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Evaluation of a new cortical strip electrode for intraoperative somatosensory monitoring during perirolandic brain surgery

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HIGHLIGHTS

- We performed a prospective multicenter medical device study.
- Polymer strips with embedded metal nanoparticles had lower impedance than the comparator device.
- The electrodes achieved good signal-to-noise-ratio.

ABSTRACT

Objective: During neurosurgical procedures, strip electrodes should have low impedance and sufficient adherence on the brain surface. We evaluated the signal quality, safety, and performance of a novel strip electrode (WISE Cortical Strip, WCS®), with conductive electrode contacts created with platinum nanoparticles embedded in a polymer base.
Methods: In a multicenter interventional, non-inferiority study, we compared WCS to a conventional strip electrode (Ad-Tech). We recorded impedance and somatosensory evoked potentials (SEP) and determined the signal-to-noise ratio (SNR). We performed direct stimulation of the motor cortex. An external clinical event committee rated safety and adverse events and users rated usability.
Results: During 32 brain surgeries in the paracentral region, WCS was rated safe and effective in signal transmission. Two seizure events were classified as probably related to the stimulation with WCS. The users rated WCS adhesion to the brain as satisfactory but reported difficulties sliding the WCS under the dura. The median (IQR) impedance of WCS was lower than for Ad-Tech: 2.7 (2.3–3.7) *vs* 5.30 (4.3–6.6) kΩ ($p < 0.005$). The SNR of SEP was non-inferior for WCS compared to Ad-Tech.
Conclusions: The impedance of WCS was lower than Ad-Tech without safety limitations. In small craniotomies not exposing the motor cortex its use may be limited.
Significance: Low impedance electrodes facilitate recordings with high SNR.

1. Introduction

Intraoperative neurophysiological monitoring (IONM) has become an important diagnostic tool that helps to guide the surgeon during neurosurgical interventions in cranial neurosurgery (Nuwer, 2008). Among standard modalities of IONM, somatosensory evoked potentials (SEP) are used to monitor somatosensory tract function and, indirectly, cortical perfusion (MacDonald et al., 2019). When recording with electrodes placed directly on the brain surface (electrocorticography, ECoG), the phase reversal of the SEP indicates the central sulcus between the somatosensory

Abbreviations: AE, Adverse Event; CD, Comparator Device; DCStim, Direct Cortical Stimulation; ECoG, ElectroCorticoGraphy; IONM, IntraOperative Neurophysiological Monitoring; IQR, Interquartile Range; MEP, Motor Evoked Potential; PRSEP, Phase reversal of the sensory evoked potential; RMS, Root Mean Square; SADE, Serious Adverse Device Effect; SEP, Somatosensory Evoked Potential; SNR, Signal-to-Noise Ratio; TD, Test Device; WCS, WISE Cortical Strip; WIN, WISE cortical strip for Intraoperative Neurophysiological monitoring.

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and the motor brain areas (Cedzich et al., 1996; Romstöck et al., 2002). ECoG electrodes are commonly shaped as strips with 4 or more contacts embedded in a polymer base layer of thickness < 1 mm. The ECoG electrodes may also serve for direct cortical stimulation (DCStim) to elicit motor evoked potentials (MEP) (Taniguchi et al., 1993; Cedzich et al., 1996; Neuloh et al., 2007; Szelenyi et al., 2007a, 2007b; Seidel et al., 2013).

For optimal use in neurosurgery, the electrodes should not only be easy to handle during placement but also should not slip from the optimal position. Change in electrode position might cause a false positive alarm by erroneously interpreting an amplitude decline as a surgical event. However, there is a trade-off between the adhesiveness of an electrode and the stiffness of the polymer strip, because the electrode should be suitable to be placed under the dura in small craniotomies.

As a further characteristic, a low impedance of the electrode is desirable when recording signals with small amplitude. A low impedance reduces the background noise, thereby enhancing the signal-to-noise ratio (SNR). An example for a signal with small amplitude are high frequency oscillations that indicate epileptogenic tissue (Burnos et al., 2016; Fedele et al., 2017a, 2017b).

As a newly developed ECoG electrode (WISE Cortical Strip, WCS®), conductive electrode contacts were created with platinum nanoparticles embedded in a polymer base. This yields a flexible strip electrode that was shown to have low impedance contacts in the experimental setting (Ravagnan et al., 2009; Corbelli et al., 2011; Marelli et al., 2011; Gnatkovsky et al., 2019).

We here present the results of a prospective multicenter medical device study that clinically validated the WCS strip electrode for application on the brain surface during neurosurgery.

2. Patients and methods

2.1. Study design

The medical device study, "WIN Study" (WIN: WISE cortical strip for Intraoperative Neurophysiological monitoring), was a prospective, interventional, non-inferiority, multi-center, open-label, one-arm and pre-market study being conducted between April 2019 to January 2020. This study was performed in accordance with the World Medical Association Declaration of Helsinki, ISO 14155:2011(E) and all local legal and regulatory requirements (including the competent authorities). All patients provided written informed consent for the study, which was approved by each institutional ethics review board: Center ID: WIN-001, Ethikkommission der Medizinischen Fakultät der LMU München (Munich, Germany), Center ID: WIN-003, Kantonale Ethikkommission Zürich (Zurich, Switzerland), Center ID: WIN-004, Kantonale Ethikkommission Bern (Bern, Switzerland), and Center ID: WIN-006, CESC delle Province di Verona e Rovigo (Verona, Italy).The trial was registered before the first patient was recruited at ClinicalTrials.gov (ID: NCT03731455). For the full details of the study beyond the results presented here we refer to the Supplementary Online Material: study workflow**,** study information, aim and endpoints (Supplementary Text S3), and adverse event (AE) classification (Supplementary Text S4).

2.2. Study population

Adult patients who were indicated for intracranial perirolandic surgery under intraoperative neurophysiological guidance for refractory epilepsy or brain tumors according to an interdisciplinary case discussion and who met the inclusion and exclusion criteria were recruited for the WIN study (Supplementary Table S5).

2.3. Test device

The test device (TD, WCS, WISE Cortical Strip, WISE Co., Milan, Italy) is a 4-contact cortical electrode strip (length: 62 mm; thickness: 0.25 mm; material of electrodes: pure platinum; exposed electrode diameter: 2.3 mm; inter-electrode distance: 10 mm center-to-center), to be positioned on the exposed surface of the brain and equipped with a cable that allows the transmission of the electrical signals to and from the IONM equipment (Fig. 1) (Ravagnan et al., 2009; Corbelli et al., 2011; Marelli et al., 2011). The TD is intended for intraoperative recording of electrical signals and stimulation on the surface of the brain in patients affected by brain tumors or epilepsy. To manufacture the TD, WISE uses supersonic cluster beam implantation, a proprietary patented technology (PCT/EP2011/054903). This allows to embed a thin, conducting metal layer (i.e., platinum) on a silicone substrate to realize a flexible, soft and thin cortical strip electrode that is biocompatible.

The electrode and the platinum contacts have been studied in detail (Gnatkovsky et al., 2019). The implanted platinum nanoparticles range between 10 nm and 100 nm in size so that the nanostructure has roughness in the same order of magnitude as has been confirmed by tunneling electron microscopy. Due to the roughness, the surface area of each contact is around 70 times larger than a flat platinum surface. The large surface area allows a highly efficient exchange of charge at the interface between the surface and the surrounding fluids. These microscopic properties become evident during application of the electrode as they result in low impedance and high capacitance of the electrode.

2.4. Comparator device

As a comparator device (CD) served a commercially available 4-contact cortical strip electrode (Ad-Tech Medical Instruments Corporation, Racine, Wisconsin, USA). The electrode is composed of a silicon strip (strip thickness 0.8 mm; platinum electrode contact diameter: 2.3 mm; distance between contact centers: 10 mm). This electrode is frequently used in IONM-guided neurosurgery and is CE- and FDA-certified for this purpose (Fig. 1).

2.5. Measurement setup

All measurements and data were obtained, recorded and stored on a neuromonitoring device (ISIS System, NeuroExplorer software version 6 or higher, Inomed Co., Emmendingen, Germany). After dura opening, the TD and/or the CD were placed on the brain surface tangentially over the central sulcus so that they covered both primary motor and primary somatosensory cortex. During measurements, the surgical field was covered by a moist gauze to ensure optimal impedance.

The neuromonitoring device measured the impedance of the electrode contact at 140 Hz. The impedance values were acquired before (at placement) and after the SEP/ECoG recordings, as well as at the end of the surgery (after MEP stimulation).

For ECoG and SEP recordings, the two strip electrodes were either placed next to each other for simultaneous recording, or they were placed consecutively for consecutive recording. This was left to the surgeon's discretion and decided upon the exposed cortex available for optimal recording of the phase reversal of the somatosensory evoked potential (PRSEP). A subdermal needle electrode placed at Fpz or a dura needle served as electrical reference.

For ECoG recording, the signal was filtered in the pass band 0.5–2500 Hz and then sampled at the sampling frequency 20 kHz. ECoG was recorded continuously.

For SEP recording, the median nerve was stimulated with square-wave pulses of 200 μsec duration, frequency range 3.7–

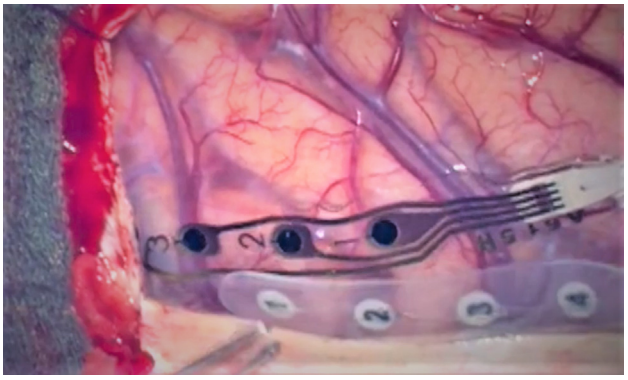

Fig. 1. Strip electrodes in the surgical field The Test Device (TD; WISE Cortical Strip WCS®) on the brain with black contacts and golden numbering. The Comparator Device (CD) is shown for comparison.

5.7 Hz, stimulation intensity <20 mA. The signal was filtered in the pass band 0.5–2500 Hz and then sampled at the sampling frequency 10 kHz. The 160 ms sweeps following the stimulation pulse were then averaged to obtain the averaged SEP. Simultaneously with the averaged SEP, we recorded ECoG in a separate window so that single sweeps could be analyzed offline. Before resection ("baseline condition"), we recorded three SEP sessions with 100 sweeps each (for more details, see Supplementary Fig. S2).

2.6. Usability assessment

After surgery, both the neurosurgeon and the person in charge of the neuromonitoring assessed adequacy of both devices to their intended use by a usability questionnaire. The closed questions with a ranking scale from 1 to 7 covered placement and repositioning, handiness, material, adhesion, and stability on the brain surface. The higher the ranking score, the more adequate was the device for its intended use. Further optional comments were collected as free text.

2.7. Data preprocessing and analysis

All post-hoc data processing and analysis was performed by an external expert in neurophysiological signal analysis who was blinded to the devices. The expert is an engineer who works at the Fondazione Don Carlo Gnocchi – Onlus (https://www.dongnocchi.it/). The statistical analysis was performed by a statistician who holds a PhD in mathematics and was a senior statistician at Quantics Consulting Ltd (https://www.quantics.co.uk), which was contracted for the biostatistical analyses.

Stimulation artefacts were used to identify the periods of SEP stimulation in the continuous ECoG recordings. Each SEP signal sweep underwent three separate filtering steps: notch filter (50 Hz), high-pass filter with cut-off frequency 30 Hz, and low-pass filter with cut-off frequency 1000 Hz.

To compute the signal-to-noise ratio of the SEP, the external expert used an algorithm taken from the literature (Burnos et al., 2016; Fedele et al., 2017b). The algorithm determines the SNR in each SEP single sweep before the signals are averaged (Fig. 2). The amplitude of the N20 peak ("signal") was defined as the root mean square (RMS) of the signal in the window (15, 25) ms after the stimulus artefact. The peak was negative for contacts over sensory cortex and positive for contacts over motor cortex. The RMS of the signal in the window (−30, −20) ms before the stimulus artefact was defined as baseline ("noise"). The SNR for each sweep was calculated as the ratio between the "signal" and the "noise". The SNR% was defined as the percentage of sweeps with SNR > 1.

2.8. Sample size calculation

A sample size of 28 was required to ensure that the study had a "reasonable probability" of 95% to observe at least one patient with TD-related Serious Adverse Device Effect (SADE) if the true SADE incidence is equivalent to the state of the art, which is taken to be 10.3%. This sample size allows to state that the TD is at least as safe as the current practice with 95% confidence by comparing the upper, one sided, 95% confidence limit (rounded to three significant digits) from an exact binomial test of the true proportion with 0.103. Additionally, if more than one SADE events were observed, the TD is at least as safe as the current practice with 80% confidence.

Further, a sample size of 28 was also required to show that quality of recorded signals (in terms of SNR%) by the TD was non-inferior to that recorded by the CD, via a two-sided, 95% level confidence interval, assuming a difference of 10 percentage units between the SNR% of the CD and TD to be acceptable.

2.9. Statistics

For statistical analysis we used the SAS software. The intra-individual impedance was compared with a paired, two-sided t-test for testing the hypothesis that the impedance of the TD was lower than the impedance of the CD. The intra-individual SNR% was compared with a paired, two-sided t-test for testing the hypothesis that the SNR% of the TD is less than 10% worse than the SNR% of the CD. Statistical significance was established at $p < 0.05$. The scores of the usability-questionnaire were analyzed with mean, standard deviation, median, IQR (interquartile range), and median score difference > 0.5 was considered significant. SADEs were binomially tabulated and binomial confidence intervals were calculated for the incidence rate.

3. Results

3.1. Patient characteristics

A total of 32 patients (51.6 ± 14.9 years of age; 19–74 years, 15 males and 17 females) were enrolled (Supplementary Table S1). 31 patients were treated for surgical removal of a brain tumor and 1 patient for epilepsy surgery.

We enrolled 32 patients instead of the 28 patients because the Swiss Competent Authority required an interim analysis after enrollment of the first 5 patients. As requested by the Swiss Competent Authority, the TD device was not used as per study protocol and thus the TD data were not fully collected in 4 out of these 5 patients. Therefore, the overall number of patients enrolled in the study had to be increased to 32 patients.

3.2. Impedance measurements

The impedance values of the TD were measured at placement before and after the SEP/ECoG recordings (median (IQR) = 2.7 (2.3, 3.7) kΩ) as well as after MEP stimulation (median (IQR) = 2.5 (1.8, 3.1) kΩ) (Table 1, Fig. 3). Across all measurements, 98.34% (296 measurements out of 301) were below 10 kΩ, which was the criterion for acceptability. On a patient-by-patient basis, the impedance measurements were stable at each time point.

The median (IQR) impedance of the CD was 5.3 (4.3, 6.6) kΩ before and after the SEP/ECoG and after MEP stimulation it was 3.3 (2.8, 4.1) kΩ. Across all measurements, 88.45% (268 measurements out of 303) were below 10 kΩ. As a main result of the study, the impedance of the TD was always lower than the impedance of the CD ($p < 0.001$, paired t-test).

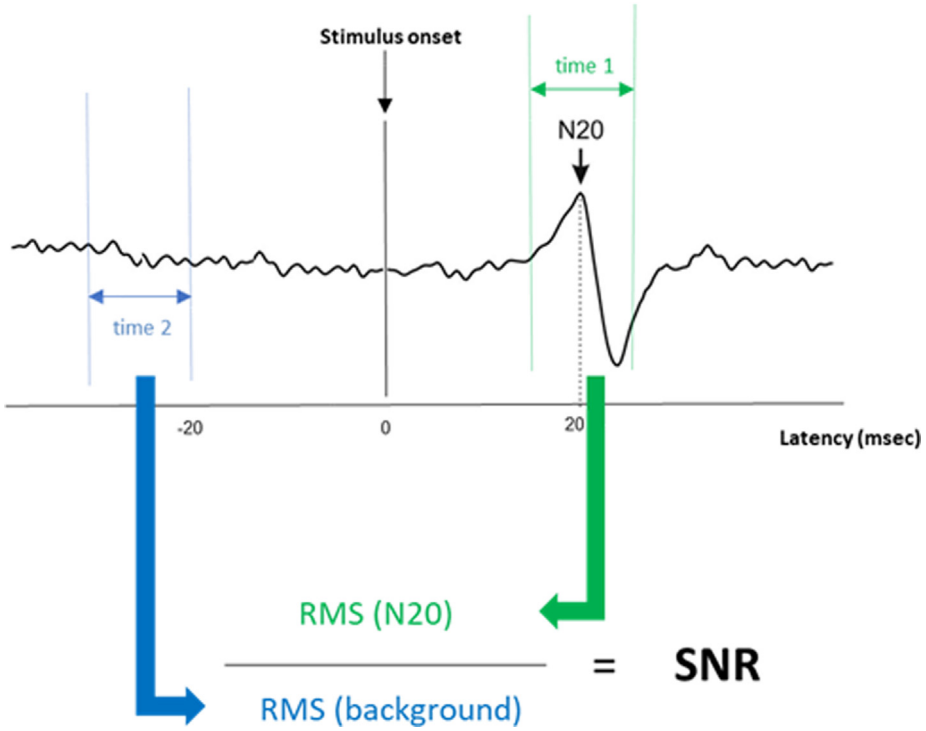

Fig. 2. Calculating the Signal-to-Noise Ratio (SNR) For calculating the SNR, the signal is taken as the Root Mean Square (RMS) around N20 in the window (15, 25) ms. The noise is taken as the RMS from the signal 20 ms before stimulus onset in the window (−30, −20) ms.

Table 1
Impedance values of Test Device and Comparator Device. Stable performance of the Test Device was confirmed by the preservation of impedance values below 10 kΩ.

	Test Device (TD)		Comparator Device (CD)	
Time point of impedance recording before	**SEP recording**	**Direct cortical stimulation**	**SEP recording**	**Direct cortical stimulation**
Total number of patients	32	27[2]	32	27
Any impedance measurements, *n* patients (%)	32 (100.0)	27 (100.0)	32 (100.0)	12 (44.4)
Max impedance across all recording times ≥ 10 kΩ, n patients (%)[1]	2 (6.3)	1 (3.7)	13 (40.6)	2 (7.4)
Number of recording times per patient – Mean (Min, Max)	2.0 (1, 3)	2.1 (1, 9)	1.9 (1, 3)	1.7 (1, 6)
Median Number of electrodes used (Min, Max)	4.0 (2, 4)	4.0 (1, 4)	4.0 (1, 4)	4.0 (1, 4)
Impedance – Mean (SD)	3.11 (1.577)	2.81 (2.232)	6.83 (6.567)	5.30 (9.887)
Impedance – Median (IQR)	2.70 (2.30,3.70)	2.50 (1.80, 3.10)	5.30 (4.30,6.60)	3.30 (2.80, 4.10)

SEP Somatosensory Evoked Potential; SD Standard Deviation; IQR interquartile range.
[1] Percentage of patients with any impedance measurement.
[2] This excludes patients with the Test Device that were excluded from the resection phase as required by the Swiss competent authority.

3.3. The SNR of the SEP

To study whether the lower impedance has an impact on signal recording, the SNR during SEP recording was analyzed. For this, TD and CD were tested consecutively in 7 and simultaneously in 25 patients, respectively.

Table 2 lists the SNR% for each enrolled patient. A positive difference indicates that the TD-SNR% was higher than the CD-SNR %. The SNR% data was missing because the data was not stored (n = 3 patients) or if the SEP stimulation artefact could not be identified in the ECoG (n = 5 patients). Accordingly, the data of 24 patients were available for further analysis. The differences in SNR% were in the range −29.3% to 21.3%. The distribution of SNR % differences is shown in Fig. 4.

We next compared the quality of the signals recorded by TD and CD. The observed mean (SD) difference in SNR% was 1.43% (12.8%) and the median (IQR) difference in SNR% was 0.67% (−2.3%, 9.8%). We performed a t-test on the observed patient-level difference in SNR% and compared the population distribution to a threshold of 10 percentage points (clinical acceptance criterion). When applying the clinical acceptance criterion, the TD appeared to be no worse than the CD (i.e., the two-sided p-value = 0.0001 was below 0.05). Thus the signal quality of the TD in terms of SNR% was non-inferior to that of the CD.

We questioned whether the missing SNR% data in 8 patients might have introduced a bias in the comparison of SNR% between TD and CD. To rule out bias, we compared the TD impedance values of the 8 patients (median (IQR) = 2.9 (2.6, 3.1) kΩ) with the TD impedance values of the remaining 24 patients (median (IQR) = 3.1 (2.6, 3.1) kΩ). We found no significant difference (p > 0.05, t-test). We therefore assume that the missing patients were randomly selected with respect to their SNR% data. Then we can further contend that the signal quality of the TD in terms of SNR% was non-inferior to that of the CD.

3.4. Usability of TD and CD

The 17 users at the four centers (11 neurosurgeons, 6 neurophysiologists) submitted a total of 63 questionnaires for 32 procedures. Overall, the mean (SD) score given by neurosurgeons for the

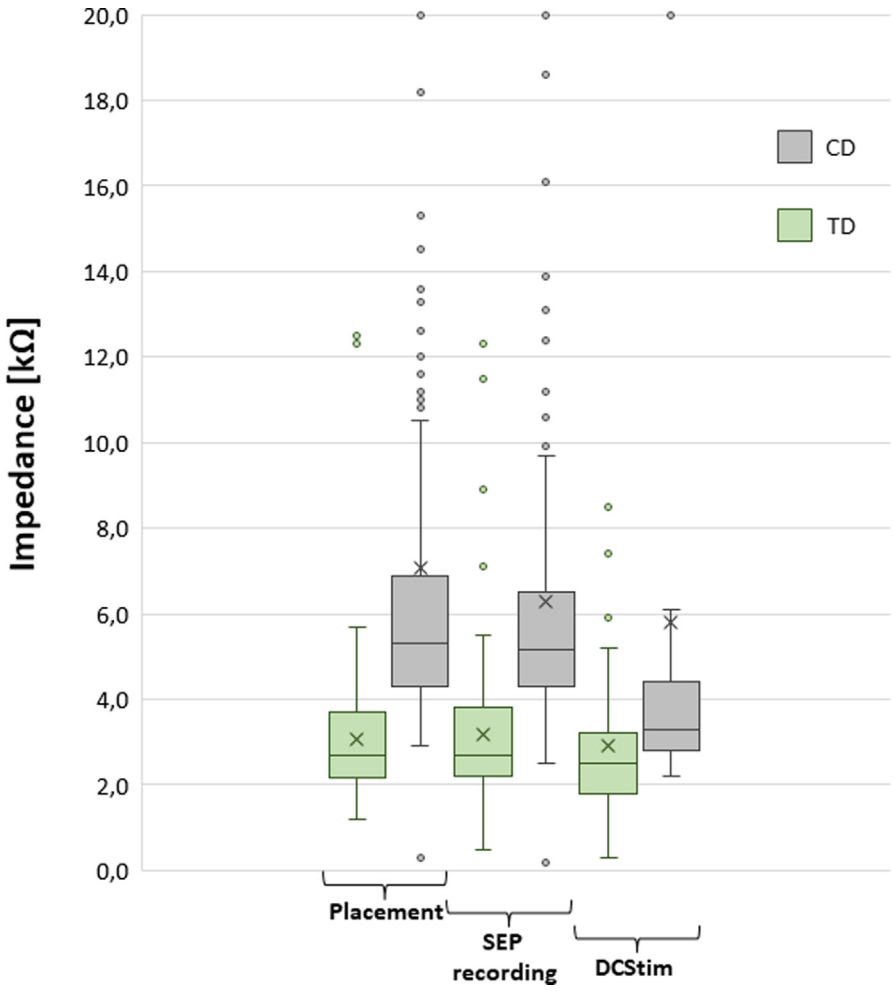

Fig. 3. Impedance values Distribution of impedance values at each recording time (i.e., Placement, Somatosensory Evoked Potential (SEP) recording, and Direct Cortical Stimulation (DCStim). The median of impedances is lower for Test Device (TD) than for Comparator Device (CD) ($p < 0.001$, t-test). TD median (IQR) = 2.9 (2.3, 3.7) kΩ. CD median (IQR) = 5.3 (4.3, 6.6) kΩ. IQR interquartile range. *Impedance values > 20 kΩ were measured only for CD and have been excluded from the graph.

TD was 5.9 (1.3) vs 5.7 (1.1) for the CD, and neurophysiologists gave a mean score of 6.1 (1.3) for TD and 5.5 (1.4) for the CD.

Only judgements on "device adhesion and conformability" on the brain surface (TD vs CD (mean (SD)): neurosurgeons: 6.6 (0.6) vs 4.9 (1.4); neurophysiologists: 6.4 (1.0) vs 5.0 (1.4)) and "device stability against movement or misplacement" (TD vs CD: neurosurgeons: 6.1(1.1) vs 5.1 (1.0); neurophysiologists: 6.4 (1.0) vs 5.4 (1.0)) were rated with a median score difference > 0.5.

As anecdotal evidence, we also collected users' comments in the optional text field. One class of comments pertained to surgeries with small craniotomies not exposing the motor cortex, where the strip electrodes had to be slid under the dura for correct positioning. In 9/32 surgeries, the neurosurgeons reported difficulties when sliding the TD (and not the CD) under the dura, because the thin TD is very flexible and lacks stiffness. We report these comments here because they reflect a limitation for the usability of the TD.

3.5. Safety and adverse events

There were not any safety issues reported. Per study protocol, any untoward medical occurrence, unintended disease or injury, or untoward clinical signs following the patient recruitment were defined as AE; overall 24 AEs were reported (full details are provided in Supplementary Table S6). Two seizure events occurred, both with the TD, and were classified as not serious and in "probable" or "possible" relationship with the TD according to the reviews by clinical event committee members. The terms are defined in the Supplementary Text S4. The relationship of AE to the surgical procedure was classified as "highly probable" in 17/24 AEs (70.8%), "probable" in one AE (4.2%), "possible" in 2 AEs (8.3%), "highly related" in one AE (4.2%) and "not related" in 3 AEs (12.5%).

In 12 out of 32 patients (37.5%) new or aggravated neurological deficits (multiple reporting) related to the surgeries were reported (Supplementary Tables S1 and S6). In 8 patients (25.0%) a new motor deficit occurred, of which minor motor deficits persisted in 4 patients (12.5%). Five (15.7%) patients presented with an aphasia, persisting in three patients (9.4%). Two patients (6.25%) experienced episodes of seizures with no further consequences. Non-neurological AEs were as follows: in one patient each (3.1%), an infection, a hemorrhage within the resection cavity not requiring another surgical procedure and a cerebrospinal fluid leakage occurred. One patient suffered from a pulmonary embolism resulting in prolonged hospital stay.

4. Discussion

As a main result of the study the TD offered a lower impedance than the CD. In SEP recordings the percentage of trials with a high

Table 2
Observed patient-level difference in Signal-to-Noise Ratio (SNR).

	Patient ID	Test Device – SNR%[1]	Comparator Device – SNR%[1]	Difference in SNR%[2]
1	WIN-001_001	99.7	99.3	0.3
2	WIN-001_002	94.7	86.7	8.0
3	WIN-001_003	n.a.	n.a.	n.a.
4	WIN-001_005	92.7	71.3	21.3
5	WIN-001_006	97.7	99.7	−2.0
6	WIN-001_007	n.a.	n.a.	n.a.
7	WIN-001_008	90.0	72.0	18.0
8	WIN-001_009	64.3	90.3	−26.0
9	WIN-001_012	83.0	92.0	−9.0
10	WIN-001_013	91.7	73.0	18.7
11	WIN-003_001	83.3	87.7	−4.3
12	WIN-003_002	89.0	91.3	−2.3
13	WIN-003_003	94.3	79.0	15.3
14	WIN-003_004	97.7	100.0	−2.3
15	WIN-003_005	98.7	94.3	4.3
16	WIN-003_006	n.a.	n.a.	n.a.
17	WIN-003_007	97.3	84.0	13.3
18	WIN-003_008	100.0	99.0	1.0
19	WIN-003_009	99.7	99.7	0.0
20	WIN-003_010	77.7	95.3	−17.7
21	WIN-003_011	66.0	95.3	−29.3
22	WIN-003_012	99.7	100.0	−0.3
23	WIN-003_013	57.3	54.7	2.7
24	WIN-003_015	99.3	87.7	11.7
25	WIN-003_016	97.7	98.3	−0.7
26	WIN-004_002	n.a.	n.a.	n.a.
27	WIN-004_003	n.a.	n.a.	n.a.
28	WIN-004_004	n.a.	n.a.	n.a.
29	WIN-004_005	n.a.	n.a.	n.a.
30	WIN-004_006	n.a.	n.a.	n.a.
31	WIN-004_007	93.3	87.3	6.0
32	WIN-006_001	67.3	59.7	7.7

The SNR% values were not calculated in the following patients: WIN-001_003, WIN-001_007, WIN-003_006, WIN-004_002, WIN-004_006, WIN-004_003, WIN-004_004 and WIN-004_005 (missing values are marked as not available (n.a.)).
[1] The SNR% is the percentage of Somatosensory Evoked Potential (SEP) trials with SNR > 1 in three recording sessions, each with 100 single trial SEP recordings.
[2] Difference between Test Device and Comparator Device.

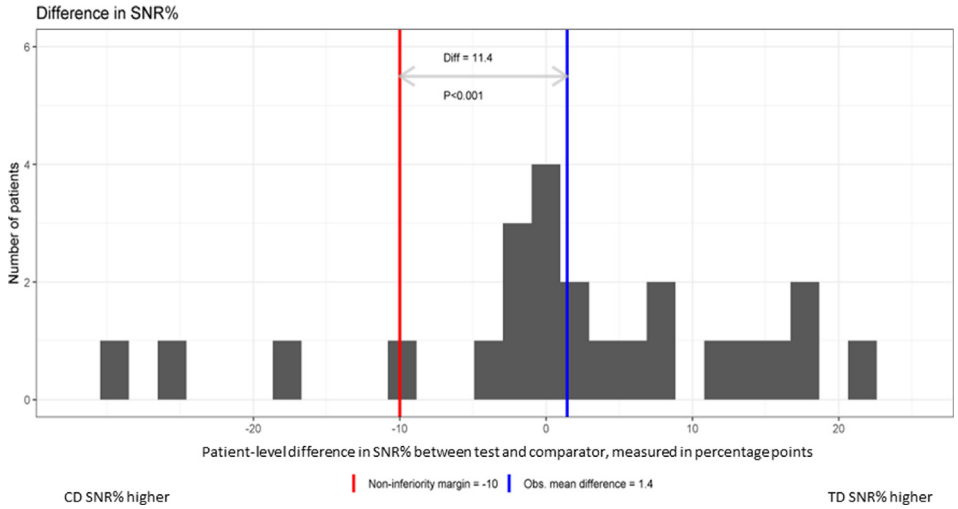

Fig. 4. Signal-to-Noise Ratio (SNR%) across the patient population The SNR% is the percentage of sweeps with SNR > 1. Histogram of the differences in SNR% across all 24 recordings (Table 2). A difference of 10 percentage points is the non-inferiority margin (red line) between the Test Device (TD) SNR% and the Comparator Device (CD) SNR%. The observed mean difference (Diff. = 1.4, blue line) is well above the non-inferiority margin.

SNR was higher for TD. No limitations with respect to safety were noted. While the TD showed better adhesion to the brain surface, due to its soft consistency, placement was difficult when partial exposure of the motor cortex required sliding of the TD underneath a dural rim.

4.1. Lower impedance of TD

The impedance of the TD (median 2.9 kΩ) was lower than the impedance of the CD (median 5.3 kΩ). This may be due the better flexibility and adhesion to the brain, leading to a larger surface

joining the electrode contact and the brain. A further reason for the lower impedance may be the rough surface structure of the platinum contact surface (Ravagnan et al., 2009; Corbelli et al., 2011; Marelli et al., 2011).

4.2. SNR in the recording

The total noise in a recording (Fedele et al., 2017a, 2017b) is the sum of.

(1) the internal noise of the brain,
(2) the noise induced by the electrode-brain interface, and.
(3) the noise of the amplifier.

The noise of the electrode-brain interface is directly proportional to the impedance of the electrode-brain interface. Therefore, a low impedance may contribute to a better SNR in a recording.

In general, a high SNR is desirable as it may improve the reliability and the speed in acquiring the targeted signal. Thus, with higher acquisition speed the IONM neurophysiologist can provide faster feedback to the neurosurgeon, which is essential to reverse signal changes before they become irreversible. In our study, the signal amplitude of the SEP was high already for both TD and CD. Consequently, the SNR and the SNR% were high and not further improved by the improvement of the impedance with the TD.

There are examples for low amplitude signals where the detection can be improved with better SNR. Among the examples are cortical evoked SEP, visual evoked potentials, cortico-cortical evoked potentials, or high frequency oscillations. We have shown earlier that the detection of high frequency oscillations can be improved with a low noise amplifier (Fedele et al., 2017a, 2017b). In view of the three sources of noise mentioned above, the detection of high frequency oscillations might be improved by reducing the impedance of the recording electrode.

4.3. Safety and usability

Given the absence of clearly TD-related SAEs during the clinical investigation with a sample size of 28, using the TD is as safe as using the CD in current clinical practice (with 95% confidence level). Overall, the users rated the usability and performance of the TD as efficient as the CD. The adhesion on the brain surface and thus the stability on the brain surface was rated better compared to the CD. Conversely, the better adhesion and the higher flexibility limited sliding of the TD underneath the dura which might be required in small craniotomies not exposing the motor cortex.

5. Conclusions

The TD had significant lower impedance than the comparator which could be related to better adhesion and conformability to the brain surface. No limitations with respect to safety were noted. The TD was suitable for direct recording and DCStim of the brain surface. In small craniotomies not exposing the motor cortex, the use of the TD might be limited.

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Author contributions

AS participated in the design of the study.
JS, AS, KS, FS performed recordings.
All authors actively participated in data acquisition and analysis.
AS and JS wrote the manuscript. All authors reviewed and edited the manuscript.

Conflict of interest

None of the authors have potential conflicts of interest to be disclosed. All authors declare that they participated in the study without receiving personal compensation. AS, KS, JS are members of the IOM board of inomed Medizintechnik GmbH and have received speaker honoraria. MCN has reviewed documentation for WISE and his institution has received research funds from WISE Srl.

Appendix A. Supplementary material

Supplementary material to this article can be found online at https://doi.org/10.1016/j.clinph.2022.07.497.

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