The European Co-ordination Hub for Open Robotics Development

Clinical Evaluation of Gait Training with Exoskeleton in Children with Spinal Muscular Atrophy (EXOTrainer)

Spanish National Research Council

Sant Joan de Déu Children's Hospital

Marsi Bionics

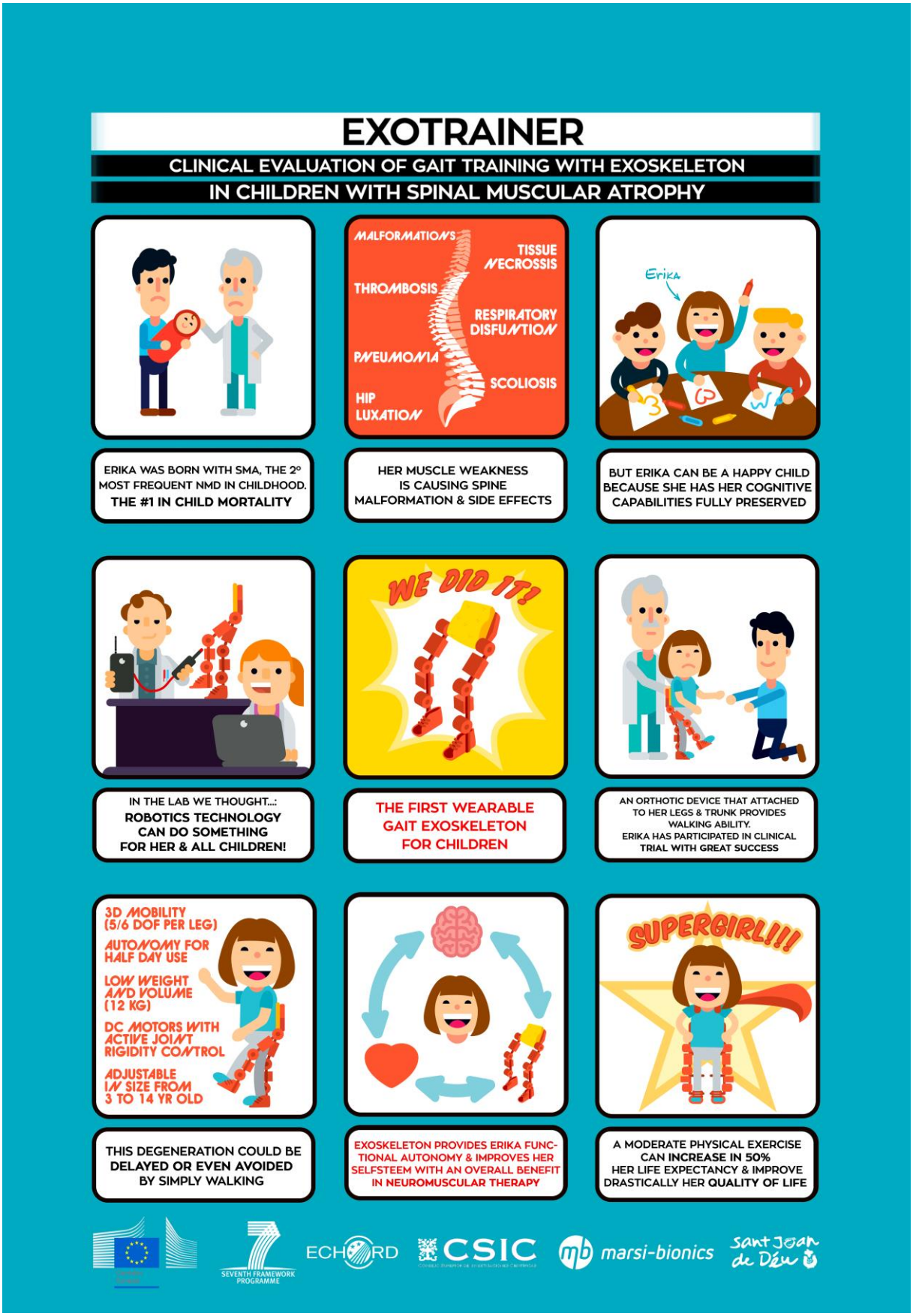
Final Report


ECHORD++

Table of contents

Section 1: Executive summary

- The goal of the project was to build a pediatric gait exoskeleton for children affected by Spinal Muscular Atrophy (SMA) Type 2.
- At the start of the project, all commercially available gait exoskeletons were indicated for adult paraplegics. The only pediatric gait exoskeleton available was a research prototype indicated for spinal cord injury, but not for neuromuscular diseases in childhood.
- This resulted in low quality of life and high mortality rate of these children affected by SMA. Clinicians considered that maintaining walking ability could improve life expectancy and life quality.
- An improvement of previous exoskeleton technology was proposed to provide: (1) spatial mobility by augmenting the number of active degrees of freedom; (2) postural balance by attaching a safety frame not supported by the child; (3) detection of child intention of motion by sensing joint residual mobility; (4) comfort for daily use of the exoskeleton by improving orthotics and physical interface between child and exoskeleton.
- Our solution was targeting to provide walking ability to this group of children as a primary impact. Besides, (1) reducing the time required to don and doff and adjust the exoskeleton size and parameters to each patient to 5 min, (2) maximize comfort using the exoskeleton, (3) maintain the degree of fatigue into clinically acceptable values, (4) keep inspiratory/expiratory frequency on acceptable values.
- After the clinical evaluation the device was demonstrated to be usable by SMA children, causing no fatigue at all and showing great comfort during walking. Scales of motor function showed a slight increase which for the short trial period is a significant result of the benefits that the therapy with exoskeleton can provide to these children. All other impact was satisfactory.


EXOTRAINER
CLINICAL EVALUATION OF GAIT TRAINING WITH EXOSKELETON
IN CHILDREN WITH SPINAL MUSCULAR ATROPHY
ERIKA WAS BORN WITH SMA, THE 2° MOST FREQUENT NMD IN CHILDHOOD. THE #1 IN CHILD MORTALITY
MALFORMATIONS
TISSUE NECROSSIS
THROMBOSIS
RESPIRATORY DISFUNTION
PNEUMONIA
SCOLIOSIS
HIP LUXATION
HER MUSCLE WEAKNESS IS CAUSING SPINE MALFORMATION & SIDE EFFECTS
Erika
BUT ERIKA CAN BE A HAPPY CHILD BECAUSE SHE HAS HER COGNITIVE CAPABILITIES FULLY PRESERVED
IN THE LAB WE THOUGHT...: ROBOTICS TECHNOLOGY CAN DO SOMETHING FOR HER & ALL CHILDREN!
WE DID IT!
THE FIRST WEARABLE GAIT EXOSKELETON FOR CHILDREN
AN ORTHOTIC DEVICE THAT ATTACHED TO HER LEGS & TRUNK PROVIDES WALKING ABILITY. ERIKA HAS PARTICIPATED IN CLINICAL TRIAL WITH GREAT SUCCESS
3D MOBILITY (5/6 DOF PER LEG)
AUTONOMY FOR HALF DAY USE
LOW WEIGHT AND VOLUME (12 KG)
DC MOTORS WITH ACTIVE JOINT RIGIDITY CONTROL
ADJUSTABLE IN SIZE FROM 3 TO 14 YR OLD
THIS DEGENERATION COULD BE DELAYED OR EVEN AVOIDED BY SIMPLY WALKING
EXOSKELETON PROVIDES ERIKA FUNCTIONAL AUTONOMY & IMPROVES HER SELFSTEEM WITH AN OVERALL BENEFIT IN NEUROMUSCULAR THERAPY
SUPERGIRL!!!
A MODERATE PHYSICAL EXERCISE CAN INCREASE IN 50% HER LIFE EXPECTANCY & IMPROVE DRASTICALLY HER QUALITY OF LIFE
SEVENTH FRAMEWORK PROGRAMME
ECHORD
CSIC
marsi-bionics
Sant Joan de Déu

Section 1.1: Milestone overview

#	Description	status
M1	Agreement on Requirements and specifications for EXOTrainer	Timely achieved
M2	EXOTrainer concept approved	Timely achieved
M3	Orthotics complements, mechanical upgrade and sensor system integrated	Timely achieved
M4	Joint motion control and intention detection	Timely achieved
M5	Prototype ready for clinical tests	Timely achieved
M6	Clinical proof of concept	Achieved

- M6: Extension was requested for the clinical tests because of the summer holidays clinical staff and families involved.

Section 1.2: Deliverable overview

#	Description	status
D1.1	Exoskeleton requirements and specifications	Timely submitted
D3.1	Progress report	Timely submitted
D4.1	Technical improvements to the exoskeleton	Timely submitted
D4.2	Exoskeleton for SMA gait training	Timely submitted
D4.3	Exoskeleton for gait training: User Guide	submitted
D5.1	Report on clinical evaluation outcome	submitted
SB	Story Board	submitted
MMR	Multi-Media Report	submitted

- D4.3 to MMR deviated from submission deadline because of the modified execution period.

Multimedia Report can be found through this video link.

Section 1.3: Technical KPIs

#	Description	status
1	DOF identification	Achieved
2	Improved Kinematics for children: size, weight, self-balance, no thoracic control needed.	Achieved
3	3D mobility	Achieved
4	Adjustable to size of patients between 4 – 8 years children	Achieved
5	Sensor Integration	Achieved
6	Gait control (Generation of foot and joint trajectories)	Achieved

Section 1.4: Impact KPIs

#	Description	status
1	Providing the ability to walk	Timely achieved
2	Acceptable time required to don and doff, and adjust from one patient to another	Timely achieved
3	Tolerance using the exoskeleton	Achieved
4	Acceptable degree of fatigue after a 10-minute walk evaluated from measurement of Respiratory Frequency (RF), Cardiac Frequency (CF) and Oxygen Saturation (Sat O2).	Achieved
5	Acceptable inspiratory/Expiratory Muscle Strength IPM/EPM and/ or SNIP (depending on patient age).	Achieved

Section 1.5: Dissemination KPIs

#	Description	status
1	Experiment Website	Timely achieved
2	Social Media (Facebook, LinkedIn, Youtube)	Timely achieved
3	Trade fairs (AUTOMATICA, Global Robot Expo, Innorobo, MEDTEC)	Achieved
4	Journal publication	Achieved
5	Conferences	Achieved

Section 1.6: Additional (unplanned) achievements

- **Ranking #2 at the 2017 UAE AI & Robotics Awards For Good, Dubai**
- **Innovation Award 2016 –WINNER- For practical innovation in the field of robotics;** Awarded by Industrial Robot; Emerald Group Publishing Limited.
- **ABC Salud 2016:** Award to the Best Technology for Health. ABC Press.
- **Fuera de Serie-Volkswagen 2016**: Award to the Social Innovation. Expansión Journal.
- **CEPYME 2015**: Award to the Best Entrepreneurial Project.

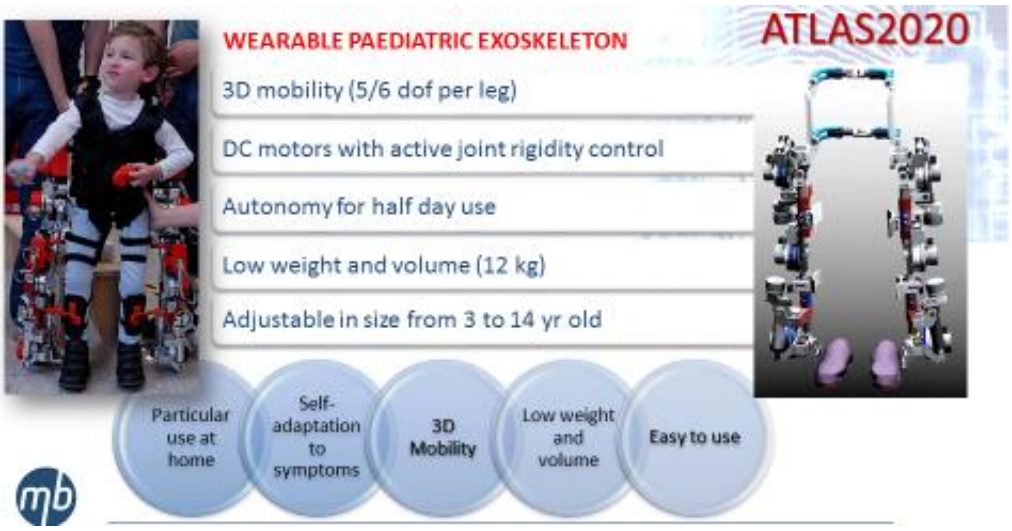
Section 2: Detailed description

Section 2.1: Scientific and technological progress

- The workplan was divided into 5 tasks.
- The first one was one of the most relevant because it required the consensus of all the multidisciplinary teams in a conceptual design. Clinicians and patient associations played a key role in the understanding of requirements and the technical teams translated them into technical specifications and all agreed in the final concept. This task required a number of meetings involving travel.
- Three research and technical tasks were the core of the project execution where the detail design and mechanical manufacturing of parts, upgrading of actuators, electronics and setting up of all components. Scientific progress on the gait control algorithm and motion intention detection. Programming of controllers and preliminary tests. Along the execution period, iterative clinical assessment of all the progress was made.
- The last task was the clinical evaluation, the most complex task in the project, which has been executed in a progressive manner, and iteratively upgrading and improvements were made to the orthotics and physical interface with the user to maximize comfort and usability. This task consisted on a series of clinical sessions for which the technical teams (Marsi Bionics and CSIC)

moved to Hospital Sant Joan de Deu in Barcelona in order to ensure the safety of the tests performed.

Section 2.2: Scientific and technological achievements



- Number of Degrees of Freedom: the exoskeleton was designed to provide 3D mobility, able to stand up, sit down, walk in straight line, make turns, go up and down slopes. This required 5 DoF per leg.
- Each DoF is actuated by variable stiffness actuators which adapt the motion of the exoskeleton to the child physical needs at each time, allowing to adapt also to the progress of the illness.
- Adjustable in size for children from 3 to 14 years old, it is a low weight exoskeleton, the lowest in weight of those exoskeletons in the market, only 12 kg that the children do not feel as the weight is transferred to the ground.
- Onboard Li-Ion batteries provide half a journey of autonomous use.
- The project started with a prototype only indicated for SCI. The new exoskeleton can be used by more groups of patients, such as those affected by Spinal Muscular Atrophy. The device is being now tested on other neuromuscular diseases like Muscular Dystrophy and Cerebral Palsy. Therefore, the number of patients that can be treated by this medical device has been increased in 400%.
- Starting the project from TRL 4 the current state of the technology is TRL6, it is now industrializing and passing safety tests, risk analysis and requesting for CE marking, and will enter the market in 2018.

Section 2.3: Socio-economic achievements

The performance of the gait exoskeleton for gait training of children affected by SMA was assessed in a clinical evaluation. 7 children were finally included in the clinical protocol. The median age of the 7 included patients was 6 years, ranging from 4 to 11 years. Although the initial project was thought to include children from 4 to 8 years old, the interest of the clinicians on testing the device on children up to 11 was considered. Three (42.9%) were males and four (57.1%) were females. The median weight was 21 kg with a range of 14.0 kg to 46.3 kg, and the median height was 115 cm with a range of 101 cm to 140 cm.

Fig. 1: Voluntary 5 year old boy affected by SMA during clinical session. Video at https://youtu.be/X_jcQaUPwjA

Measured variables:

• Tolerability

- Observing the child's skin after walking 5 meters

- Number of times the child needs to rest

- Degree of fatigue after walking 5 meters (from 0 to 10)

- Secondary Variables:
  - Evaluate the percentage of patients who manage to walk with the exoskeleton for 5 meters.
  - Functional motor scales
  - Degree of satisfaction of families and children with the new device.

Results:

During the 15 weeks of clinical evaluation the training sessions were designed to progressively increase the time and distance walked. Therefore, in the initial sessions children walked 1.5 meters and finalized walking the maximum distance that the available room allowed. After the third evaluation session, the tree children above 8 years old in age were finally excluded because their joint range of motion restricted a normal gait.

The **time to don and doff** was reduced from 8 minutes in the initial sessions to 3 minutes in the last sessions.

Statistical results of the evaluation are detailed:

1. **Distance walked:** Of the total of 23 sessions of which this value is available, the walked distance in median was of 6 meters. For sessions it was observed that in the first session walked 1.5 meters of median and in the seventh 12.4 meters of median.

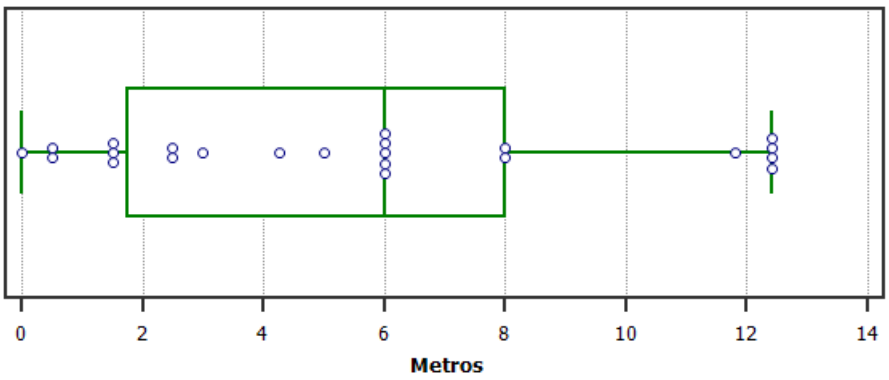


Fig. 2: Distance walked (meters)

2. **Walking time:** Of the total of 20 sessions with this variable available, the median walking time was 3 minutes, reaching 5.1 minutes in the seventh session.

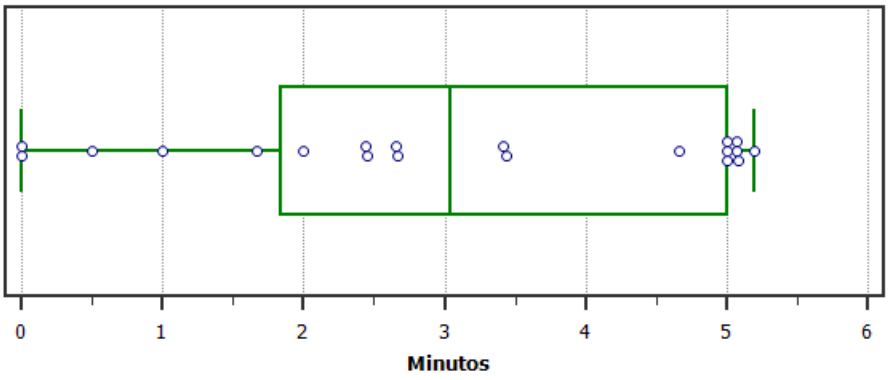


Fig. 3: Walking time (minutes)

3. **Time required to walk 5 meters**: Of the 13 sessions in which the walking time of 5 meters was evaluated, the median was 2.1 minutes.

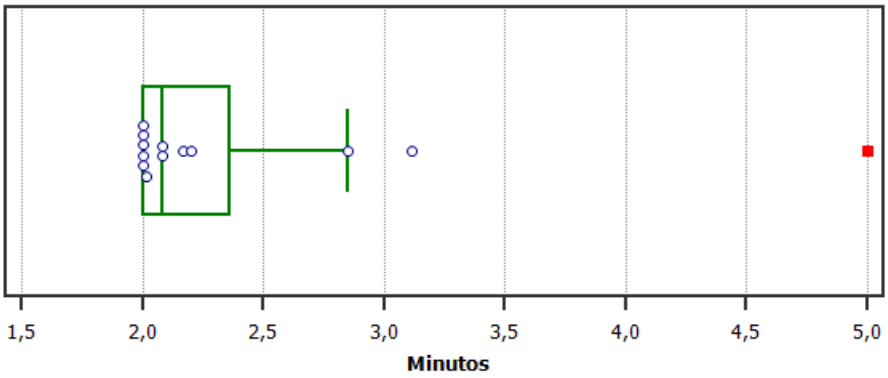


Fig.4: Time required to walk 5 meters (minutes)

4. **Number of times the child needs to rest:** Of the 29 sessions in which the number of breaks was evaluated, no rest was needed in 23 (79.3%).

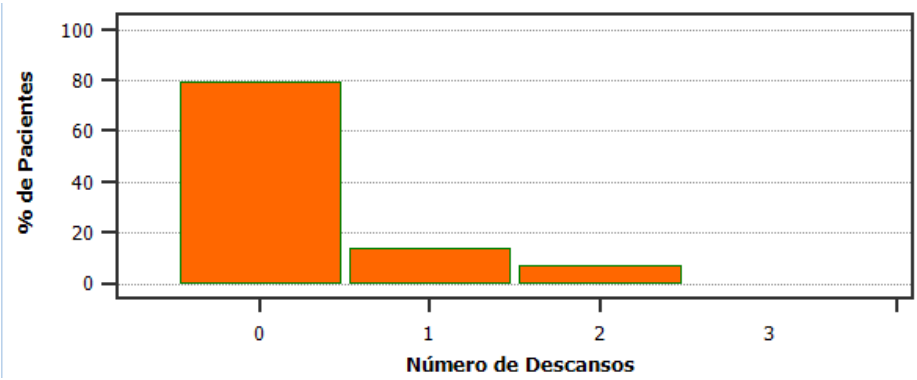


Fig.5: Number of rests needed

5. **Degree of fatigue:** During each training session the degree of fatigue was measured in the scale from 0 (no fatigue) to 10 (very high fatigue). Of the 25 sessions in which this variable was measured, the median value was 2, starting from 6 in the first training sessions and ending on 0 in the final sessions.

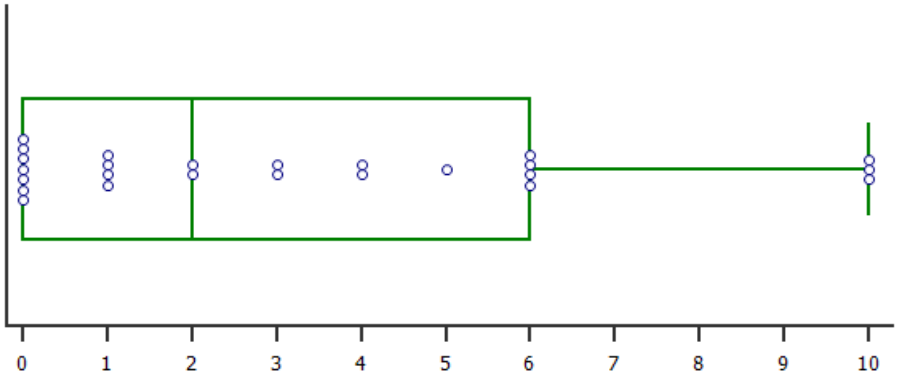


Fig. 6: Degree of fatigue (0-10)

6. **Skin tolerance:** Small marks or scratches in the skin of the underarms were observed only in 6 (20%) of the 30 sessions, progressing from 57% in the first session to 0% in the fourth session and forthcoming sessions.
7. **Blood pressure, respiratory frequency, cardiac frequency**: Measurements did not show any significant difference before and after the training sessions.
8. **Functional scales:** Both Hammersmith and Brook scales were measured at the first session (basal) and one week after the last session. Both scales showed an increment of 1 point which is a result showing a functional benefit in just 15 weeks of training.

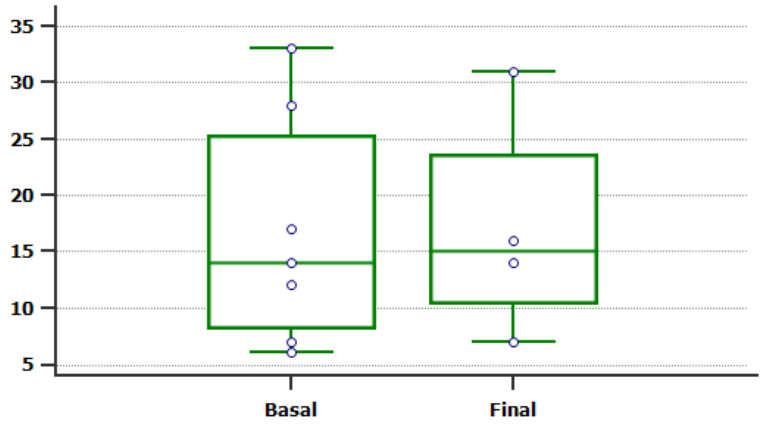


Fig. 7: Hammersmith functional motor scale for SMA

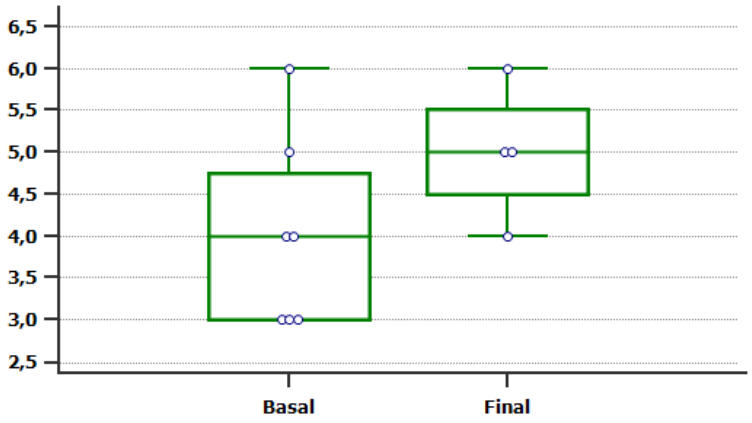


Fig.8: Muscular exploration: Brook scale

9. **Muscular examination:** Muscle examination was performed during the basal and final visit, in which muscle balance, joint balance and respiratory muscle strength were assessed.
    a. Respiratory Muscle Strength: The strength of the muscle was measured at both visits for inspiration / expiration and aspiration pressure.

    The maximum inspiratory pressure in the mouth was a median of 34.0 cmH2O at the baseline visit (N = 7), with a range of 15 to 120 cmH2O, and of 26.5 cmH2O at the final visit (N = 4), with A range of 15 to 64 cmH2O.

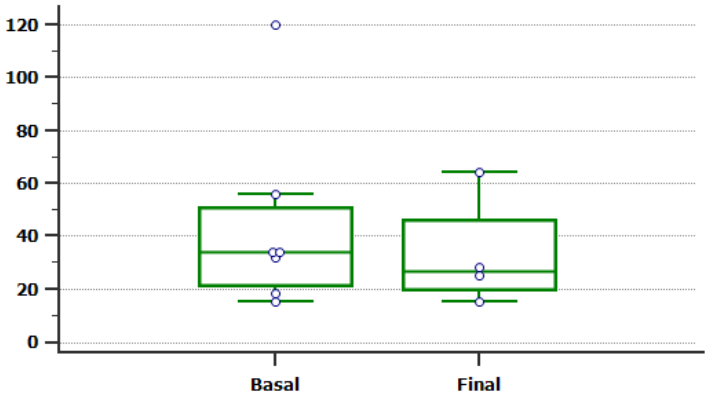


Fig. 9: Muscle examination - Maximum Inspiratory Pressure in Mouth (IPM) - [cm H2O]

The maximum expiratory pressure in the mouth was median of 29 cmH2O at the basal visit (N = 7), with a range of 17 to 67 cmH2O, and of 26 cmH2O at the final visit (N = 4), with a range of 20 At 34 cmH2O.

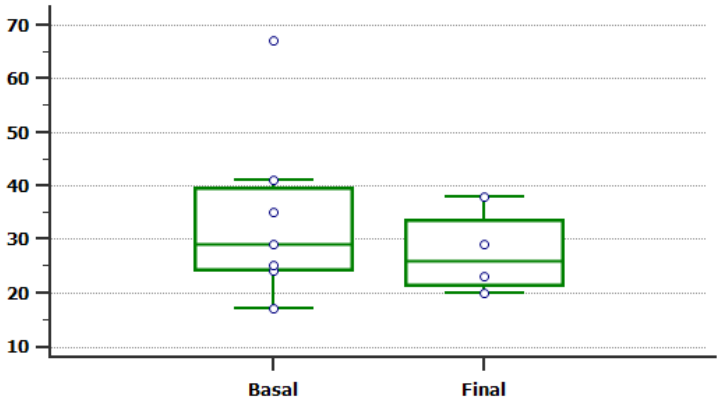


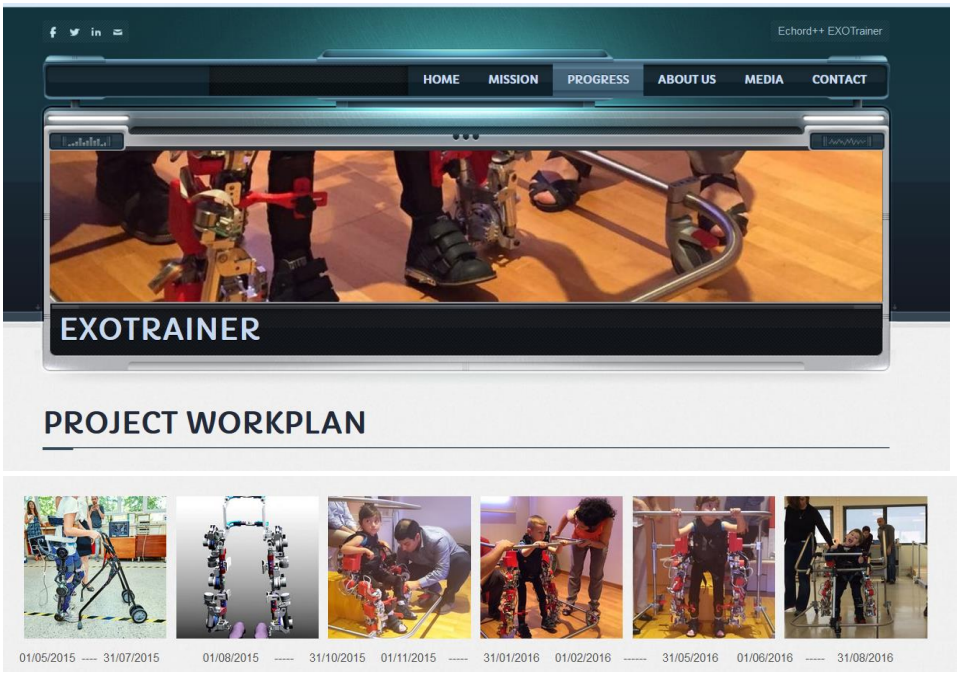
Fig. 10: Muscle examination - Maximum Expiratory Pressure in Mouth (EPM) - [cm H2O]

The deviation from initial to final examinations is not significant enough to be considered, as It can be perfectly justified within the variability that may exist between one day and another.

The overall assessment pf the EXOTrainer project by the clincal team is very successful. A relevant testimonial of the project by Dr. Anna Febrer, Head of Rehabilitation at Sant Joan de Déu Childrens Hospital can be found following this video link.

Section 2.4: Dissemination activities

- The project website was launched at the very beginning of the project execution and has been updated continuously showing the project progress. Milestones are presented through videos demonstrating achievements. Project mission and media dissemination are also shown on the website. http://www.exotrainer.weebly.com/



- The project progress was also broadcasted through social media, making use of Marsi Bionics facebook, twitter and youtube channels.
- Once the prototype was operative and with care of not disturbing clinical evaluation, a number of Trade Fairs were considered for dissemination:

AUTOMATICA 2016, Munich

Global Robot Expo 2017, Madrid

Future plans to show at Innorobo 2017 and MEDTEC 2017

- Conferences

  First Meeting on Technological Innovation and low cost for Rare Diseases and Disabilities | Burgos 7/10/2015
  Gait Exoeskeletons for the therapy of neuromuscular diseases in childhood. Dr. Elena García (CSIC) [Agenda]

  Festival of Capabilities CAPFEST 2015 | Tenerife 4/12/2015
  Bionics Exoeskeletons for the therapy of Spinal Muscular Atrophy. Invited Talk. Dr. Elena García (CSIC)

  Invited Talk at the Medical College Ourense | Ourense 21/04/2016
  Paediatric gait exoskeletons and other service robots. Invited Talk. Dr. Elena García (CSIC)

  Cure SMA international Conference. Familiy Poster Session | Los Angeles 17/06/2016
  An exoskeleton for the therapy of SMA type 2. Manuel Prieto (Marsi Bionics)

  International Conference on Climbing and Walking Robots CLAWAR2016 | London 12-14/09/2016
  Control architecture of the ATLAS2020 lower-limb active orthosis. D. Sanz-Merodio, J.Sancho, M. Perez, E. Garcia
  WINNER- Industrial Robot Innovation Award

  International Conference on Climbing and Walking Robots CLAWAR2016 | London 12-14/09/2016
  Mechanical description of ATLAS2020, a 10-DoF pediatric exoskeleton. J.Sancho, M. Perez, D. Sanz-Merodio, A. Plaza, M.Cestari, E. Garcia
  WINNER- Industrial Robot Innovation Award

- Scientific Journals

  M.Cestari, D. Sanz-Merodio, E. Garcia **Preliminary Assessment of a Compliant Gait Exoskeleton | Soft Robotics 2017**
  (Article in Press)

- Specialised Journals

  SmartHEALTH | 19/6/2015
  Innovación biónica por la calidad de vida [Online article]

  Adjacent Government Digital - ISSN 2055-7612, page 236| February 2015
  Wearable gait exoskeletons for the therapy of neuromuscular diseases. [Article]

- Online News, Releases and Bulletins

  Sant Joan de Déu Research Foundation | Barcelona 19/8/2015
  Proyecto para el desarrollo de un exoesqueleto robótico para niños con Atrofia Muscular Espinal, Dra. Anna Febrer MD (Hospital U. Sant Joan de Deu) [Online article]

DIGITAL TRENDS | 10/6/2016
This pint-sized exoskeleton is helping disabled kids walk again (or for the first time) [Online article]

GIZMODO | Australia 15/6/2016
Here is the World's first exoskeleton for children [Online article]

MARCA ESPAÑA | 25/7/2016
The first exoskeleton for children with spinal muscular atrophy has been created in Spain [Online article]

- Activities to the general public

XI Jornada Anual de Familias de FUNDAME | Madrid 7/2/2015
Presenting EXOTrainer Exoskeleton for Spinal Muscular Atrophy. Dra. Elena García (CSIC), Dra. Julita Medina (Hospital U. Sant Joan de Deu)

EXOTrainer Demonstration | Valencia 3/12/2015
Presenting EXOTrainer Exoskeleton for Spinal Muscular Atrophy during the *International Day* of People with *Disability,* Museo de las Ciencias Príncipe Felipe, Ciudad de las Artes y las Ciencias de Valencia.

- Courses and Round Tables

Course for medical profesionals: Muscular diseases in childhood and adolescence | Madrid 26/4/ 2015, Hospital U. Ramón y Cajal
Curso de Formación para profesionales de la CAM: Enfermedades Musculares en la Infancia y Adolescencia (XII), Mesa redonda: Miopatías en la infancia y adolescencia (III).

Exoesqueletos biónicos. Una alternativa terapéutica en las enfermedades neuromusculares. Dr. I. Pascual Pascual (HU La Paz), Dr. E. Tizzano Ferrari (H. Val d'Ebron), Dra. Elena Garcia (CAR, CSIC_UPM) [download Flyer]

- Press Releases and other Media Coverage

Press Release | 08/6/2016
The first pediatric gait exoskeleton for Spinal Muscular Atrophy
Dr Elena García. CSIC . Link

BUSINESS INSIDER UK | 15/6/2016
Spain just made an exoskeleton to help disabled children walk [Online article]

ABC | 08/6/2016
Primer exoesqueleto para niños con atrofia muscular [Online article]

EL MUNDO | 08/6/2016
La armadura biónica de Álvaro [Online article]

20minutos | 28/7/2015
Un exoesqueleto español permite andar a niños [Online article]

LASEXTA NOCHE| 26/06/2016

NEW CHINA TV | 9/06/2016 [link]

LA SEXTA - MAS VALE TARDE | 9/06/2016 [link]

EUROPA PRESS TV | 8/06/2016 [link1] [link 2]

ANTENA3 TV | 8/06/2016 [link]

TVE - TELEDIARIO | 29/07/2015 [link]

Section 3: Resource usage summary

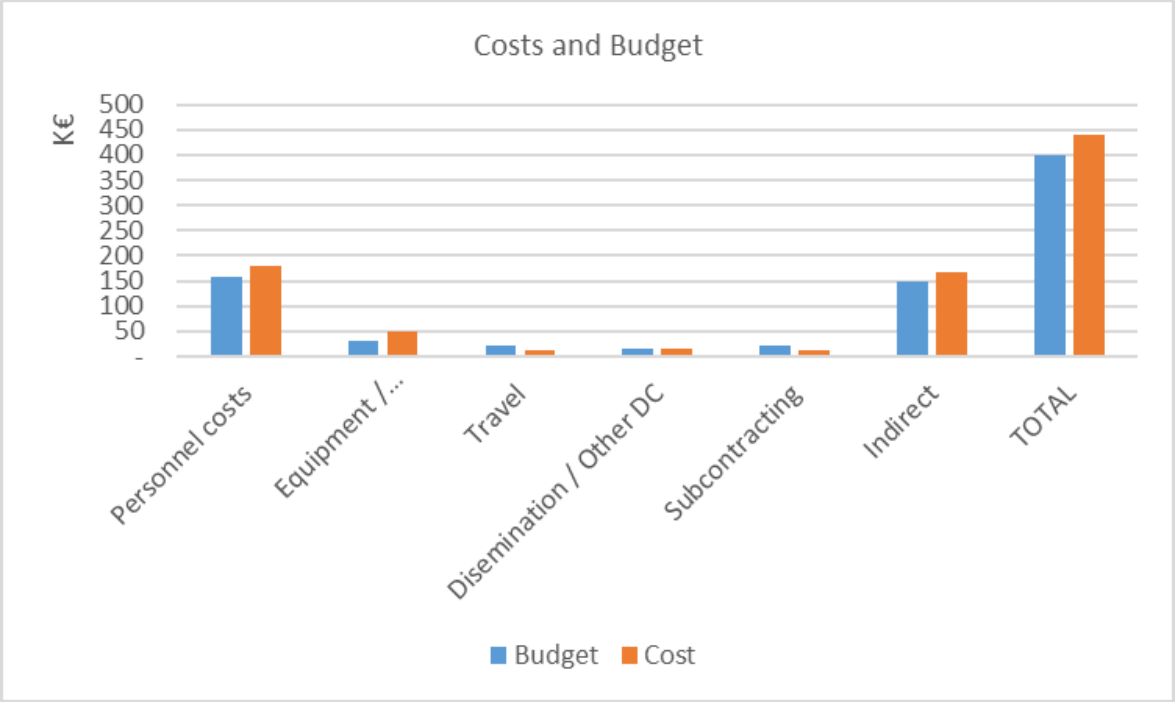
- The project costs have been aligned to the budget requested except for the manufacturing costs of the exoskeleton. Due to the requirements of the particular illness it had to be a new prototype with very different components, not an uptate of the previous prototype as initially considered. The expenses of manufacturing all parts of the new exoskeleton exceeded in 25.000€ the budget for consumables and it has been covered by Marsi Bionics.

CSIC	Budget	Cost
Personnel costs	51.000,00 €	51.080,12 €
Equipment / Consumables	6.872,00 €	3.090,84 €
Travel	2.540,00 €	4.073,72 €
Disemination / Other DC	3.700,00 €	3.500,00 €
Indirect	51.000,00 €	49.731,84 €
TOTAL	115.112,00 €	111.476,52 €

Marsi Bionics	Budget	Cost
Personnel costs	60.000,00 €	60.008,10 €
Equipment / Consumables	21.430,00 €	46.925,79 €
Travel	13.790,00 €	9.074,60 €
Disemination / Other DC	2.700,00 €	9.233,50 €
Indirect	58.751,92 €	75.145,19 €
TOTAL	156.671,92 €	200.387,18 €

HSJD	Budget	Cost
Personnel costs	47.500,00 €	68.000,00 €
Equipment / Consumables	3.000,00 €	697,52 €
Travel	6.000,00 €	1.022,83 €
Disemination / Other DC	9.128,00 €	1.800,00 €
Indirect	39.376,80 €	42.912,21 €
Subcontracting	23.000,00 €	13.927,00 €
TOTAL	128.004,80 €	128.359,56 €

TOTAL EXOTrainer	Budget	Cost
Personnel costs	158.500,00 €	179.088,22 €
Equipment / Consumables	31.302,00 €	50.714,15 €
Travel	22.330,00 €	14.171,15 €
Disemination / Other DC	15.528,00 €	14.533,50 €
Subcontracting	23.000,00 €	13.927,00 €
Indirect	149.128,72 €	167.789,24 €
TOTAL	399.788,72 €	440.223,26 €



Section 4: Deviations and mitigation

- The clinical evaluation in Task 5 was initially scheduled to run from April to June 2016, however, due to the initial modification of the project runtime because of the delays with the Amendment signature with the EC, the project started on May 1st instead of January 1st, and this modified in 4 months the whole project runtime.
- This made the clinical evaluation coincide with summer holidays. Clinicians involved in the project and voluntary patients and families were not available for the clinical trials during this period. We had to wait to October 1st to start the 3-month clinical trials. Our project deadline was then extended to January 31, 2017 after request to ECHORD++ and agreement.
- Please take into consideration that this extension was not caused by a delay in the project execution, which followed the initial schedule tightly. The EXOTrainer exoskeleton was ready for clinical trials in due time, but the dates, which coincided with summer holidays, were the cause to extend the execution period.

Section 5: Future work

Marsi Bionics is transferring to the market this project results. Technology Transference agreements between CSIC and Marsi are fully defined and active, assuring our potential for growing our target markets. Towards this purpose, in 2016 Escribano Mechanical and Engineering SL has become part of Marsi Bionics corporate structure by acquiring a 24% of the company. Apart from the financial push this private investment means for the business, Escribano will be a key ally for the industrial manufacturing of the products, as part of Marsi Bionics plan for scalability.

Escribano's manufacturing plant has a 5,600 m2 factory extended to other 7,000 m2 on two adjacent buildings, one of them newly built. Two plants of this new building have been transferred to MARSI for

offices and R&I labs. In the other new building, around 1000 m2, have been equipped for manufacturing the mechanical pieces of Marsi's exoskeletons.

With all this, Marsi Bionics expects to launch EXOTrainer results to the market by early 2018.

Cost benefit for health institutions and systems

During Phase 1 of UE funded I4SME, Marsi Bionics have also deeply analyzed the potential savings to National Health Systems from implementing exoskeleton-related rehabilitation paradigms. The following tables show the main conclusions as an average per European Country:

III. SAVINGS IN HEALTH EXPENDITURE DUE TO THE USE OF MARSI BIONICS' PRODUCTS

Estimation of savings around muscular atrofia based on surveys and internal market studies (€)

Medical services	Potencial Savings (survey responses)	Potential savings estimate
Medication	None	0
Medical tests	quaterly and annual	900
medical visits	monthly and quaterly	600
Physiotherapy visits	weekly and monthly	1120
IQ main disease	none	0
IQ comorbidity	1 or more surgical interventions	1200
Hospitalization	depending on intensity	210
Medical supply		1000
Socio-health services	weekly and monthly	1200
Home-care workers	daily	3150
Total savings per patient per year		**9380**

Estimation of the potential total saving per affection

Pathologies	Cases	Total saving
Muscular atrophy	157	1.468.776
Muscular dystrophy	346	3.245.522
Miopatía	96	900.218
Spina bifida	470	4.406.329
Para- and tetraplegics	864	8.104.320
Cerebral palsy	2105	19.741.617
Total potential saving		**37.866.782**

Cost benefit for families

A similar study was performed to estimate the potential savings to affected families that could incorporate a gait exoskeleton as a daily use therapy at home. Current related average costs (not covered by NHS) are estimated around € 20.000 per year and family. Of these costs 50% at least could be potentially reduced with the use of exoskeletons.

Distribution channel: As a result, from I4SME Phase 1, we have made a selection of those countries in Northern Europe which National Health Systems are likely to provide coverage to our products. For these countries, usual distributors of orthopaedics will be reached during Phase 2 to sign distribution agreements. In Southern Europe, current agreements with SEUR logistics will be used as distribution channel, and also signed agreement with Centro Ortopédico de Valencia will provide direct sales point to patients.

Clients:

Currently hospitals and rehabilitation centers help Marsi Bionics to gain visibility. These hospitals will provide great support during our market launch stage. Physicians have a crucial role, because their trust on our product generates the interest of patients and family. Below, some doctors showing their interest in carrying out the multicentric clinical evaluations (to obtain CE and FDA marking) in the

hospitals where they develop their activity are cited. Marsi Bionics has been collaborating with these physicians and hospitals from the beginning of its activity.

Dr. Gustavo Lorenzo (Paediatric Neurology unit) and **Dra. Blanca Palomino** (Rehabilitation Unit): Hospital Universitario Ramón y Cajal (Madrid, Spain).

Dra. Anna Febrer and **Dra. Julita Medina** (Paediatric Rehabilitation unit): Hospital Sant Joan de Déu (HSJD, Barcelona, Spain).

Dr. Laurent Servais (Neuroscience and Paediatric Neurology unit): Institute of Muscle-Oriented Translational Innnovation, I-MOTION (Paris, France).

Dr. Juan Ignacio Marín (Cerebral Injury Rehabilitation unit): Aita Meni Hospital (Bilbao, Spain).

Dra. Susana Quijano-Roy (Neuromuscular Diseases unit): Hôpitaux Universitaires Paris lle France Quest (Paris, France).

Continue Research and Development to widen the number of pathologies that can benefit from exoskeleton-based therapy:

Marsi Bionics has a close cooperation with associations of patients of different neurodegenerative diseases, where patients and families provide much valuable information regarding the potential daily use of our exoskeletons. Forming part of projects of research clinical, patients collaborate as volunteer for taking biomechanical data and clinical trials, which allows optimizing the gait pattern in our exoskeleton, therefore playing an essential role in the research and technological advances. Consolidated agreements with several patients' associations:

SMA Europe through Institute of Muscle-Oriented Translational Innovation (I-MOTION), which Marsi collaborates with since 2015. I-MOTION is a platform of Paediatric Neuromuscular diseases for clinical trials. It has four tutors, The Institute of Miology, AFM-Telethon, the Assistive Publique-Hôxpitaux de Paris (AP-HP) and the University Piere and Marie Curie (UPMC). I-Motion is specialized in these of innovative therapies and technologies. The use of our exoskeletons in this European reference institute with the stimulated collaboration of SMA Europe Association will present great prescribing/networking effect in the European region.

FundAME: Marsi and FundAME have a close collaboration since the start of the SMA exoskeleton development.

ASPACE: Association of children with Cerebral Palsy is currently collaborating with us in the development of a new exoskeleton paying attention to the spasticity effect.

The Parent project (Duchenne-Spain branch). The Parent Project association is actively involved in the develop of a partial exoskeleton for Duchenne Muscular Distrophy in a project recently funded by Spanish Economics and Competitiveness Ministry.

A number of proposals are being submitted to H2020 and other national funds to provide funding for these research actions.

Section 6: Lessons learned (optional)

This has been the most wonderful project ever. All the teams have been enthusiastic and so much motivated, and the successful project results are the consequence of this. We are all grateful to Echord++ for funding this research giving all of us the opportunity to give hope to these children, their families and clinicians. The intensive and very hard work we faced during real trials with real patients was completely compensated by the enormous satisfaction of seeing such a happiness in their smiles.

Please let me just remark that this research was previously submitted to FP7 calls without success, never receiving funding. This project would not have been realized without the funding from Echord++.

It is true that we faced a number of issues during execution, but however mitigated with success:

- The first issue was financial. What at the very beginning was thought of as an upgrading of an existing prototype, at the end due to the requirements of the particular illness it had to be a new prototype with very different components. The expenses of manufacturing all parts of the new exoskeleton which was not included in the project budget was covered by Marsi Bionics crowdfunding campaign (www.marsibionics.com/crowdfunding)
- A second issue was technical. Due to the fact that we faced for the first time in the research community an exoskeleton for children with neuromuscular diseases, we had to face during the life time of the project new challenges not foreseen, and a solution had to be found for each of them in the runtime. The whole team have learnt so much from the voluntary children involved in the clinical trials. They helped us very much in interpreting problems and looking for solutions. The clinical evaluation progressed in an iterative manner by updating step by step at every clinical session. The final prototype was demonstrated to fit perfectly within the affection, but a number of iterations were need to reach the final result. This would have been very difficult to achieve with children that do not preserve their cognitive capabilities. However, after the expertise gained through this project we are now ready to face affections showing non-cognitive capabilities such as Cerebral Palsy.