

# Groundbreaking Therapeutic Technological Method for Neurological Injuries Motor Recovery

BioXtreme has developed a ground-breaking therapeutic technological method that has clinically demonstrated 100% additional improvements of motor recovery for stroke victims. Currently, there are 25 million neurological injury casualties worldwide annually and

this figure is steadily growing. The two thirds who survive, experience a highly limited and prolonged rehabilitation period. This tremendous growing pressure has led, during the last decade, for a dramatic growth in new technologies and products, intended to shorten motor recovery process and to reduce the total costs. The most effective

products bring automation and efficiency to the traditional therapy methods. However, they do not offer any new treatment methods or concepts, resulting in limited additional improvement vs. traditional non-automatic neuro-rehab.

BioXtreme's new method and products are based on an adaptive instinct, for changes in the environmental forces, in which a unique robotic system that applies Error-Enhancement Forces during motor practices, triggers the patient to an immediate instinctive correction, without the use of cognition.

This core technology has been specifically tailored for the rehabilitation facilities and process, along with 3-dimensional virtual reality exercises, both controlled by an adaptive therapy software.

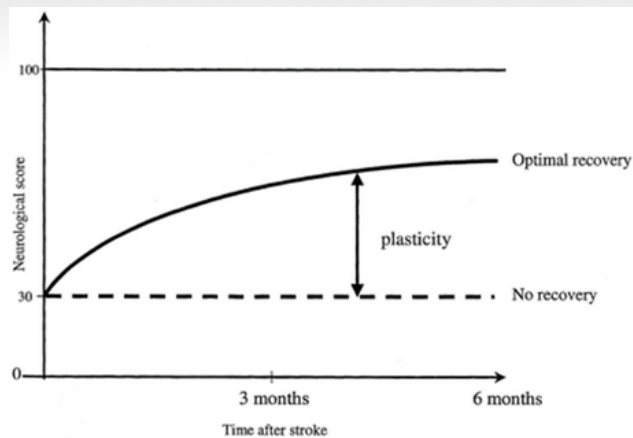
## Neurological Rehabilitation

There are currently 25 million neurological injury casualties worldwide annually and this number is steadily growing. The two thirds who survive stroke or other brain injuries, have to struggle with an extreme reduction in their quality of life and to experience a highly limited and prolonged rehabilitation period, more often than not, not resulting in a full recovery. This rehabilitation period is estimated to cost approx. \$300B annually for the healthcare systems.

This growing pressure has resulted in the last decade in:

1. A creation of a perpetual state of lack of hospital beds, manpower and equipment, which has led to cuts in hospitalization days and treatments that further restrict the process.
2. A dramatic growth in new technologies and products, intended to improve and shorten the recovery process.

The rehabilitation period is driven mostly by the movement recovery process. The most critical phase of rehabilitation is the post-acute phase, which occurs during the first 6 months after the injury, during which the brain's plasticity increases. After this phase, although patients can still undergo processes and treatments, the effect of rehabilitation is significantly diminished.



## An overview of the principles in motor learning and in neurological rehabilitation

### Motor learning – Existing methods

- ✓ Repetition of motor practice
  - Limited to the level of individual’s natural talent
  - Limited to individual’s ability of motor practice repetitions, limited by Neuro-Injuries
- ✓ Repetition of motor practice, combined with cognitive instruction & correction
  - Unnatural & complicated - to cognitively change existing motor patterns
  - Neuro-Injuries generally limit the use of cognition

### Motor recovery in Neuro-Rehabilitation

- ✓ Repetition of motor practice
  - Practice on natural & gaming tasks
  - Practice on computerized virtual reality gaming tasks
- ✓ Repetition of motor practice, combined with cognitive instruction & correction
  - Practice on natural & gaming tasks combined with therapist’s oral & physical guiding
  - Practice on computerized virtual reality gaming tasks, combined with robotics' physical guiding
- ✓ Existing effective Neuro-Rehab devices
  - The most effective technologies that have been developed are primarily concerned with streamlining the process and existing treatment

methods. These include exercising games in a virtual reality environment that enhance patient motivation and challenge, along with assistive robotics to guide the patient and correct his movement errors.

- These existing technologies bring efficiency & automation to traditional therapy method but do not offer any new treatment or concept, therefore resulting in a very limited additional improvement vs. traditional non-automatic neuro-rehab.
- The robotic systems require supervision during treatment and an effort to adjust, harness and calibrate the systems for each patient, which makes it difficult for the caregivers and the existing manpower. In this manner, achieving additional improvements is very limited and requires many treatments and practice cycles.

## BioXtreme's New Therapeutic Technology and Products

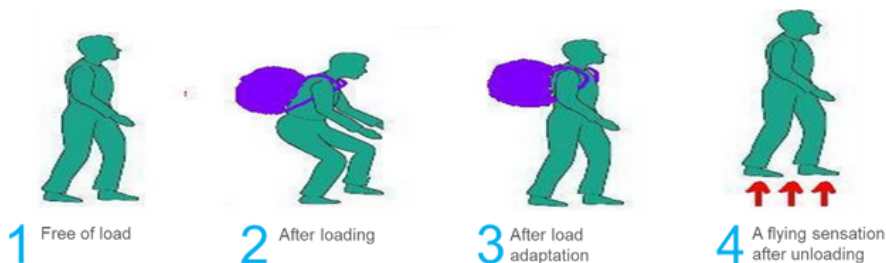
An adaptive instinct for changes in environmental forces and “After Effect” According to

researches, the brain appears to predict forces that are necessary for an upcoming movement and programs muscle activations accordingly (Lackner and DiZio, 1994; Shadmehr and Mussa-Ivaldi, 1994). When force prediction is incorrect, movement errors drive adaptation of the motor commands (Thoroughman and Shadmehr, 1999). In the following examples, which we know from daily life, this process

is divided into

several steps and is demonstrated in the illustration below:

1. A stage where isometric or dynamic motion occurs, without error.
2. A stage in which external force is added and applied to the body, resulting in an error.
3. A stage where there is an adaptive instinctive force response of the subject, which corrects the error.
4. A stage where the external force is removed, thereby resulting in an error in the opposite direction.





The final step is called After Effect. Once achieved, it proves that a change has been made in the subject's movement patterns. Reaching this stage was actually created by the subject automatically, without the use of cognition.

### BioXtreme method principle: Motor Improvement by Error Enhancement Forces

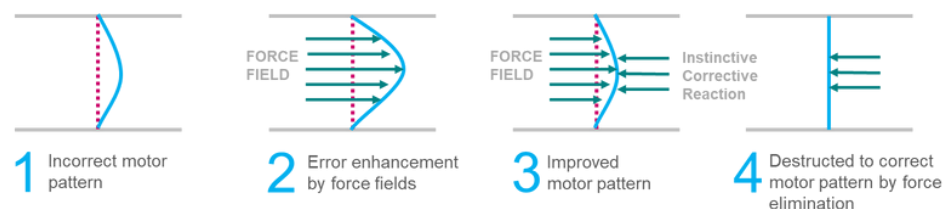
Based on this adaptive process, BioXtreme has developed an automatic motion learning method, based on the following steps, which are analogous to the steps previously described:

1. A stage in which the subject performs a movement with an error, measured by the system.
2. A Stage where the system applies a force acting in the direction that increases the error.
3. A stage where an adaptive instinctive force response occurs by the subject, which rectifies the magnified error.
4. A phase in which the force applied by the system is removed, resulting in a movement without error performed by the subject.

Second example (for comparison of analogue phases):



BioXtreme's basic method principles:

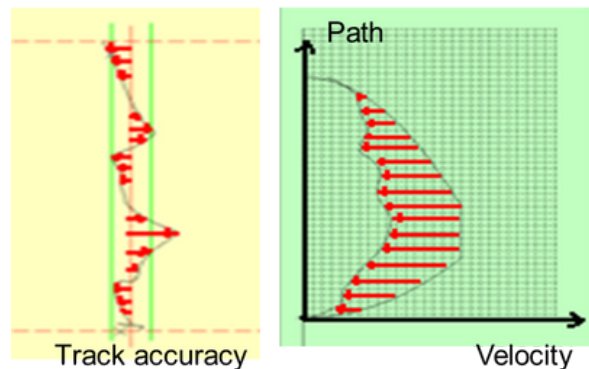


One of the most important principles of the method is that the greater the error, the greater the force the system uses to increase it.

As we know from the examples given in daily life, after the fourth phase inverse processes will occur, which will lead to an adaptive reduction of forces in order to correct the error created, a phase called washout. Therefore, this step may also occur

in the basic operation of the system, as described, especially in cases where the subject's error is a typical repetitive error. And how will the system deal with dynamic instability or vibration errors?

The second important basic principle, which addresses these issues, is that the system measures, calculates and applies the forces in real time, throughout the movement, gradually in each level and stage of treatment.



Since forces that increase errors can create (in some cases) a chaotic state and excessive entanglement of movement, the principle of error ranges is added whereby the system reduces the forces to even the correctional forces, to control and stabilize the exercise.

movement errors are divided into different parameters, such as position, speed, acceleration and force.

According to the principle of the method, the forces that act will increase the type of error that corresponds to the movement requirements.

BioXtreme's novelty method and technology are globally patent protected.

## deXtreme™

The first application for upper limb

- A robotic arm engaged to the upper limb for motor detection & error enhancement.
- Rehab motor tasks implemented in 3D VR games to motivate practice.
- A full rehab product consists of user-friendly working interfaces for patient & therapist.
- Therapy programming & results presentation.

The treatments included in the system are designed to improve position accuracy and stability, and increase range of motion, while completing tasks.

## System interfaces

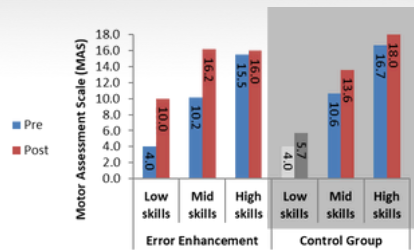
The system has convenient interfaces for both patient and the operator/therapist:

1. Easy transition between treatment in which the patient sits in the system seat and treatment in which the patient sits in a wheelchair.
2. Minimal transition between right-side practice and left-hand practice.
3. Convenient grip with minimum patient's harness to the robot arm handle.
4. Automatic adjustment of treatment and therapeutic parameters, along with easy setting ability for the therapist.
5. Motivational and challenging practice games.
6. Easier access and treatment ability also for patients who are more limited, for example have difficulty gripping the system handle or raising their arm. Anti gravitation forces.. armrest for people with grip difficulty..
7. System is mobile and not anchored which means it's not limited to one treatment room.
8. Immediate feedback on success and progress, for the patient and the therapist.
9. Automatic and rapid adjustment of patient practice ranges, depending on the patient's ability and dimensions.

## BioXtreme's Clinical Trials & Validation

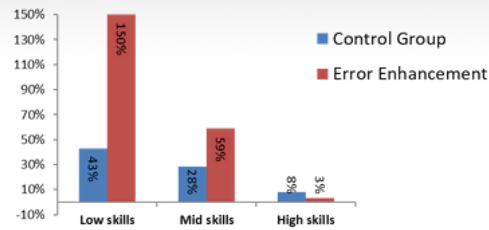
### 1. First experiment

- a. Performed on the first prototype, which included two-dimensional movement, without lifting of the limbs.
- b. The trial protocol consisted of 3, 15-minutes long treatments per week for a treatment period of 4 weeks.
- c. 18 stroke survivors subjects with hemiplegia or hemiparesis completed the study protocol. They were divided into a control and a research group, both performed the same movements, with the difference that for research subjects, the system applies the principle forces derived from the method of error enhancement.
- d. After the completion of the clinical trial and examination of the results, an article detailing the trial and results was written, led by Sciences and Biomedical Engineering Department, Ben-Gurion University, Israel, and published by International Journal of Therapy and Rehabilitation.



Upper motor skills of patients who received Error Enhancement treatment (left-side – light background), compared to patients in the control group (right-side – dark background)

- ▶ Motor skills before the treatment (blue), and after the treatment (red), were diagnosed using MAS (Muscle Assessment Scale)
- ▶ Results are grouped by patients' motor skills before the treatment (Low skill<sup>(\*)</sup>, Mid skills and High skills).



Comparison between Error Enhancement and control group.

- ▶ Improvement of patients with mid skills who received Error Enhancement treatment was **more than double**: 59% improvement on Error Enhancement, compared to 28% the control group.
- ▶ Improvement of patients with low skills who received Error Enhancement treatment was **more than 3 times higher**: 150% on Error Enhancement, compared to 43% on literature<sup>(\*)</sup>
- ▶ No significant improvement for patients with high skills on both groups (there isn't much to improve)

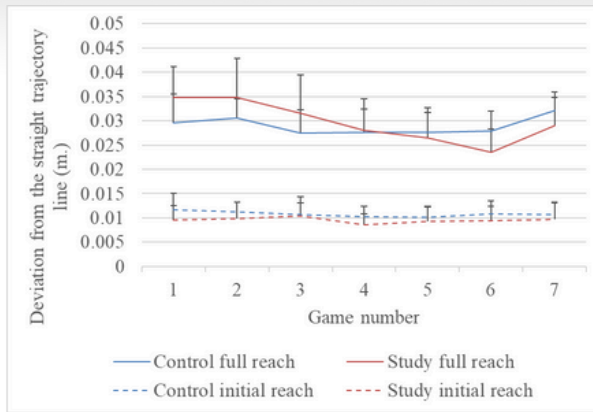
\*No patients with low skills were included in the control groups. Instead, results from literature are presented: "Stroke patients and long-term training is it worthwhile? A randomized comparison of two different training strategies after rehabilitation". Birgitta Langhammer Oslo University; Lindmark Uppsala University & Stanghelle Sunnaas Rehabilitation Hospital)

## 2. Clinical interim tests on patients

- Performed on the beta system developed by the company, from which the final product is derived.
- This step allows for customization and upgrading of the complete rehabilitative system developed, for optimal patient and rehabilitation alignment.

## 3. A quantitative experiment on healthy subjects

- Performed on the rehabilitative beta system.
- Experiment was conducted with the participation of 41 healthy subjects, who were divided into a control group and a research group, both practicing in a 20-minute treatment. Both groups performed the same movements, with the difference that for research subjects, the system applies the principle forces derived from the method of error enhancement.
  - Although the trial did not include brain injury victims, its success rate in a big group of subjects, alongside the fact that it is a practice adapted to a poor motor level of brain injury, gave BioXtreme the reassurance in the complex system that was developed, and additional feedback to optimize and upgrade the system even further.
- In the context of this experiment, an article was, by Department of Physical Therapy, University of Haifa, Israel, and published by the International Journal: Advances in Experimental Medicine and Biology.



Mean deviations per game-set of the hand trajectory from the straight line between groups.

Dashed lines illustrate the deviations at the first 300 msec of the game set. Complete lines illustrate the mean deviations from the straight line of a complete movement between groups. Error bars indicate the group standard deviations.

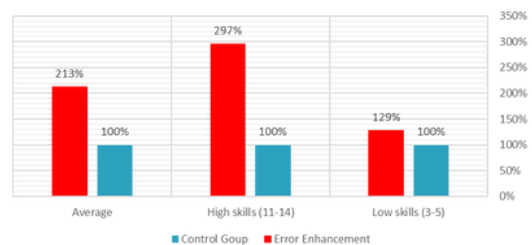
#### 4. Current experiment - ongoing 3rd clinical trial

- Targeted: 40 stroke survivors subjects with hemiplegia or hemiparesis, divided into research and control group.
- Duration: 2 weeks/a total of 6 treatments (3 per week)/20 minutes per treatment. Both groups performed the same movements, with the difference that for research subjects, the system applies the principle forces derived from the method of error enhancement.
- 14 subjects (out of the planned 40) have completed the trial so far.

#### PRE/POST M.A.S SCORE



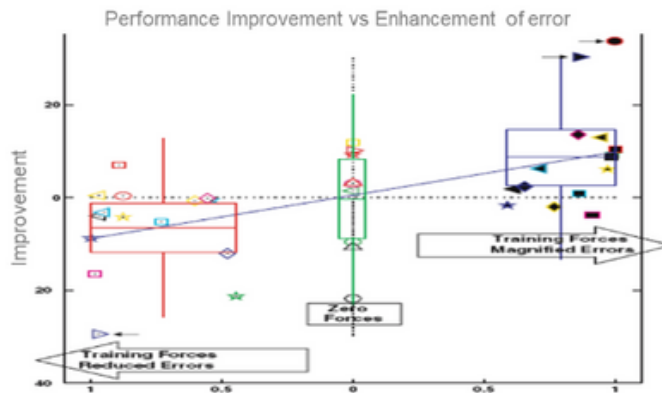
#### Error Enhancement/Control – Summarized Comparison





## 5. Unaffiliated clinical validation on Error Enhancement

Several academic researches of leading universities have also proved the great potential of Error Enhancement.



"Improvements occurred only when the training forces magnified the original errors, and not when the training forces reduced the errors"

Evaluation of Robotic Training Forces that Either Enhance or Reduce Error, **Northwestern University**  
Patton JL1, Stoykov ME, Kovic M, Mussa-Ivaldi FA

## Summary

BioXtreme has developed therapeutic technological method and products, based on an adaptive instinct for changes in the environmental forces, in which a unique robotic technology automatically applies forces, aimed to increase the errors during motion practice. By this, the patient is triggered to an immediate Instinctive correction without the use of cognition.

The company's clinical results in trials on its first product for upper limb rehabilitation show over 100% additional improvements and double progression rates in the rehabilitation measure for the study groups, compared with the control groups who performed the same exercises without treated by the method effect.

BioXtreme believes that this groundbreaking product and technology has a high potential to dramatically improve the capabilities of rehabilitation systems, expand patient rehabilitation, and streamline the process.