How rapidly acquiring reproducible intraoperative FVEP waveforms: is something changing?

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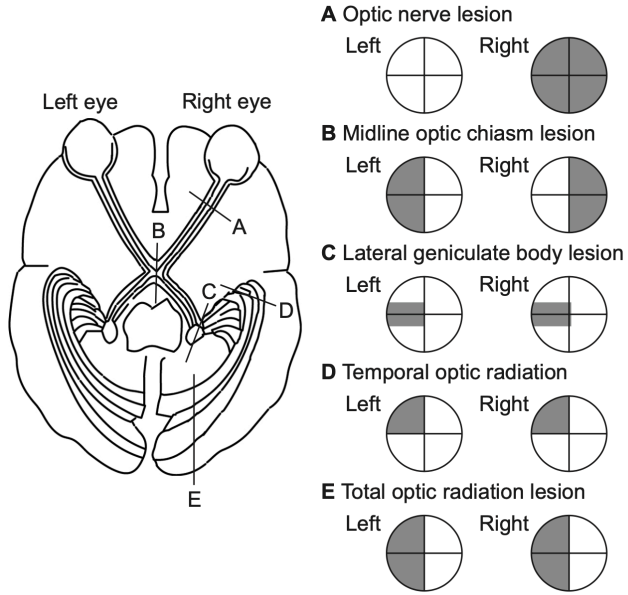
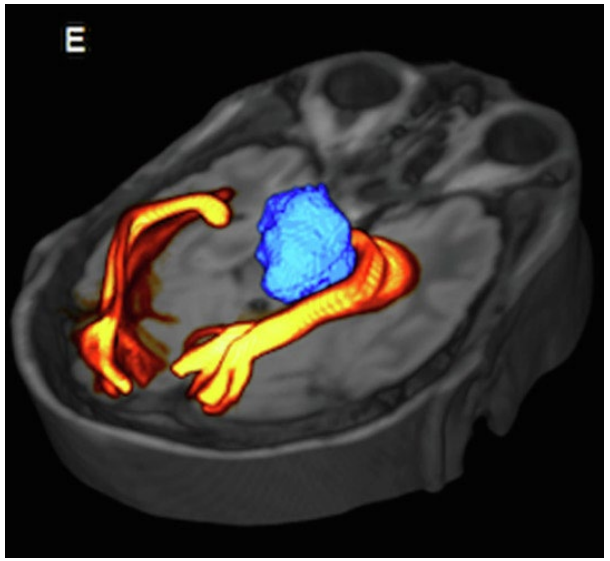
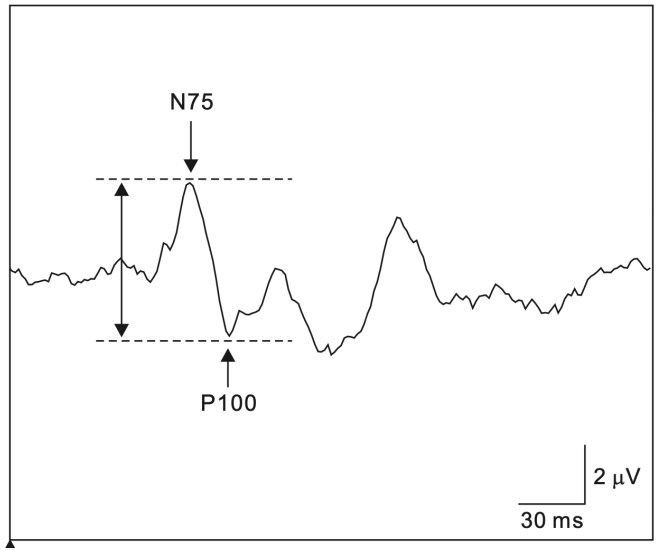
Aim

- Surgeries pose a risk of **visual impairment in the intraoperative period** include particularly tumorectomy at the **optic chiasm of pituitary adenomas, craniopharyngiomas, tuberculum sellae meningiomas, and other intrinsic brain tumors** that are close to either the **optic nerves, visual tracts, or temporal-occipital cortices.**
- Over the past five years, the scientific community has shown **increasing interest** in the use of VEPs intraoperatively.
- to determine **how to improve** the reliable of intraoperative monitoring of **flash visual evoked potential (FVEP)** and its relationship with visual **outcome** in the neurosurgery field.

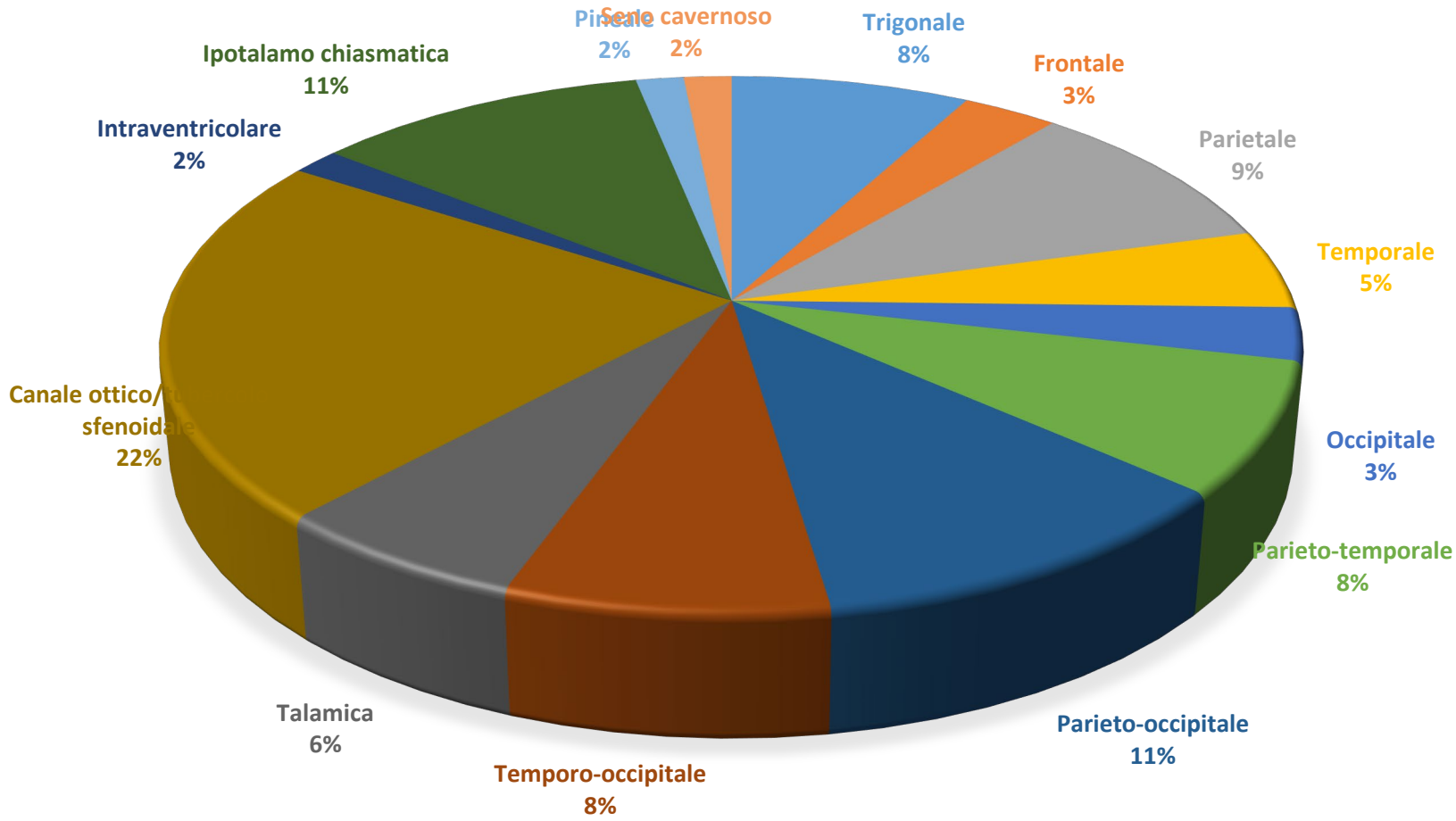




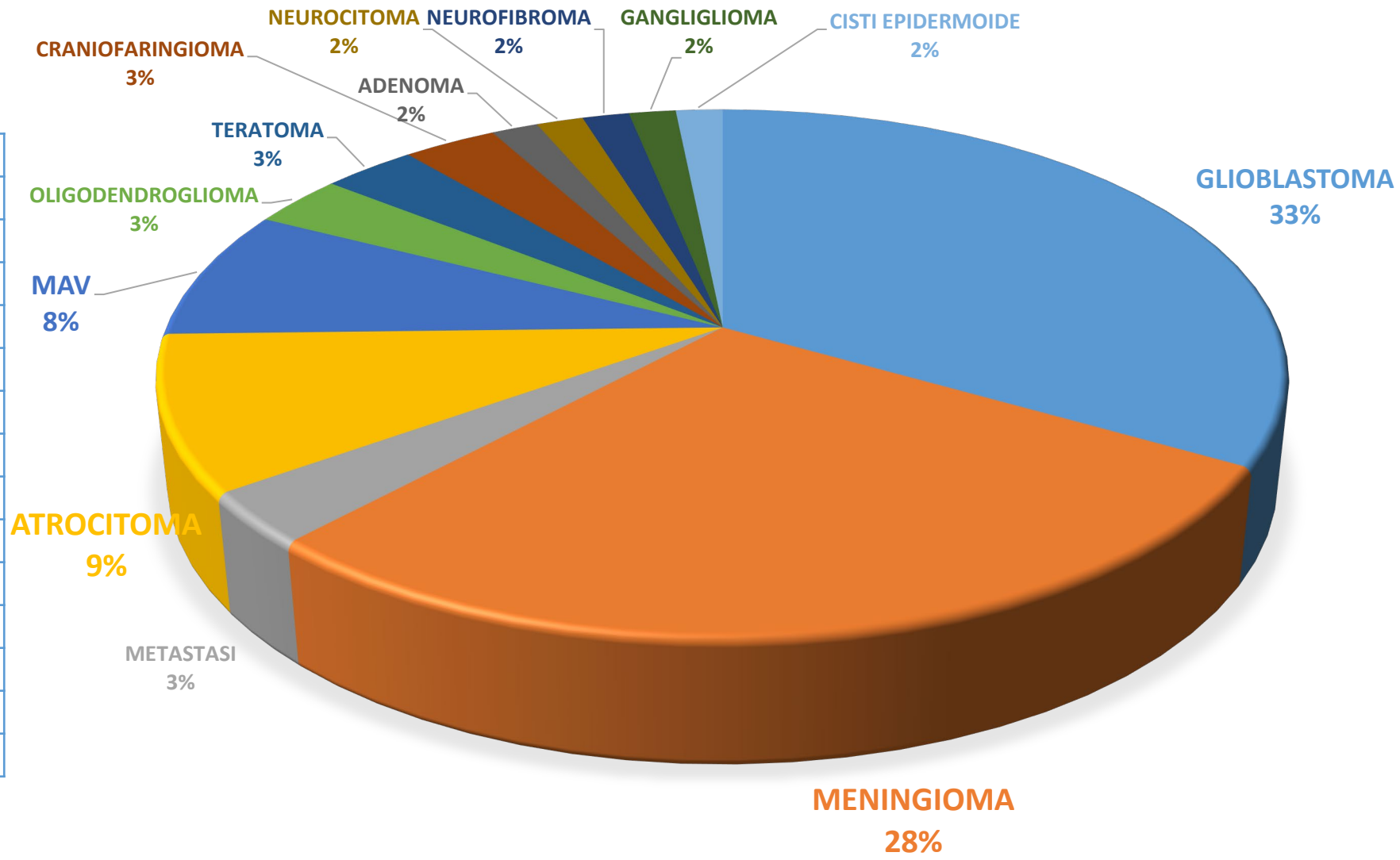


This study included **63 patients** who underwent craniotomy for the resection of a brain lesion located close to the visual pathways or associated areas.
Mean age 48, sd 16 y

	N°	%
TRIGONALE	5	8
FRONTALE	2	3
PARIETALE	6	9
TEMPORALE	3	5
OCCIPITALE	2	3
PARIETO-TEMPORALE	5	8
PARIETO-OCCIPITALE	7	11
TEMPORO-OCCIPITALE	5	8
TALAMICA	4	6
CANALE OTTIO/TUBERCOLO SFENOIDALE	14	22
INTRAVENTRICOLARE	1	2
IPOTALAMO CHIASMATICA	7	11
PINEALE	1	2
SENO CAVERNOSO	1	2
	63	



	N°	%
GLIOBLASTOMA	21	33
MENINGIOMA	18	29
METASTASI	2	3
ATROCITOMA	6	10
MAV	5	8
OLIGODENDROGLIOMA	2	3
TERATOMA	2	3
CRANIOFARINGIOMA	2	3
ADENOMA	1	2
NEUROCITOMA	1	2
NEUROFIBROMA	1	2
GANGLIGLIOMA	1	2
CISTI EPIDERMOIDE	1	2
	63	

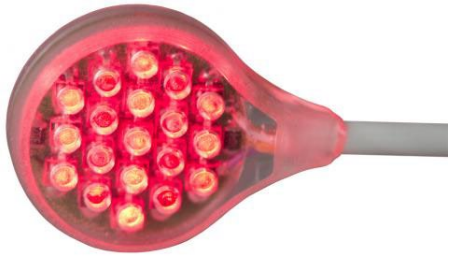


Material and methods

Intraoperative Monitoring of VEPs

- Intraoperative FVEPs were recorded from occipital subcutaneous corkscrew electrodes placed on **Oz, O1, O2** with preferred reference at the vertex, and Cz, with the ground electrode made of linked A1 and A2 (reference electrodes A1 and A2) (international 10/20 EEG system) and **directly (dFVEPs)** in the occipital cortex with subdural strip
- Signals were averaged over typically 50 sweeps for every VEP
- bandpass filtering 10–100 Hz (1-1000),
- length 200 msec
- The duration of the stimulation was **8 msec** (10-20 ms)
- stimulation intensities 10 000 to 20 000 Lx (adjusted to the minimum stimulation intensity that produced the maximum amplitude)
- at a rate of 0.9 Hz (1-2 Hz).

Flash stimulation



LED flash goggles for VEP stimulation 1.5mm touchproof connector, Diameter 18.6mm.
Each device contains 19 red (654 nm) diodes that provide illuminance up to 25000 Lux.

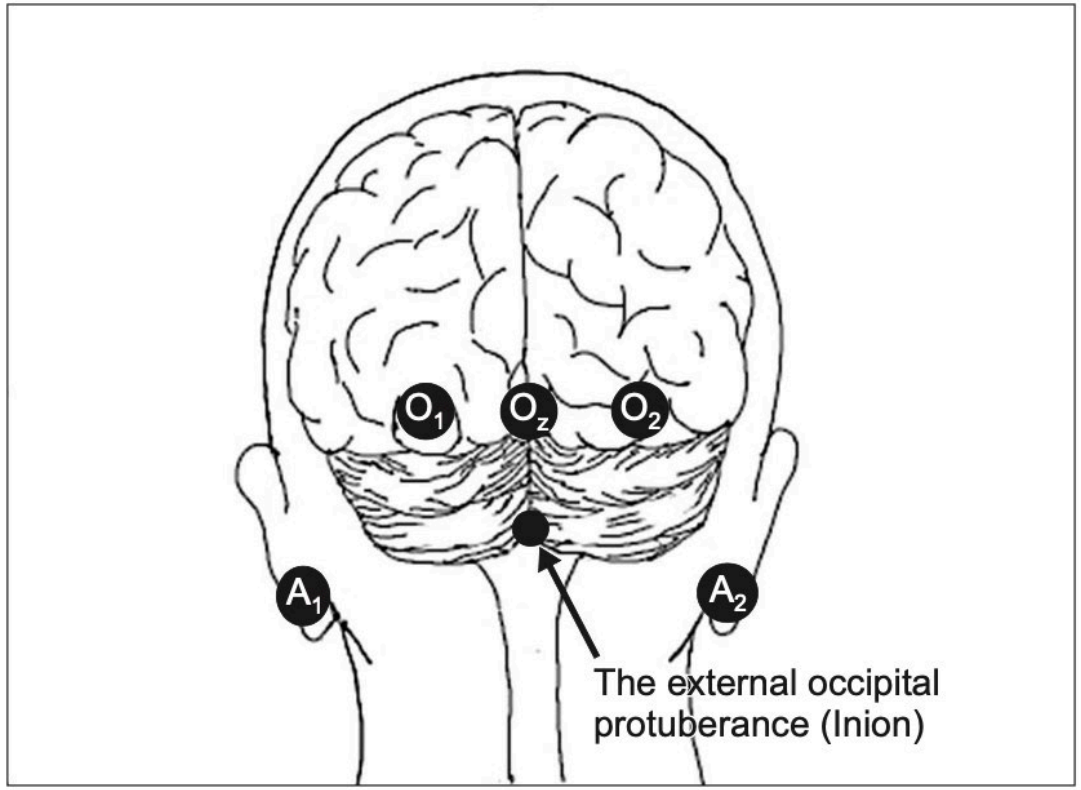
The **goggles**, which were placed over the patients' eyes, were carefully protected from **scialytic operating room lamps and from the microscope light with a film of aluminum**. A soft tissue was used to separate the aluminum and the patient's skin.

Material and methods

ERG

- Left and right eyes were excited sequentially, and VEPs were performed for one eye at a time, alternating periods of VEP recordings for the other eye
- The **ERGs** were recorded with a pair of subdermal electrodes placed laterally to every patient's eye.
- The amplitude of ERGs was monitored with peak-to-peak amplitude.
- Changes in ERGs could either occur with **dark or light adaptation or be due to displacements of goggles** or of their aluminum protection.
- A new VEP baseline was obtained at the beginning of the lesion resection after the microscope was brought into place.
- total intravenous anesthetic (TIVA)
- The VEP baselines were updated with ERG changes

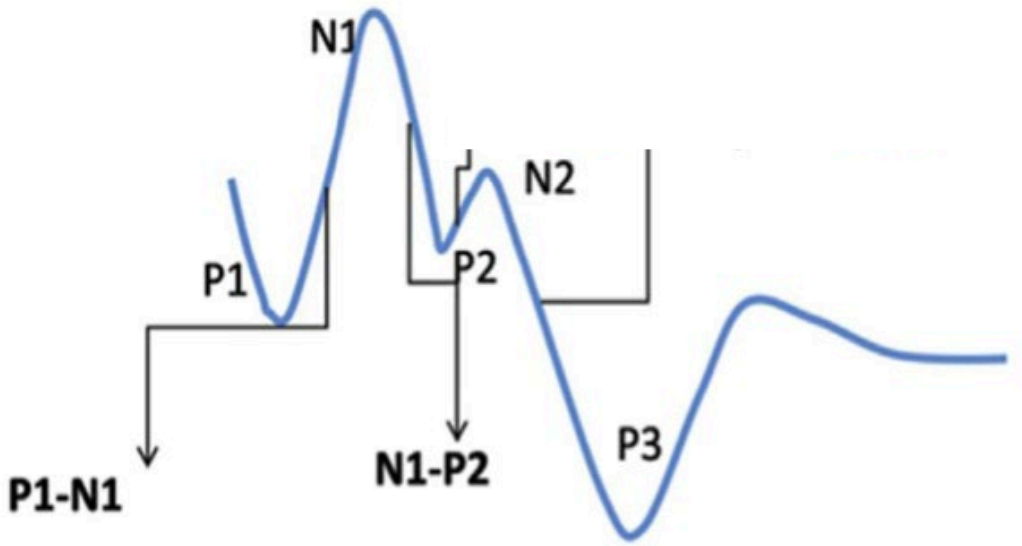
Intraoperative Monitoring of VEPs



VEPS recording: parameters and alarm criteria

Parameters

- **VEP latency** was specifically examined as a parameter for evaluating VEPs in six of the studies: none of these were deemed to be statistically significant (Jashek-Ahmed et al. BMC Neurol 2021)
- **The FVEP amplitude was measured**
  - from the first negative peak after 60 ms **(N1)** to the following positive peak **(P1) (Houlden DA et al, Can J Neurol Sci. 2019)**
  - from the peak-to-peak amplitude of **N2–P2** waves.



Gutzwiller EM et al. Intraoperative monitoring with visual evoked potentials for brain surgeries. J Neurosurg. 2018

VEPS recording: parameters and alarm criteria

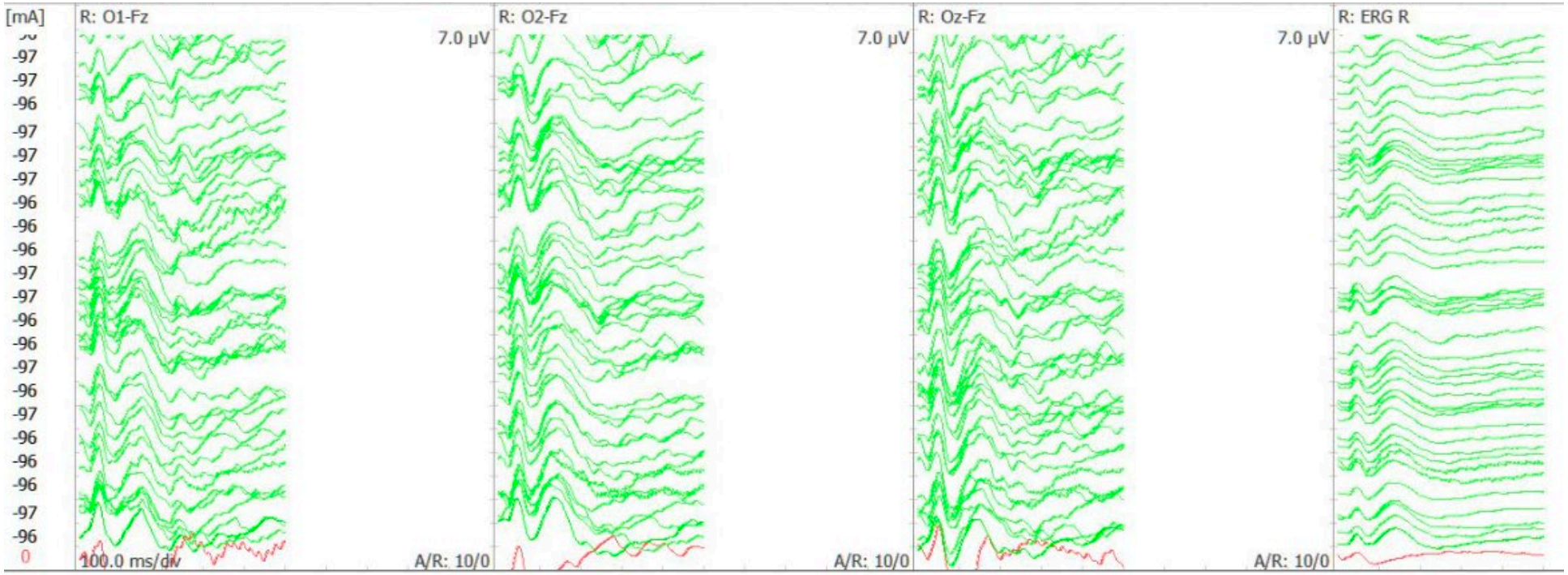
Alarm criteria

- The alarm was defined as a reproducible (20%) **50%** decrease or more in the peak- to-peak amplitude of **N1-P1/N2–P2 waves**, **with concomitant stable ERGs**.
  - In such case, the **alarm** was communicated to the surgeon.
- **For improvement**—a greater than **50% increase** in baseline VEP amplitude;
- **For deterioration**—a greater than **50% decrease** in baseline VEP amplitude was required
- The evaluation of proportions (sensitivity and specificity) and performances (positive and negative predictive values) was defined as:
  - **true negative** (no permanent decrease in VEP amplitude and no new postoperative visual deficit);
  - **true positive** (permanent decrease in VEP and new postoperative visual deficit);
  - **false negative** (no permanent decrease in VEP, but new postoperative visual deficit);
  - **false positive** (permanent decrease in VEP, but no new postoperative visual deficit).

Gutzwiller EM et al. Intraoperative monitoring with visual evoked potentials for brain surgeries. J Neurosurg. 2018

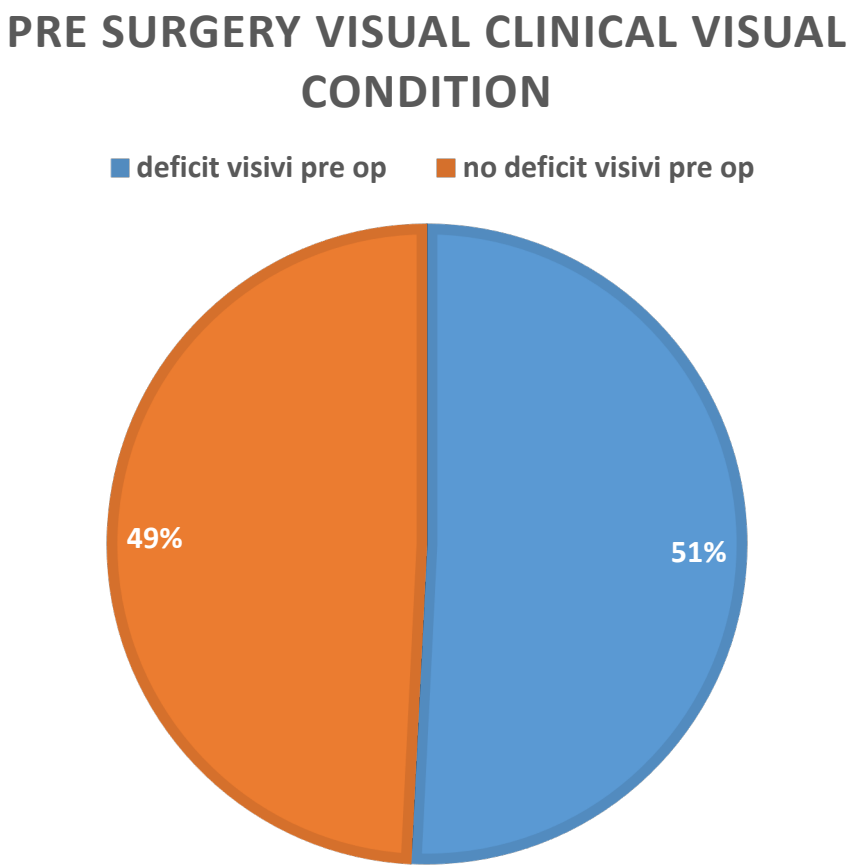
Results

- FPEVs were monitorable for **72%.**
- Only in **11%** cases we alerted the surgeon for significant change in amplitude parameters during surgery.



Factors that Affect Flash VEP

- **Preoperative visual function (51%)**
- **Body temperature**
  - The optic pathway, which is a polysynaptic pathway, is considered sensitive to hypothermia. Compared to VEP latency at 37°C, **latency at 33°C is extended by 10–20%.**
  - Decreases in body temperature gradually cause the **VEP amplitude to attenuate** and latency to extend, and **waveforms completely disappear at 25–27°C**
- **Partial pressure of carbon dioxide in the blood**
- **Hypoxemia and hypotension**
  - VEP amplitude is decreased and latency is extended under conditions of extreme hypoxia and hypotension.
- **Hemodilution**
- **Turning of the skin flap**



Hayashi H, Kawaguchi M. Intraoperative monitoring of flash visual evoked potential under general anesthesia. Korean J Anesthesiol. 2017

Factors that Affect Flash VEP

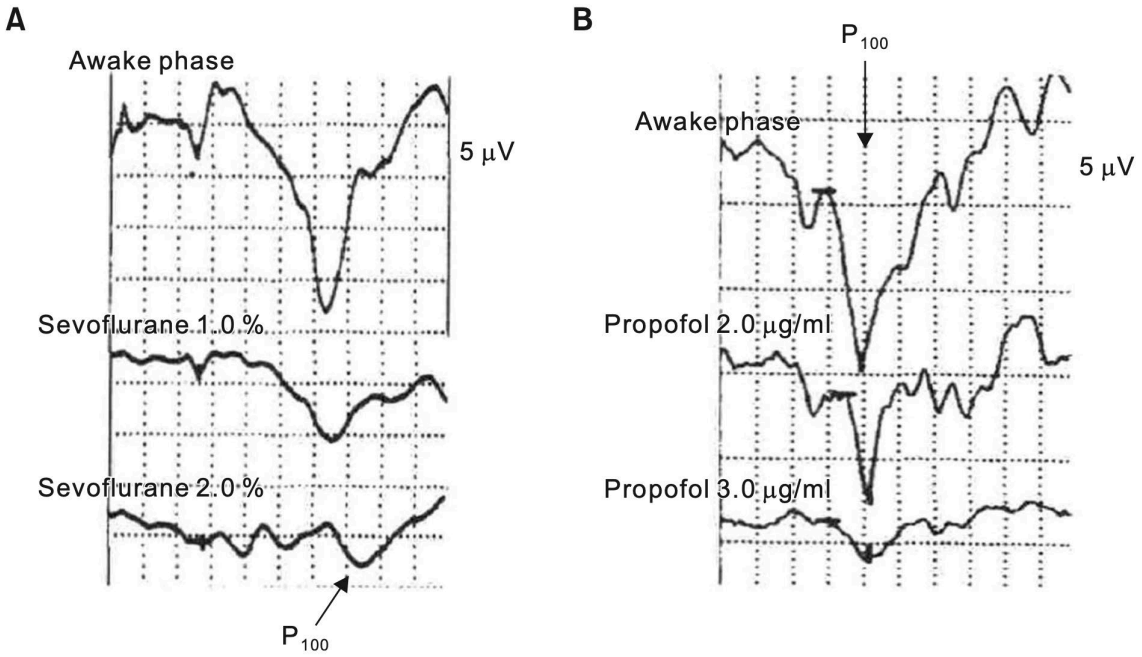


Table 2. Effects of Various Anesthetics on Flash VEP

Inhaled anesthetic gases	Isoflurane	↓↓
	Sevoflurane	↓↓
	Desflurane	↓↓
	Nitrous oxide	↓↓
Intravenous anesthetics	Thiopental	↓↓
	Propofol	↓
	Fentanyl	— or ↓
	Remifentanil	— or ↓
	Ketamine	↓↓
Muscle relaxants	Vecuronium	—
	Rocuronium	—

↓↓: strong suppressive effect, ↓: small suppressive effect, —: no suppressive effect. VEP: visual evoked potential.

Hayashi H, Kawaguchi M. Intraoperative monitoring of flash visual evoked potential under general anesthesia. Korean J Anesthesiol. 2017

Dotto PF et al.

Gender-based normative values for pattern-reversal and flash visually evoked potentials under binocular and monocular stimulation in healthy adults.

Doc Ophthalmol. 2017

- The FVEP waveform was composed by successive deflections, named in order of appearance.
- The first and the second positive deflections were named P1 and P2, respectively, and their preceding negative deflections, N1 and N2.
- **29.1%** of tested women presented a **hardly recognized N1–P1 complex**, leading to a remarkable low lower limit for both stimulation conditions.
- **The N2–P2 complex was easily recognizable in all cases and about 3 times larger than N1–P1 both in men and women.**

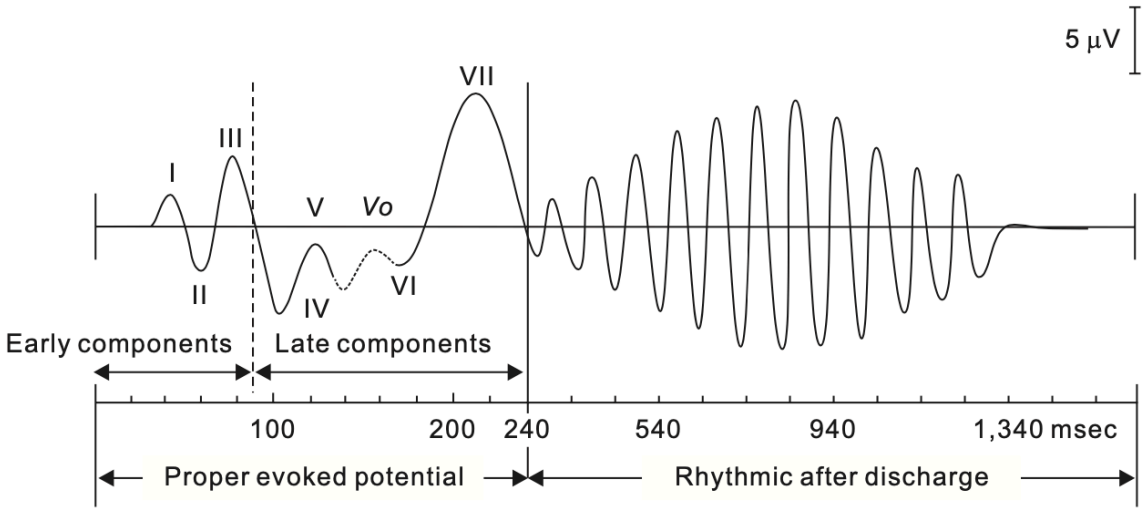


Fig. 5. Schematic diagram of VEP waveform induced by flash stimulation. Upward is negative (Partial modification from Electroenceph Clin Neurophysiol 1961; 13: 165-72).

Table 2 Normative values for transient flash VEP according to gender

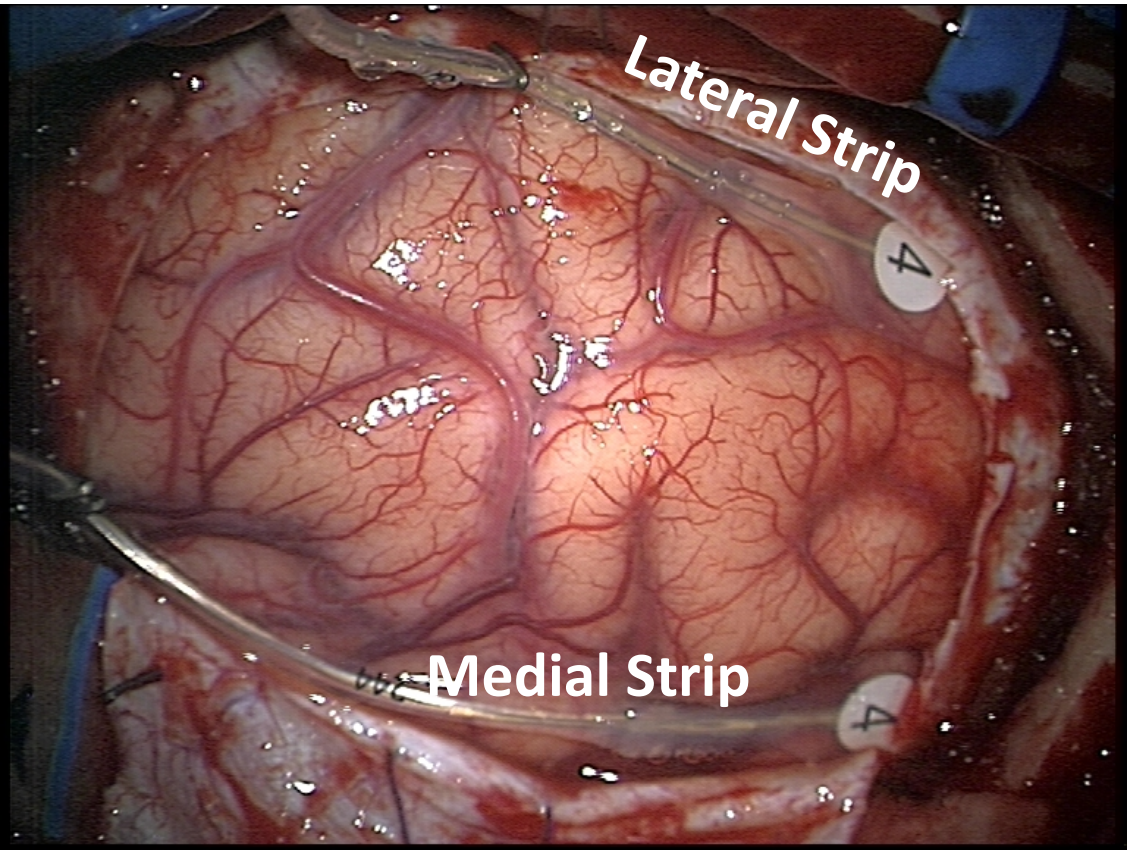
Variable	Condition	Men ($n = 25$)						Women ($n = 24$)						Statistical model	P value
		Mean	SD	Normal limit[a]	Median	Percentile[b]	Adherence (KS)	Mean	SD	Normal limit[a]	Median	Percentile[b]	Adherence (KS)		
N1–P1 amplitude (μV)	Monocular	4.3	1.8	.6	4.3	1.9	Yes	4.5	2.4	.0					4
	IAD	1.4	.9	.0	1.2	2.7	Yes	1.2	1.0	.0					6
	Binocular	7.7	4.2	.0	7.1	2.7	Yes	7.2	4.1	.0					0
	BSR	1.7	.8	.1	1.7	.6	No	1.6	.6	.4					2
N2–P2 amplitude (μV)	Monocular	9.8	4.0	1.8	10.2	4.0	Yes	14.6	4.9	4.8					02*
	IAD	3.1	2.8	.0	2.1	9.3	No	2.1	1.3	.0					7
	Binocular	15.2	5.5	4.2	15.2	5.9	Yes	22.6	7.8	7.0	22.4	8.9	Yes	*t* Test	<.002*
	BSR	1.7	.9	.0	1.4	.9	No	1.6	.6	.4	1.5	.9	No	Mann–Whitney	.73
N1 peak time (ms)	Monocular	42.1	2.2	46.5	42.5	45.4	Yes	41.3	3.8	48.9	41.7	47.9	Yes	*t* Test	.33
	IOD	1.7	1.1	3.9	1.5	3.5	Yes	1.3	1.1	3.5	1.2	3.8	No	Mann–Whitney	.18
	Binocular	42.4	2.3	47.0	42,5	45.8	Yes	40.9	3.4	47.7	41.2	44.5	Yes	*t* Test	.08
P1 peak time (ms)	Monocular	54.0	4.0	62.0	54.0	60.8	Yes	51.9	4.3	60.5	52.0	57.8	Yes	*t* Test	.09
	IOD	2.2	1.7	5.6	2.5	4.5	Yes	1.3	1.2	3.7	1.0	3.4	No	Mann–Whitney	.03
	Binocular	54.4	2.6	59.6	54.0	58.5	Yes	51.3	5.7	62.7	52.2	57.8	No	Mann–Whitney	.01
N2 peak time (ms)	Monocular	65.1	5.6	76.3	65	74.2	Yes	62.8	4.3	71.4	63.0	70.0	No	Mann–Whitney	.11
	IOD	2.5	2.0	6.5	1.5	5.9	No	2.4	1.6	5.6	2.0	5.0	No	Mann–Whitney	.86
	Binocular	65.7	5.1	75.9	64.0	73.5	Yes	61.8	4.3	70.4	62.5	66.9	No	Mann–Whitney	.02
P2 peak time (ms)	Monocular	106.1	17.6	141.3	107.0	128.3	Yes	108.9	14.4	137.7	110.2	126.8	Yes	*t* Test	.55
	IOD	1.9	1.1	4.1	2.0	3.5	Yes	1.4	1.3	4.0	1.2	3.4	No	Mann–Whitney	.15
	Binocular	104.9	17.8	140.5	104.5	129.0	Yes	107.8	14.7	137.2	106.5	129.0	Yes	*t* Test	.53

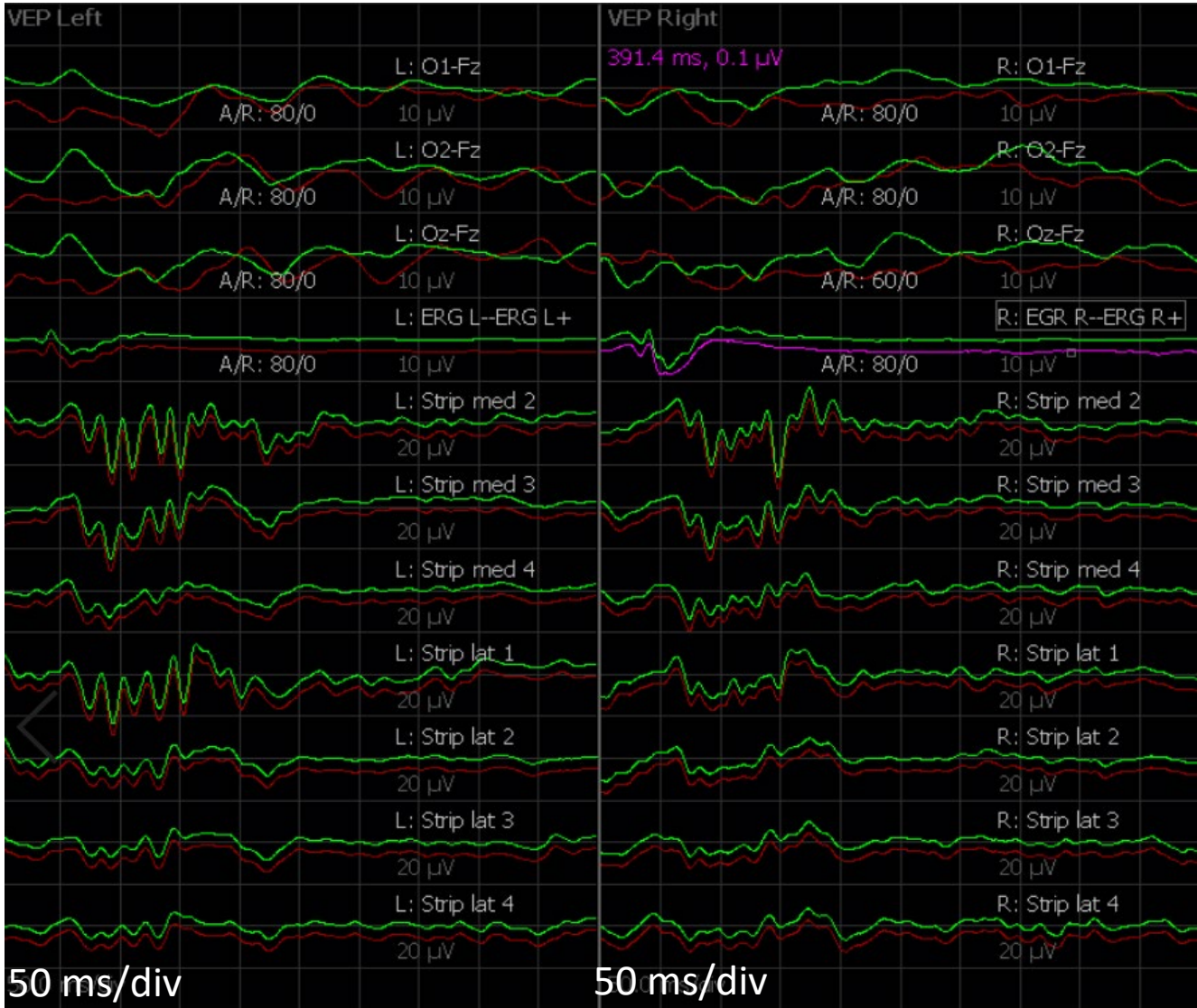
IOD inter-ocular peak-time difference, *IAD* inter-ocular amplitude difference, *BSR* binocular summation ratio

Recording	Transcranial m (ds) uV	Direct strip m (ds) uV
N1-P1	7,14 (4)	44,37 (20)
N2-P2	7,84 (5)	46 (23)

Dotto PF et al. **Gender-based normative values for pattern-reversal and flash visually evoked potentials under binocular and monocular stimulation in healthy adults.** Doc Ophthalmol. 2017

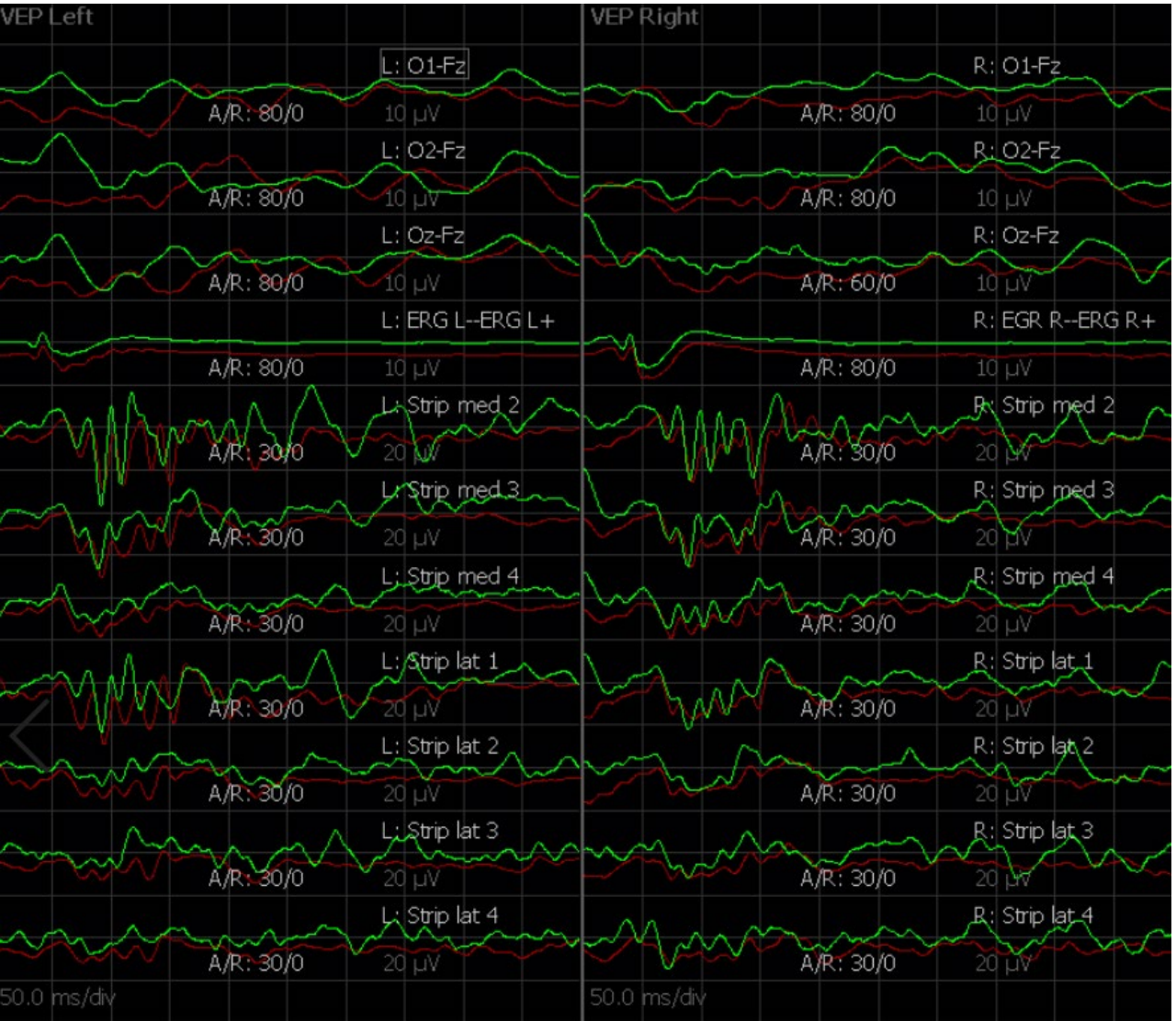
VEP cortical strip recording





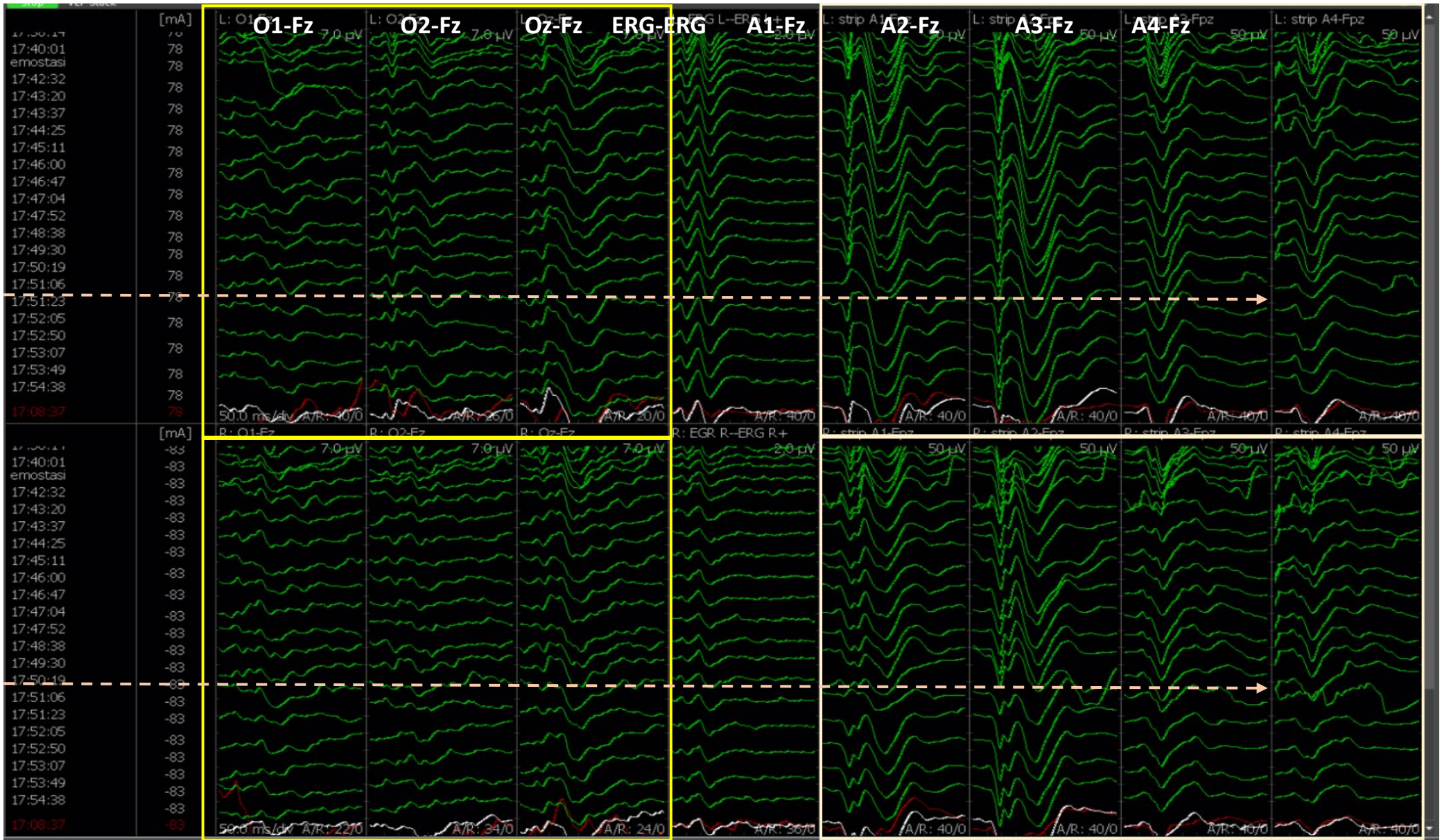
VEP Monitoring

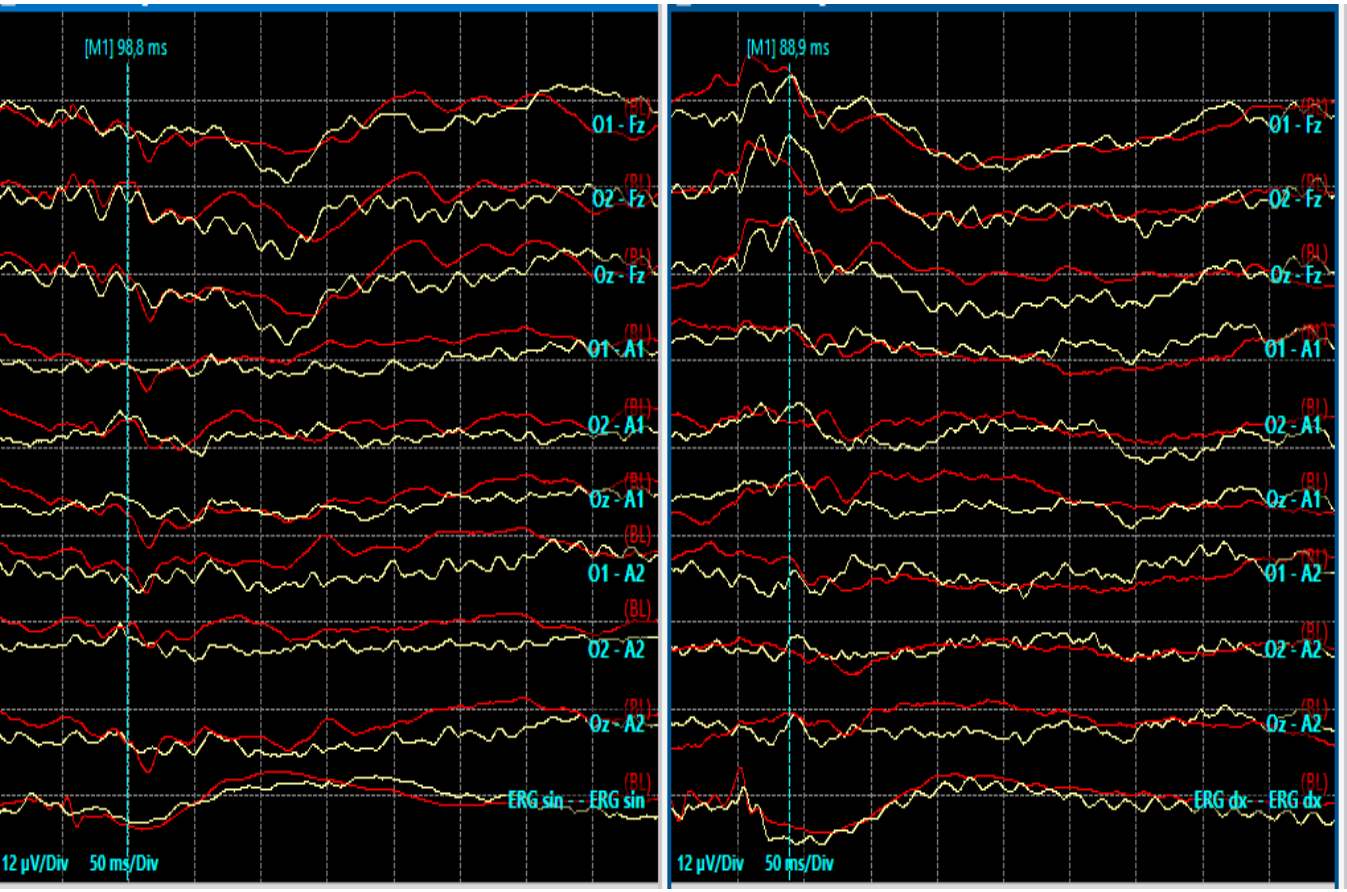
Tumor approach and removing

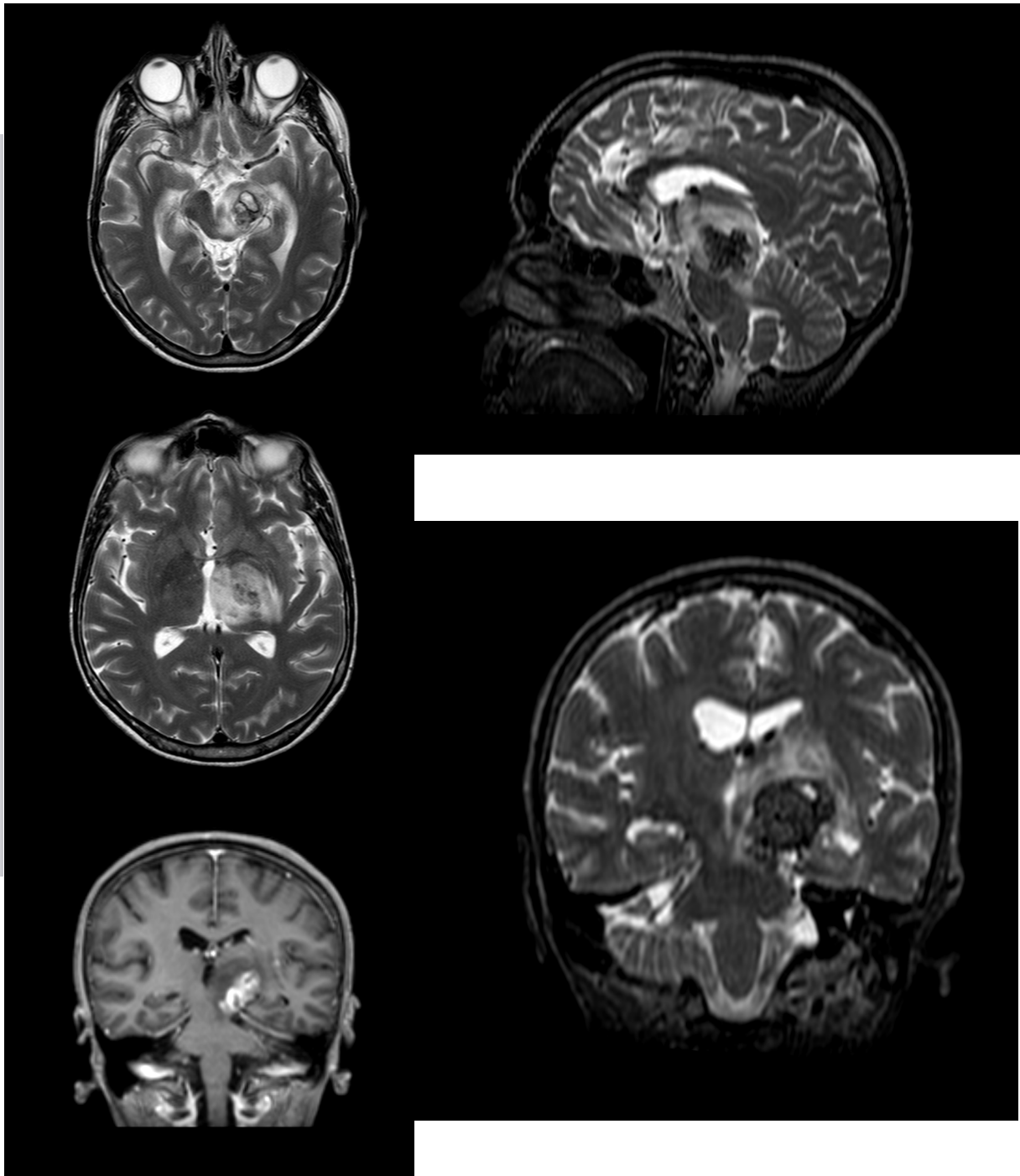


At the end of removing

TPEV *vs* Dpev


O1-Fz
O2-Fz
Oz-Fz
ERG-ERG
A1-Fz
A2-Fz
A3-Fz
A4-Fz
[mA]
17:40:01
emostasi
17:42:32
17:43:20
17:43:37
17:44:25
17:45:11
17:46:00
17:46:47
17:47:04
17:47:52
17:48:38
17:49:30
17:50:19
17:51:06
17:51:23
17:52:05
17:52:50
17:53:07
17:53:49
17:54:38
17:08:37
7.0 µV
2.0 µV
50 µV
50.0 ms/div
A/R: 40/0
A/R: 26/0
A/R: 20/0
R: EGR R--ERG R+
A/R: 22/0
A/R: 34/0
A/R: 24/0
A/R: 36/0


[M1] 98,8 ms
O1 - Fz
O2 - Fz
Oz - Fz
O1 - A1
O2 - A1
Oz - A1
O1 - A2
O2 - A2
Oz - A2
ERG sin - ERG sin
12 µV/Div 50 ms/Div
[M1] 88,9 ms
O1 - Fz
O2 - Fz
Oz - Fz
O1 - A1
O2 - A1
Oz - A1
O1 - A2
O2 - A2
Oz - A2
ERG dx - ERG dx
12 µV/Div 50 ms/Div



Results

- For total or subtotal removal in 90% of cases after the surgery:
  - **77%** remained in the same clinical preoperative condition (34% no visual deficit, 43% same visual deficit)
  - **11%** worsened (of which 5% showed significant change of FPEVs only recording directly on the occipital cortex)
  - **7%** improved.

• Metriche

- Il tasso di errore (error rate)
  - E R R = F P + F N/ T P + T N + F P + F N
- L'accuratezza (accuracy)
  - A C C = T P + T N/T P + T N + F P + F N = 1 – E R R
- La precisione (precision)
  - P R = T P/ T P + F P
- Il richiamo (o recall) o sensitività (sensitivity).
  - R e c a l l = T P/ T P + F N
- La specificità (specificity)
  - S P = T N /T N + F P
- Il tasso dei falsi positivi (False Positive Rate).
  - F P R = F P /T N + F P

Amplitude N1-P1

CONDIZIONE REALE	CONDIZIONE PREVISTA: PP 19	CONDIZIONE PREVISTA: PN 44
P+N 63		
P 10	TP 6	FN 4
N 53	FP 13	TN 40

Amplitude N2-P2

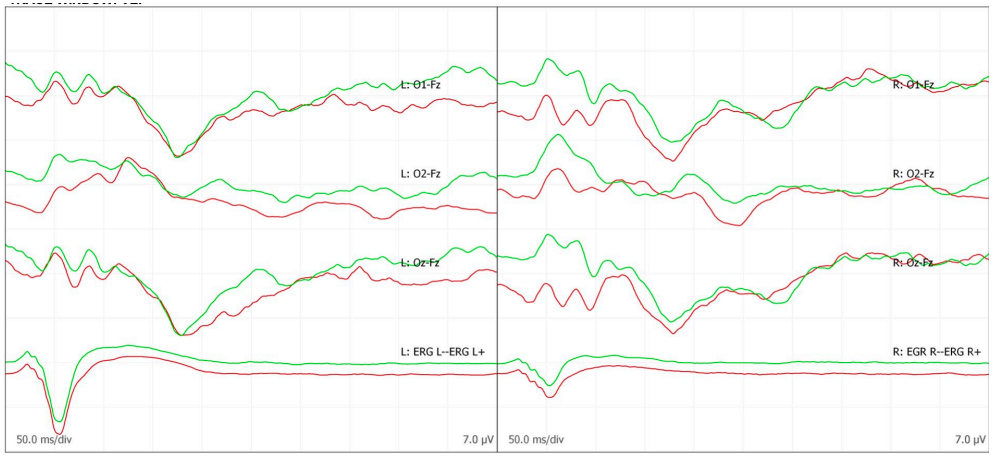
CONDIZIONE REALE	CONDIZIONE PREVISTA: PP 16	CONDIZIONE PREVISTA: PN 47
P+N 63		
P 10	TP 6	FN 4
N 53	FP 10	TN 43

	N1-P1	N2-P2
error rate	27%	**22%**
accuracy	73%	**78%**
precision	31.5%	**37%**
sensitivity	60%	60%
specificity	75%	**81%**
False Positive Rate	24.5%	**19%**

Discussion and conclusions

- The use of **FPEVs recorded from strips placed directly on the occipital cortex** makes it possible to obtain cortical components that are more stable and of greater amplitude than FPEVs from transcranial electrodes.
- **Technical adjustments** allow rapidly acquiring reproducible FVEP waveforms for timely reporting of significant FVEP change resulting in prompt surgical action to obtain lower postoperative visual deficit rate
- Therefore to improve FPEV usefulness we suggest **co-recording** of FPEV by transcranial electrodes and putting the strip directly on the occipital cortex: this method for rapidly acquiring reproducible FVEP waveforms allowed for timely reporting of significant FVEP change resulting in prompt surgical action to obtain lower postoperative visual deficit rate, differently from the previously considered difficult to obtain during surgery and, when obtained, a poor predictor of postoperative visual function.

Conclusions



• the relevance of using **ERGs** to calibrate stimulus intensity ensuring adequate stimulation that saturates the visual pathway;

- the usefulness, whenever possible, of recording **tPEV and dPEV** simultaneously;

- greater monitorability of dPEV (greater definition of the visual cortical component);

- dPEV may be more sensitive to the postoperative clinical outcome (recording from the cortex and in the vicinity of the lesion) than tPEV (recording electrodes positioned at the craniectomy margins)

- reliability of the **N2-P2 complex: less error rate, more precision and specificity**

- **limit**: pre- and post-operative assessment with visual field study