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Intraoperative somatosensory activity monitoring by semiparametric analysis of thermal neuroimaging

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Abstract

Thermal neuroimaging systems detect the emitted heat radiation of the exposed cerebral cortex. The main contributor to thermal radiation of the cortex is regional cerebral blood flow. Through neurovascular coupling it is well known that changes in regional cerebral blood flow can be traced back to local neural activity. We now exploit this relationship by a novel statistical data analysis framework to unveil neural activity induced by somatosensory evoked potentials. This is achieved by incorporating deterministic as well as random effects into a semiparametric regression model which is then subject to statistical inference. The method was applied to a cohort of nine intraoperative cases with promising results. Functionally active sites corresponded with anatomical localization, electrophysiological and intraoperative optical imaging validation. The semiparametric regression framework estimates and visualizes statistically evoked somatosensory activity by incorporating deterministic experimental conditions as well as random effects of thermal imaging systems. These deterministic conditions can be adopted to general electrical stimulation protocols so that the the framework allows to unveil arbitrary evoked cortical activity intraoperatively. Knowledge about eloquent areas is of vast importance since the removal of potential eloquent tissue during neurosurgical tumour resections might cause significant post-operative functional deficits to the patients.

Keywords

Neurosurgery; Primary Sensory Cortex; Penalized Splines; Semiparametric Regression; Thermography

1 Introduction

Thermography is a method that measures the emitted temperature radiation of tissue. This radiation depends on the tissue's composition and dynamic processes like perfusion. It is a non-invasive and contactless approach to real time measurements of small temperature gradients. Current devices use uncooled infrared focal plane array microbolometers for sensing electromagnetic radiation at 7.5 μm to 14 μm wavelength with a spatial resolution of up to 170 μm at 20 cm object distance at 50 frames per second. In comparison to actively cooled thermographic imaging systems, microbolometer FPA devices don't require expensive stirling cyclic coolers or liquid nitrogen coolers making the intraoperative application possible. The detected infrared radiation originates from the tissue's surface and also interferes with the environment due to heat flow, convection effects and cooling tissue making thermal images highly dynamic and highly non-stationary over time.
As stated, temperature variations also originate from metabolic changes. In medical applications of thermography, the perfusion state of tissue can be used to identify pathologies like fever, breast cancer and vascular disorders [7]. In neurosurgery, the detected temperature gradients derive from near surface perfusion- and neural activity related heat transfers. Gorbach et al. [5] and Shevelev et al. [12] demonstrated the applicability of thermography for tumour diagnostics. Steiner et al. [13] further showed the detection of an ice-cold saline solution applied through a central line as tool for tissue perfusion diagnostics using methods of multivariate statistics.
In this study, we focus on neurosurgical interventions for resection of brain tumours. Anaplastic and infiltrative (malignant) tumours are characterized by weak differentiation between healthy and pathological tissue hampering the resection. Especially in case of tumour growth beneath functional areas, it is essential to minimize postoperative functional deficits in order to retain the patient's quality of life as long as possible. For this purpose, we extend prior findings regarding the detection of functional areas using intraoperative thermal imaging (TI) by means of a sound mathematical framework and statistical inference methods. Hereby it is now possible to design and analyse various experimental conditions and setups using the same framework. Compared to prevalent functional imaging modalities like intraoperative optical imaging, TI is robust against various environmental conditions as it is a whitelight-independent method and is not affected by light reflections at the cortex.

2 Related Work

In a seminal paper, Friston et al. employed the general linear model (GLM) for analysis of functional imaging [3]. The authors of [4] gave an comprehensive overview of current developments. They also showed how to include experimental conditions into the general linear model to understand the neural activity under various conditions. Since then, research has been done on extending this framework onto other modalities like SPECT[8] and PET[6]. An extension to the deterministic model is described (among others) by Rupport et al.[11] as semiparametric regression or partially linear models and originates back to 1988[10]. These models combine the deterministic components of common GLMs with nondeterministic components like B-Splines[1] allowing to catch non-linear behaviour.
Shevelev showed the general ability to measure neural activity by recording the heat distribution of rat brains in 1993 [12]. Gorbach [5] extended these results and had shown that thermal detectable sensor and motor activity can be extracted from thermal images given a cooled high-sensitive infrared camera. These findings require the data to fulfil certain data constraints like not showing low-frequent temporal behaviour besides neural activity.

3 Materials and Methods

Semiparametric regression is a method which combines both parametric and nonparametric components in order to establish a robust method allowing the incorporation of some degree of uncertainty. The nonparametric terms typically describe some dominant correlation pattern which is difficult to describe deterministically. In the following we will first give a short review of the GLM and then show its extension into a semiparametric linear model. Given these prerequisites we will then discuss necessary components to model the challenges of thermal imaging in order to recognize small thermal signatures correlating with regional cerebral blood flow.

3.1 General Linear Model

The GLM provides a framework with sound statistical foundation enabling statistical inference about specific experimental conditions. We will give a brief overview of the general framework and discuss necessary extensions towards semiparametric regression. The timeseries y_i of pixel i is modelled as a linear combination of the assumed experimental conditions X weighted by $\beta^i = [\beta_1^i \ \beta_2^i \ ...]$, whereas β_n^i can be seen as contribution of the $n-$th experimental condition to the pixel's timecourse.

$$\begin{aligned} y_1 &= X\beta^1 + e \\ y_2 &= X\beta^2 + e \\ &\vdots \\ y_n &= X\beta^n + e \end{aligned} \tag{1}$$

For the whole dataset $Y \in \mathbb{R}^{n\times m}$ the model can be represented as matrix notation:

$$Y = X\beta + e \tag{2}$$

Equation 1 describes the most generic case wherein the measured data $y_i \in \mathbb{R}^m$ with $1 \leq i \leq n$ is described by the design matrix $X \in \mathbb{R}^{m\times p}$ containing p experimental conditions, weights $\beta^i \in \mathbb{R}^m$ and normal distributed noise $e \sim N(0, \sigma)$. Each column of the design matrix depicts a linear confound to the model, whereas confound j is weighted by β_i^j. An estimate of β is given by the normal equations

$$\tilde{\beta}_{OLS} = (X'X)^{-1}X'Y \tag{3}$$

The temporal behaviour of thermographic time courses is best described by a low-frequent non-linear function which distracts the assumptions of GLM (stationary signal). Therefore, we now extend the rather simple GLM by a penalized non-parametric component in order to catch dominant background signals.

3.2 Penalized Splines

A convenient method for non-parametric estimation of non-linear behaviour is the penalized spline (p-Spline) framework. We will give a brief review of p-Splines, whereas more detail can be found in [2] and [11]. A p-Spline is linear smoother fit by penalized least squares. Herein, a smoothness penalty λ is introduced in order to trade-off variance and bias. Since penalized splines aim to find a low rank approximation of the given signal $y \in \mathcal{R}^n$, the used basis must be chosen by care. A simple choice would be a truncated polynomial basis which is easy to implement. Yet, it might cause numerical instabilities, since it doesn't require orthogonal basis vectors. This issue is solved by choosing a B-Spline basis. B-Splines can be seen as piecewise polynomial function of some arbitrary degree over a restricted domain $t_0 \leq x \leq t_m$ with $m \leq n$ knots. De Boor[1] gave a recursive definition of a k-th order B-Spline basis by

$$B_{i,1}(x) = \begin{cases} 1 & x \in [t_i; t_{i+1}] \\ 0 & \text{otherwise} \end{cases} \tag{4}$$

and

$$B_{i,k}(x) = \frac{x - t_i}{t_{i+k-1} - t_i} B_{i,k-1}(x) + \frac{t_{i+k} - x}{t_{i+k} - t_{i+1}} B_{i+1,k-1}(x) \tag{5}$$

which yields the linear approximation of a signal $\widehat{y_i}$

$$\widehat{y_i} = \sum_{j=1}^{m} a_m B_{j,i}(x_i) \tag{6}$$

given coefficients a_j. Suppose our signal contains normally distributed random and fixed effects. The nonparametric random effects are modelled as degree k B-Spline by $Z = B_{;k}$ and our p fixed effects as X. Both of them are stacked into $G = [Z, X]$. Since we only want to penalize the coefficients of Z, we utilize the d-th order difference operator D_d to prevent steep changes in a_i. The optimization problem now reads

$$\min_b ||y - Gb||_2^2 \text{ wrt. } \sum_i ||D_d a_i||_2^2 < C \tag{7}$$

given $b = [\beta, a]$ and some arbitrary constant $C \in \mathcal{R}$. By introducing the Lagrange multiplier λ, we arrive at the (dual) penalized least squares problem

$$\min_b \; ||Y - Gb||_2^2 + \lambda ||D_d b||_2^2, \lambda \geq 0 \tag{8}$$

using some basic algebra, this problem can be solved by a penalized version of the normal equations:

$$\widehat{b}(\lambda) = (G^T G + \lambda P)^{-1} G^T y \tag{9}$$

wherein the Lagrange multiplier λ controls the smoothness of the nonparametric component. $P = blkdiag(0_{p \times p}, D_d^T D_d)$ is our d-th order penalty matrix to enforce smoothness of the nonparametric component.
The parameter λ controls the smoothness of $\widehat{y}$ and can also be seen as a trading-off bias and variance of the resulting fit. For automated parameter estimation, several criterion were proposed like General Cross Validation (GCV), Mallow's C_p and even the corrected Akaike's information criterion is applicable [11]. GCV is a commonly used criteria to control λ of the dual problem formulation in 9 to optimize λ. This criteria efficiently approximates the leave-one-out cross validation yielding [11]:

$$GCV(\lambda) = \sum_{i=1}^{n} \frac{RSS(\lambda)}{1 - n^{-1} tr(S_\lambda)} \tag{10}$$

with

$$RSS(\lambda) = ||y - \widehat{y}||_2^2 \tag{11}$$

and smoothing matrix $S_\lambda = G(G^T G + \lambda P)^{-1} G^T$. By means of these results, we are also able to formulate Akaike's information criterion (AIC):

$$AIC(\lambda) = log(RSS(\lambda)) + 2tr(S_\lambda)/n \tag{12}$$

3.3 Statistical Inference

A core step of each statistical signal analysis framework is testing for significant effects. In terms of the mixed model formulation of the discussed semiparametric model, we are only interested in the significance of fixed effects (parametric component). Assuming iid. errors $e \sim N(0, \sigma I)$, the coefficients variance $var(b)$ of the general linear model is

$$var(b) = \sigma^2 (G^T G)^{-1} \tag{13}$$

Since we penalize some values of b, we can not use this result, since it neglects the bias-variance tradeoff we introduced. Fortunately, the variance of penalized splines can be formulated analogously to ridge regression:

$$var(b; \lambda) = \sigma^2 (G^T G + \lambda P)^{-1} G^T G (G^T G + \lambda P)^{-1} \tag{14}$$

By letting λ go to 0, the variance of the penalized regression reduces to $var(b)$:

$$\lim_{\lambda \to 0} var(b;\lambda) = \sigma^2 (G^T G)^{-1} G^T G (G^T G)^{-1} = var(b) \tag{15}$$

This result is especially useful in cases where only some small penalization is necessary and $(G^T G + \lambda P)^{-1}$ requires costly computations. The t-statistics of the penalized spline regression model can be computed by

$$t = cb/(\sqrt{c\ var(b;\lambda)\ c^T}) \tag{16}$$

The contrast vector is denoted by $c \in \mathbb{N}^p$ with $\sum_i c_i = 0$. It allows testing the significance of a specific coefficient b_j or of some arbitrary combination of b_js.
The t-statistics is distributed $t \sim T_{m-p}$ in general linear model and $t \sim T_{m-df_{fit}}$ in our penalized model. The degrees of freedom of the fit are approximated by $df_{fit} = trace(S_\lambda)$ with smoothing matrix S_λ[11]. This now enables us to test wrt. a significance level α: $p(t) > (1-\alpha)$. Since we are employing a massively-univariate approach, we face the multiple comparison problem. It states, that the number of false-positives increases proportional to the number of tests when not correcting α. To circumvent the multiple comparison problem, we employ a conservative bonferroni corrected $\alpha_B = \alpha/n$ with n being the number of tests.

3.4 Intraoperative Functional Thermography

Thermographic imaging systems require specific preprocessing steps prior to the application of the inference framework. The characteristics originate from the behaviour of uncooled infrared imaging systems with focal plane array IR detectors. Microbolometer FPA detectors convert incident electromagnetic radiation of the mid- to long IR range into electrical resistance changes, which are then computed into temperature values. Hereby, the detector element, the optics and the camera body heats up until a convergence temperature is reached, more so when the whole device is encased by a sterile cover as in the designated intraoperative setting. This heating typically induces non-linear temperature drifts. In thermography, a common correction method for this issue is a periodic gain and offset correction called non-uniformity correction (NUC) [14]. This normalizes the computed temperatures and hereby gives a temperature and drift normalized image just after the NUC occurred. When evaluating timeseries, the NUC typically induces a jump discontinuity and changes the low frequency time-behaviour of the timeseries. This behaviour is demonstrated by the mean temperature curve of a thermographic recording (blue curve) in figure 1.

3.4.1 Thermal Model for Neural Activity

As known from fMRI experiments, neural activity initiates the neurovascular coupling chain. Latter induces changes in regional cerebral blood flow which yields changes in tissue temperature by hypo- or hyperthermic behaviour. These changes typically propagate through several tissue layers before they can be detected by an IR camera. Because of this behaviour, we expect the signal to resemble a smooth bell-like curve. We therefore approximate the expected neural activation signal in the thermographic time course as gaussian function

$$\frac{\alpha}{\sigma\sqrt{2\pi}} exp((-(t_i - \mu)/2\sigma)^2) \tag{17}$$

Here, μ models the time of maximum signal intensity and σ describes the steepness of the temperature change. We further expect μ to correlate with the depth of the focal activation, meaning that a neural activity in deeper tissue layers leads to a weaker amplitude of the measured signal. In this case, the signal's shape is also expected to have less curvature and therefore higher σs. The experimental conditions can now be modelled as of dilated and shifted variants of equation 17 (depending on the actual experimental protocol) and stacked into X.

3.4.2 Background Signals

The NUC not only induces an jump discontinuity, but it also induces a slope correction into the data (see for example [14]). As a result, adjacent pixel's time series follow a similar trajectory. We can further observe various high-frequent effects like periodic patterns at heart rate as well as irregular components. We assume both of them to correlate with vascular processes that lead to cortical heat transfers. To account for these signal components, we add two B-Spline components to the model, Z_1 consists of a less amount of knots to catch low-frequent non-linear behaviour. We further introduce a second B-Spline Z_2 component to address high-frequent behaviour. Attention has to be paid to the high-frequent B-Spline component, since it is also capable of fitting low-frequent drift and neural activation behaviour. To prevent this, we add a specific penalty to the wavelet transformed W signal estimate Xb. Given the previously discussed experimental conditions X and our random effects Z_1, Z_2 we get $G = [X, Z_1, Z_2]$. This yields the following minimization problem

$$\min_b ||Gb - y||_2^2 + \lambda ||PWGSb||_2^2 \tag{18}$$

with $S = blkdiag(0_{noFixedEffects}, 1_{noRandomEffects})$ the penalty is applied to the B-Spline components. By $P = blkdiag(I_{128}, 0_{m-128})$ only the lower dyads 1 through 6 of the wavelet transform are included in penalty computation. These lower dyads can be seen as a approximation of the low-frequency components of y. This approach enables us to penalize low-frequent behaviour of the estimated signal and can be thought of an high-pass filter. Analogously to the derivation in section 3.2, we arrive at

$$\widehat{b}(\lambda) = (G^T G + \lambda S^T G^T W^T P^T PWGS)^{-1} G^T y \tag{19}$$

3.4.3 Incorporating Discontinuities

As stated, the NUC introduces a step into the data (see figure 1). To account for this issue, we estimate the temporal position t_js of each NUC. For each t_j, we now add an additional knot at this timepoint to the high-frequent B-Spline model. This approach introduces additional flexibility into the model since it is possible to account for steep changes at respective time points.

4 Results and Discussion

In order to quantify the performance of the proposed framework, we first evaluate the quality of the results on artificial data. Subsequently, the methods were employed on intraoperative recordings and the results were compared to intraoperative optical imaging (IOI).

4.1 Simulation

As discussed earlier neural activity leads to heat transfers correlating with haemodynamic responses. These responses can be approximated by a Gaussian function which is replicated for each stimulation interval. Since thermal data typically contains low- and high-frequent temporal behaviour as well as device specific artefacts, it is helpful to employ existing intraoperative recordings as baseline dataset. This dataset is then augmented by a synthetic activity function allowing the quantification of the framework's performance.
We model the activation pattern by equation 17 with parameters $\sigma = 10$ and $\mu = 15$ s at varying α. The activation pattern is added to a circular area with radius 5 yielding 347 activated time courses and 306853 baseline time courses. We have chosen to use a small radius since we also expect activation focii of the same spatial extent in our measurements. Given a resolution of 250 μm per pixel, the resulting activation is 2 cm in diameter.

We evaluated AIC and GCV as criterion for optimizing μ, σ and λ of equation 17. For reasoning about significant activations, we employed two thresholding levels: t_{Bonf} ($t \geq 5.8$) and $t \geq 3.0$.
The resulting true positive rate at varying signal strengths is shown in figure 2. The first value, $\alpha = 0.03$, denotes a signal with Signal-To-Noise ratio of approximately 1, hereby all evaluated methods yielded suboptimal performance with AIC3.0 showing best TPR of 0.15. At a SNR of roughly 4, we see good TPR values for AIC3.0 (0.986) and acceptable 0.781 for GCV3.0. The three approaches AIC3.0, AIC5.8 and GCV3.0 resulted in good performance at a SNR of 6 with $TPR > 0.87$. The FPR values of all four approaches can be seen in table 1. GCV 5.8 showed nearly perfect FPR with only 25 pixels being wrongly classified, yet at cost of a decreased overall performance. The results indicate that AIC seems to be appropriate for optimizing the parameters of the proposed framework. Depending on the actual signal strength, the very conservative Bonferoni corrected significance testing yields good true positive rates. Since minimal FPRs are required for medical decision support systems, we employ AIC 5.8 for reasoning about activations in patient datasets.

4.2 Somatosensory Evoked Potentials

Thermographic sequences were recorded during tumour resections with all patients suffering from a neoplasm near the central sulcus. All intraoperative procedures were approved by the Human Ethics Committee of the Technische Universität Dresden (no. EK 323122008). The patients were under general anaesthesia wherein focal activations of the primary somatosensory cortex were provoked by contralateral median nerve stimulation.
In the described cases a standard electrical stimulation protocol was applied to the patient's median nerve. This protocol consists of 10 periods where each period starts with 30 s stimulation followed by 30 s rest. We expect - potentially delayed - changes in metabolism of and near hand areal of the primary somatosensory cortex leading to a focal change in vascularization. The expected behaviour of the timeseries is included as confound into the design matrix of the proposed semiparametric model. Since both the shape σ and the time to peak μ of the neural activation (see equation 17) are unknown, we estimate them by a grid search allowing efficient parameter estimation for all pixels at once.
Prior to the analysis using thermal and optical imaging we validated sensory activity of the exposed cortical tissue by electrophysiological measurements (phase reversal). Table 2 lists the results of analysing the thermographic recordings by the proposed framework. Column activation lists the results after testing the parameter of the activation function with respect to significance level α_{Bonf}. By positive we denote datasets with a dense cluster of pixels with high t-statistics ($t > t_{bonf}$) within Gyrus postcentralis (see figure 1). We further compared these focal activations with the results of concurrent optical imaging measurements[9]. In all cases of a clear positive thermographic signal and parallel intraoperative optical imaging, we found that the spatial position of the activation in both modalities is similar. Because of the higher penetration depth of optical imaging and its well-researched methods, the spatial extent of the found activation is typically larger in this modality.
Case 4 and 7 showed weak activations. By weak we denote results, when only focal centers with sparse significant (wrt. to t_{bonf}) t-statistics are found. One such example is case 4. In this measurement a significant temperature increase is detected in a vessel on Gyrus postcentralis. Also a sparse activation pattern is found on Gyrus postcentralis that correlates with the detected weakly activated area in optical imaging. The anatomic localization of weak and positive classified results was further evaluated. In all cases we found that the position of the estimated statistically significant eloquent sites correlates with the expected functional activity on the primary sensory cortex resulting from contralateral electrical stimulation of the median nerve.
Two datasets (case 6 and 8) showed no statistically significant activation on Gyrus postcentralis at all. In both cases, these results disagree with Optical Imaging's findings, since analysis of latter data yielded a significant activation on Gyrus postcentralis. The exposed cortex of case 8 showed a strong convexity and the Gyrus postcentralis was located at the trepanation's boundary, what hampers the quality of the

measured IR radiation. Additionally, it is quite difficult to orient a thermal imaging device and a microscope for optical imaging to the same area of the cortex with comparable resolution and orientation. Therefore, we expect these challenges to degrade the sensitivity of the thermal imaging device, preventing the measurement of significant temperature changes. Since we further base our analysis on the Bonferoni corrected t-statistic, we already lose overall sensitivity especially in cases of low SNR (as seen in our simulation experiments). The Bonferroni correction is a very conservative approach when facing the multiple comparison problem, while other approaches might produce better results in cases with weak or degraded SNR. Both technical reasons in summation cause these inaccurate results.
In general, we demonstrated the applicability of the semiparametric regression for analysis of thermal imaging data of the human cortex during neurosurgical interventions for unveiling the position of the sensoric cortex. The results of the statistical inference were further validated by comparison with simultaneous optical imaging recordings. We unveiled a clear correlation between the detection of neural activity by intraoperative thermal imaging with intraoperative optical imaging.

5 Summary

In this study we showed the gain of extending the GLM framework by semiparametric methods for the detection of focal neural activity in intraoperative thermal imaging data. The data was acquired during neurosurgical resection of brain tumours near Gyrus postcentralis. Neural activity on the sensory cortex was provoked intraoperatively by somatosensory evoked potentials whilst the heat distribution of the cerebral cortex was measured using the thermal imaging system. Former is a standard method that induces neural activity by stimulating the patient's median nerve by a predefined protocol. The measurements were done using a standard infrared thermographic imaging system capable of detecting temperature gradients as low as 30 mK. The proposed penalized semiparametric model includes the expected thermal behaviour of neural activity as well as characteristic random effects of thermal imaging devices. Latter are described by periodic discontinuity points, non-linear temporal drifts in-between and autoregulatory perfusion patterns. In 7 of 9 cases our method yielded promising results at locating the source of neural activity at the trepanated somatosensory cortex. The results were validated by anatomic localization, intraoperative electrophysical measurements (phase reversal) and intraoperative optical imaging. As OI yielded plausible results in the two other cases as well we assume low signal amplitudes due to imperfect intraoperative camera setups as main cause for these false-negatives. We further employed the conservative Bonferoni correction to solve the multiple comparison problem, which might further account to this issue.
In general, we demonstrated the overall applicability of the semiparametric framework to recordings of intraoperative thermal imaging. Thermal imaging in conjunction with the proposed framework is novel approach to visualize statistically significant eloquent areas of the exposed cortex. The framework allows incorporating arbitrary experimental setups for the evocation of neural activity. The visualization of neural activity during neurosurgical tumour resections allows to guide medical decision regarding the extent of tumour mass removal. Postoperative functional limitations or deficits significantly affect the patient's outcome for what reason tissue resections require robust intraoperative schemes to unveil neural activity. Further work will focus on more sophisticated preprocessing schemes as well as approaches to the multiple comparison problem to operate at lower signal-to-noise levels. Latter decreases the required overall time and number of repetitions of the employed intraoperative electrical stimulation protocols and by this the intraoperative delay. Because of the model's flexibility, we also expect applicability to other pre- and intraoperative imaging modalities.

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Table 1: FPR of various approaches for parameter optimization and significance testing.

AIC 3.0	AIC 5.8	GCV 3.0	GCV 5.8
0.023	0.0002	0.042	0.0001

Table 2: Results of intaoperative SSEP analysis.

case	sex / age	pathology	location	preop. clinical condition	activation TI	IOI
1	m / 58	metastasis adeno-ca.	precentral l.	hemiparesis r. (4/5)	positive	correlation
2	f / 33	metastasis mamma-ca.	parietal l.	facioplegia	positive	no OI
3	m / 79	metastasis melanoma	frontoparietal r.	hemiparesis l. arm (3/5) l. leg (4/5)	positive	correlation
4	f / 72	glioblastoma	parietal r.	hemiparesis l. leg (3/5)	weak	weak correlation
5	m / 69	glioblastoma	parietooccipital l.	symptomatic seizures	positive	correlation
6	m / 72	astrocytoma grade III	parietal l.	hemiparesis brachiofacial	none	weak signal
7	f / 60	metastasis RCC	parietal l.	no paresis	weak	no OI
8	f / 70	glioblastoma	parietal l.	hypesthesia 4th and 5th finger r.	none	strong signal
9	f / 84	anaplastic meningioma	frontoparietal l.	progressing half-side-disability	positive	no OI