

Transcranial versus direct cortical stimulation for motor-evoked potentials in supratentorial tumor resection: preliminary results of the TRANSEKT trial [Abstract]

Tammam Abboud, Maximilian Stein, David Wasilewski, Kathleen Seidel, Arthur Wagner, Katharina Faust, Florian Ringel, Dorothee Mielke, Bernhard Meyer, Veit Rohde, Andrea Szelenyi

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CMAP latency discrepancies facilitate identification of the trigeminal and facial nerves during resection of complex cerebello-pontine angle tumors.

Fares Komboz¹, Angelina Nazarenus¹, Veit Rohde¹, Tammam Abboud¹

¹ Universitätsmedizin Göttingen, Göttingen, Germany

Differentiating between the trigeminal nerve (TN) and the facial nerve (FN) during microsurgical resection of large, complex skull base and cerebello-pontine angle (CPA) tumors with altered anatomy can be tricky. Direct nerve stimulation (DNS) of TN motor axons often elicit compound muscle action potential (CMAP) responses of the ipsilateral facial muscles recorded simultaneously in both TN and FN muscle recording channels. Some studies retrospectively mention latency differences between CMAPs recorded after TN-DNS (ca. 5 ms) and after FN-DNS (ca. 7 ms.). However, the literature does not reveal any statistical evidence to these reports. In this study, we aim to prospectively record facial muscle CMAPs elicited by TN- and FN-DNS during CPA surgery.

Methods: 18 patients underwent CPA surgeries with intraoperative neuro-monitoring (IONM). To map the TN and the FN, DNS was performed with a bipolar concentric DNS probe (single pulse constant current stimulation, 3 Hz repetition rate, maximum intensity of 0.5 mA and a pulse width of 0.2 msec). CMAPs were recorded from the orbicularis oculi, oris and masseter. Latencies of the CMAPs elicited by TN-DNS vs FN-DNS were compared at the patient-level and muscle-level via a Wilcoxon signed-rank test.

Results: TN-DNS elicited in all facial muscles an average CMAP latency of 2.61 ± 2.18 ms, whereas FN-DNS elicited a significantly longer CMAP latency of 4.37 ± 1.61 ms ($p < .00001$, $n=30$). This latency difference also applied at the individual muscle level, i.e. the orbicularis oris (TG: 2.14 ± 1.03 , F: 4.62 ± 1.74 , $p = 0.005$, $n=10$), the orbicularis oculi (TG: 2.46 ± 1.23 ms, F: 4.32 ± 1.43 ms, $p = 0.005$, $n=10$) and to a lesser extent the masseter (TG: 3.24 ± 3.27 ms vs F: 4.19 ± 1.60 ms, $p=0.09$, $n=10$).

Conclusions: The prospectively recorded values seem to differ from the previously reported literature. In complex skull-base surgeries, both anatomy and DNS might be misleading as to the identity of the TN and the FN. In such cases, a better knowledge of CMAP latency differences might reveal electrophysiological signatures specific to each cranial nerve, hereby guiding the surgeon and maximizing IONM reliability.

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Transcranial versus Direct Cortical Stimulation for Motor-Evoked Potentials in Supratentorial Tumor Resection: Preliminary Results of the TRANSEKT Trial

Tammam Abboud¹, Maximilian Stein⁷, David Wasilewski^{4,5}, Kathleen Seidel⁶, Arthur Wagner², Katharina Faust^{4,5}, Florian Ringel³, Dorothee Mielke⁸, Bernhard Meyer², Veit Rohde¹, Andrea Szelenyi³

¹ University Medical Center Göttingen, Göttingen, Germany; ² Rechts der Isar Hospital, Munich, Germany; ³ LMU Klinikum, Munich, Germany; ⁴ University Hospital of Düsseldorf, Düsseldorf, Germany; ⁵ Charite- Berlin University Medicine, Berlin, Germany; ⁶ Inselspital Bern, Bern, Switzerland; ⁷ University Medical Center of Johannes Gutenberg University Mainz, Mainz, Germany; ⁸ University Hospital Augsburg, Augsburg, Germany

Intraoperative monitoring of motor-evoked potentials (MEPs) during resection of supratentorial brain tumors under general anesthesia is commonly performed using either transcranial electrical stimulation via scalp electrodes (TES) or direct cortical stimulation via a strip electrode placed on the precentral gyrus (DCS). To date, evidence favoring one method over the other is lacking.

Methods: TRANSEKT is a multicenter, randomized, double-blind, exploratory parallel-group trial conducted at six neurosurgical centers in Germany and Switzerland. Adult patients with supratentorial tumors adjacent to the corticospinal tract and no or mild preoperative paresis were randomized to intraoperative monitoring with TES-MEP or DCS-MEP. A bihemispheric threshold

criterion was applied for TES-MEP monitoring, whereas an amplitude-based criterion was used for DCS-MEP. The primary endpoint was deterioration of motor function at discharge or 7 days after surgery, assessed using the Medical Research Council scale. Secondary endpoints included predictive accuracy of MEP monitoring, extent of tumor resection, and safety outcomes.

Results: A total of 137 patients were randomized and 114 patients were included in the final analysis (DCS $n = 54$; TES $n = 60$) with a dropout rate of 17%. Mean age was 60 years and 56% of patients were male. Postoperative deterioration of motor function occurred in 13/54 patients (24%) in the DCS group and in 12/60 patients (20%) in the TES group ($p = 0.6$). Sensitivity for predicting postoperative motor deficits was comparable between techniques (DCS 44%, TES 29%; $p = 0.399$), while specificity was high in both groups and non-inferior for TES compared with DCS (DCS 86%, TES 94%; $p = 0.021$).

Residual tumor was detected in 33% of patients in the DCS group and in 30% in the TES group, with no significant difference between groups ($p = 0.63$). Intraoperative seizures occurred in 4/114 cases (3.5%). Three-month mortality was 16%, with one death directly related to surgery.

Conclusions: Preliminary results of the TRANSEKT trial demonstrate no significant difference between TES-MEP and DCS-MEP regarding postoperative motor deterioration or extent of tumor resection. Superiority of one monitoring technique over the other could not be confirmed, supporting individualized technique selection based on surgical context and institutional expertise.

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Ultrasound-Triggered Nano-TiO₂ Delivery of Temozolomide: A Novel Approach for Managing Chemoresistant Glioblastoma Multiforme

Ubaidullah Mian¹, Sajjad Ullah²

¹ khyber medical college, Peshawar, Pakistan; ² Khyber Teaching Hospital, Peshawar, Pakistan

Glioblastoma multiforme (GBM) remains the most aggressive primary brain tumor in adults, with poor prognosis despite maximal safe resection followed by chemoradiotherapy using temozolomide (TMZ). Chemoresistance, tumor infiltration, and limited drug penetration across the blood-brain barrier significantly compromise treatment efficacy. Sonodynamic therapy (SDT), which utilizes ultrasound to activate sonosensitizers and generate reactive oxygen species (ROS), has emerged as a promising non-invasive strategy. This study evaluates the therapeutic potential of ultrasound-activated nano-TiO₂ loaded with temozolomide in overcoming chemoresistance and facilitating surgical resection of GBM.

Methods: Nano-TiO₂ particles were synthesized and conjugated with temozolomide to create a multifunctional nanoplateform. Physicochemical characterization assessed particle size, morphology, drug loading efficiency, and stability. In vitro experiments were conducted on GBM cell lines, including chemoresistant models, to evaluate cytotoxicity, ROS generation, apoptosis induction, and synergistic effects under ultrasound activation. In vivo efficacy was examined in orthotopic GBM models, assessing tumor volume reduction, survival outcomes, and histopathological changes. Safety and systemic toxicity were also evaluated.

Results: Ultrasound activation significantly enhanced the cytotoxic efficacy of nano-TiO₂-temozolomide (nTiO₂-TMZ) compared to temozolomide alone. In chemoresistant GBM cell lines, treatment with TMZ alone resulted in a $22.4 \pm 3.1\%$ reduction in cell viability at 48 hours, whereas nTiO₂-TMZ with ultrasound exposure reduced viability by $61.8 \pm 4.7\%$ ($p < 0.001$). Reactive oxygen species (ROS) generation increased 3.4-fold in the ultrasound-activated group compared to control ($p < 0.001$).

Flow cytometry demonstrated significantly higher apoptosis rates in the combination therapy group (early + late apoptosis: $58.2 \pm 5.6\%$) versus TMZ alone ($27.9 \pm 4.2\%$, $p < 0.001$). Caspase-3 activation and Bax/Bcl-2 ratio were significantly elevated ($p < 0.01$). Colony formation assays showed a 68% reduction in clonogenic survival compared to control ($p < 0.001$).

In vivo, orthotopic tumor models treated with ultrasound-activated nTiO₂-TMZ demonstrated a 55–65% reduction in tumor volume compared to TMZ monotherapy ($p < 0.01$). Median survival increased from 32 days (TMZ alone) to 49 days in the combination group (log-rank $p = 0.002$). No significant systemic toxicity or organ damage was observed ($p > 0.05$).