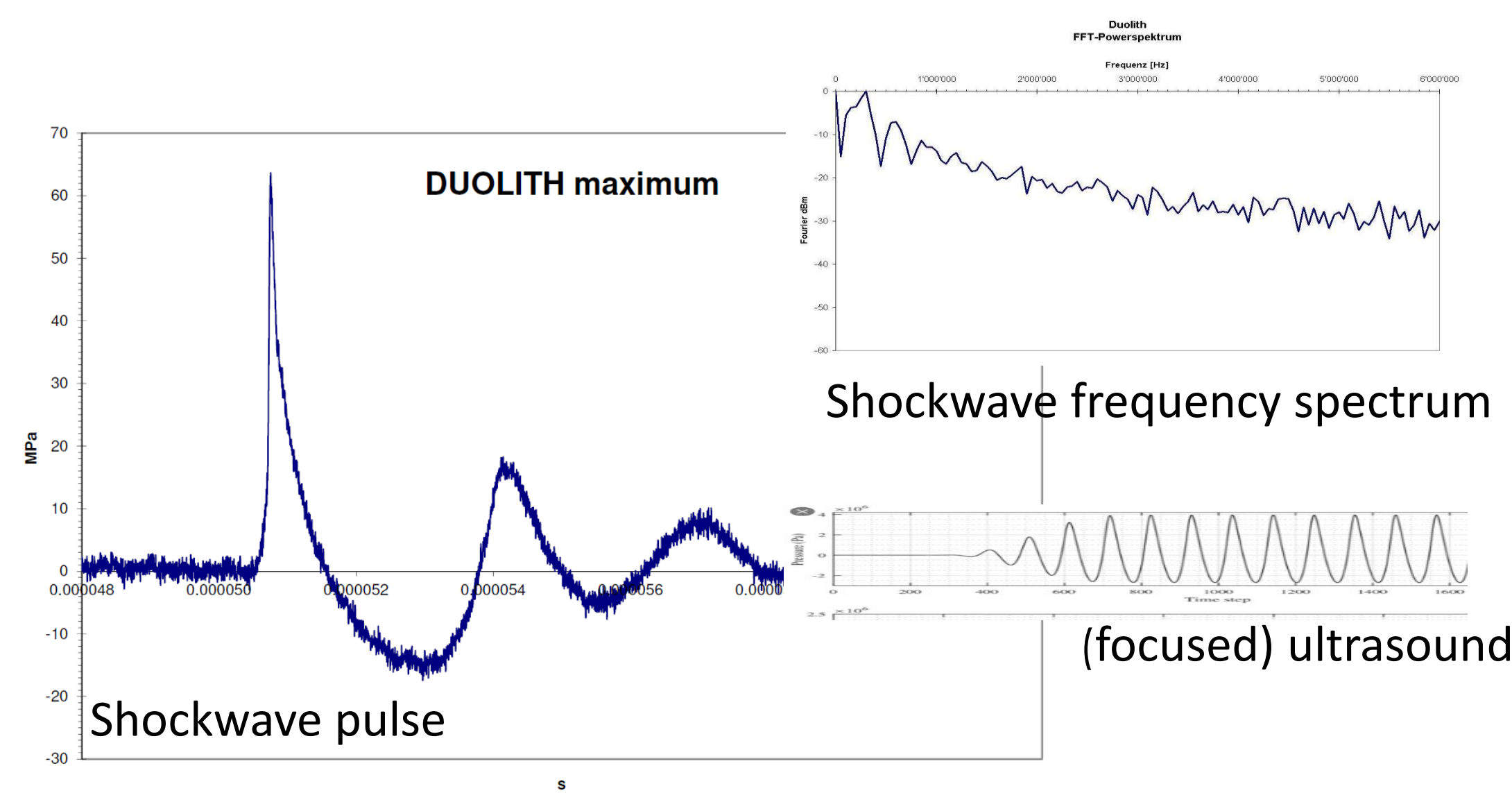


# LONGTERM RESULTS OF ALZHEIMER'S DEMENTIA TREATED WITH TRANSCRANIAL PULSE STIMULATION.

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## Introduction

- TPS are shockwaves pulses .
- Shock waves consist of all sound frequencies from audible sound to ultrasound. With a steep leading edge (no heat)
- Compared to the TPS focused ultrasound is a continuous train of pulses with relatively low pressure amplitude



- Shockwaves are used in medicine since 1980: Urology, Orthopaedics, Cardiology, Dermatology, Aesthetics

**Shockwave interaction** with soft tissue is called **“mechanotransduction”** which results in:

- ❖ Release of nitric oxide (eNO)
- ❖ Increased cell wall permeability, BBB opening
- ❖ Increased cell metabolism
- ❖ Release of growth factors like VEGF, BMP, TGF-β, GABA, BDNF resulting in **angiogenesis and neurogenesis**
- ❖ Anti-inflammatory effect
- ❖ Vasodilatation
- ❖ Stimulation of stem cells (proliferation, migration and differentiation)
- ❖ Stimulation of the innate immune system
- **No noteworthy side effects**

## Method

### Feasibility study

6 patients with unmodified standard medication were treated with TPS and assessed with the CERAD Plus score over 3 years.

### Treatment protocol

6000 pulses/session with 0.2mJ/mm<sup>2</sup> at 5Hz.

Initially 6 sessions of TPS in 2 weeks. After 12 weeks without any treatment all patients received a maintenance treatment with one TPS session monthly.

Follow up before the initial booster after 2, 4 and 12 weeks, after 1 year and after 2 years and after a further 2-weeks booster and after 3 years.

Due to the skull dependent attenuation of the energy, the energy flux density in the brain tissue itself is 0.03mJ/mm<sup>2</sup> to 0,05 mJ/mm<sup>2</sup>.

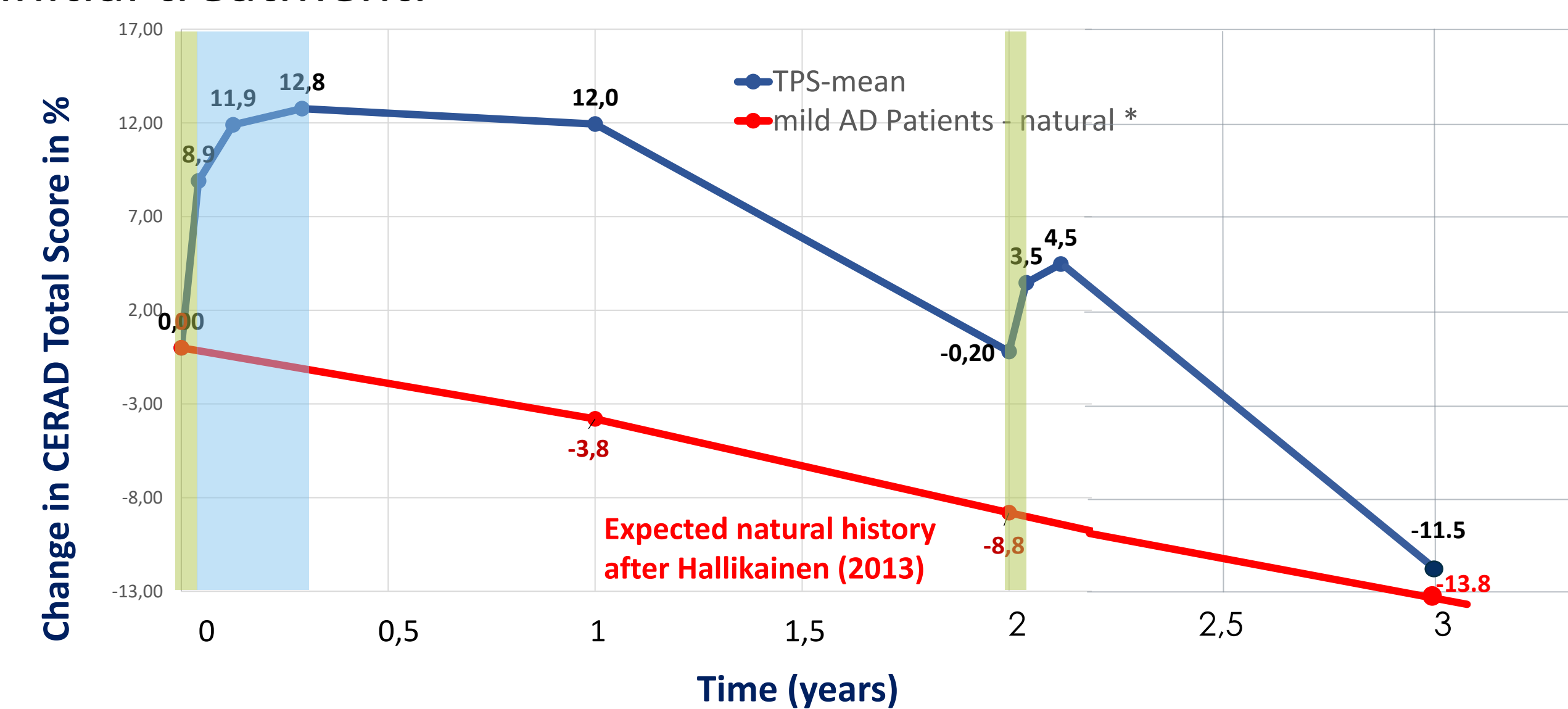
With this low energy flux density smaller than 0,25 mJ/mm<sup>2</sup> no noteworthy side effects are not expected.

50 % of the pulses were delivered scattered to the fronto-basal region, the parietal and temporal lobes, the precuneus and occipital lobe. 50% of the pulses were delivered aiming to the regions of special interest: basal ganglia, hippocampus...



## Results

- After the initial treatment (booster) and the 3 months follow-up the patient received one TPS maintenance treatment of 6000 TPS every month. This proved sufficient for the first year.
- Because unfortunately not tested during the 2nd year, cognitive abilities deteriorated unnoticed.
- The booster treatment after 2 years achieved approximately only 40% improvement compared to the initial treatment.



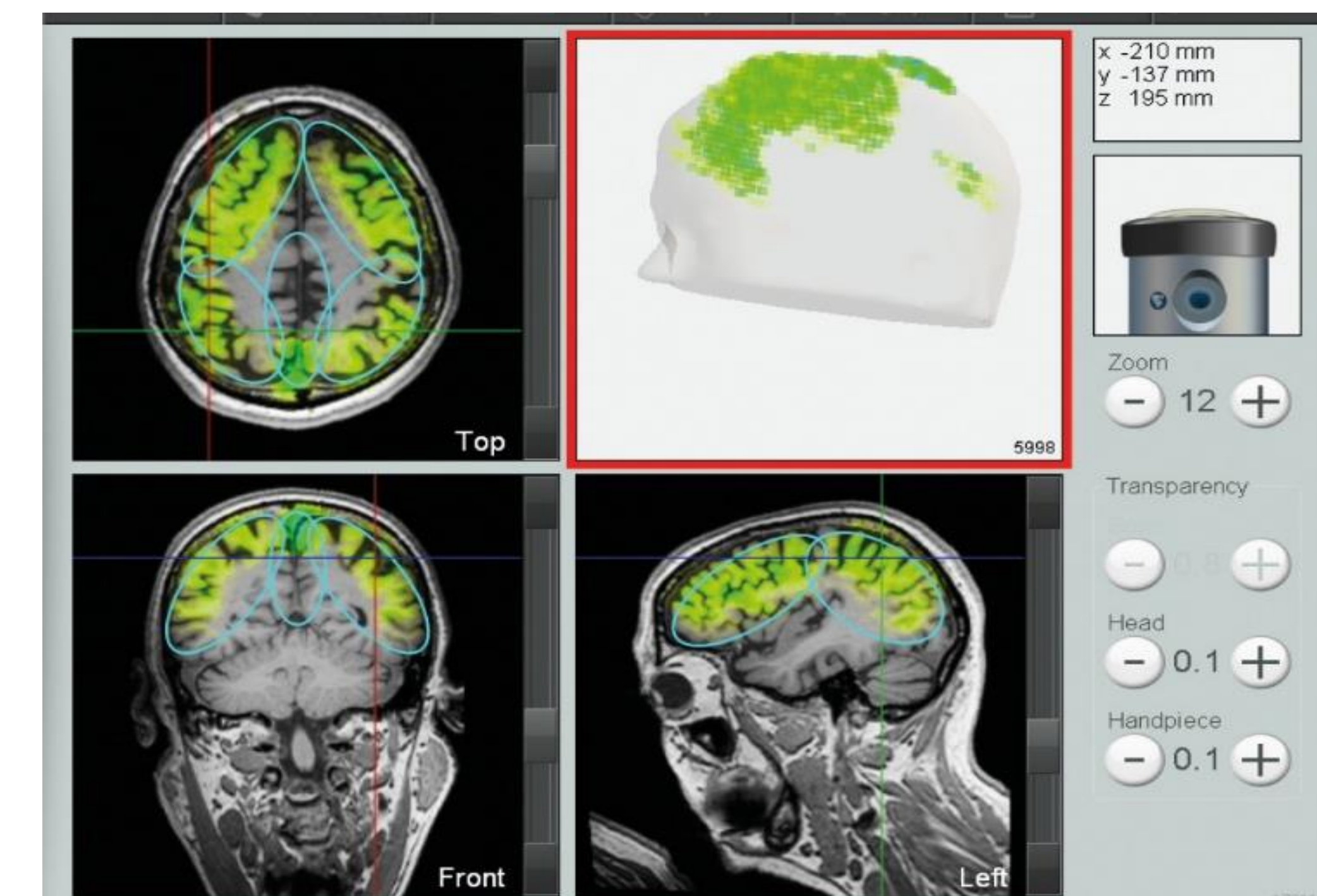
- Baseline at 66,5 points in the total CERAD score
- 6 TPS sessions in 2 weeks (booster)
- 3 months Follow-up without treatment
- Maintenance TPS every 6 weeks

Could an optimized treatment strategy with 2-weeks booster TPS every 6 months possibly maintain the results over a longer period of time?

## Discussion

Compared to other physical treatment methods of the brain the monthly repeated TPS of Alzheimer's patients is effective and safe over years. It is free of pain and provokes no side effects, especially no heat in the tissue. It is not necessary to shave the patient's head.

The new BodyTrack system is using individual MRI Data. The effective focus of the TPS is precisely indicated. This might further improve the outcome.



Body Track System

It was a methodological mistake not to test the patients more frequently neuropsychologically. It is conceivable that more frequent testing and earlier boosters (every 6 months?) would achieve a better long-term result.

Till this day there have been reported positive experiences with the TPS of the brain concerning Parkinson's disease [5], unresponsive wakefulness [3], stroke recovery, spine injury. With the European approval (CE sign) for the treatment of Alzheimer's disease the device Neurolith® (Storz Medical) is qualified for broader clinical use.

[1] Beisteiner R, Matt E, Fan C, Baldysiak H, Schönfeld M, Philippi Novak T, Amini A, Aslan T, Reinecke R, Lehrne J, Weber A, Reime U, Goldenstedt C, Marlinghaus E, Hallett M, Lohse-Busch H. Transcranial Pulse Stimulation with Ultrasound in Alzheimer's disease – A new navigated focal brain therapy. Advanced Science 2019  
 [2] Lohse-Busch H, Reime U, Falland R. Symptomatic treatment of unresponsive wakefulness syndrome with transcranially focused extracorporeal shock waves. Neuro Rehabilitation 35(2014) 235-244  
 [3] Lohse-Busch H, Reime U, Falland R. Focused extracorporeal shock waves (ESW) improve pareses in 8 cases of spinal cord injury and 3 cases of myelomeningocele. ISMST Milano 2014 and Poster Istanbul 20 14  
 [4] Widenfalk J, Lipson A, Jubran M, Hofstetter C, Ebendal T, Cao Y, Olsen L. Vascular endothelial growth factor improves functional outcome and decreases secondary degeneration in experimental spinal cord contusion injury. Neuroscience 2003;120(4):951-60  
 [5] Lohse-Busch H. Transcranial pulse stimulation (TPS) improves and stabilizes Parkinson symptoms over years. Preprint in ResearchGate DOI: 10.13140/RG.2.2.17406.72009