



the
art of
shock
wave

NEUROLITH®
Transcranial Pulse Stimulation (TPS®)
in Alzheimer's disease





STORZ MEDICAL – Our approach to treating patients with Alzheimer’s disease

STORZ MEDICAL has been using shock waves for the extracorporeal treatment of kidney stones (Extracorporeal Shock Wave Lithotripsy, SWL) since the late 1980s. Today, we also employ shock waves with great success in the treatment of musculoskeletal disorders and pseudarthrosis (Extracorporeal Shock Wave Therapy, ESWT), for the stimulation of angiogenesis, in the treatment of wound-healing disorders and in therapy for angina pectoris (Cardiac Shock Wave Therapy, CSWT).

What are shock waves?

Shock waves are acoustic pulses that have been used successfully for the treatment of various medical conditions since 1980. They enable physical energy to have a therapeutic effect in locally confined tissue regions. Thanks to this property, shock waves induce mechanotransduction¹, the

stimulation of growth factors (VEGF)^{2,3} and the release of nitric oxide (NO)⁴. This improves cerebral blood flow and promotes the formation of new blood vessels (angiogenesis) and neural regeneration.

Shock waves vs ultrasound

Shock waves are related to ultrasound. Nevertheless, the two technologies are fundamentally different. Whereas ultrasound is essentially a continuous wave with frequent oscillations, shock waves are characterized by a single pressure pulse followed by a tensile wave of lower amplitude. Ultrasound exerts a high-frequency alternating load on the tissue, causing the tissue to absorb the ultrasound energy. As a result, the tissue may heat up – an effect not observed in the application of shock waves.

Transcranial Pulse Stimulation (TPS®)

In the mid-1990s, shock waves were discovered to be effective in the treatment of neurological conditions such as post-traumatic spasms and spastic paralysis (Dr Lohse-Busch, Bad Krozingen)^{5,6}. 2015 saw the first treatment of Alzheimer’s patients with shock waves, performed at Vienna University. In 2018, authorization was obtained for Transcranial Pulse Stimulation (TPS®) using the NEUROLITH® system – as the only procedure of its kind to date – for the »treatment of the central nervous system of patients with Alzheimer’s disease«.^{7,8}

Today, neurological conditions such as Parkinson’s disease and depression are among the priority areas of our ongoing clinical research and development activities.

05 | TPS® method of action



09 | BodyTrack® system



07 | TPS® treatment



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¹ d’Agostino, M. C. et al.: International Journal of Surgery, 24(Pt B):147-153, 2015.

² Yahata, K. et al.: Journal of Neurosurgery, 25(6):745-755, 2016.

³ Hatanaka, K. et al.: American Journal of Physiology-Cell Physiology, 311(3):C378-85, 2016.

⁴ Mariotto, S. et al.: Nitric Oxide, 12(2):89-96, 2005.

⁵ Lohse-Busch, H. et al.: NeuroRehabilitation, 35(2):227-233, 2014.

⁶ Lohse-Busch, H. et al.: NeuroRehabilitation, 35(2):235-244, 2014.

⁷ Beisteiner, R. et al.: Advanced Science, 7(3):1902583, 2020.

⁸ Popescu, T. et al.: Alzheimer’s & Dementia, 7(1):e12121, 2021.



Knowledge application in neurology – The TPS® method of action

The clinical symptoms of Alzheimer's disease are caused by a progressive loss of neurons. This results in atrophy of the brain, especially in the cerebral cortex. The progressive death of neurons also leads to the disruption of synaptic connections between nerves, i.e. links responsible for the transmission and processing of information.^{9,10} Impaired information processing is one of the root causes of memory loss.

Based on the knowledge gained to date, destructive protein molecules that develop outside the neurons and disrupt their function are thought to be the triggering factor in the pathogenesis of Alzheimer's disease. One of these molecules, the beta-amyloid protein, accumulates – and is deposited – in the brain of Alzheimer's patients, forming structures called plaques which reduce cerebral blood flow and, consequently, interfere with the oxygen and energy supply to the brain cells.¹¹

Effects^{12,13} of TPS®

- Modulation of neural responses
- Reduction of cortical atrophy
- Stimulation of neuroplasticity
- Improvement of brain performance in patients with Alzheimer's dementia
- Improvement of axonal status in the stimulated area

⁹ Van Hoesen, G. W. et al.: Hippocampus, 1(1):1-8, 1991.

¹⁰ Van Hoesen, G. W. et al.: Cerebral Cortex, 10(3):243-251, 2000.

¹¹ Bush, A. I.: Trends in Neurosciences, 26(4): 207-214, 2003.

¹² Beisteiner, R. (Medical University of Vienna): Transcranial Pulse Stimulation (TPS) as a revolutionary new brain therapy, 46th Polish Psychiatric Congress, Stettin, 2021.

¹³ Matt, E. et al.: Journal of Translational Medicine, 20(1):26, 2022.

TPS® treats the frontal lobe, parietal lobe and precuneus regions of the brain.



Prof. Lars Wojtecki, MD
Hospital zum Heiligen Geist,
Kempen
Academic teaching hospital of
Düsseldorf University,
Germany



“ TPS® is a new therapy for Alzheimer's disease, which is, in my experience, very well tolerated. My first treatments showed amazingly positive effects in patients. There is initial scientific evidence of the clinical benefits in humans and of the effects on network connectivity in the brain. ”

TPS

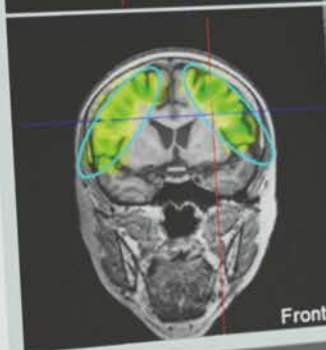
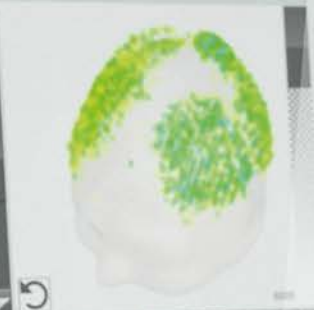
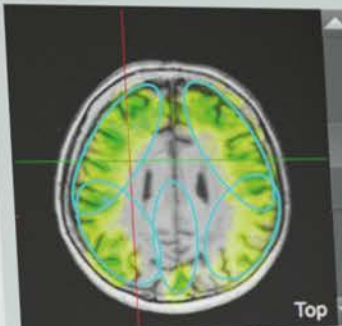
0.25
Energy (mJ/mm²)

6000
Pulses

4
Frequency (Hz)

6000
Total pulses

1.962
Total energy (J)



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TPS® treatment of Alzheimer’s disease: an effective and safe procedure

TPS® can stimulate deep cerebral regions, reaching as far as 8 cm into the brain. Owing to the short duration of TPS® stimulation, tissue heating is avoided. The pulses applied to the treatment area thus exert their maximum clinical effectiveness. TPS® treatment is performed through the closed skull. The patient is not immobilized during the session and able to move freely.

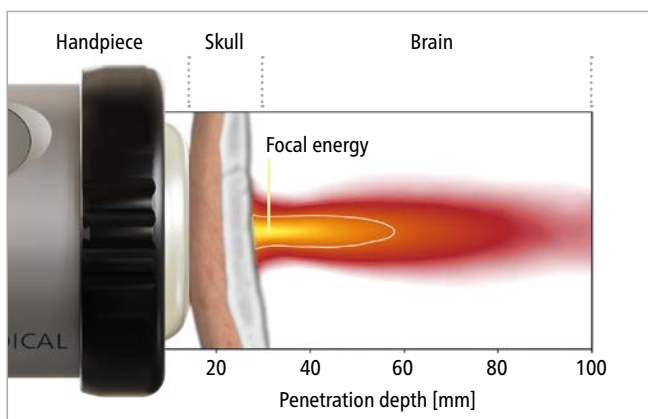
Based on the collected efficacy data, a follow-up study published in 2021 investigated the potential beneficial effects of TPS® treatment on the cortical atrophy characteristic of Alzheimer’s disease (AD).⁸ Data from 17 patients were included in the pre- and post-analysis. The authors of the study found correlations between the neuropsychological improvements and the increase in cortical thickness in AD-critical brain regions. AD patients who benefit from TPS® appear to have reduced cortical atrophy. Over 3500 treatment sessions have already been carried out with the NEUROLITH® system in over 50 treatment centres worldwide.

Advantages of TPS®

- 6 treatment sessions in 1 – 2 weeks
- Outpatient treatment (30 minutes/session)
- No head shave necessary
- Significant neuropsychological improvements (CERAD)⁷
- Indications of reduced cortical atrophy⁸

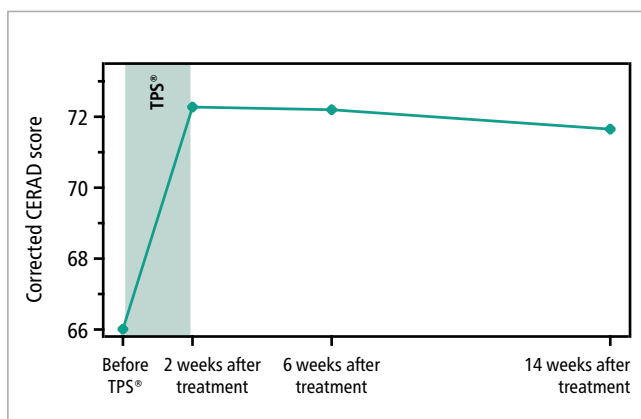
¹⁴Lohse-Busch, H.: Neurologie & Rehabilitation, 52:KV4–05, 2019.

TPS® energy distribution



Improvement over 3 months

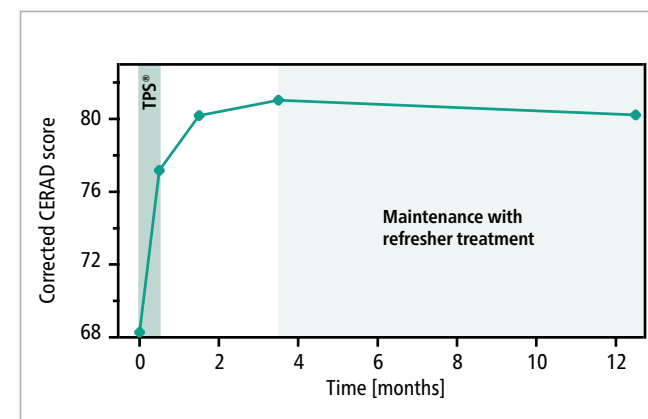
TPS® treatment: 6 sessions in 2 weeks⁷



Improvement over 12 months with refresher treatment

TPS® treatment: 6 sessions in 2 weeks

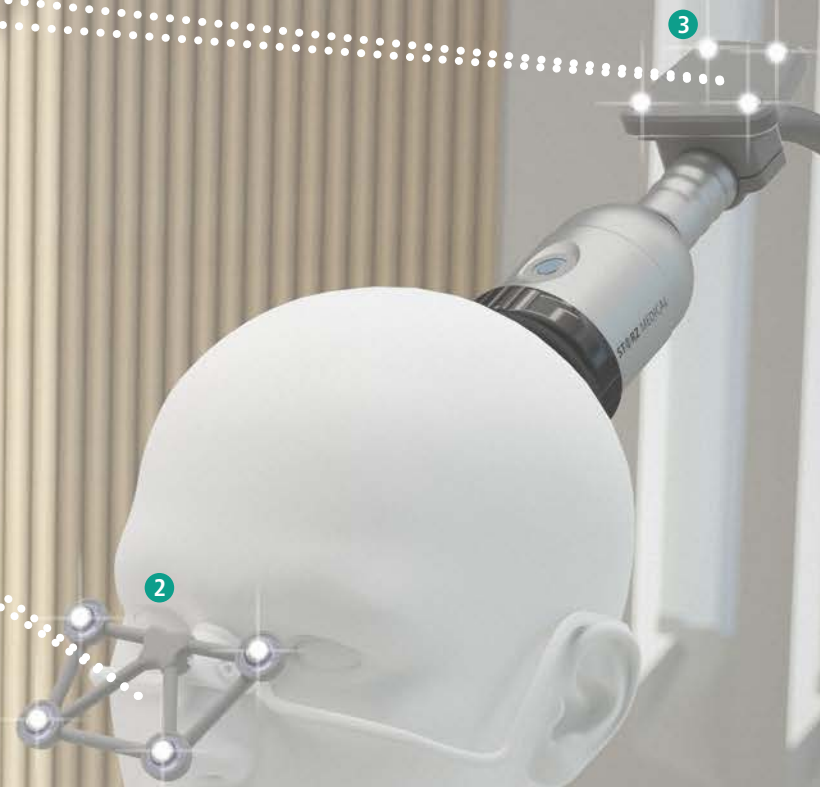
Refresher treatment: 1 session every 5 weeks (after 3 months)¹⁴





BodyTrack® system consisting of:

- 1 3D camera
- 2 Patient glasses with detection lenses
- 3 TPS® handpiece with detection lenses



BodyTrack® – Real-time treatment documentation with 3D visualization

The BodyTrack® system is the heart of the patented NEUROLITH® solution. Simple and rapid calibration ensures that the shape of the head matches the patient's MRI data. In this manner, each pulse applied can be visualized and documented in real time. Additionally, real-time detection of the handpiece position enables automatic visualization of the treated regions. The use of personalized MRI data allows specific characteristics of the patient's brain to be taken into account. Every time

the handpiece position changes, the visualization of the target regions in the loaded MRI scans is automatically updated. The energy applied is highlighted in colour. The BodyTrack® system is a unique tool for visualization and control of the TPS® pulses applied and of treatment progress.

Another benefit of the BodyTrack® system is that the user can define patient-specific treatment areas and target regions.

Advantages of the BodyTrack® system

- Use of personalized MRI data
- Visualization of MRI data in 3 planes
- Coloured visualization of the treatment region
- Real-time visualization of TPS® pulse distribution
- Documentation of the energy applied and of treatment progress

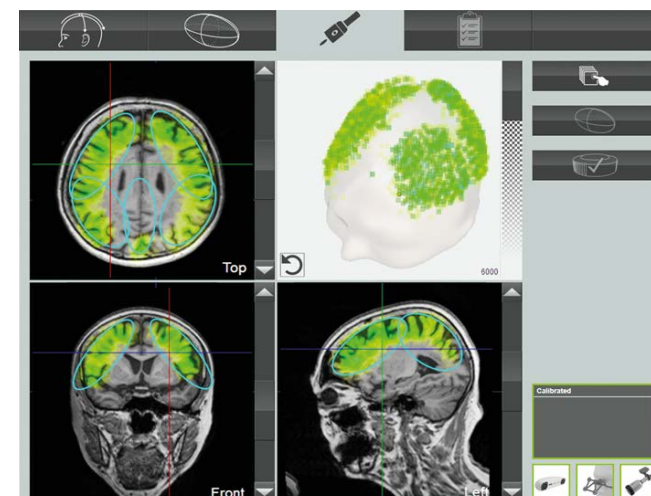
Manually controlled calibration: steps 1 (red) and 2 (blue)



Manually controlled calibration: step 3 (green)



Real-time coloured visualization of TPS® treatment





STORZ MEDICAL's service offering for healthcare practice marketing and therapist training

STORZ MEDICAL's TPS® website (www.tps-neuro.com) is the place to go for patients and their relatives seeking to find out about Alzheimer's disease and the new TPS® treatment. As a therapist, you can choose to be listed on the website so that patients can locate their nearest specialist on an interactive map. We support your patient education efforts by providing brochures that help to explain the TPS® treatment clearly and concisely. After their treatment has started, patients and their relatives can document their personal experiences using the TPS® diary specifically developed for this purpose.

As a new user, you will benefit from STORZ MEDICAL's special service. You will receive full, individual user training on the NEUROLITH® system to familiarize yourself with the device. Supporting materials are available that help you refresh your knowledge as needed: a quick reference guide provides an at-a-glance overview of what is important in the everyday use of the system. More advanced knowledge can be obtained by reading the informative manual, and clear, straightforward videos are available to explain the most important issues.

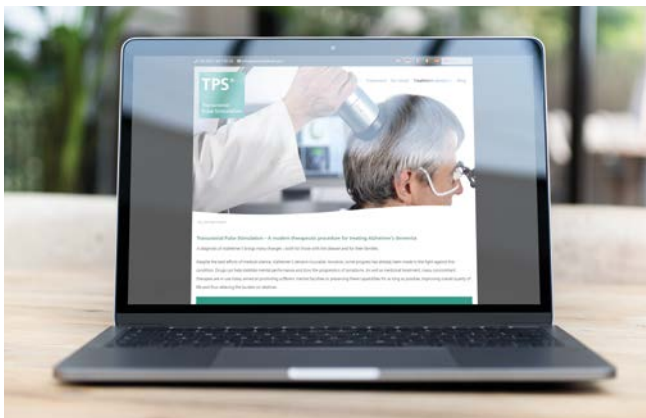
Our offering at a glance

- TPS® website providing information for patients and their relatives
- Online directory for therapists
- Helpful patient information materials for initial consultation
- Full user training



To find out more about Transcranial Pulse Stimulation (TPS®), visit www.tps-neuro.com

The TPS® website informs patients and their relatives about the new treatment.



Dr Teris Cheung, PhD
The Hong Kong
Polytechnic University
School of Nursing
Hong Kong



“ I am very satisfied with TPS® as it is very user-friendly and has a real-time treatment visualization. More importantly, TPS® has proved to be effective and safe in the treatment of my patients. I consider TPS® to be a breakthrough in brain treatment and stimulation! ”



www.storzmedical.com



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