
Auditory cueing	• Necessary components are considered and included in the prototype.	• Synchronization between the symptom's detection and the launching of the cues is not completely satisfactory. • Detection of the FoG must be improved for a better administration of the cueing.	• Additional initiatives or new projects must be started for satisfactory development and implementation.	Medium
Server-based platform – DMS	• Prototype specification and implementation were satisfactory at the project level.	• In a real implementation, it must be improved communication, data privacy, and security aspects.	• For a real introduction of telehealth in Parkinson's Disease management many aspects must be improved: technology adoption, patient empowerment, doctor's trust, etc.	Low

was to **concentrate efforts on the final development and possible industrialization of a novel wearable sensor for the detection and measurement of the movement-related symptoms in the mid-stage of Parkinson's disease.** The main ideas and the value analysis of this initiative can be found in the reference [11].

The additional identified technologies (auditory cueing and the server-based platform) were initially discarded for immediate actions, waiting for new opportunities. Among others, the main reasons were:

- For an innovative and effective auditory cueing system, it is necessary to have a good detection device (mainly, able to detect severe movement disturbances and FoG episodes in real time) and able to automatically launch the generation of the auditory cueing.
- The server-based platform is, in essence, a very good idea. It is a solid step through the consolidation of the main eHealth ideas and initiatives. At that time, we considered that it was too early since the development of the necessary interoperability and sharing measures of personal data was still very country dependent.

In this way, the REMPARK partners owning the IPR of the family of AI-based algorithms to be included in a possible manufacturable sensor device decided to go away and start a series of necessary actions for the materialization of this idea.

2.2.2 Related challenges

Once it was decided to progress for the obtention of a new wearable sensor device for helping the PD community in the detection, measurement, and following of the disease evolution, it was necessary to face some important points:

- To determine the best development context. It seems that research or innovative action is not the correct environment to get a final product, ready to be launched to the market and society.
- To decide which is the correct final product format, compatible with the above ideas. The initial thought was to go to the materialization of a medical device, but this must be refined.
- To determine the most advantageous organization to correctly advance in these objectives. The main question is about the suitability of a Spanish university (Universitat Politècnica de Catalunya) as the main

owner of the IPR, for covering all the necessary stages to cover the objective in an agile way.

- To obtain resources and enough funding to cover the complete initiative.

After a complete analysis of the needs and opportunities, it was decided that the most efficient way to work was under the modality of SME (Small and Medium Enterprise), trying to get resources from the available EU actions at that moment (SME Instruments action).

With this idea, Universitat Politècnica de Catalunya (UPC) was signing a technology transfer contract, for the commercial exploitation of the IPR related to REMPARK results, with Sense4Care SL, an SME company created in 2012, and participated by the UPC. Part of the UPC researchers, taking part in REMPARK, were co-founders and owners of this company.

Sense4Care was proposing the PARK-IT project (*Unobtrusive, continuous and quantitative assessment of Parkinson's disease: hard evidence for optimal disease management with information technologies*), which was granted with an SME Instruments – phase I action, under contract number 672228 in 2015. With this funding, Sense4Care was able to study and take conclusions about the market opportunity, and associated business model for the presented initiative.

2.3 The PARK-IT Project: Main Conclusions

The aim of the phase 1 project, called PARK-IT, was to confirm the feasibility of a successful launching to the market of the future product. As the technical aspects of the sensor were verified during the REMPARK project, achieving over 90% sensitivity and over 90% specificity, the key for the phase 1 project was to confirm that there is sufficient market demand for the PARK-IT product. It was distributed into three different tasks:

- Market and stakeholder analysis: in order to determine the key market and its size, market drivers, and routes to market and to identify the key stakeholders in order to establish possible partnerships with them.
- Development of a detailed Plan for regulatory aspects and IP Management, including a CE medical device certification plan.
- Drafting an elaborated business plan, including target and value proposition, possible distribution channels and price strategy, manufacturing cost, gross margin, marketing strategy, and the establishment of the company structure and organization...

Sense4Care was developing the PARK-IT work along the project's scheduled time, analyzing the market opportunities and concrete needs, and identifying the possible users of the proposed solution.

An important conclusion was that the PARK-IT product can be considered a **Class IIa medical device** and a detailed plan for regulatory aspects and IP management was elaborated. As a final conclusion, what this feasibility study was demonstrating is that, once the project is completed, PARK-IT should be the market-leading solution, with a significant target market and a clear business strategy to achieve a successful market launch.

The conclusion of the action was that Sense4Care should submit an application to phase 2 of the SME Instrument action, in order to obtain the necessary budget for the required work to do.

2.3.1 The following steps

After the conclusions obtained from the PARK-IT project, it was time for the preparation, study, and edition of a new project proposal, with the same title and the PARK-IT2 acronym, that was submitted to the SME Instruments – phase 2 action. PARK-IT2 received the necessary support and funding, starting the associated works at the beginning of 2017, under contract number 756861. This project, with a scheduled duration of 24 months, was organized around the following work packages:

- WP1. Redesign of PARK-IT in order to obtain a version "ready-to-market." The estimated duration was 14 months, starting at the beginning of the project.
- WP2. CE medical device certification. The estimated duration was 16 months, starting when the redesign should be in an advanced state, and finishing at the end of the project.
- WP3. PARK-IT demonstration pilot. The estimated duration was 11 months, to be started with the newly redesigned prototype would be available and finish at the end of the project.
- WP4, WP5, and WP6 have a transversal character and were scheduled throughout the whole project duration. They must cover: the communication and dissemination parts, the IPR and commercialization-business strategies, and the global management of the project.

During the execution, it was decided to add a new and necessary WP7 on "Ethics requirements and protection of personal data." Finally, after a

Figure 2.1 Redesigned PARK-IT wearable prototype.

proposed and accepted Amendment to the contract, the duration of PARK-IT2 was enlarged by 6 months, concluding in a satisfactory way on October 2019.

The completely redesigned wearable sensor during the project PARK-IT2 project (shown in Figure 2.1) was the prototype originating the actual medical device, commercialized by Sense4Care, with the STAT-ON™ registered name.

2.4 Conclusion

A summary of the findings and technological advances found in the REMPARK project development are presented. An analysis of opportunity is done, motivating the proposal and work done in the frame of the PARK-IT2 initiative, which generated the precursor of the current STAT-ON™ medical device.

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