BioElectric Stimulation in Postpolio: preliminary perspectives

- the technology
- ongoing research
- pathophysiology
- 1st clinical results

BEST

PostPolio

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Our Approach

- **Technology**
  Focus on bio-electric stimulation (BEST), proprietary, developed and owned by KFH

- **Segmentation**
  unique products per indication / target group

- **Clinical Proof**
  studies, medical marketing with data

- **Strong Medical Support**
  exceptional for small device company

- **Differentiate**
  design, technical, branding

- **International from day 1**
  (FDA plus CE mark)
<table>
<thead>
<tr>
<th>Indication</th>
<th>n</th>
<th>Study Design</th>
<th>Location</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PostPolio</strong></td>
<td>25</td>
<td>Open label, longitudinal follow-up</td>
<td>4 countries</td>
<td>Completed, see Results</td>
</tr>
<tr>
<td><strong>MS (multiple sclerosis)</strong></td>
<td>22</td>
<td>Randomized, controlled</td>
<td>University College, Hasselt Belgium</td>
<td>Ongoing final results Q2 2008, see Interim Results</td>
</tr>
<tr>
<td><strong>FMS (fibromyalgia)</strong></td>
<td>50</td>
<td>Double blind, Placebo controlled Randomized</td>
<td>University Hospital, Leuven Belgium</td>
<td>Ongoing final results Q4 2008, see Protocol Summary</td>
</tr>
<tr>
<td><strong>Recovery after sport</strong></td>
<td>16</td>
<td>Double blind, Placebo controlled Randomized</td>
<td>University College, Hasselt, Belgium</td>
<td>Completed, 48 hrs gain in muscle strength, publication pending</td>
</tr>
<tr>
<td><strong>Venous leg ulcers</strong></td>
<td>50</td>
<td>Double blind, Placebo controlled Randomized</td>
<td>5 University Hospitals, Belgium</td>
<td>Ongoing final results Q2 2009</td>
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</table>
R & D Strategy

<table>
<thead>
<tr>
<th>Lifestyle</th>
<th>Medical - Home Use</th>
<th>Medical - Clinic</th>
</tr>
</thead>
</table>

Lifestyle applications:
- 5) Jet lag
- 6) Stress
- 7) Insomnia
- etc

1) KFH Energy
2) KFH Sport
3) KFH Medic
4) KFH Novo

Cash flow invested

R & D Platform

Clinical segments
Technological developments

MINIATURIZATION

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**BEST - rationale for applications**

<table>
<thead>
<tr>
<th>Mechanisms of Action</th>
<th>Application</th>
<th>Clinical Utility</th>
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</thead>
<tbody>
<tr>
<td>↑ ATP production</td>
<td>Mitochondrial Insufficiency</td>
<td>Alleviate pain and fatigue post polio syndrome fibromyalgia MS other</td>
</tr>
<tr>
<td>↓ Inflammatory cytokines</td>
<td></td>
<td></td>
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<tr>
<td>↑ Protein synthesis</td>
<td>Tissue Regeneration</td>
<td>Chronic leg ulcers e.g. venous, diabetic Pressure sores (decubitus)</td>
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<tr>
<td>Galvanotaxis</td>
<td></td>
<td></td>
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<tr>
<td>Stimulation of fibroblasts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑ Membrane Transport</td>
<td>Functional Recovery</td>
<td>Sport - recovery Sports injuries</td>
</tr>
<tr>
<td>- proline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- amino acids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Ca++, K+, Na++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑ ATP production</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
MET  How does it work?

By boosting energy production

- ATP formation driven by a proton gradient
- Water exists as an equilibrium
  \[H_2O = OH^- + H^+\]
- LOW current enhances proton (H+) supply
- Within a narrowly defined window of current intensity

⇒ more is NOT better
BEST - Mechanisms of Action

- Significantly higher ATP production at cellular level  
  (Seegers 02, Cheng 82)
- Increased protein synthesis  
  (Cheng 82, Bourguignon 87)
- Enhanced transport across cell membranes  
  Amino acids, proline, calcium, etc  
  (Nessler 87, Bourguignon 89)
- Cellular migration - galvanotaxis of WBCs and keratinocytes  
  (Gardner 99, Ojingwa 02)
- Stimulation of fibroblasts  
  (Cruz 99, Alvarez 83)

✓ BEST acts at cellular level, NOT nerve stimulation
✓ enhances energy metabolism and stores
✓ supports / restores homeostasis
BEST, a promising technology

BEST = Microcurrent ElectroTherapy
(1/1,000,000 of 1 Ampere)

How does it work?

by boosting energy

by restoring homeostasis
(physiological balance)

at cellular level

✓ nerve stimulation
✓ muscle stimulation

✓ nerve stimulation
× muscle stimulation
✓ cell
PP fatigue

Peripheral (physical)

- Physical fatigue a major problem for PP patients
  (Schanke, 2001)

- Neurophysiological evidence that local muscle factors determine ability to recover from fatiguing exercise
  (Rodriquez, 1991)

- Medical literature: abnormal changes in muscles of PP patients
  - anatomy
  - function
  - energy metabolism
**PP fatigue, pathophysiology**

**Muscle energy metabolism changes**

**PP differences**
- ATP resynthesis lower \((p < 0.001)\)
- ATP utilization higher \((p < 0.001)\)

↬ Energy imbalance in PP muscle cells, explaining
  - prominent muscle fatigue
  - slow recovery

Enzyme-histochemical properties, showing metabolic ratios (ATP use vs ATP production)

**PP patients,**

↑ ATP usage

Grimby, 1996
PP fatigue, pathophysiology

Muscle fiber changes

Control (age and sex matched)                   PP patient (ambulant)

PP differences
- almost exclusively Type I muscle fibers
- fibres are hypertrophied (much bigger)

- 'all or none' phenomenon, no differentiated use of muscle fibers
- muscle strength ± normal, but
  - muscle fatigue more prominent
  - recovery slower

muscle biopsy, cross section Tibialis Anterior

Grimby, 1996
PP fatigue, pathophysiology

Summary

PPS patients

- muscle fiber composition changes over time
- these type I fibers hypertrophy
- function in an ‘all or nothing’ way
- muscle strength ± normal BUT
  - fatigue sets in earlier
  - recovery time slower
- muscle energy metabolism out of balance
  (energy use higher than production)

overall picture consistent with (over)compensation and overuse, leading to mitochondrial insufficiency
BEST in PostPolio study
Study Design

- 25 postpolio patients, 4 countries, open label
- 3 months daily (1h) BEST use, at home, + 3 months extension
- Patient Reported Outcomes, weekly or monthly, on
  - Fatigue ~ BFI (Brief Fatigue Inventory)
  - Endurance ~ Borg RPE (Rate of Perceived Exertion)
  - Pain ~ BPI (Brief Pain Inventory)
BESTIPP study
Study Results

- In addition, the 1st 5 postpolio patients also underwent a full gait analysis

  - video plus computerized gait analysis, muscle strength, EMG, blood tests
  - energy consumption (O2 cost)

- Results
  - increase in walking speed and gait length
  - no change in gait, strength or O2 cost

แจก no obvious effect on gait within 3 months of BEST
BEST in PostPolio study

Results

Improvements (vs baseline) in all 3 endpoints

(3 patients dropped out within 1st 2 weeks)

- around 3 in 4 patients benefited
- 1 in 2 experienced significant improvements (> 30%)
- no side effects were observed
- treatment protocol well accepted as home treatment
BESTIPP study
Study Results

Maintenance effect
- 11 patients completed another 12 weeks
treatment 1 to 2 times per week

BEST appears to maintain effects over 6 months
10 patients > 2 years treatment, benefits maintained, stable
Clinical Proof of Concept
therapy resistant chronic ulcers

Before MET

6 weeks later
(completely healed)
Prescribing Information

USA

Prescription needed from medical professional

FDA labeling: chronic pain

Safety

attractive to use, as there are virtually no side effects
KFH current intensity too low to cause even skin irritation

as a pre-caution, we advise not to use BEST on patients with pacemakers, active cancer or during pregnancies

Practical

easy to use at home, we recommend 1 hour treatment per day
convenient to sit or lie down whilst being treated
available in US rental try out $100 per month purchase for $500

www.kfamericas.com
BEST and Postpolio

- There is no magic wand
- Many postpolio issues remain a challenge
- Progress likely to be through small steps
- We believe BEST is one such step

Thank You
Disclaimer: The following are unofficial notes which have not been read by or approved by the speaker.

- A micro current electrotherapy called BioElectric Stimulation Therapy (BEST) has great potential but it has not been well accepted by the medical community for two reasons – lack of medical evidence and lack of investment capital.
- Technology is quite old. Kingfisher Healthcare has a few patients who are approaching three years on this device/treatment.
- Kingfisher is trying to provide clinical evidence through its research.
- BEST was designed with the user in mind. It is small and portable.
- Research Study – started with 25 patients looking at fatigue, endurance and stamina.
- Twelve-week study. Some subjects stayed on for another six months. Collected weekly questionnaires from the patients and analyzed data.
- Full gait analysis done on first five postpolio patients. Stopped with those patients. Conclusion was that Kingfisher should not make any claims on the gait because these patients had established gait patterns for many years and it would be hard to change.
- For the group as a whole, 22 patients, everyone appeared to benefit but the pattern is consistent that at least one-half saw improvements; little side effects; and patients found it quite easy to treat themselves at home.
- Eleven patients agreed to go through another 12 weeks.
- Maintenance therapy – 1, 2 or 3 times a week as needed.
- Ten patients are using the treatment over two years.
- In U.S., a prescription is needed for the device.
- Product is safe; no side effects.
- Home-based therapy, one hour a day.
- Dr. Snyman believes BEST would be a useful addition to treating postpolio. Asked the directors if they would be interested in trying this device.

Comments/questions:
- Question -
  - Were the patients receiving anything other than the BEST – any medication that could have reduced fatigue?
  - Answer: No other meds. Some went to therapists which Kingfisher asked them to do. Nothing new happened during the study. Some reduce analgesics.
- Comment –
  - The majority of postpolio patients are taking several meds for depression or something that could have influenced the changes observed.
Answer: No changes in their lifestyle or work. If Kingfisher were to participate in a randomized clinical trial, they would have to be extremely careful about what the patients could and could not do during the study.

- **Question** –
  - Level of activity – were they wheelchair bound or ambulatory? Would we limit to only those who could work, with or without braces?
  - Answer: Some patients were in wheelchairs, the rest were in varying degrees of ambulation. It was not a randomized study.

- **Comment** –
  - Kingfisher understands that randomized data would be required before acceptance.

- **Comment** –
  - Why not try something that, as far as can be shown, is safe?
  - Answer: It is not entirely proven. If there was interest, Kingfisher would do a randomized study. To have a good, well-matched sample is complicated.

- **Question** –
  - Over what muscle groups was the electricity applied and was the muscle group or overall body fatigued?
  - Answer: Four electrodes were applied – hand to hand, foot to foot, to treat the whole body. It was not designed as a muscle stimulation but Kingfisher is trying to help with fatigue.

- **Comment** –
  - PHI has received emails from people about this device. Joan will contact Dr. Snyman about the next steps.

- **Question** –
  - If this technology doesn't do any harm and possibly does good, is there any reason not to try it?
  - Answer: If people are interested, Kingfisher could send the device to try.

- **Comment** – Kingfisher has a huge respect for these patients and would like to help them. Cannot do so without having people such as those on the call try the device or tell him a study should be done.

- **Comment** – IRB would require sufficient evidence that there is a good chance that good results will be seen. They want to see evidence as to why they should approve the study.

- **Comment** – PHI would be interested to know what Dr. Grimby thinks of this device.