

Universitätsspital Basel  
Hals-, Nasen-, Ohrenklinik  
Prof. Dr. biomed. Ing. J.H.J. Allum

UniversitätsSpital Zürich  
Klinik für Ohren-, Nasen-, Hals-, und Gesichtschirurgie  
Prof. Dr. Rudolf Probst

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Arbeit unter Leitung von PhD Flurin Honegger und  
CI – Audiologe und Akustiker Daniel Abels

**Relationship of Neural Response Telemetry (NRT) and electrically evoked stapedius reflex threshold (ESRT) to Cochlear Implant comfortable (C) and threshold (T) programming values.**

**INAUGURAL-DISSERTATION**

zur Erlangung der Doktorwürde der Medizinischen Fakultät  
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vorgelegt von  
Patrizia Maria Savoia  
von Zürich ZH

Genehmigt auf Antrag von Prof. Dr. med. Rudolf Probst  
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## 1. Abstract

**Objective:** The purpose of this study was to investigate if either the intraoperatively measured neural response telemetry thresholds (TNRT) or the electrically evoked stapedius reflex thresholds (ESRT) could predict the contour of behaviourally programmed T-Levels (minimal stimulation) and/or C-Levels (maximum stimulation) (creating a patient's MAP, including the set of parameters of electrode stimulation that gives the patients best hearing) equally well on two different types of Cochlear implant (CI) devices, the Nuc24RCS/RCA (Nucleus 24) System and Nuc24RECA (Nucleus Freedom) System.

**Methods:** Data from 50 patients with a minimal age of 6 years was used. 12 patients received the Nucleus 24 implant and 38 patients the Nucleus Freedom implant. In the Nucleus 24 group data from 11 patients (92%) was available for both measurements (TNRT and ESRT), and in the Nucleus Freedom group from 34 patients (89%). T- and C-levels were measured one and six months after first fit. By using the technique of Lai et al (13) the electrode array offset of C and T values was removed with respect to ESRT and TNRT values of each subject (hereafter termed TcorrESRT respectively TcorrNRT and CcorrESRT, respectively CcorrNRT). These corrected T- and C- levels were correlated with intraoperative threshold values for 4 electrodes (4, 10, 14 and 20).

**Results:** Correlations (R) with the corrected C and T levels were higher for ESRT compared to TNRT. This difference was present for both Nucleus devices. The average correlation coefficients of all electrodes were the highest comparing ESRT to C levels (Freedom device 0.79 one month after first fit, respectively 0.74 six months after first fit; Nucleus 24 device 0.81 one month after first fit, respectively 0.74 six months after first fit). The correlations were highest for the mid-array electrode 14. However, TNRT correlations for T and C were not significant for the Nucleus 24 device ( $p>0.05$ ).

**Conclusions:** Once the C and T values were corrected, ESRT are better correlated with C and T CI speech processor settings than TNRT. Presumably, improvement in ESRT techniques could yield even more accurate predictions of the C and T level profiles. Across the array, wound through the cochlea, correlations didn't show an improvement according to the distance to the acoustic nerve from base (electrode 4) to apex (electrode 20).

## 2. Introduction

Some 4 weeks after the implantation of a cochlear implant, the speech processor controlling stimulation levels needs to be programmed in an optimal way for the patient's speech understanding. This is a time-consuming procedure, and it is based on patient's behavioural responses to determine the minimum or threshold (T) levels and maximum comfortable (C) levels. Careful attention of the programmer is required especially for young children. Thus, objective techniques that aid this process will reduce the time required for the task and presumably increase its accuracy.

One objective method, neural response telemetry (NRT), measures electrically evoked compound nerve action potentials (ECAP's) of the acoustic nerve using the implant electronics to stimulate at one implant electrode and record at another (1). The first Nucleus cochlear implant (CI) with this capability was the Nucleus 24 (RCS/RCA). With introduction of the new Nucleus Freedom (24RECA) implant, improved linearity and signal- to-noise ratios (1, 2) were available in the implant electronics and with these presumably more accurate NRT thresholds (TNRT) could be measured. The threshold is based on the minimum stimulation level required to observe an ECAP. Several studies with these devices investigated whether the measurement of TNRTs could predict behaviourally obtained T- and C-levels in order to create a patient's MAP either for children (3) or for adults (4-7). These studies showed considerable variability in the correlations between the NRT and the T- and C-levels across electrodes. Due to this variability a prediction of an accurate MAP from TNRT was considered difficult (7).

An alternative method to determine the threshold response of the auditory nerve is to electrically evoke a stapedius reflex. The threshold (ESRT) obtained by observation of stapedius muscle contractions can also be used to predict processor T- and C-levels (8). An advantage of the ESR compared to the NRT technique is that the response involves the reflex loop to the facial motorneuron and back to the stapedius muscle. Thus a greater amount of central processing is involved in contrast to NRT, where the measurement includes a singular neural answer of the acoustic nerve. Both methods, TNRT and ESRT can be used intra-operatively under anaesthesia (8). ESRT has been used to predict speech processor C- and T-levels in several studies, in adult (9-12) and paediatric populations (11). These studies concluded that ESRT is a useful technique to predict speech processor values.

To our knowledge, a comparison of the correlations of TNRT and ESRT to the C- and T-values has not been published to date. Therefore the principal aim of this study was to investigate whether the TNRTs or ESRTs predict the C- and T-levels with a greater precision. We were also interested in investigating whether the predictions changed between one and six months after first speech processor fitting, and whether correlations are better for mid-array regions of the electrode where a priori the electrode carrier should be closer to the nerve endings than at the basal part of the cochlear (9).

In this study we included patients provided either with the Nucleus 24 RC or the Nucleus Freedom 24RE system in order to explore whether the technological changes in the NRT Freedom system improved correlations between TNRT and C and T levels. Another change between the two devices was the use of modiolus “hugging” (contour advanced) electrode, introduced with the Nucleus Freedom system which presumably should improve the weaker correlations previously observed for basal electrodes (9).

### 3. Methods

Data from 12 users of the cochlear implant Nuc24RCS/RCA (Nucleus 24) and 38 users of the newer Nuc24RECA (Nucleus Freedom) was used in this study. Both implants are manufactured by the Cochlear Company, Melbourne, Australia. All participants in this study were implanted at the Cochlear-Implant Centre at the University Hospital Basel, Switzerland, between 2002 and 2009. Of these subjects 28 (56%) were female and 22 (44%) were male with ages between 7 and 65 years (mean age of 35 years). Children younger than 6 years were excluded from this study, as generally below this age C- and T- levels can only be based on behavioural observation of facial expressions rather than verbal responses. In 14 patients (28%) the cause of deafness was congenital.

#### *Data collection*

Intraoperative data were collected after measurement of the electrical impedance of the inserted electrode array. The dimension of this data is Current Level (CL), which is an internal unit of the cochlear implant, describing the acoustic intensity which is encoded with electric charge. First, ESRT measurements on all even numbered electrodes were performed stepping 10 Current Level (CL) up from 180 CL with a stimulation rate of 900/s, pulse width 25  $\mu$ s, duration 0.5 sec until a contraction of the stapedius muscle was observed in the operating microscope by the surgeon and the audiologist. Then stimulation levels were reduced in steps of 5 CL until no contraction was observed and then increased again in steps of 3 CL until a contraction was again observed. This final level was taken as the ESR threshold (ESRT).

Second, NRT measurements were taken on a reduced number of electrodes used for ESRT measurements. First the automatic “visual” technique of the manufacturer (1, 5) was used with a stimulation rate of 250/s and recording at 2 electrodes apically from the stimulated electrode. If less than 10 different CLs were used for the automatic TNRT detection, 7 stimulation levels above the maximum level used for the automatic technique, each level separated by 3 CLs, were added to determine an amplitude growth function for the electrode. Off-line the correct alignment of negative and positive peaks (typically at 300 and 550 ms) in the compound nerve action potential was checked across recordings from a single electrode, and then the NRT threshold was determined as the x-axis intercept of the regression line in the amplitude growth function.

NRT data was available for all patients. Due to anatomic reasons (absent stapedius muscle, for example) ESRT data was available for 11/12 patients in the Nucleus 24 group and 34/38 patients in Nucleus Freedom group).

We chose to analyze data from 4 electrodes at basal (electrode 4), medial (electrode 10 and 14) and apical (electrode 20) segments of the electrode array.

Behaviour C- and T-levels for the speech processor settings were first determined 4 weeks after the CI implantation. These levels were obtained using a 6 level loudness scaling display with the following displayed levels: hardly perceptible (set to T), soft, good, loud but comfortable (set to C), loud, too loud. The ESRT and NRT levels obtained intraoperatively were available to the programming audiologist. Standard stimulation rates of 1200/s, 25  $\mu$ s pulse width, 2 bursts over 0.5 sec with 0.5 sec between bursts were used for testing C and T levels. Maps were set with 10 electrodes per stimulation frame being set initially and 12 electrodes after 2 weeks. The stimulation algorithm used for all patients was ACE (2).

Initially (first 2-3 sessions) only T values were determined with C levels set at T+15. The speech processor (MAP) C and T levels settings were raised or lowered until the MAP was acceptable to the patient. For the first 2 weeks 2-3 programming sessions were scheduled. Thereafter, sessions were conducted once per week until 1 month, then every 2-3 weeks. MAP levels at 1 and 6 months were used for this study.

#### *Data analysis*

For regression analysis we first used the technique of Lai et al (13), removing the mean electrode array offset of C and T values with respect to ESRT and NRT values of each subject (hereafter termed TcorrESRT respectively TcorrNRT and CcorrESRT, respectively CcorrNRT) before performing subject regressions for each electrode. At this stage, data of 6 Nucleus 24 and 3 Nucleus Freedom patients-electrode correlations were rejected from analysis because one or more of the electrode correlation coefficients R were lower than the 5% range of the rest of the correlations. Finally, electrode correlations were calculated for the remaining patients (6 Nucleus 24 and 35 Freedom patients) fitted with each implant type.

The last step was to test whether there was significant difference between the TNRT- and ESRT – correlations. As the observed data was not distributed according to normal distributions we used a bootstrap approach. For this analysis, we used the MATLAB Version 7.10 (R2010a), Statistics Toolbox Version 7.3 (R2010a). We established the working hypothesis  $H_0: R_1 = R_2$ , alternatively  $R_1 < R_2$ , where 1 stands for TNRT and 2 for ESRT. The calculations were performed with the statistic program “R 2.13.1” using the publicly available package Cocor (Comparing correlations), which includes functions to compare two correlations based on either dependent or independent groups (14).

This package uses 6 different tests (Pearsons and Filon's (1898); Dunn and Clark's (1969); Steiger's (1980) modification of Dunn and Clark's (1969); Raghunathan, Rosenthal and Rubin's (1996) modification of Pearson and Filon's (1989); and Silver, Hittner and May's (2004) modification of Dunn and Clark (1969) using the backtransformed average Fisher's (1921); Zou's (2007) confidence interval).

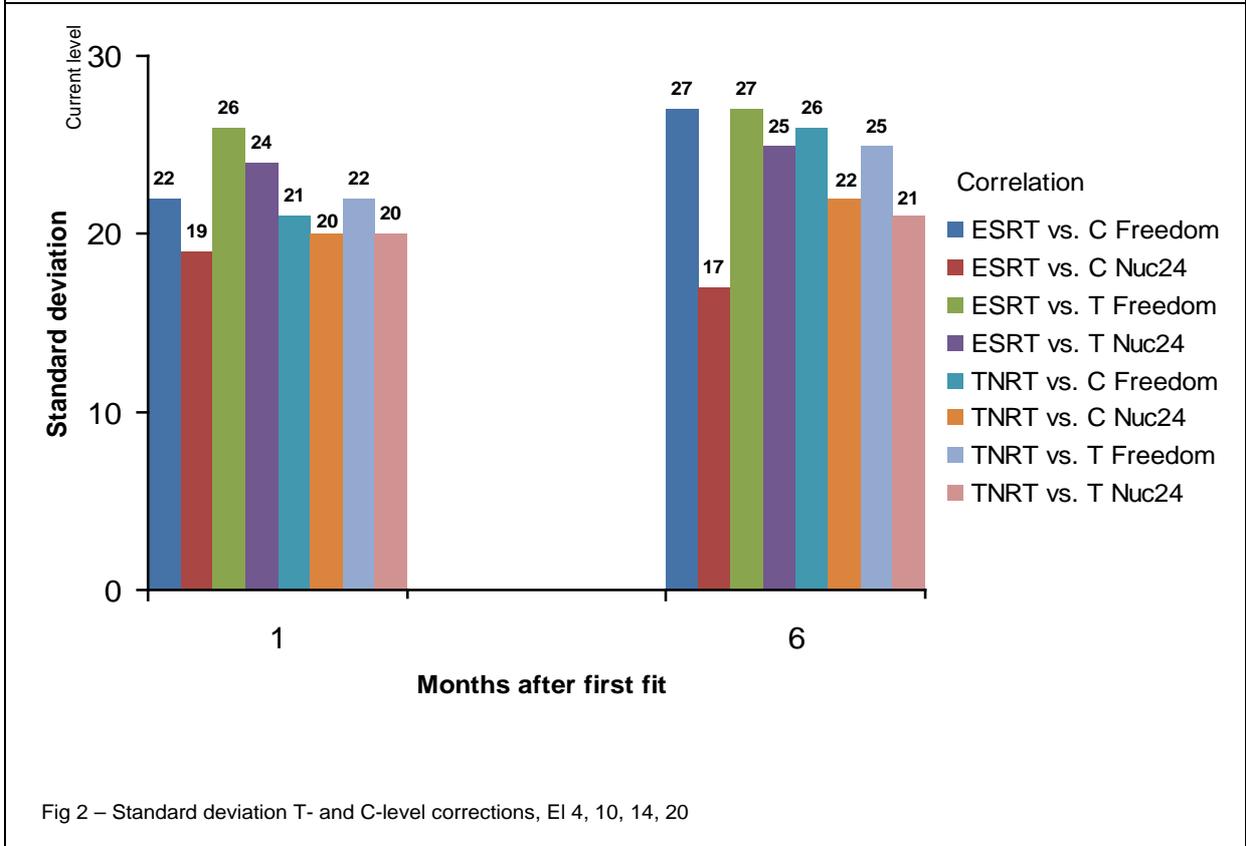
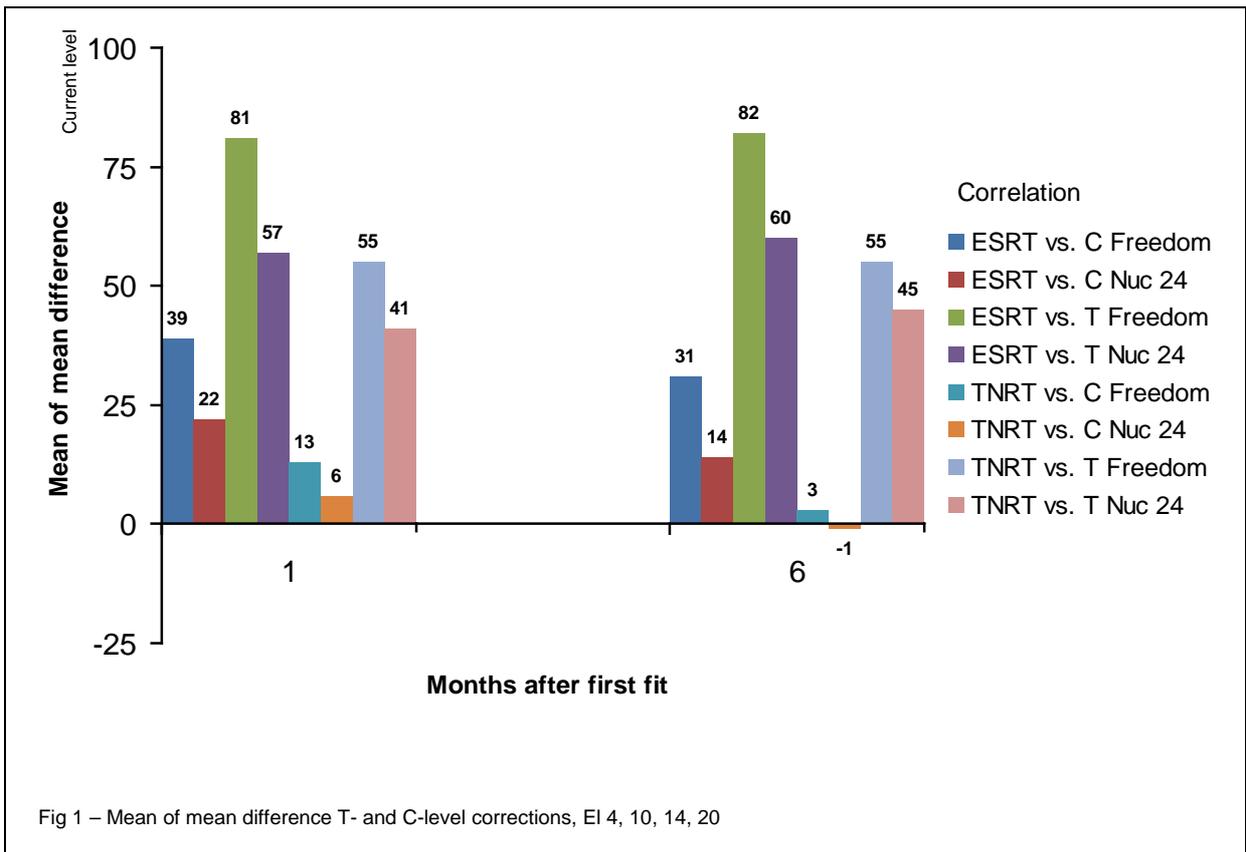
To reject H0 we established that 4 of these tests must reject our working hypothesis with  $p < 0.05$ . If correlations were significantly different this is marked by a star symbol in the plots of Figs 7 to 10.

#### **4. Results**

##### *Mean of mean difference and standard deviation of C and T level corrections*

We calculated for both TNRT and ESRT T and C value corrections prior to regression analysis (using the technique of Lai et al (13), as described in the methods above). Figure 1 illustrates the mean corrections and Figure 2 the respective standard deviations. The x-axis illustrates the time point, the dimension of the y-axis are Current level (CL). We observe a similar effect of corrections at 1 and 6 months. Corrections depending on the Nucleus 24 device are lower. The established mean electrode array offset of C values with respect to TNRT indicate the lowest correction between C values and corresponding CcorrNRT values for both devices, comparing to the further calculated corrections.

Standard deviations of these corrections varied from 19 to 26 CL at 1 month and from 17 to 27 CL at 6 months.



*Global relationship between T- and C-levels and NRT/ESRT one and six months after first fit*

Table 1 shows the correlations R (across all electrodes) of the corrected T- or C-values (TcorrESRT, TcorrNRT, CcorrESRT and CcorrNRT), to TNRT and ESRT values one month after first fit for all patients and across the four single and all electrodes. The significant correlations are indicated by bold type. Correlations are shown for both implant devices. The largest R value was found between CcorrESRT and ESRT values 1 month after first fit over all electrodes for Nucleus 24 device (R 0.81). Fig 3 on page 13 shows this correlation with the highest slope value of 1.07 (see Table 3).

The graphical displays of the global correlations (across all electrodes) between the corrected T- or C-values to TNRT and ESRT are shown for both implant devices on the Figures 11 to 17 in the attached files.

In Table 2, the same correlations are shown 6 months after first fit. As already seen one month after first fit, the largest R value appears between CcorrESRT and ESRT values over all electrodes for Nucleus 24 device (R 0.74). Fig 4 shows the equivalent graphical interpretation. The graphical interpretations of the global correlations are shown in attached file on the Figures 18 to 24, equivalent to Figs 11 to 17.

Using the equation of straight line for the graphical interpretations with the equation written  $y = mx + b$ , m is the slope value and b the y-intercept, where the line crosses the y-axis. The slope and intercept values for the correlations of each tested electrode for the Freedom device are shown in Tables 3 and 4. Dimension of intercept values are Current level (CL). Corresponding slope and intercept values for the Nucleus 24 device are not provided as these were not consistently significant. Note that to obtain the true intercept values, the intercept values in Tables 3 and 4 must be added to corrections applied to offset C and T values prior to correlation analysis.

One month after first fit		EL 4		EL 10		EL 14		EI 20		All	
		R	p	R	p	R	p	R	p	R	p
Freedom	TNRT vs. T	0.63	<b>0.000</b>	0.44	<b>0.006</b>	0.67	<b>0.000</b>	0.7	<b>0.000</b>	0.63	<b>0.000</b>
	TNRT vs. C	0.64	<b>0.000</b>	0.59	<b>0.000</b>	0.63	<b>0.000</b>	0.71	<b>0.000</b>	0.67	<b>0.000</b>
N24	ESRT vs. T	0.76	<b>0.000</b>	0.67	<b>0.000</b>	0.83	<b>0.000</b>	0.62	<b>0.000</b>	0.72	<b>0.000</b>
	ESRT vs. C	0.83	<b>0.000</b>	0.86	<b>0.000</b>	0.93	<b>0.000</b>	0.75	<b>0.000</b>	0.79	<b>0.000</b>
	TNRT vs. T	0.48	0.423	0.6	0.748	0.75	0.958	0.86	0.202	0.17	0.261
	TNRT vs. C	0.17	0.946	0.72	0.888	0.7	0.855	0.78	0.653	0.07	0.631
	ESRT vs. T	0.83	<b>0.010</b>	0.58	0.062	0.52	0.103	0.73	<b>0.011</b>	0.63	<b>0.000</b>
	ESRT vs. C	0.72	<b>0.046</b>	0.97	<b>0.000</b>	0.87	<b>0.001</b>	0.88	<b>0.000</b>	0.81	<b>0.000</b>

Table 1 - Correlations (R) and p-value (p) one month after first fit. Significant correlations are indicated by bold type.

Six months after first fit		EL 4		EL 10		EL 14		EI 20		All	
		R	p	R	p	R	p	R	p	R	p
Freedom	TNRT vs. T	0.61	<b>0.000</b>	0.51	<b>0.001</b>	0.63	<b>0.000</b>	0.71	<b>0.000</b>	0.63	<b>0.000</b>
	TNRT vs. C	0.62	<b>0.000</b>	0.7	<b>0.000</b>	0.63	<b>0.000</b>	0.75	<b>0.000</b>	0.65	<b>0.000</b>
N24	ESRT vs. T	0.77	<b>0.000</b>	0.67	<b>0.000</b>	0.83	<b>0.000</b>	0.61	<b>0.000</b>	0.71	<b>0.000</b>
	ESRT vs. C	0.83	<b>0.000</b>	0.85	<b>0.000</b>	0.9	<b>0.000</b>	0.75	<b>0.000</b>	0.74	<b>0.000</b>
	TNRT vs. T	0.5	0.064	0.51	0.747	0.63	0.801	0.62	0.613	0.17	0.251
	TNRT vs. C	0.32	0.940	0.85	0.416	0.7	0.938	0.75	0.987	0.017	0.913
	ESRT vs. T	0.75	<b>0.032</b>	0.46	0.153	0.51	0.111	0.63	<b>0.038</b>	0.56	<b>0.000</b>
	ESRT vs. C	0.6	0.114	0.95	<b>0.000</b>	0.86	<b>0.000</b>	0.85	<b>0.001</b>	0.74	<b>0.000</b>

Table 2 - Correlations (R) and p-value (p) six months after first fit. For details see legend to Table 1.

One month after first fit		EL 4		EL 10		EL 14		EI 20		All	
		Slope	Inter.								
Freedom	TNRT vs. T	0.65	58.3	0.45	102.2	0.62	69.6	0.64	56.6	0.65	60.8
	TNRT vs. C	0.72	49.4	0.71	55.2	0.67	57.7	0.69	45.3	0.78	37.3
	ESRT vs. T	0.77	52.7	0.44	108.9	0.62	74.4	0.52	95.3	0.61	77.8
	ESRT vs. C	1.07	-4.25	0.73	49.2	0.86	24.5	0.74	51.9	0.83	33.0

Table 3 – Shape and intercept values (Inter) of Freedom one month after first fit.

Six months after first fit		EL 4		EL 10		EL 14		EI 20		All	
		Slope	Inter.								
Freedom	TNRT vs. T	0.63	62.1	0.53	89.4	0.58	74.7	0.68	49.1	0.67	57.4
	TNRT vs. C	0.78	41.3	0.71	55.5	0.62	65.5	0.78	29.7	0.78	37.3
	ESRT vs. T	0.72	64.2	0.43	12.0	0.64	71.1	0.51	96.8	0.60	80.7
	ESRT vs. C	0.99	14.3	0.73	50.0	0.82	29.6	0.79	40.5	0.79	42.3

Table 4 – Shape and intercept (Inter) values of Freedom six months after first fit.

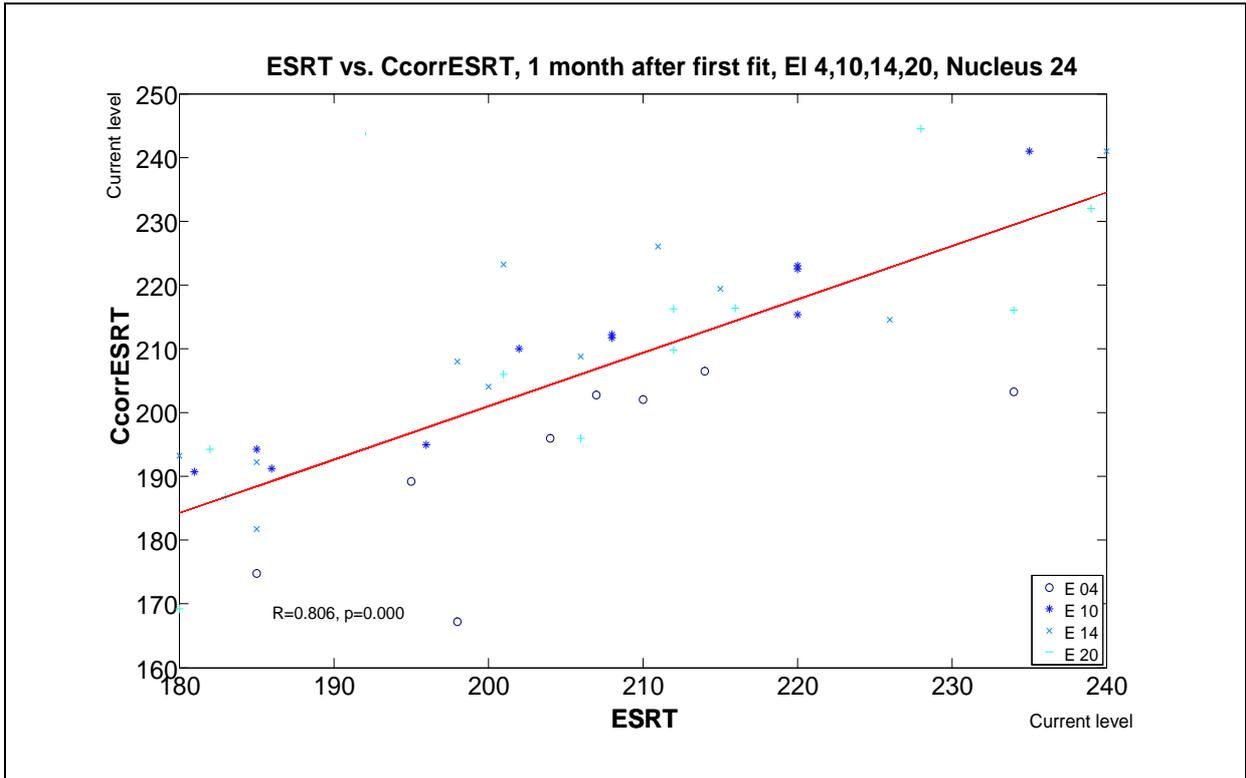


Fig 3 - ESRT vs. C level, corrected for mean electrode offset with respect to ESRT (CcorrESRT), 1 month after first fit, all electrodes, Nucleus 24

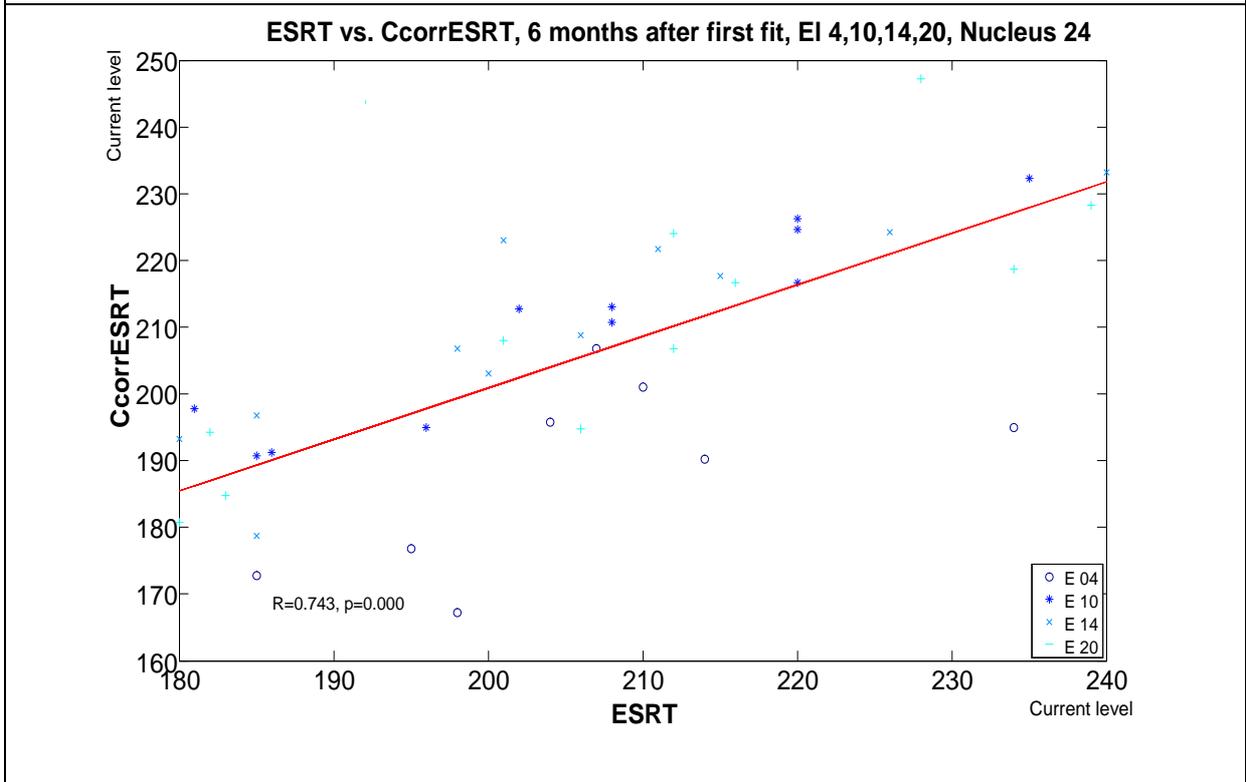


Fig 4 - ESRT vs. C level, corrected for mean electrode offset with respect to ESRT (CcorrESRT), 6 months after first fit, all electrodes, Nucleus 24

*Electrode specific relationship between T- and C-levels and NRT/ESRT one and six months after first fit.*

Electrode 14 showed the highest correlations (see Tables 1 and 2). For this reason we decided to create a graphical interpretation for these correlations. The highest correlations ( $R \geq 0.9$ ) appear between ESRT and corrected C-levels (CcorrESRT) one and six months after first fit in the Freedom device. These correlations are shown in Figs 5 and 6. Figs 25 to 31 in the attached file show correlations between corrected T- and C-levels for the NRTT and ESRT of electrode 14 one month after first fit, regressions for both devices are displayed separately. Likewise for 6 months after first fit in Figs 32 to 38.

The correlations between TNRT, ESRT and the T- and C- levels comparing one and six months after first fit did not show any change over time.

Electrode 14 slope value for T was 0.62 and intercept value was 70 CL for the Freedom after 1 month.

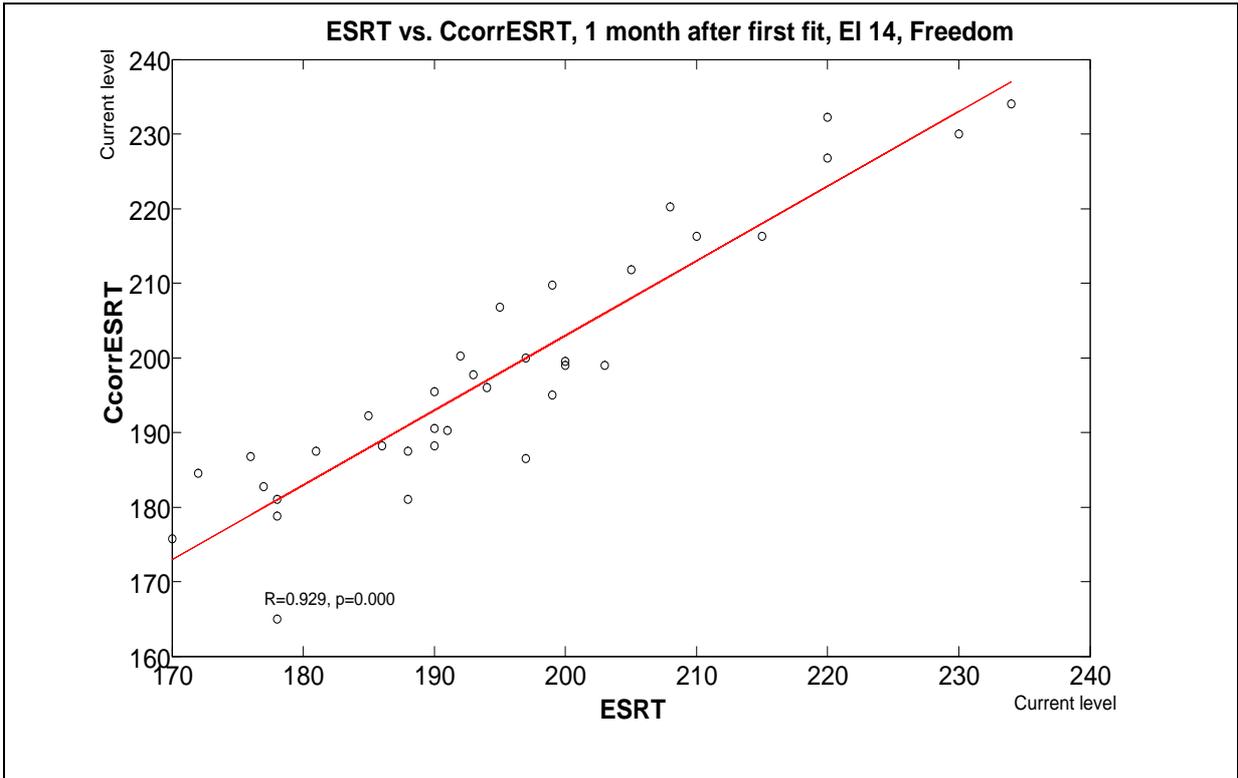


Fig 5 - ESRT vs. C level, corrected for mean electrode offset with respect to ESRT (CcorrESRT), 1 month after first fit, electrode 14, Freedom

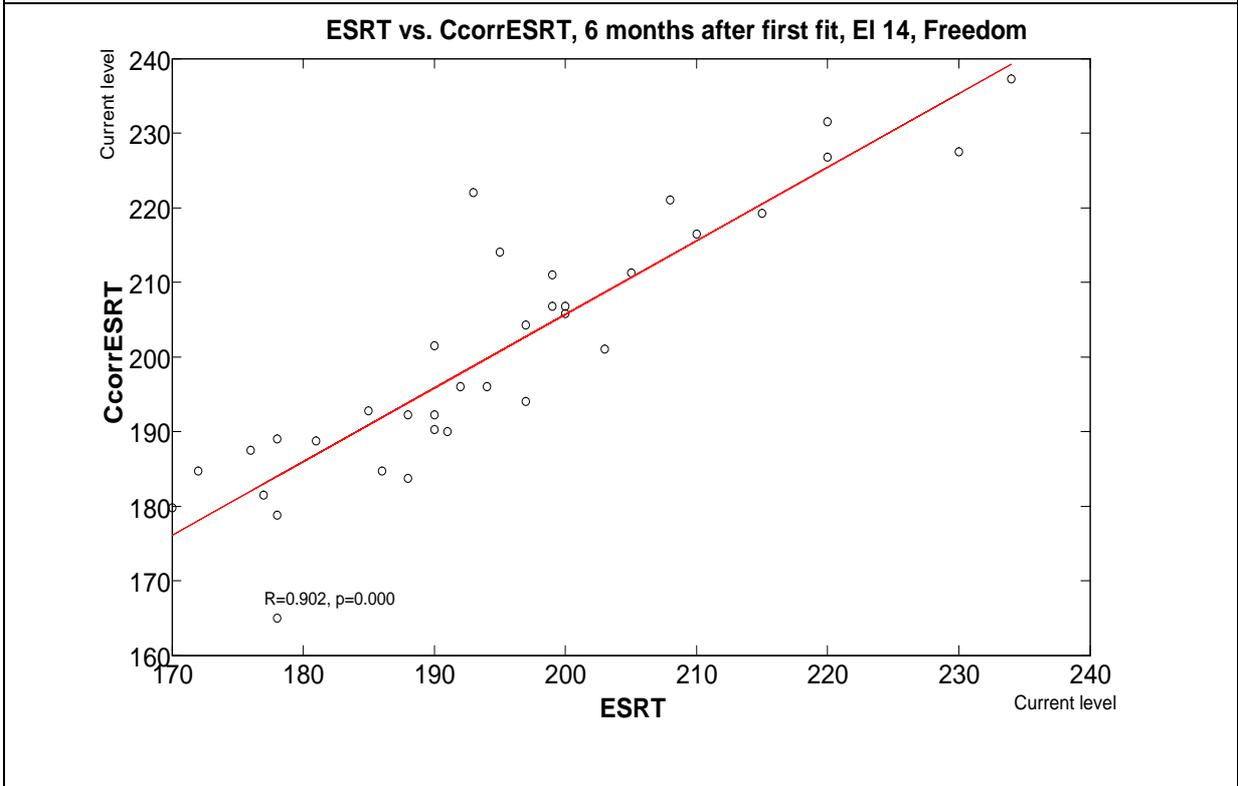


Fig 6 - ESRT vs. C level, corrected for mean electrode offset with respect to ESRT (CcorrESRT), 6 months after first fit, electrode 14, Freedom

### *Differences between correlation – based on ESRT and NRT*

As explained in the methods above, the last step was to test whether there were significant differences between the TNRT- and ESRT correlations.

Figures 7 to 10 illustrate the bootstrapped means (columns in Fig 7 to 10) and confidence intervals (vertical bars in Fig 7 to 10) for R values. Fig 7 and 8 illustrate these values for the Nucleus Freedom device, T- and C- level separately, Fig 9 and 10 for the Nucleus 24 device. The mean values correspond to those listed in Tables 1 and 2, likewise the significance (p) values (significant correlations are indicated in bold type). Looking at the confidence intervals, we see that for the Freedom device TNRT correlations have larger confidence intervals than ESRT correlations. Also, the confidence Intervals for the Freedom device are smaller than those for the Nucleus 24 device.

Significant differences were estimate based on passing 4 of 6 possible tests as explained in the methods above. Pairs of correlations which pass the aforementioned test and are thus considered to be significantly different are marked with a star-symbol in the corresponding plots in Fig 7 to 10. Although good correlations were achieved with ESRT for the Freedom device, these were only significantly better for C and T levels at 6 months, specifically for electrode 14, compared to TNRT. For the Nucleus 24 system significant differences were also observed especially at 1 month.

### Freedom Mod. Threshold Level

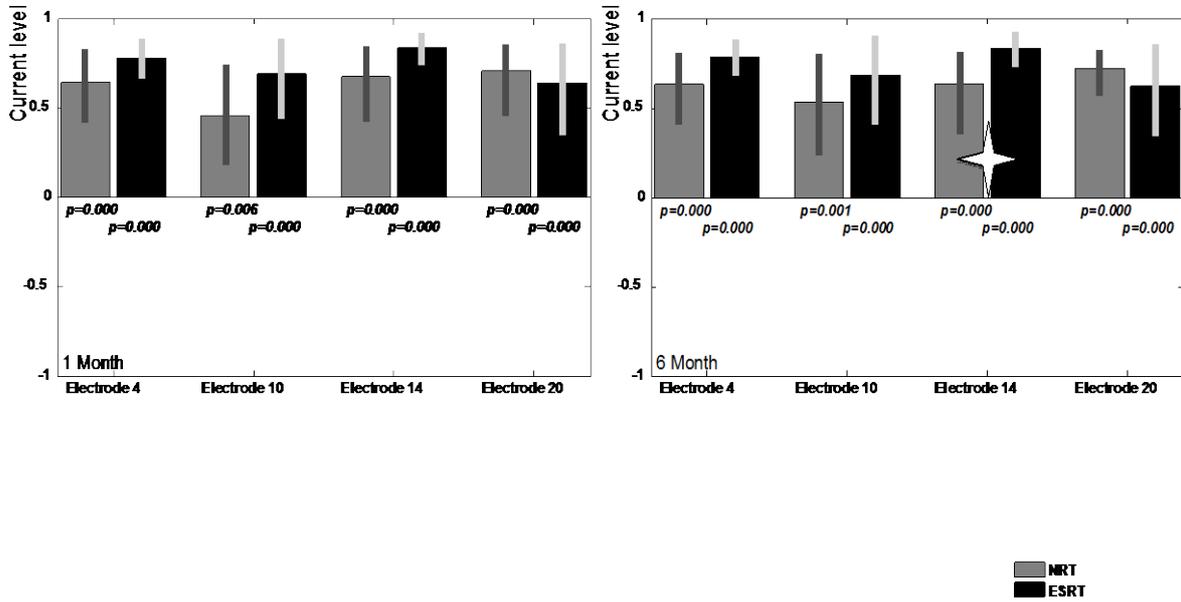


Fig 7 – Bootstrapped means and confidence intervals for correlations, T level, Freedom device

### Freedom Mod. Comfortable Level

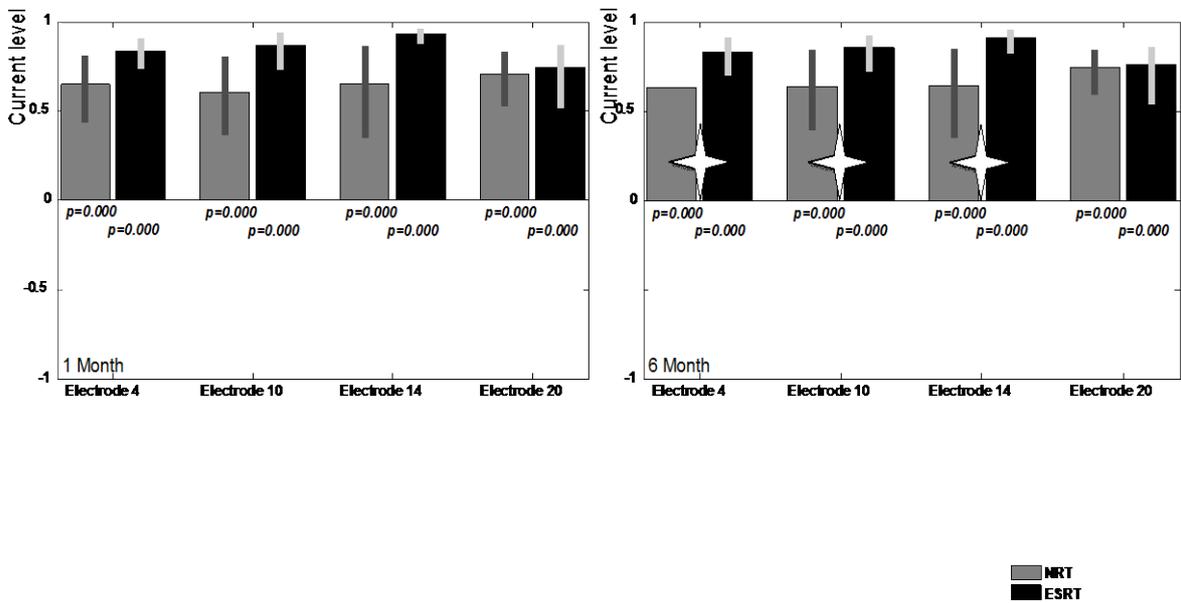


Fig 8 – Bootstrapped means and confidence intervals for correlations, C level, Freedom device

### Nucleus 24 Mod. Threshold Level

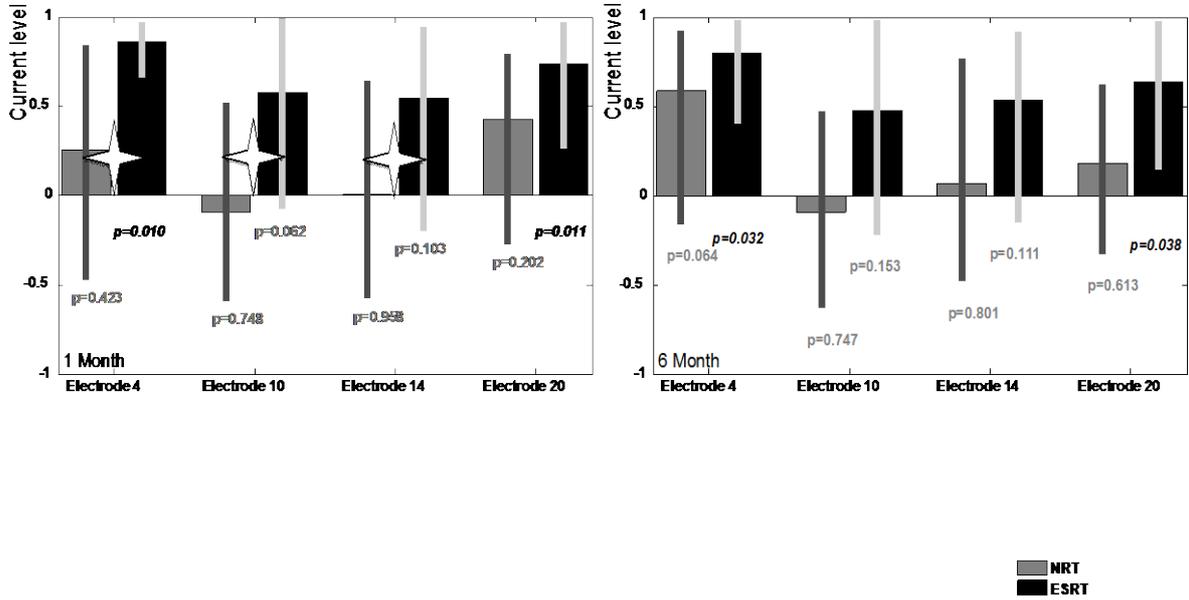


Fig 9 – Bootstrapped means and confidence intervals for correlations, T level, Nucleus 24 device

### Nucleus 24 Mod. Comfortable Level

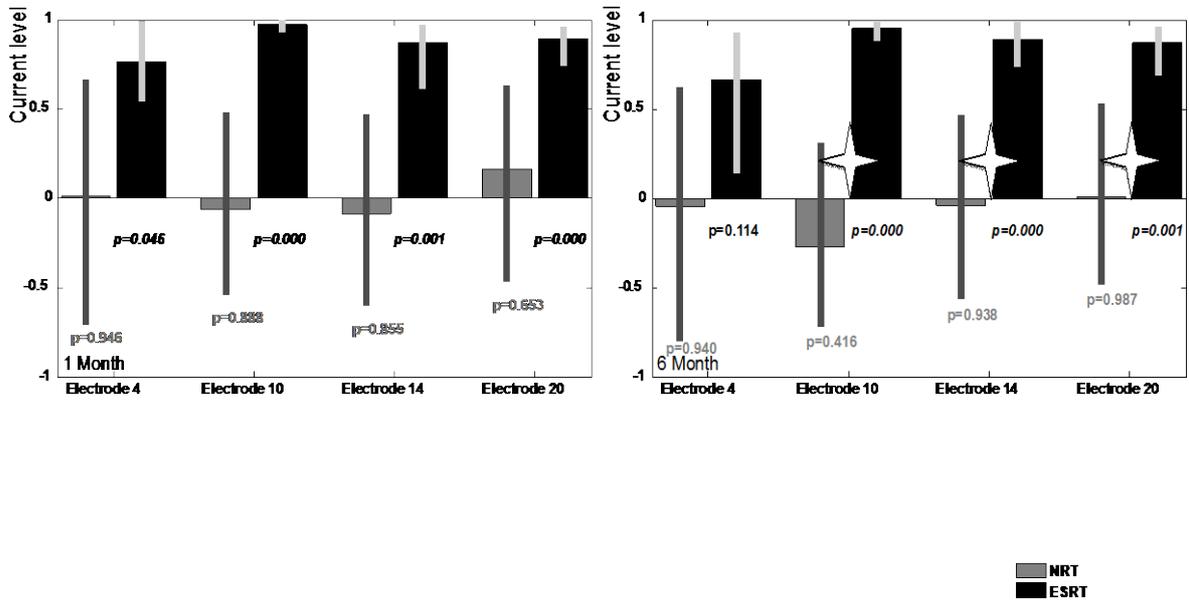


Fig 10 – Bootstrapped means and confidence intervals for correlations, C level, Nucleus 24 device

## 5. Discussion

Both the measurements of NRT and ESRT are performed easily and quickly. NRT measures responses of the auditory nerve. ESRT is dependent on a signal from the auditory nerve reaching the brainstem and activating the motor neurons of the M. stapedius. Thereby it provides more information on the integrity of auditory pathways.

The major aim of this study was to provide information whether NRT or ESRT thresholds best determine stable T- and C-levels for CI speech processor MAPs. The results indicate that ESRT would be a better predictor for a behavioural-based MAP than TNRT.

Using strict comparison criteria we determined that a significant difference was evident on several electrodes (2 of 4 tested) comparing either the correlations to the C- or to the T-levels. Given that ESRT correlations were always larger than those of TNRT we assume that with less strict statistical criteria more electrodes would have shown significance, that is, not only electrodes 10 and 14. The lack of statistical significance of correlations and wide confidence intervals showed that TNRT correlated worse to the behaviourally programmed T- and C levels in the Nucleus 24 group. Considering the ESRT correlations as a comparison standard this result implies that the changes between the Nucleus 24 and Freedom systems led to better TNRT estimates.

Comparing the results one and six months after first fit there is, in general, little change in the ESRT and TNRT correlations for the Freedom device. Typically, C levels increase over time with a gradual reduction in T levels to widen the dynamic range between T and C (16). The small change in the correlations would therefore imply that C and T levels at 1 and 6 months are correlated with one another.

Data was collected at different locations in the electrode array so that it was possible to follow the correlation trends from apex to base. If we examined the best correlations across electrodes, those for ESRT with C, then there was little difference across the array. Our expectation that the basal electrode 4 would have a worse correlation due to a greater distance to the acoustic nerve endings, comparing to apical electrode 20 was not completely fulfilled (see Table 1 and 2).

Henkin et al (16) analysed the interaction between the T- and C-levels and the different cochlear segment over one, three and six months in Nucleus24 users. Their results showed a lower significance in the T- and C-levels in apical segments than those at medial and basal segments. This is a similar trend to that we found.

We used the technique of Lai et al (13) to reduce scatter between subjects and electrodes by removing the mean offset first. This action needs to be taken into account together with the error of 20 Current levels that can be expected when attempting to predict C or T values. Once this has been done the C and T levels as predicted by ESRT levels can be estimated.

Our correlations are based on different stimulation rates. For ESRT the stimulation rate used was 900/s. For NRT the rate was 250/s. For behavioural C or T level estimation a stimulation rate of 1200/s was used. Thus it is possible that better correlations were obtained with ESRT due to the more similar rate used with C and T behaviour testing. Another factor is that ESRT testing provides stimulation to the facial motoneuron in the brainstem with its function to percept loudness and to convert it in electrical potential, which is lacking for the nerve responses of NRT. In ESRT measurement the stapedial reflex is directly stimulated and a contraction of the muscle is observed. It is possible that identifying the muscle electrographic activity rather than observation of the muscle contraction might improve the ESRT measurement technique.

## 6. Figure Legends

- Figure 1. Mean of the mean difference between ESRT and TNRT levels and respectively T- and C-level corrections for each subject considered for all 4 electrodes, Electrode 4, 10, 14, 20. The means are shown for each correction performed.
- Figure 2. Standard deviation of the T- and C-level corrections depicted in Figure 1
- Figure 3. ESRT vs. C levels corrected for mean electrode offset (CcorrESRT), 1 month after first fit, regression across all electrodes (4,10,14,20), for the Nucleus 24 device.
- Figure 4. ESRT vs. CcorrESRT, 6 months after first fit, all electrodes, Nucleus 24
- Figure 5. ESRT vs. CcorrESRT, 1 month after first fit, electrode 14, Freedom
- Figure 6. ESRT vs. CcorrESRT, 6 months after first fit, electrode 14, Freedom
- Figure 7. Bootstrapped means (columns) and confidence intervals (vertical bars) of correlation coefficient R for the correlations between corrected T levels and TNRT and ESRT levels when measured with the Freedom device. The means are for 1 and 6 months after first fitting. The p and R values are also listed in Tables 1 and 2. The stars with 4 points indicate TNRT and ESRT means which are statistically different based on 4 of 6 tests (see methods).
- Figure 8. Bootstrapped means and confidence intervals of correlation coefficient R for the correlations between corrected C levels and TNRT and ESRT levels when measured with the Freedom device.
- Figure 9. Bootstrapped means and confidence intervals for correlations between corrected T levels and TNRT and ESRT levels when measured with the Nucleus 24 device.
- Figure 10. Bootstrapped means and confidence intervals for correlations between corrected C levels and TNRT and ESRT levels when measured with the Nucleus 24 device.
- Figure 11. NRT vs. T levels corrected for mean electrode offset (TcorrNRT) 1 month after first fit, regression across all electrodes (4, 10, 14, 20), for the Freedom device. Each point is for one subject and one electrode
- Figure 12. NRT vs. TcorrNRT, 1 month after first fit, all electrodes, Nucleus 24  
Equivalent to Fig 11, for Nucleus 24 group
- Figure 13. ESRT vs. TcorrESRT, 1 month after first fit, all electrodes, Freedom
- Figure 14. ESRT vs. TcorrESRT, 1 month after first fit, all electrodes, Nucleus 24
- Figure 15. NRT vs. CcorrNRT, 1 month after first fit, all electrodes, Freedom
- Figure 16. NRT vs. CcorrNRT, 1 month after first fit, all electrodes, Nucleus 24
- Figure 17. ESRT vs. CcorrESRT, 1 month after first fit, all electrodes, Freedom
- Figure 18. NRT vs. TcorrNRT, 6 months after first fit, all electrodes, Freedom
- Figure 19. NRT vs. TcorrNRT, 6 months after first fit, all electrodes, Nucleus 24
- Figure 20. ESRT vs. TcorrESRT, 6 months after first fit, all electrodes, Freedom

Figure 21. ESRT vs. TcorrESRT, 6 months after first fit, all electrodes, Nucleus 24  
Figure 22. NRT vs. CcorrNRT, 6 months after first fit, all electrodes, Freedom  
Figure 23. NRT vs. CcorrNRT, 6 months after first fit, all electrodes, Nucleus 24  
Figure 24. ESRT vs. CcorrESRT, 6 months after first fit, all electrodes, Freedom  
Figure 25. NRT vs. TcorrNRT, 1 month after first fit, for electrode 14 only, Freedom  
Figure 26. NRT vs. TcorrNRT, 1 month after first fit, electrode 14, Nucleus 24  
Figure 27. ESRT vs. TcorrESRT, 1 month after first fit, electrode 14, Freedom  
Figure 28. ESRT vs. TcorrESRT, 1 month after first fit, electrode 14, Nucleus 24  
Figure 29. NRT vs. CcorrNRT, 1 month after first fit, electrode 14, Freedom  
Figure 30. NRT vs. CcorrNRT, 1 month after first fit, electrode 14, Nucleus 24  
Figure 31. ESRT vs. CcorrESRT, 1 month after first fit, electrode 14, Nucleus 24  
Figure 32. NRT vs. TcorrNRT, 6 months after first fit, electrode 14, Freedom  
Figure 33. NRT vs. TcorrNRT, 6 months after first fit, electrode 14, Nucleus 24  
Figure 34. ESRT vs. TcorrESRT, 6 months after first fit, electrode 14, Freedom  
Figure 35. ESRT vs. TcorrESRT, 6 months after first fit, electrode 14, Nucleus 24  
Figure 36. NRT vs. CcorrNRT, 6 months after first fit, electrode 14, Freedom  
Figure 37. NRT vs. CcorrNRT, 6 months after first fit, electrode 14, Nucleus 24  
Figure 38. ESRT vs. CcorrESRT, 6 months after first fit, electrode 14, Nucleus 24

## 7. Figures

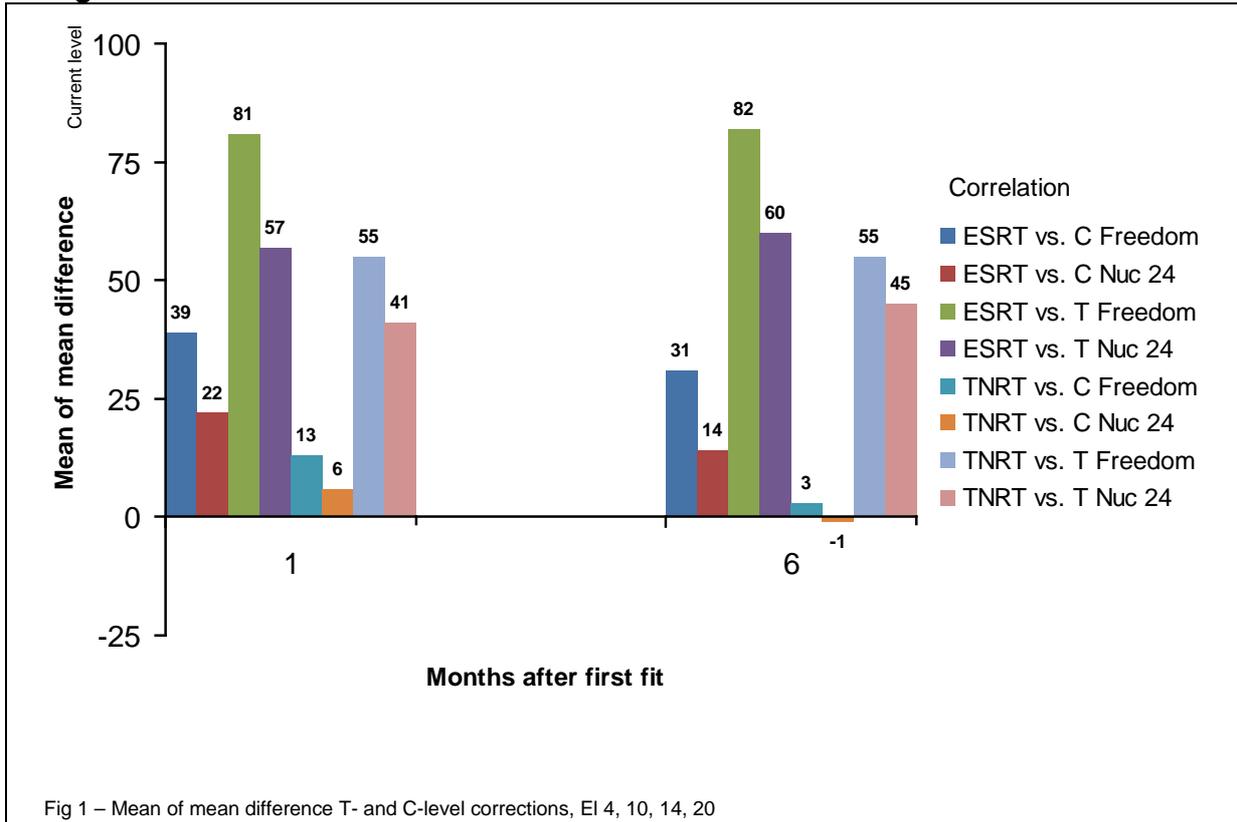


Fig 1 – Mean of mean difference T- and C-level corrections, EI 4, 10, 14, 20

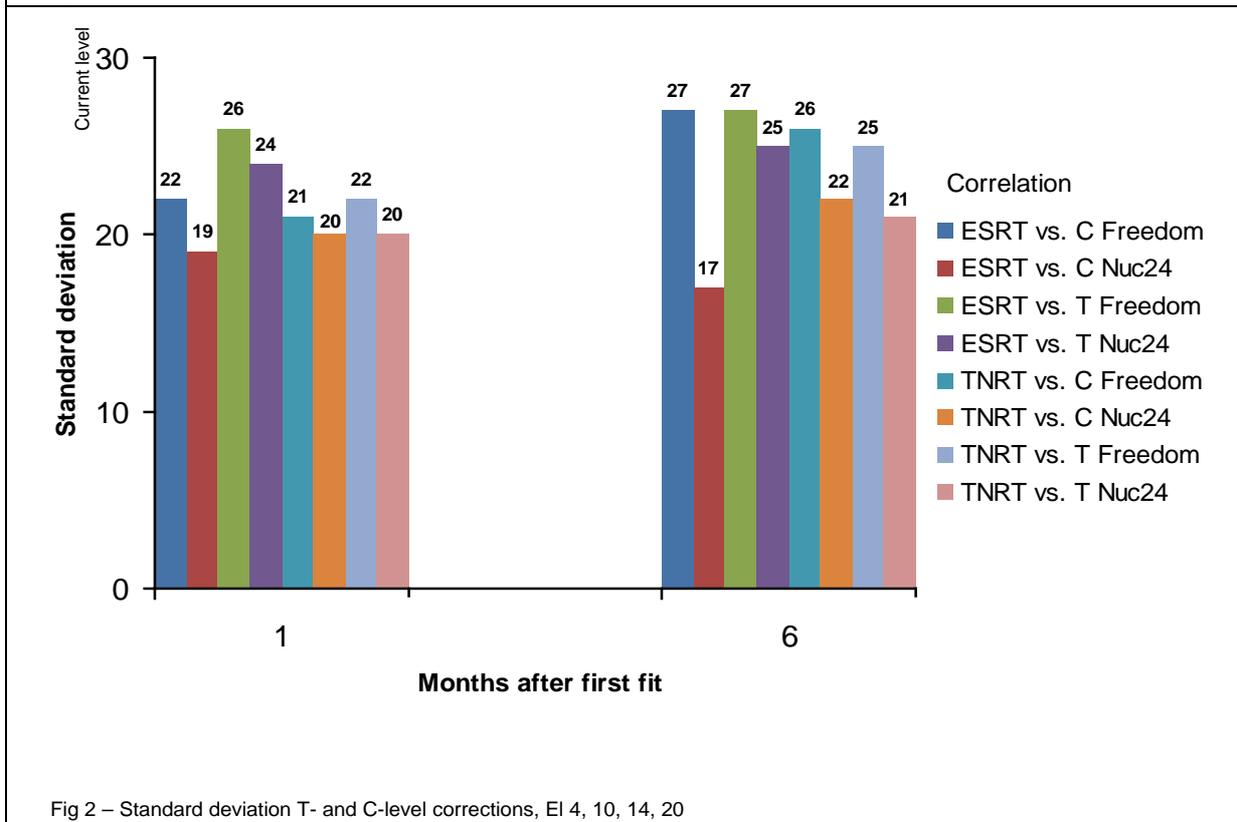


Fig 2 – Standard deviation T- and C-level corrections, EI 4, 10, 14, 20

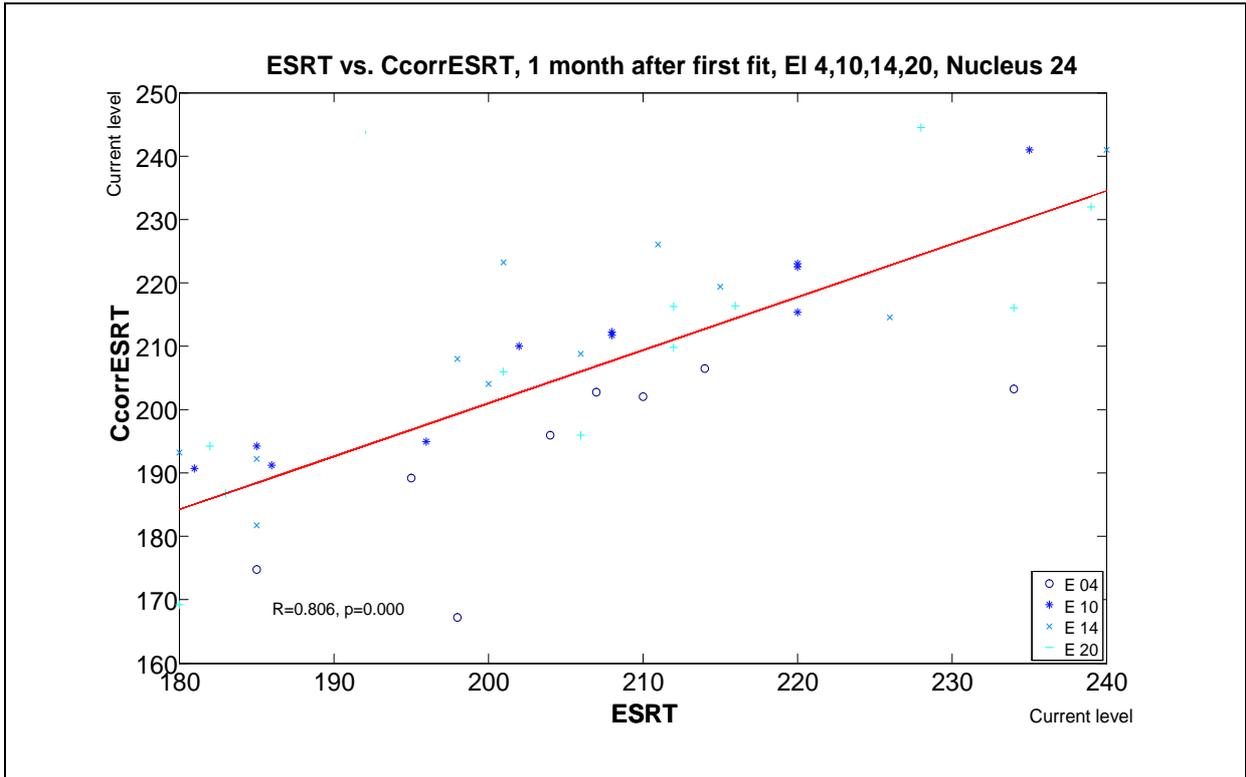


Fig 3 - ESRT vs. C level, corrected for mean electrode offset with respect to ESRT (CcorrESRT), 1 month after first fit, all electrodes, Nucleus 24

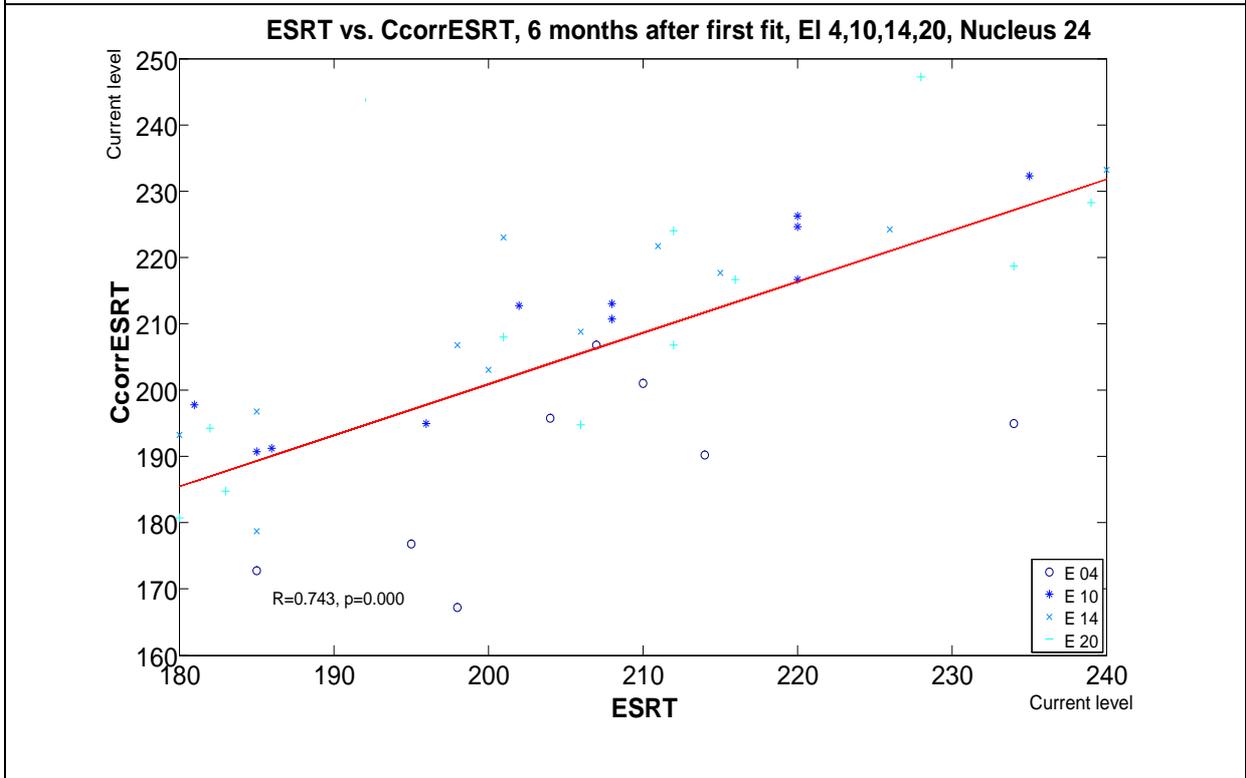


Fig 4 - ESRT vs. C level, corrected for mean electrode offset with respect to ESRT (CcorrESRT), 6 months after first fit, all electrodes, Nucleus 24

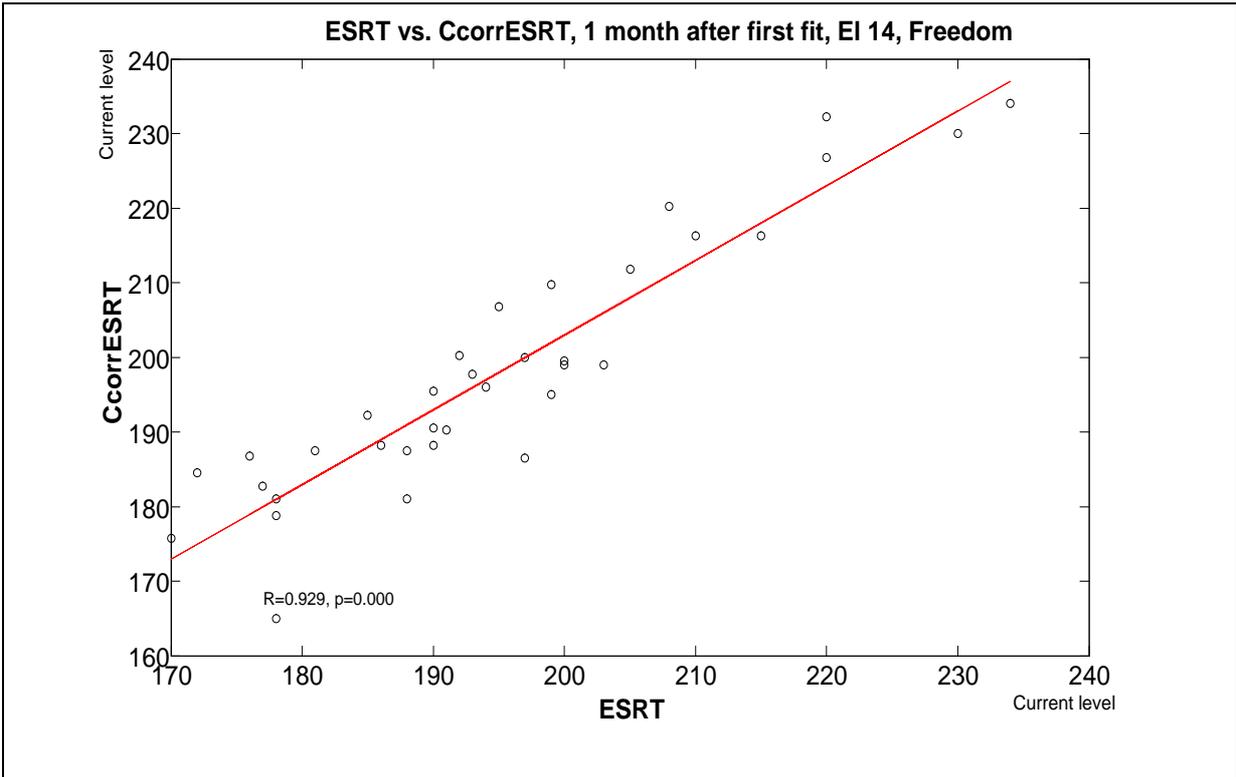


Fig 5 - ESRT vs. C level, corrected for mean electrode offset with respect to ESRT (CcorrESRT), 1 month after first fit, electrode 14, Freedom

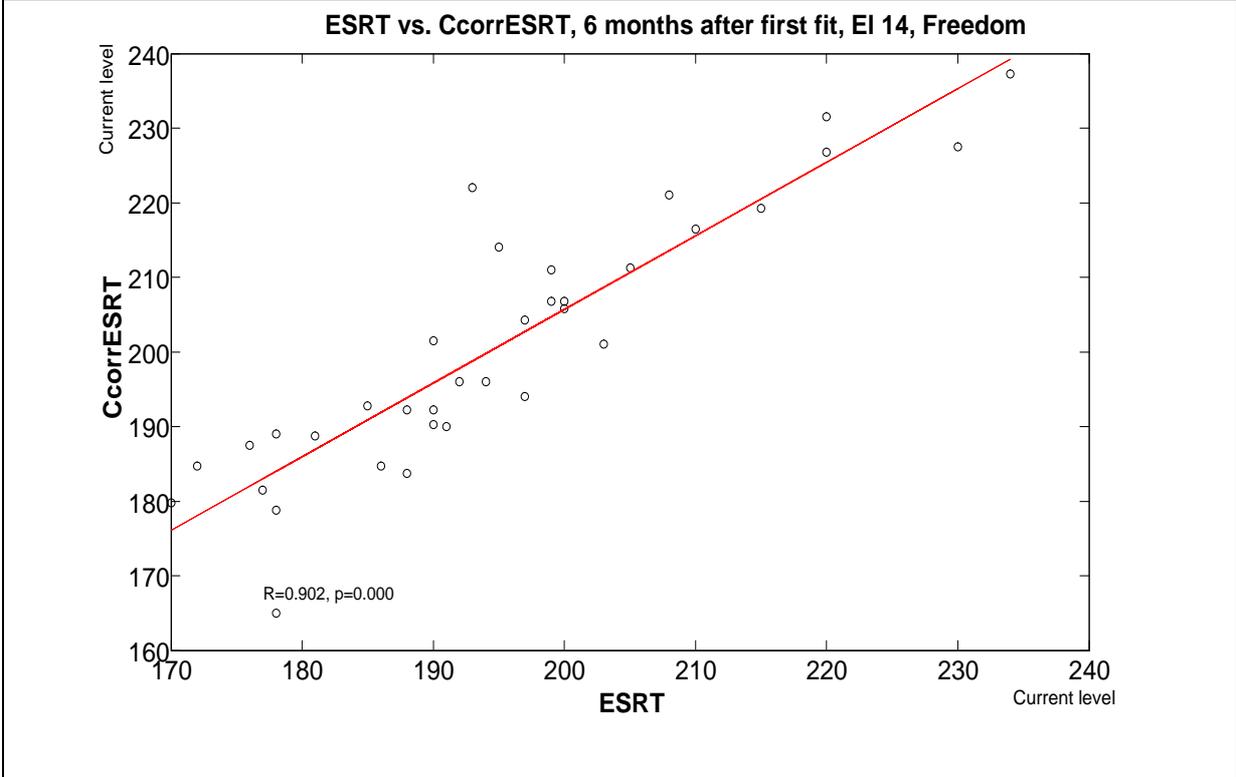


Fig 6 - ESRT vs. C level, corrected for mean electrode offset with respect to ESRT (CcorrESRT), 6 months after first fit, electrode 14, Freedom

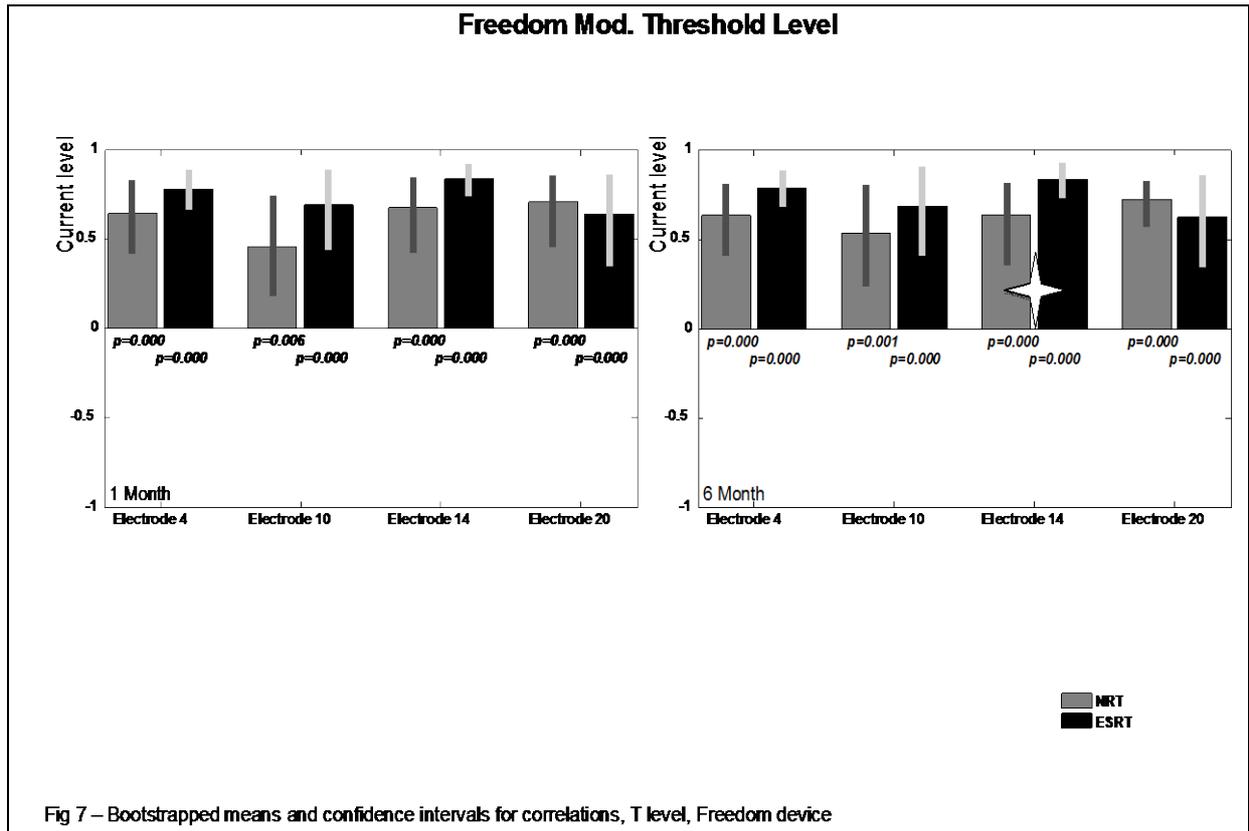


Fig 7 – Bootstrapped means and confidence intervals for correlations, T level, Freedom device

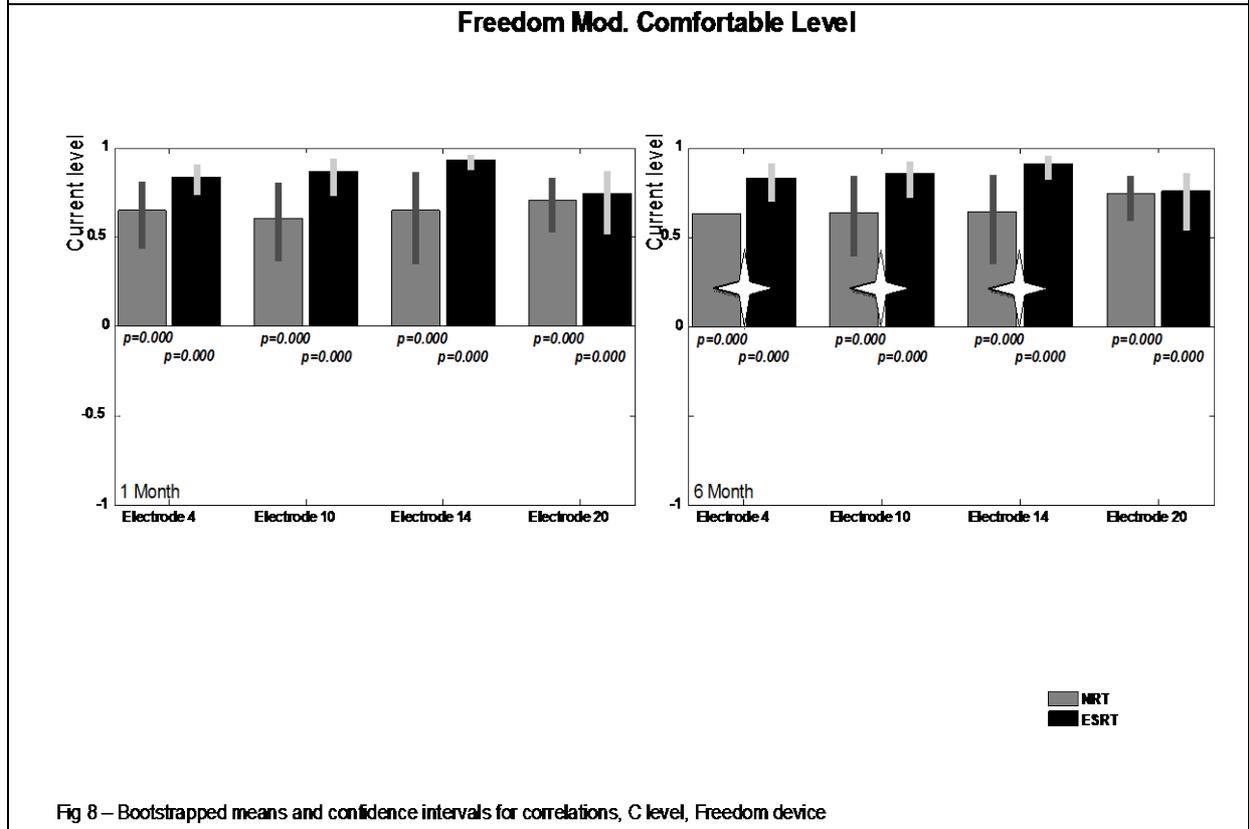


Fig 8 – Bootstrapped means and confidence intervals for correlations, C level, Freedom device

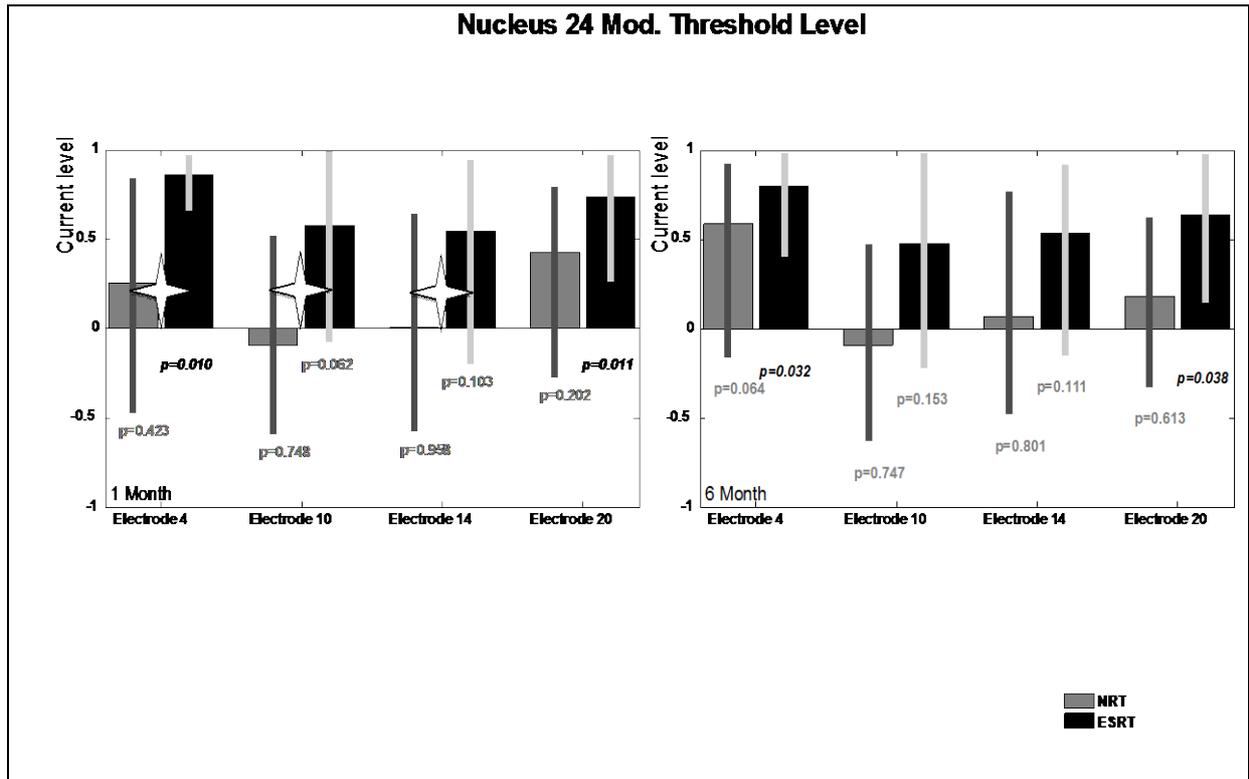


Fig 9 – Bootstrapped means and confidence intervals for correlations, T level, Nucleus 24 device

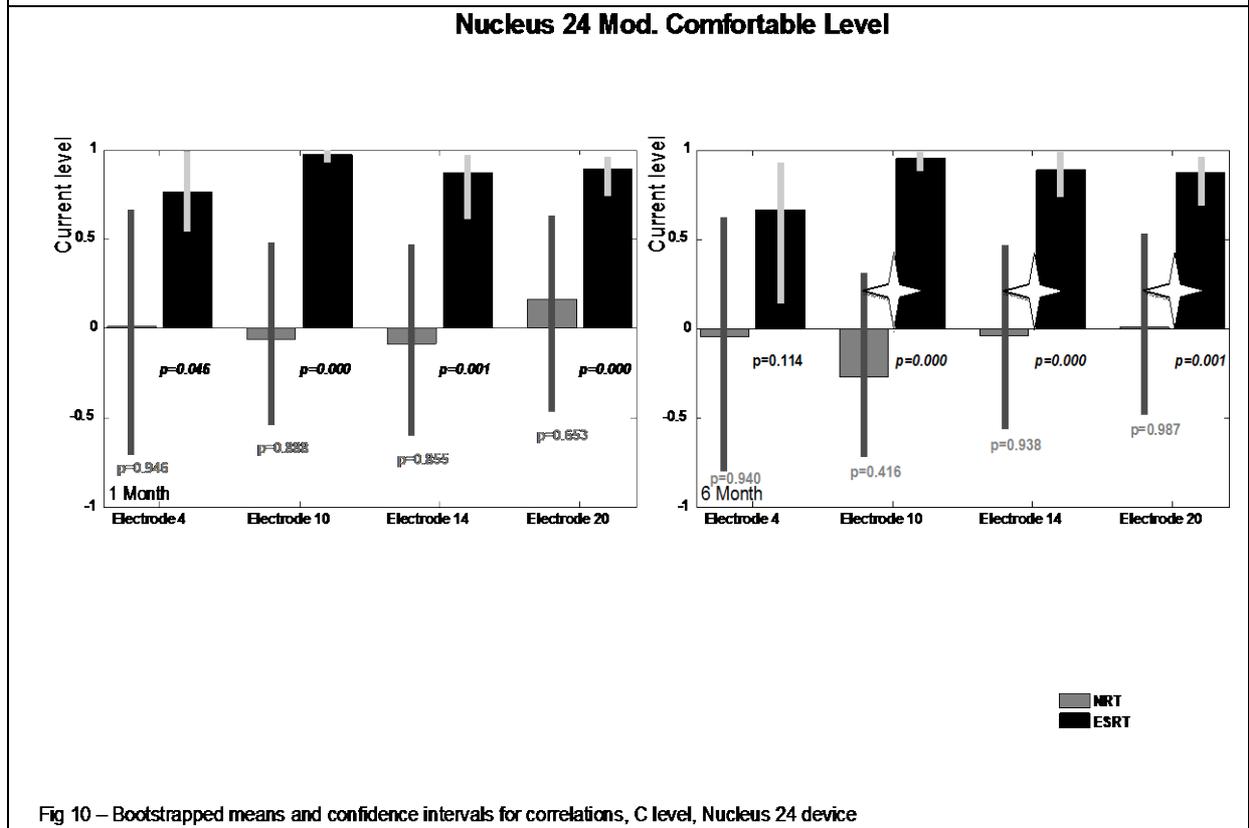


Fig 10 – Bootstrapped means and confidence intervals for correlations, C level, Nucleus 24 device

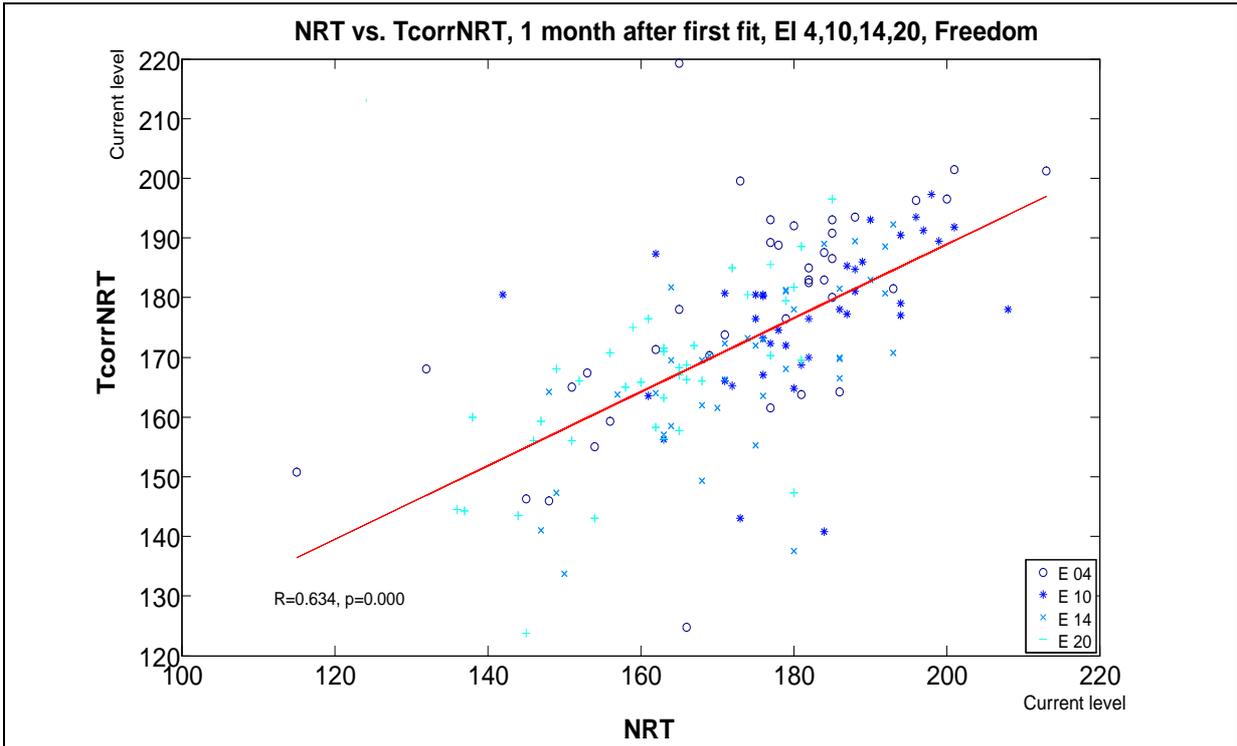


Fig 11 – NRT vs. T level, corrected for mean electrode offset with respect to NRT (TcorrNRT), 1 month after first fit, all electrodes, Freedom

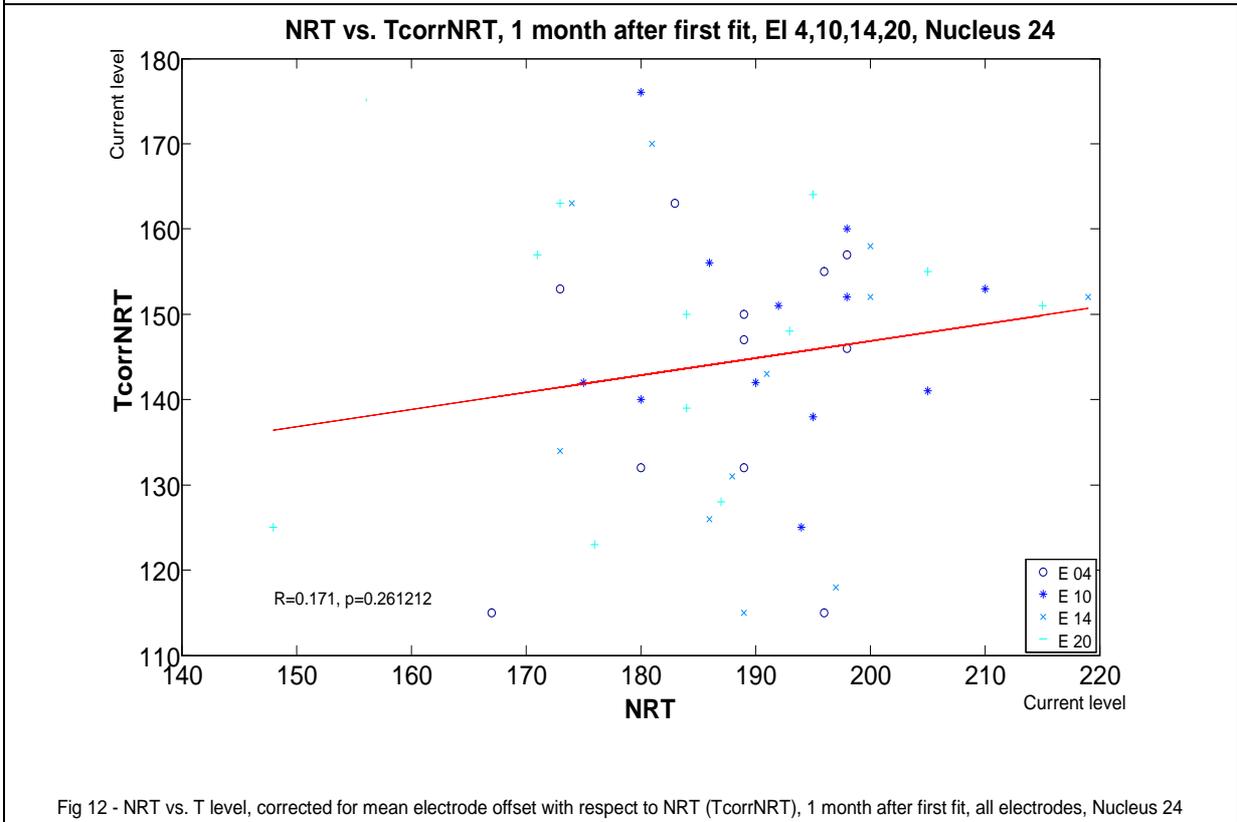


Fig 12 - NRT vs. T level, corrected for mean electrode offset with respect to NRT (TcorrNRT), 1 month after first fit, all electrodes, Nucleus 24

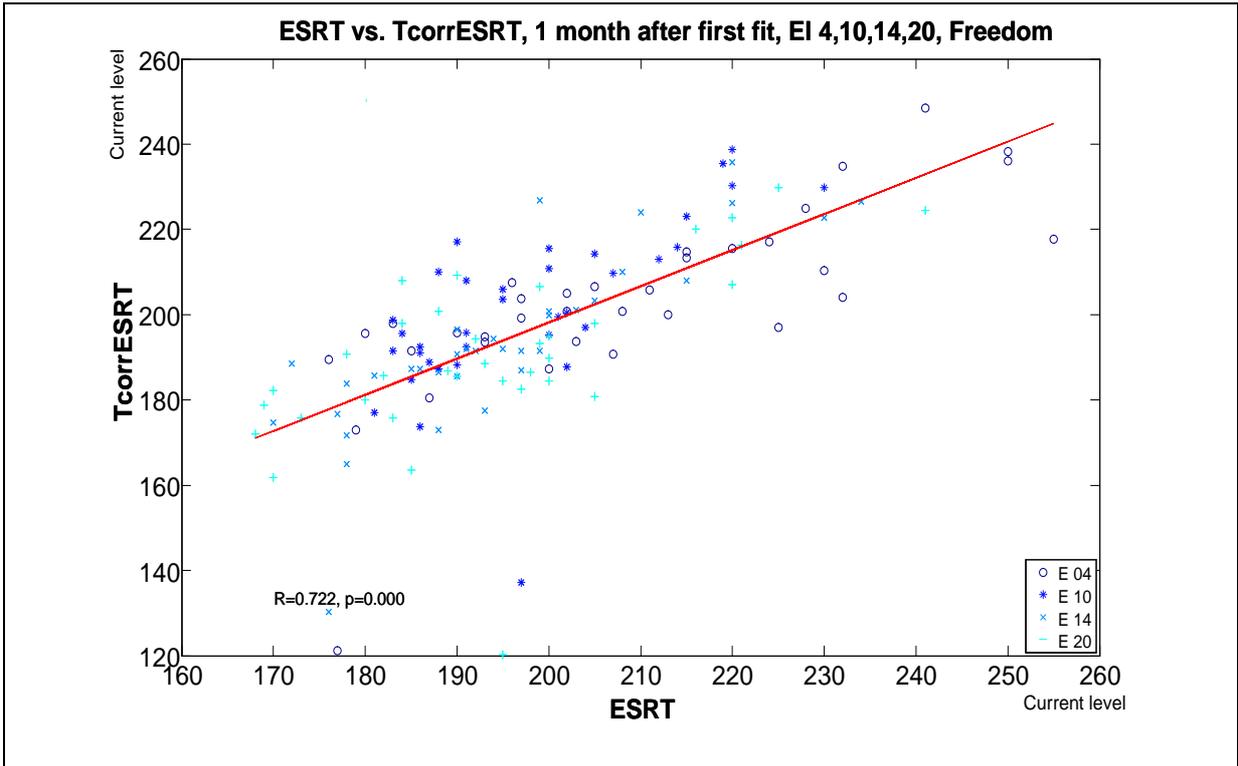


Fig 13 - ESRT vs. T level, corrected for mean electrode offset with respect to ESRT (TcorrESRT), 1 month after first fit, all electrodes, Freedom

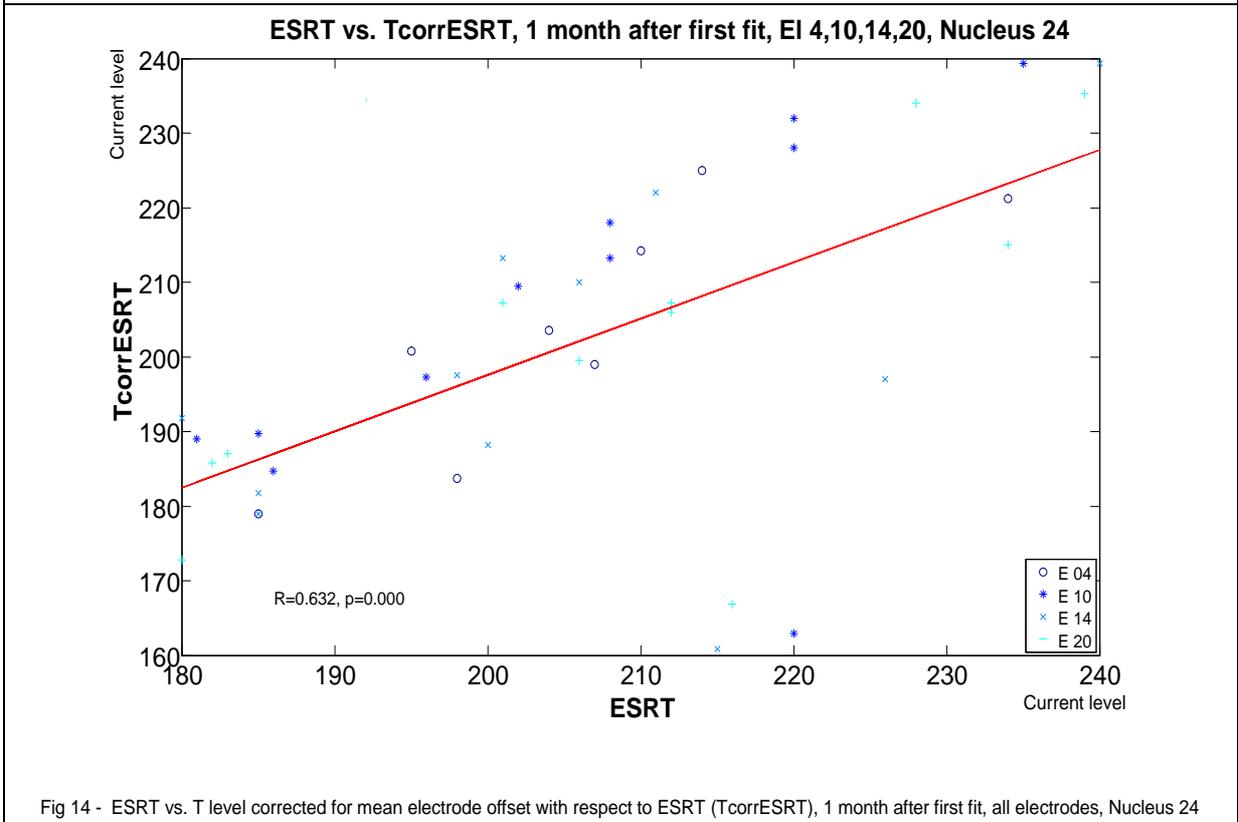


Fig 14 - ESRT vs. T level corrected for mean electrode offset with respect to ESRT (TcorrESRT), 1 month after first fit, all electrodes, Nucleus 24

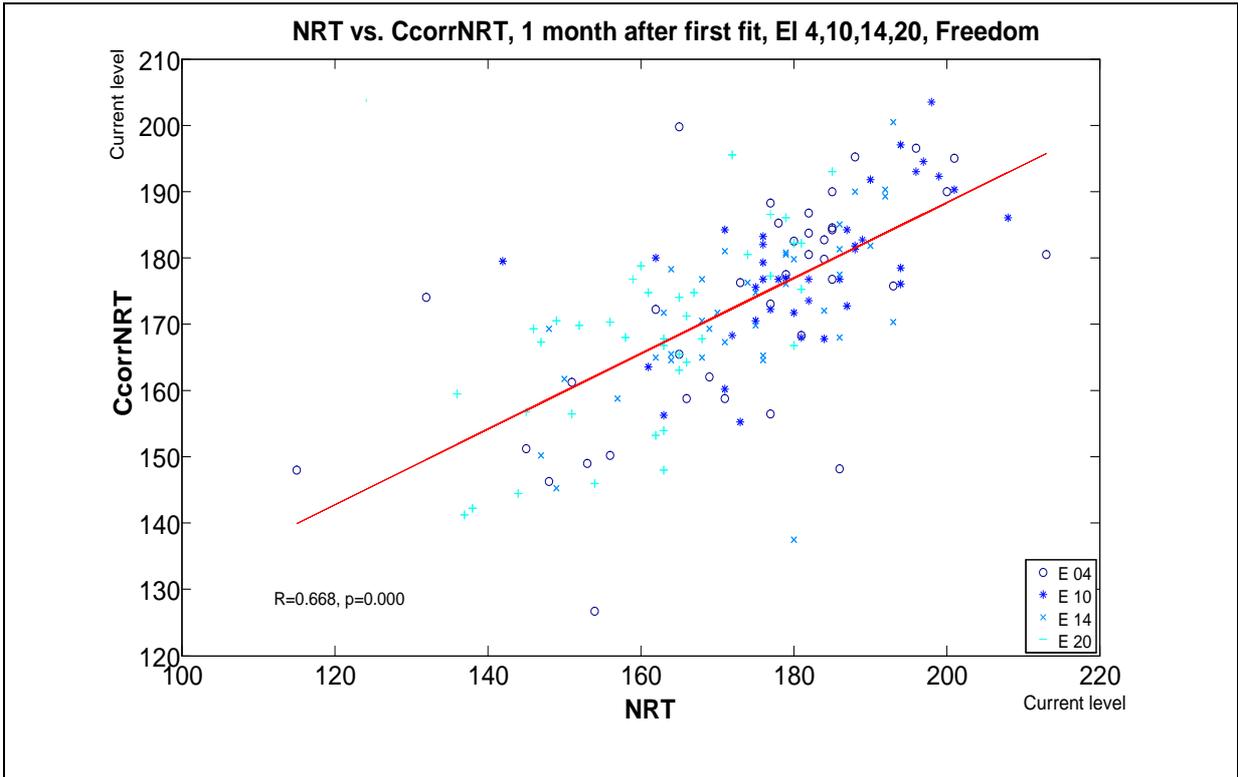


Fig 15 - NRT vs. C level, corrected for mean electrode offset with respect to NRT (CcorrNRT), 1 month after first fit, all electrodes, Freedom

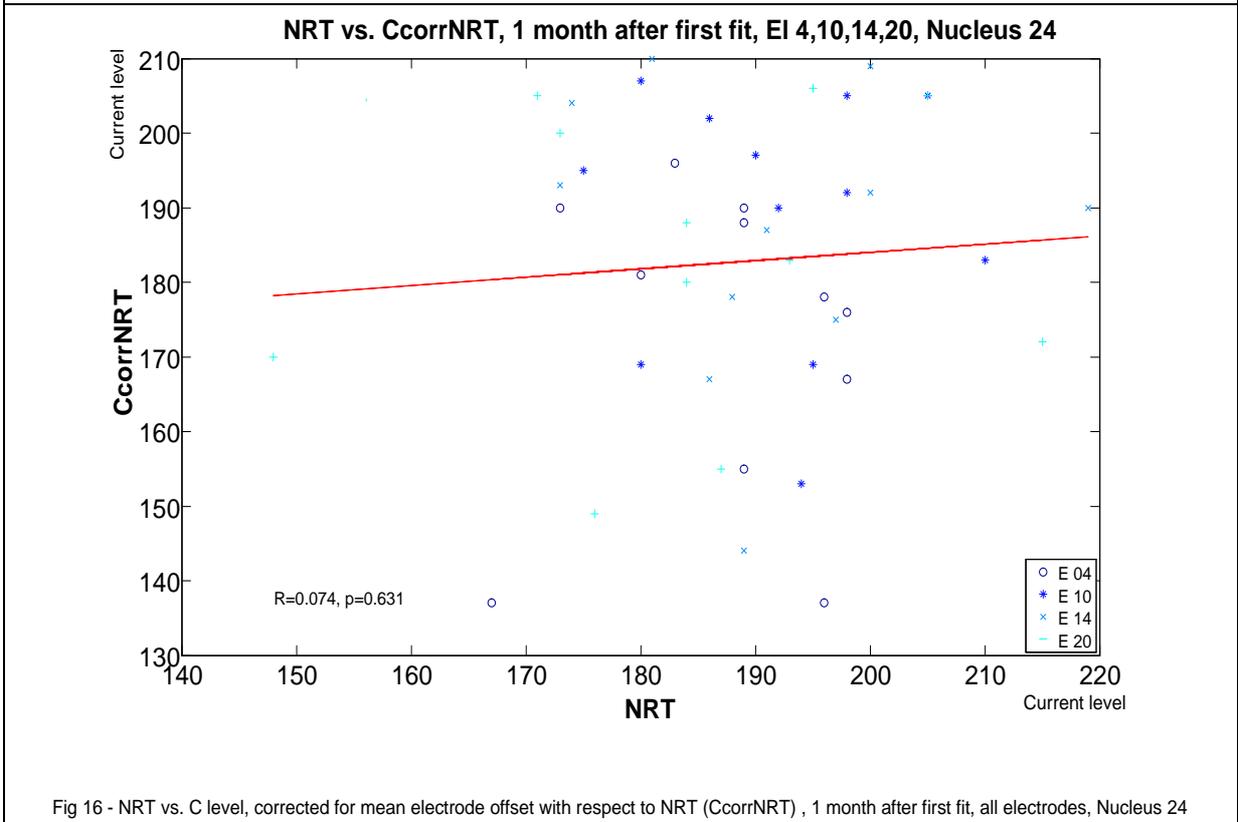


Fig 16 - NRT vs. C level, corrected for mean electrode offset with respect to NRT (CcorrNRT), 1 month after first fit, all electrodes, Nucleus 24

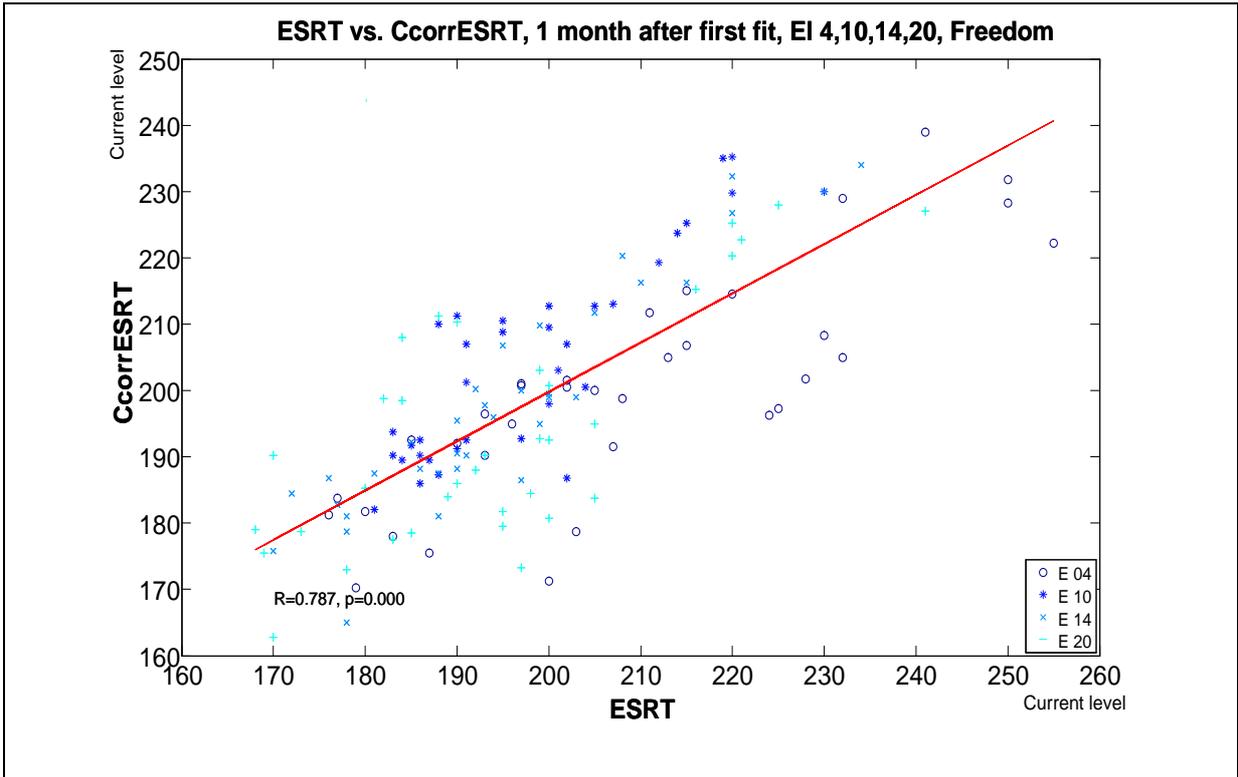


Fig 17 - ESRT vs. C level, corrected for mean electrode offset with respect to ESRT (CcorrESRT), 1 month after first fit, all electrodes, Freedom

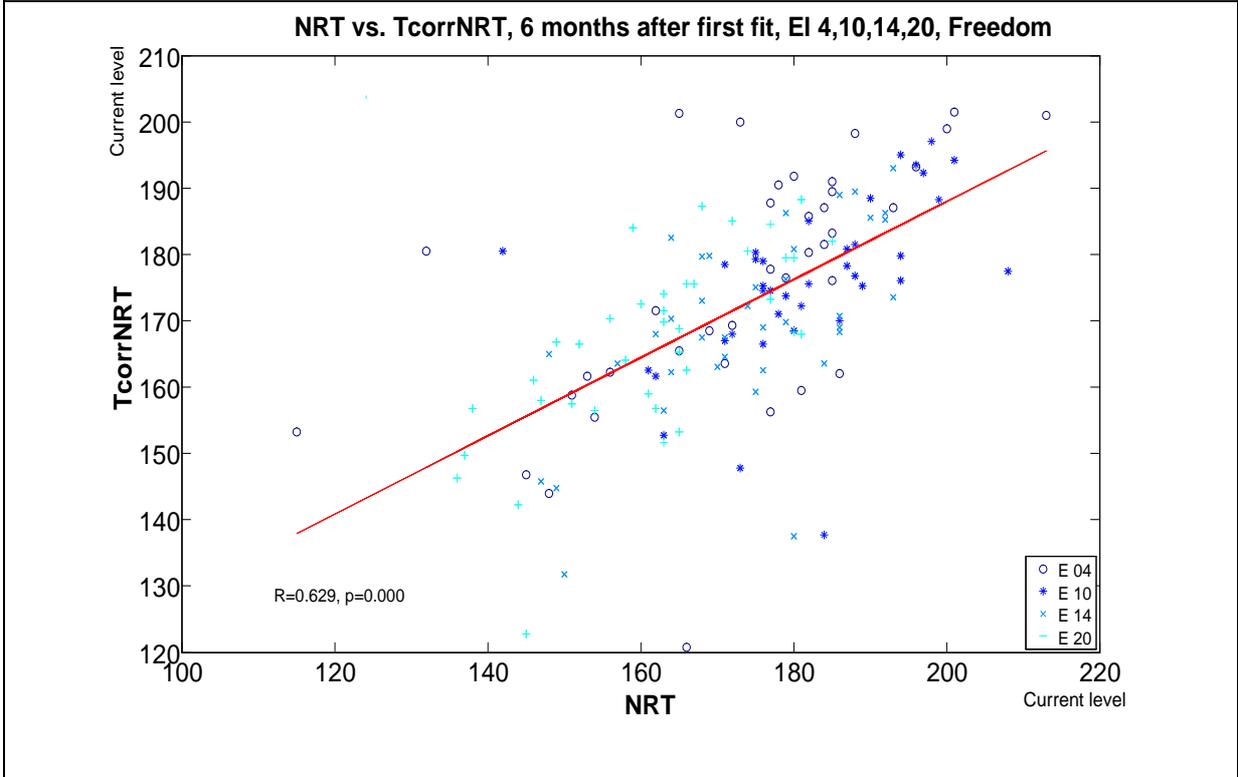


Fig 18 - NRT vs. T level, corrected for mean electrode offset with respect to NRT (TcorrNRT), 6 months after first fit, all electrodes, Freedom

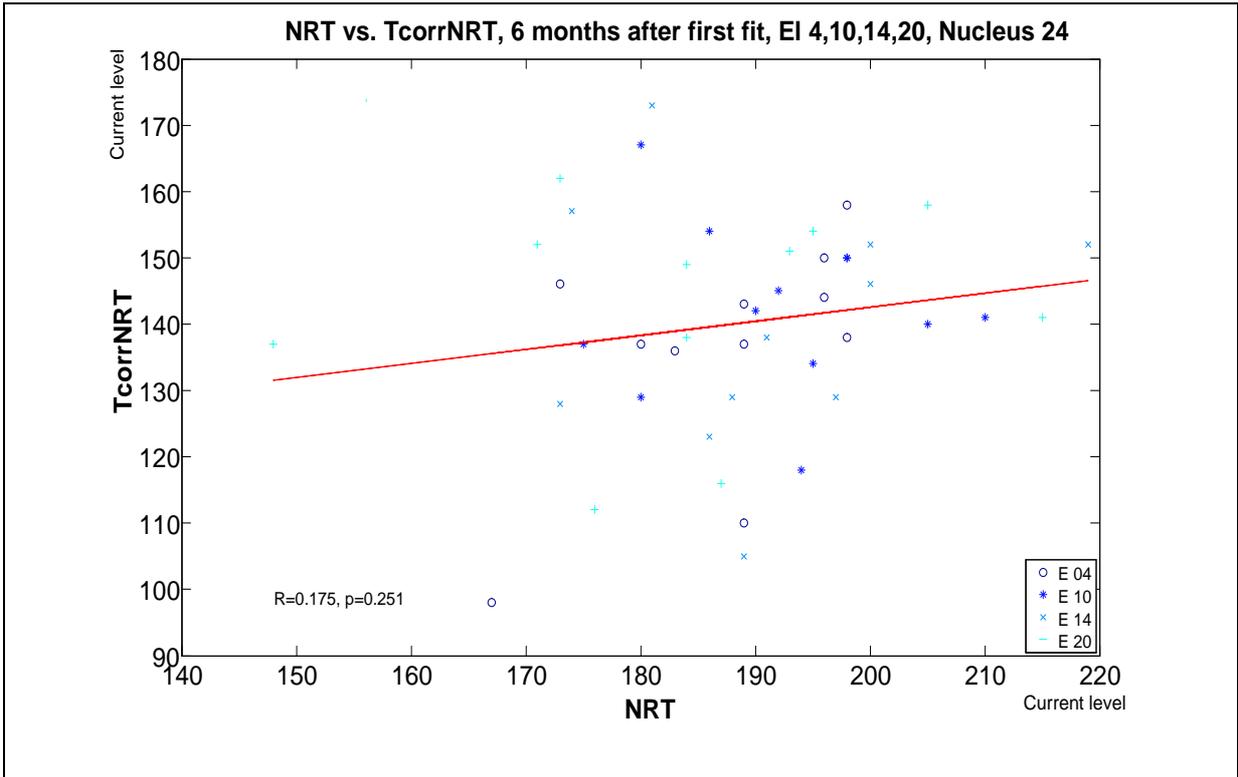


Fig 19 - NRT vs. T level, corrected for mean electrode offset with respect to NRT (TcorrNRT), 6 months after first fit, all electrodes, Nucleus 24

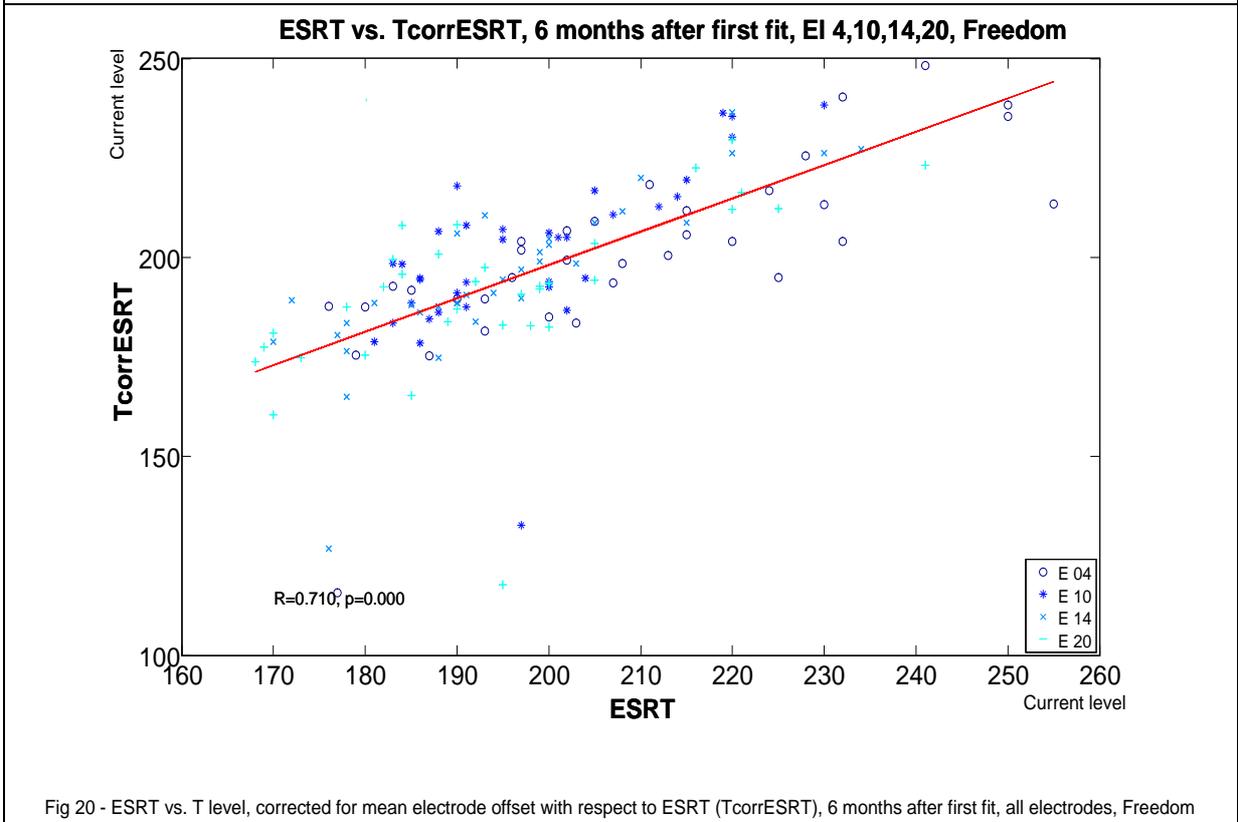


Fig 20 - ESRT vs. T level, corrected for mean electrode offset with respect to ESRT (TcorrESRT), 6 months after first fit, all electrodes, Freedom

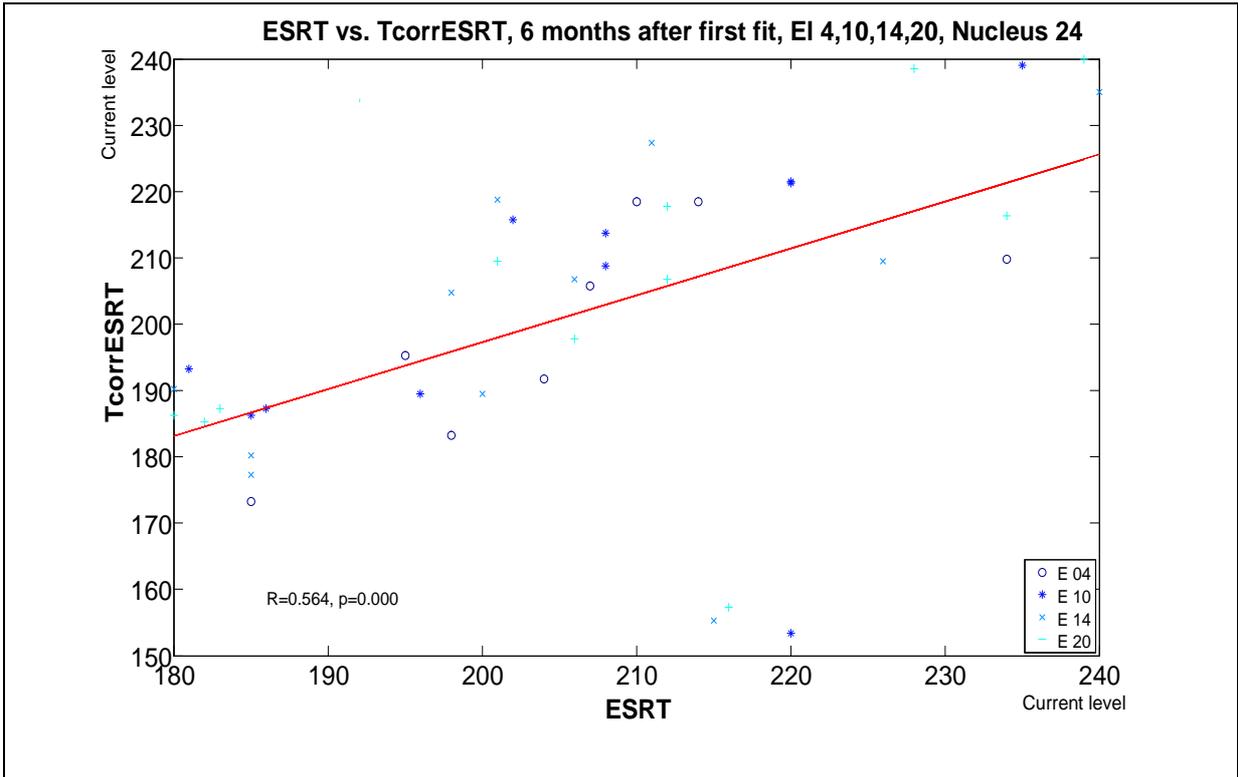


Fig 21 - ESRT vs. T level, corrected for mean electrode offset with respect to ESRT (TcorrESRT), 6 months after first fit, all electrodes, Nucleus 24

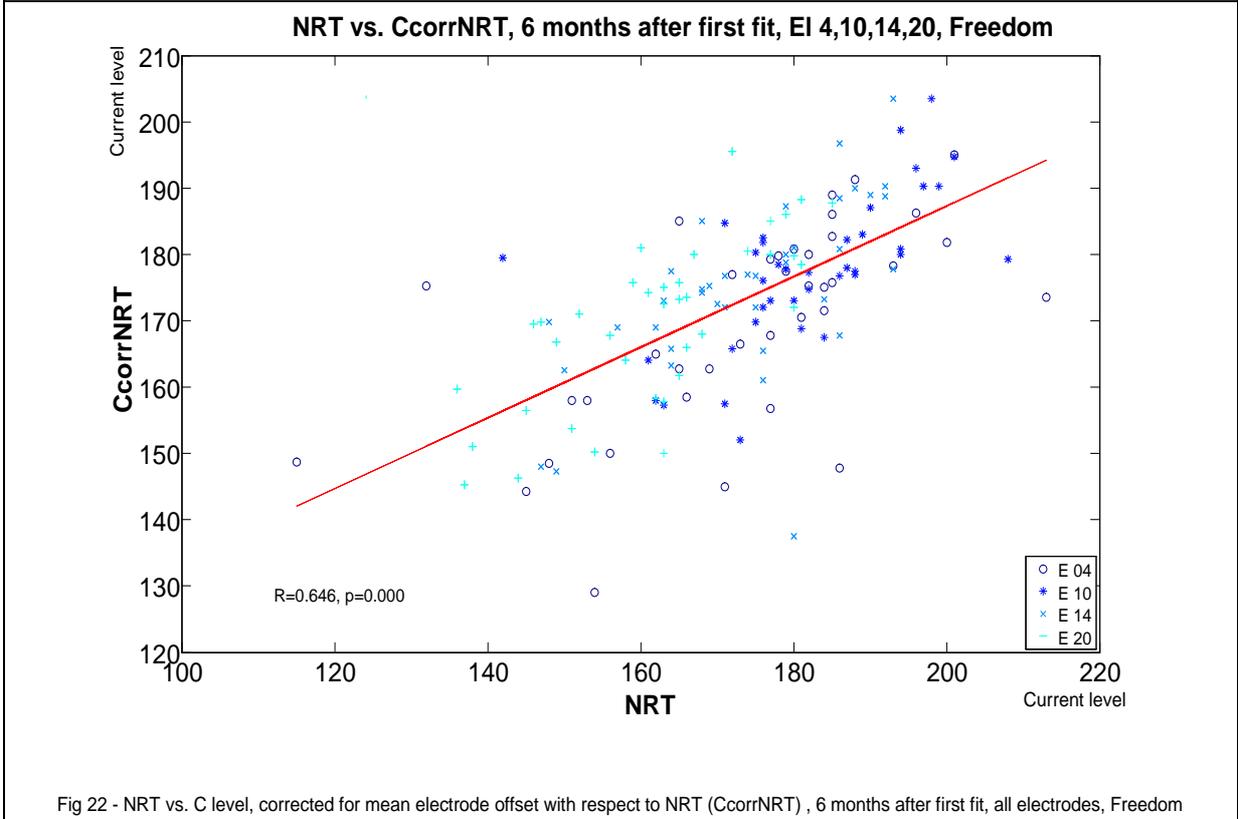


Fig 22 - NRT vs. C level, corrected for mean electrode offset with respect to NRT (CcorrNRT), 6 months after first fit, all electrodes, Freedom

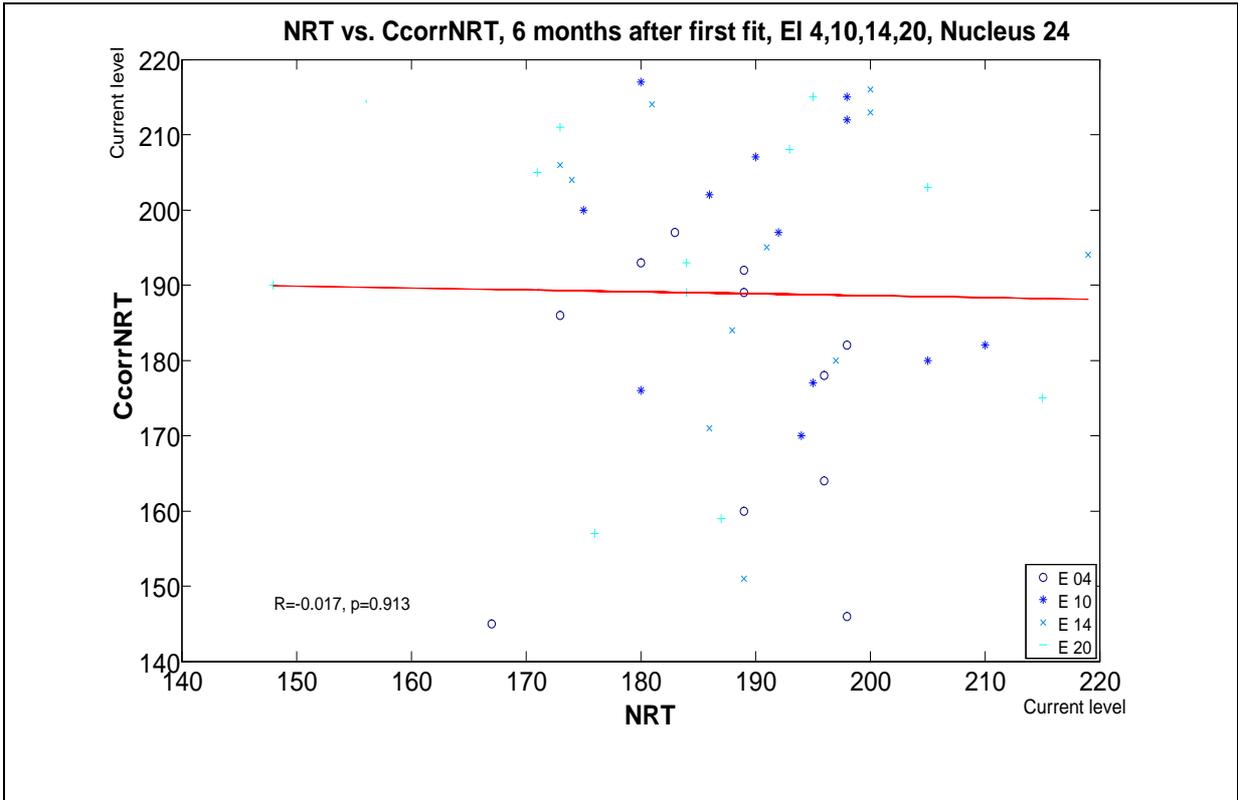


Fig 23 - NRT vs. C level, corrected for mean electrode offset with respect to NRT (CcorrNRT), 6 months after first fit, all electrodes, Nucleus 24

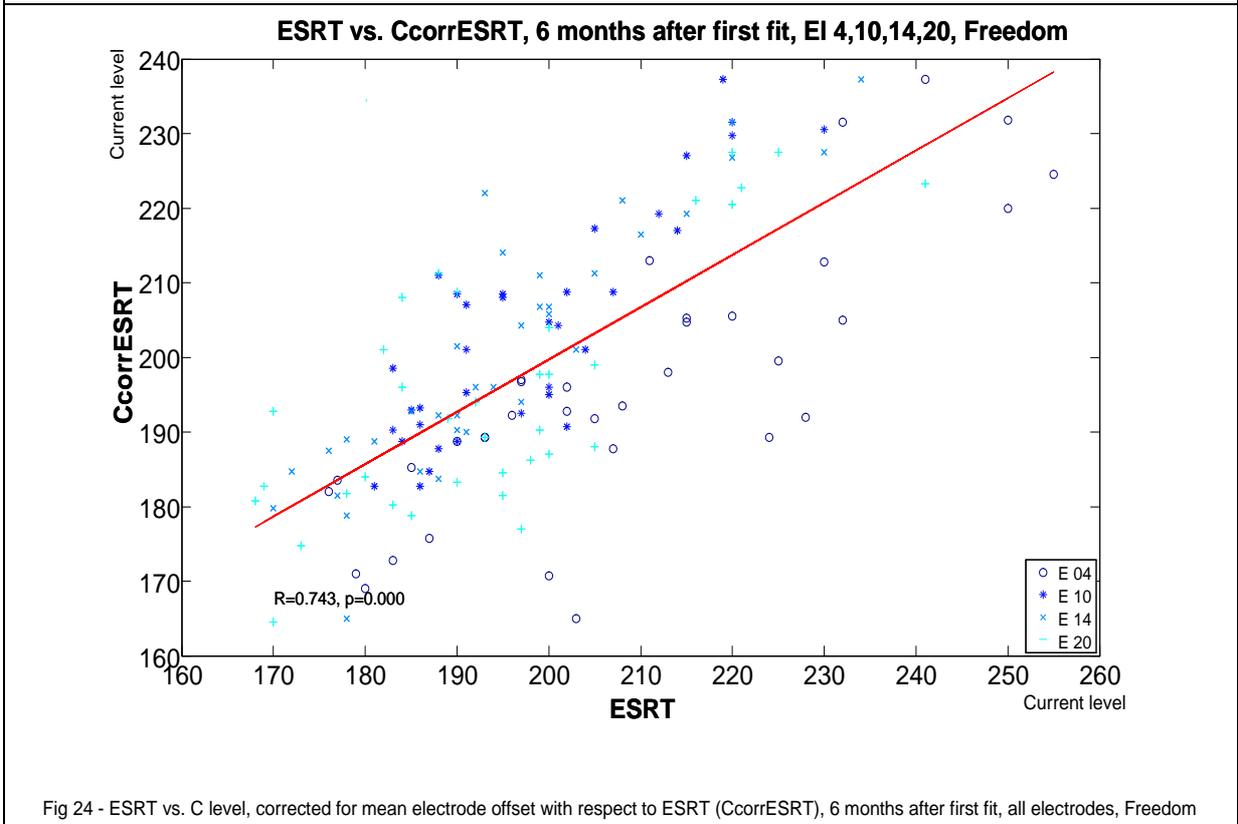


Fig 24 - ESRT vs. C level, corrected for mean electrode offset with respect to ESRT (CcorrESRT), 6 months after first fit, all electrodes, Freedom

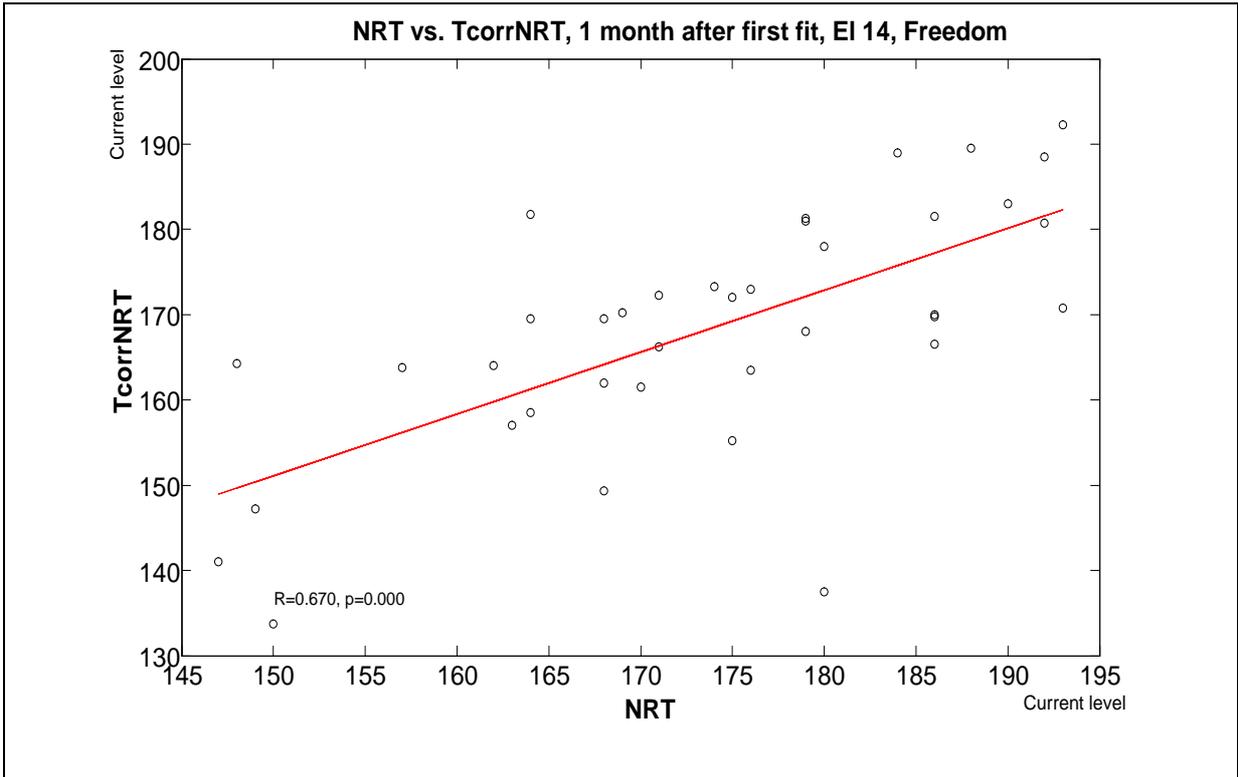


Fig 25 - NRT vs. T level, corrected for mean electrode offset with respect to NRT (TcorrNRT), 1 month after first fit, electrode 14, Freedom

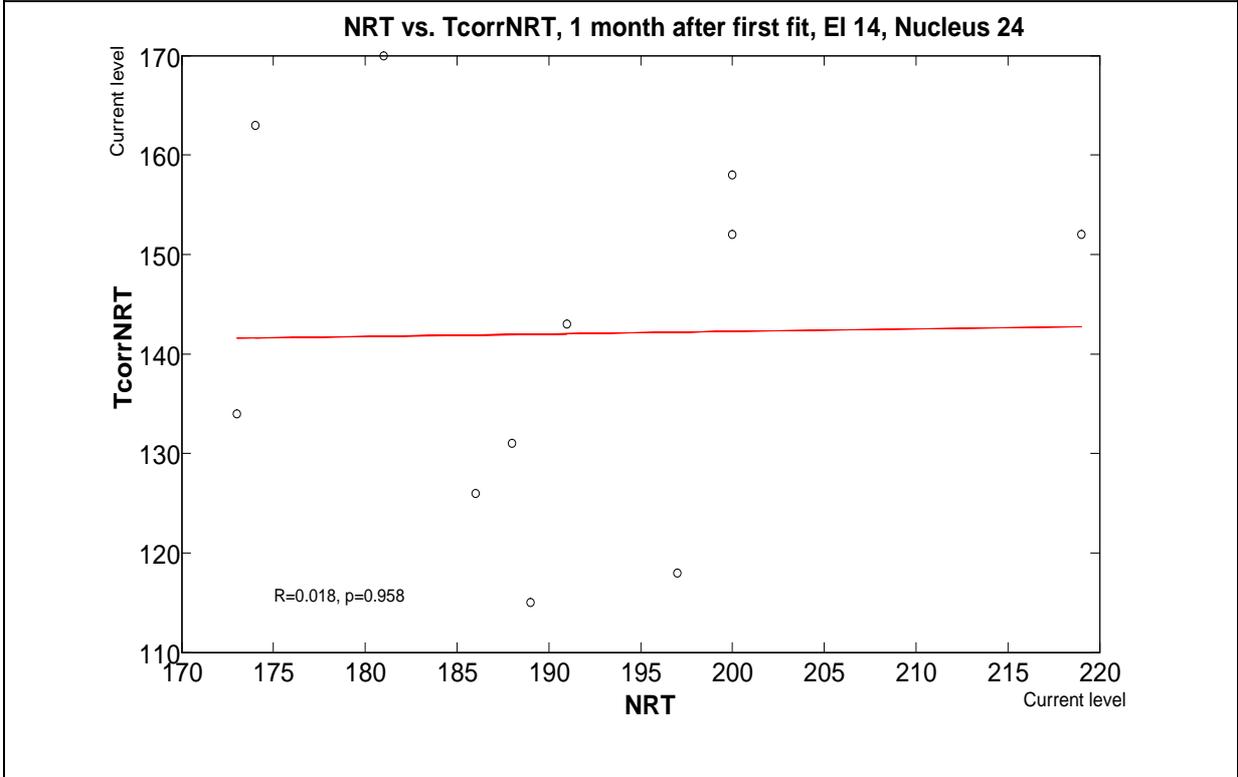


Fig 26 - NRT vs. T level, corrected for mean electrode offset with respect to NRT (TcorrNRT), 1 month after first fit, electrode 14, Nucleus 24

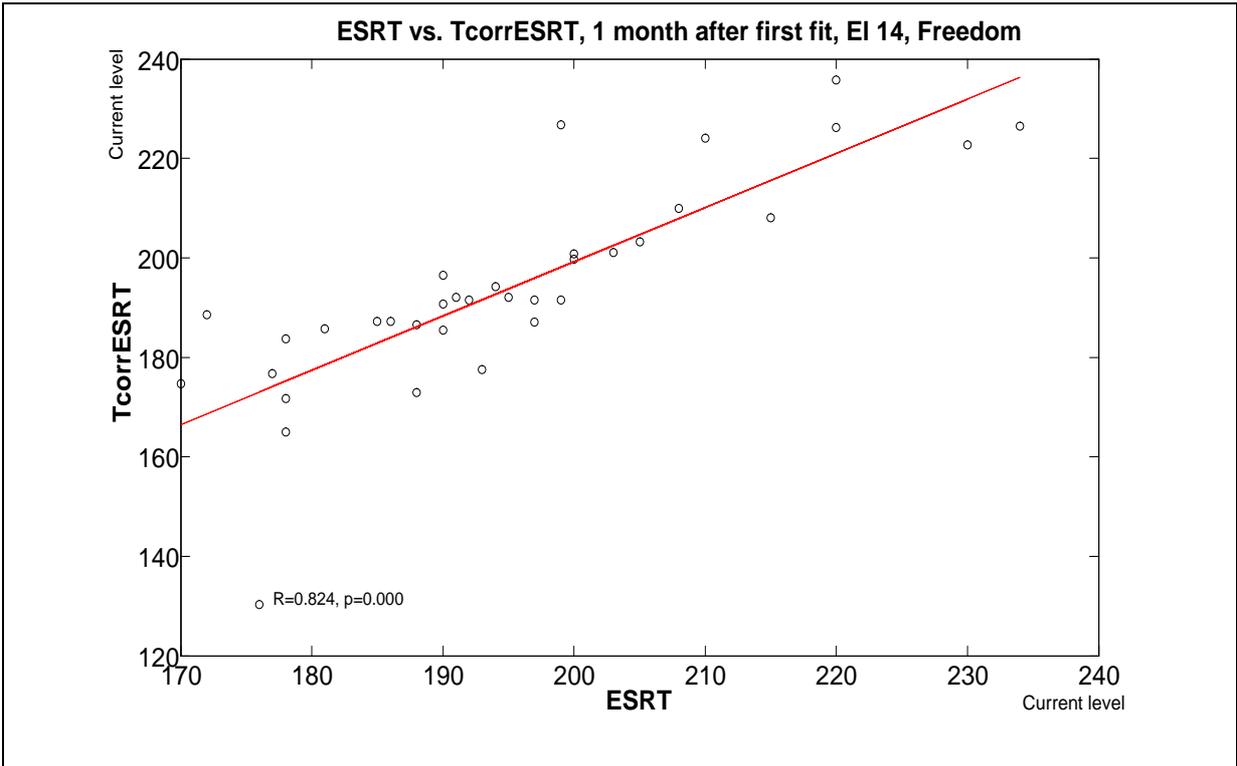


Fig 27 - ESRT vs. T level, corrected for mean electrode offset with respect to ESRT (TcorrESRT), 1 month after first fit, electrode 14, Freedom

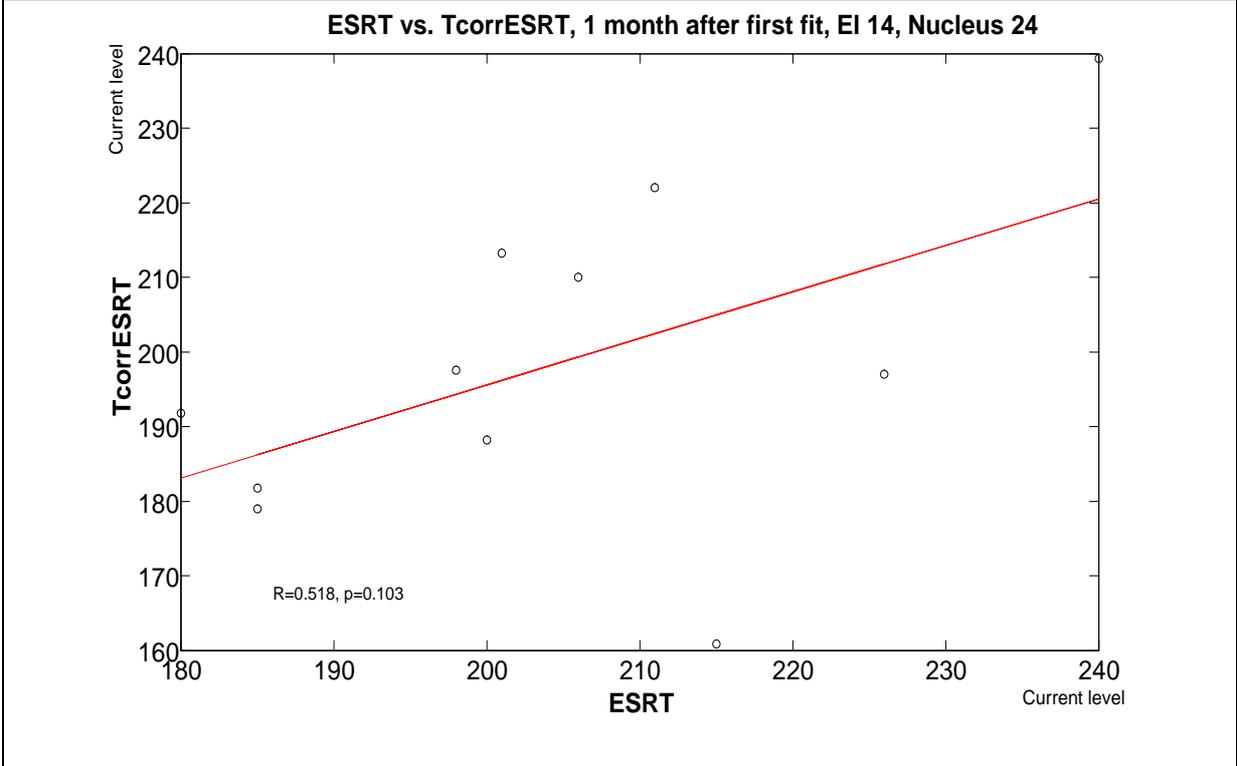


Fig 28 - ESRT vs. T level, corrected for mean electrode offset with respect to ESRT (TcorrESRT), 1 month after first fit, electrode 14, Nucleus 24

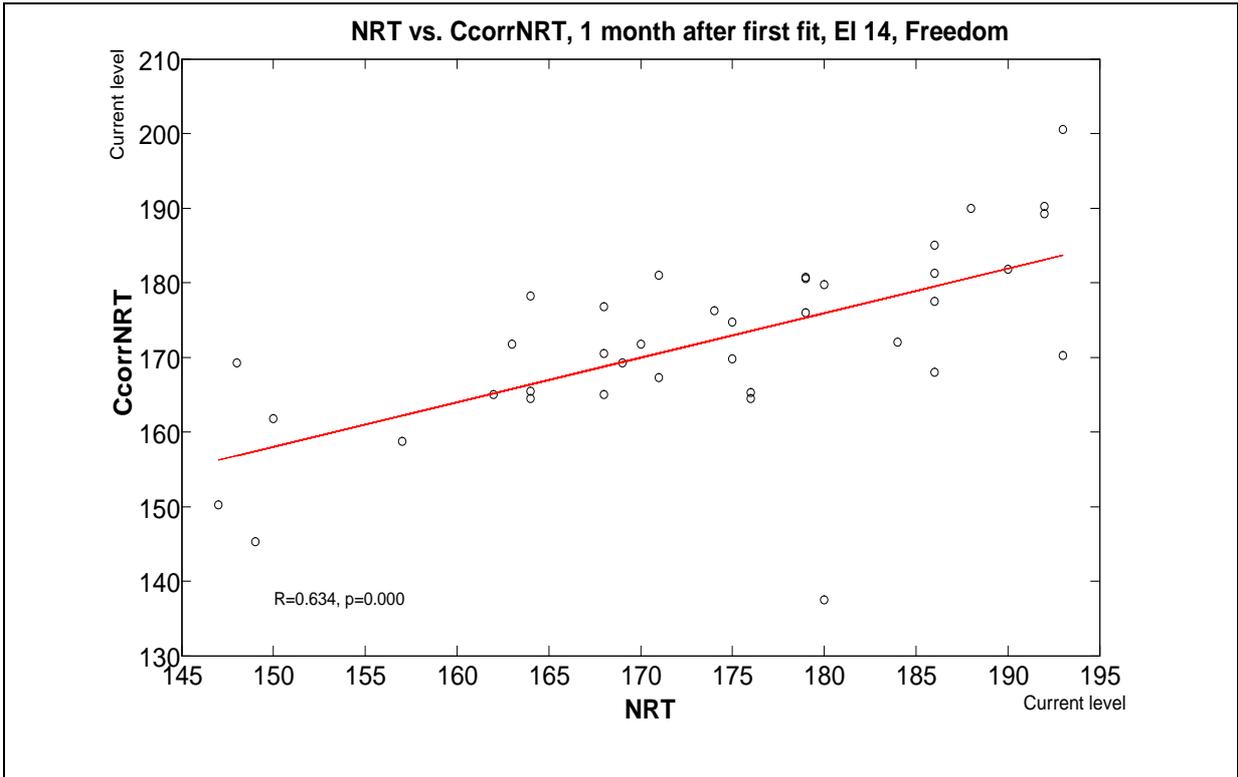


Fig 29 - NRT vs. C level, corrected for mean electrode offset with respect to NRT (CcorrNRT), 1 month after first fit, electrode 14, Freedom

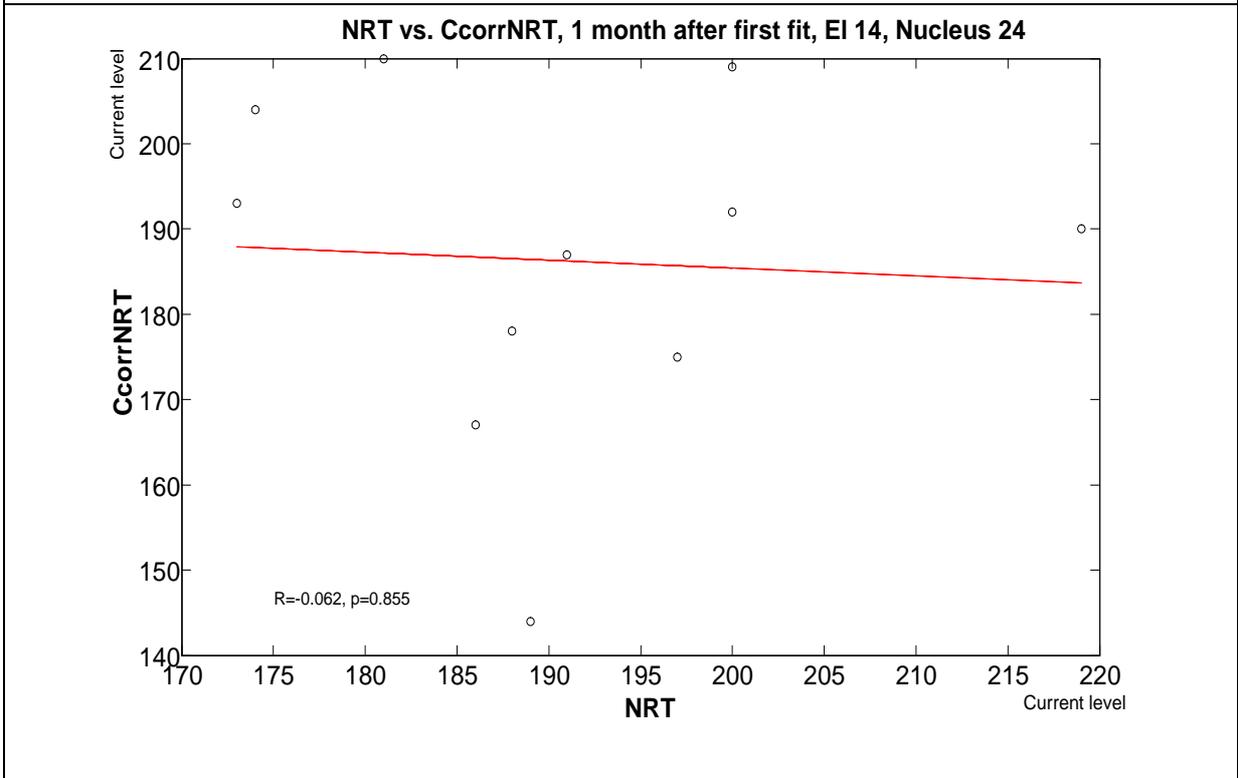


Fig 30 - NRT vs. C level, corrected for mean electrode offset with respect to NRT (CcorrNRT), 1 month after first fit, electrode 14, Nucleus 24

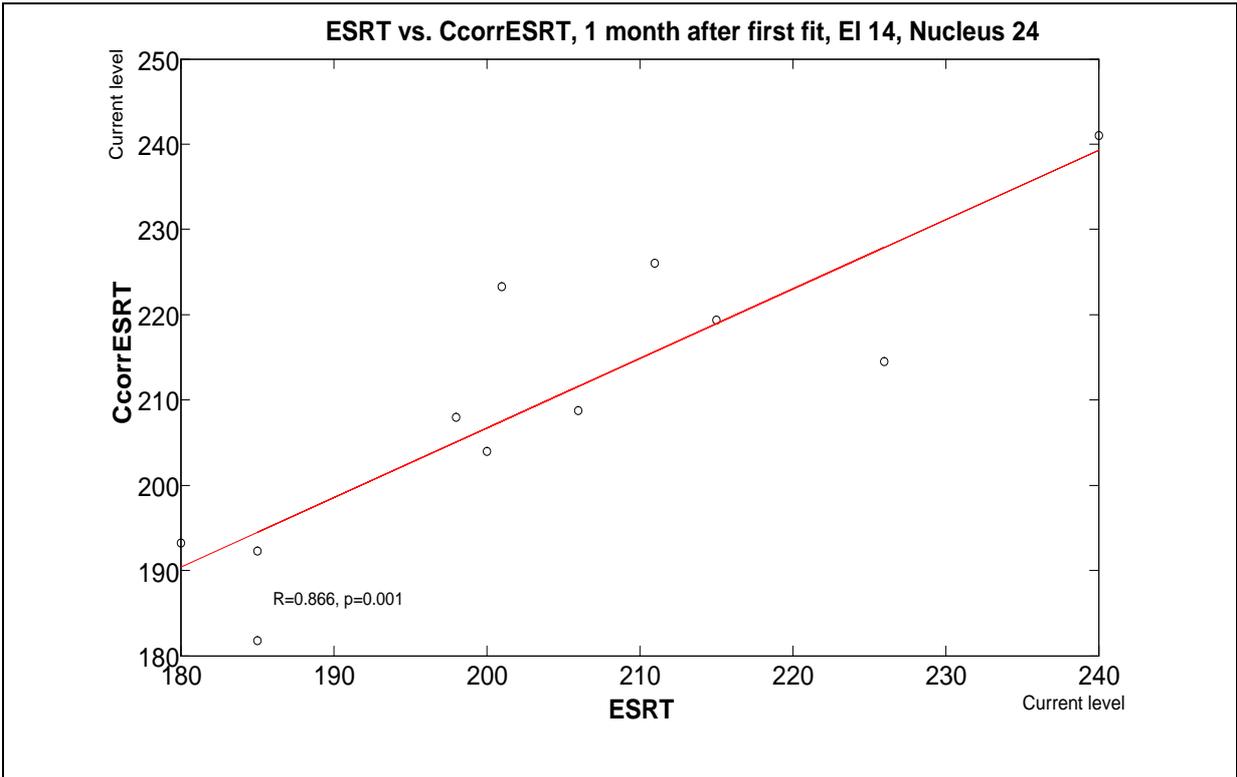


Fig 31 - ESRT vs. C level, corrected for mean electrode offset with respect to ESRT (CcorrESRT), 1 month after first fit, electrode 14, Nucleus 24

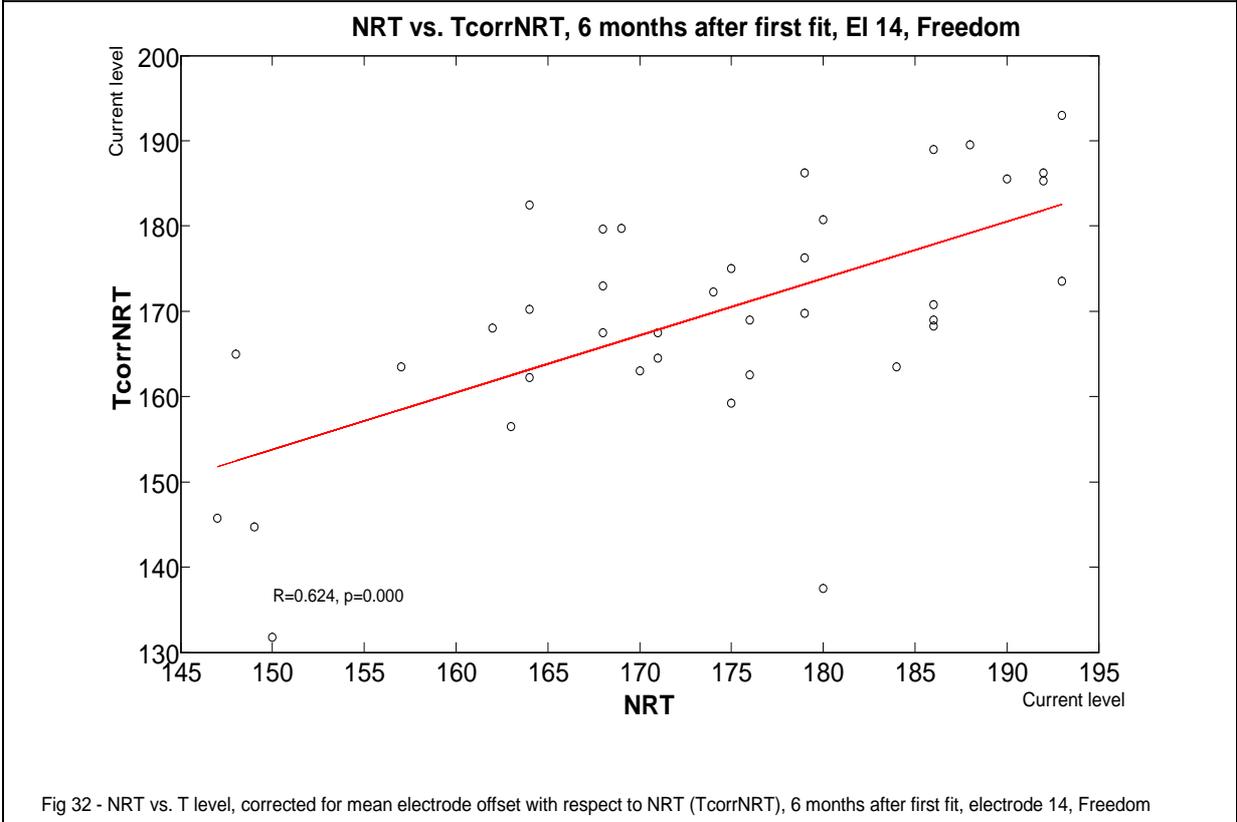


Fig 32 - NRT vs. T level, corrected for mean electrode offset with respect to NRT (TcorrNRT), 6 months after first fit, electrode 14, Freedom

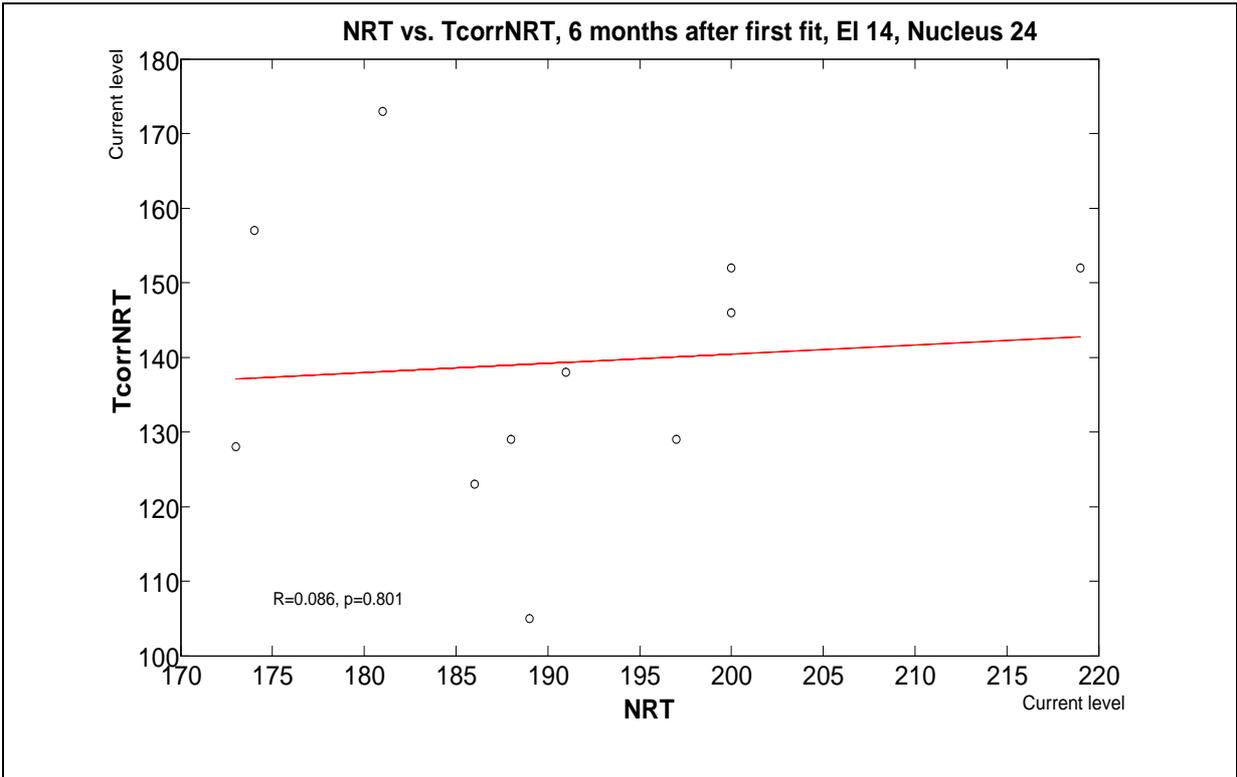


Fig 33 - NRT vs. T level, corrected for mean electrode offset with respect to NRT (TcorrNRT), 6 months after first fit, electrode 14, Nucleus 24

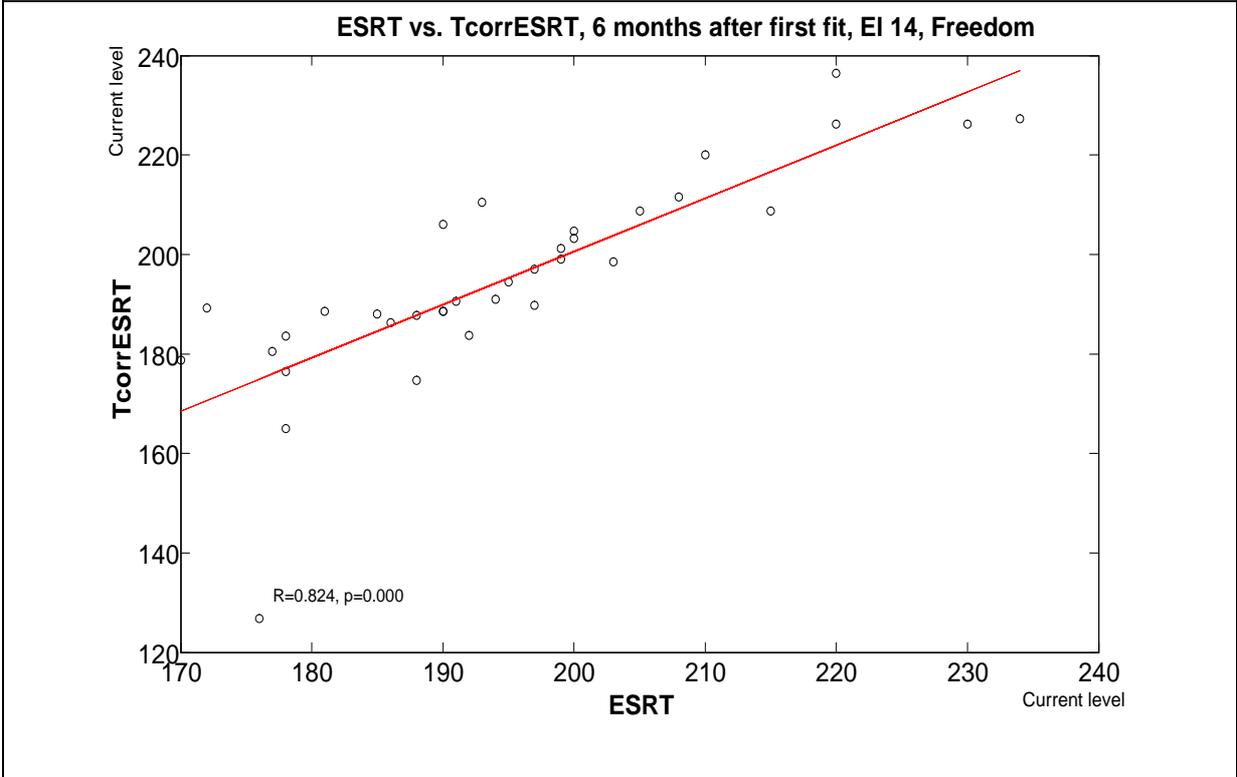


Fig 34 - ESRT vs. T level, corrected for mean electrode offset with respect to ESRT (TcorrESRT), 6 months after first fit, electrode 14, Freedom

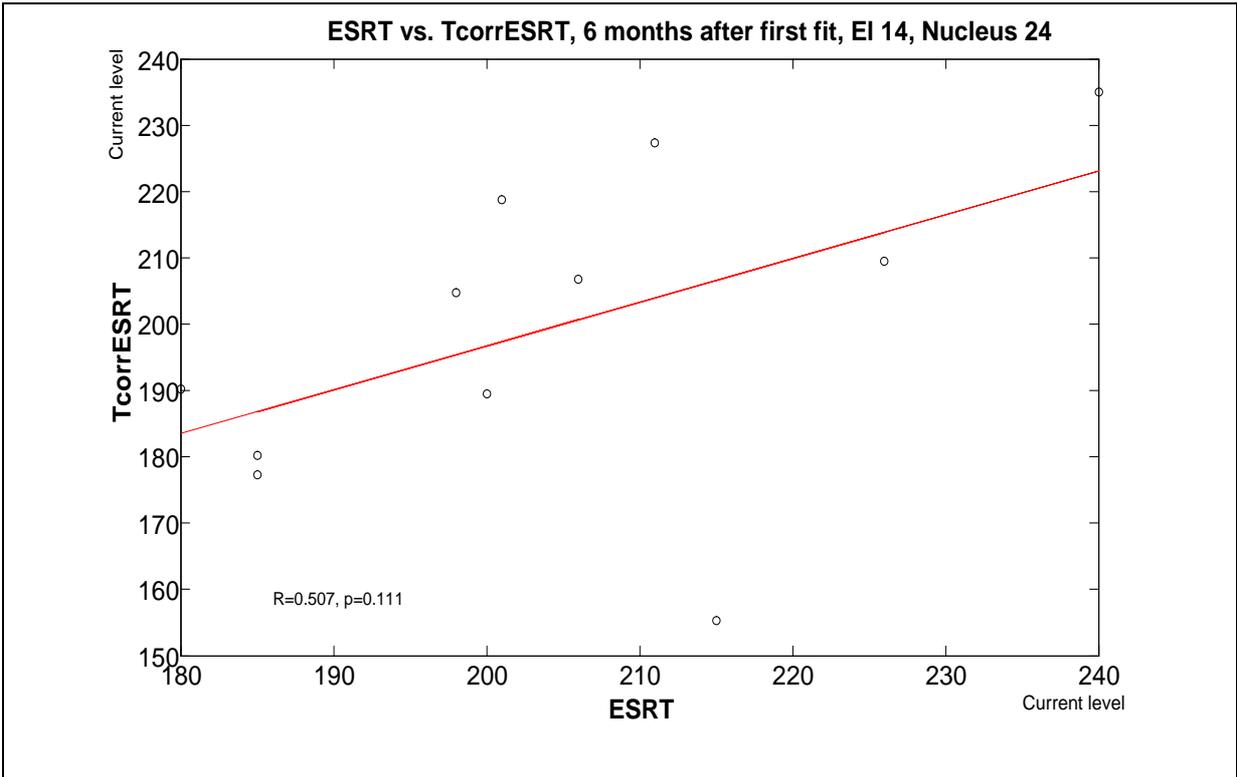


Fig 35 - ESRT vs. T level, corrected for mean electrode offset with respect to ESRT (TcorrESRT), 6 months after first fit, electrode 14, Nucleus 24

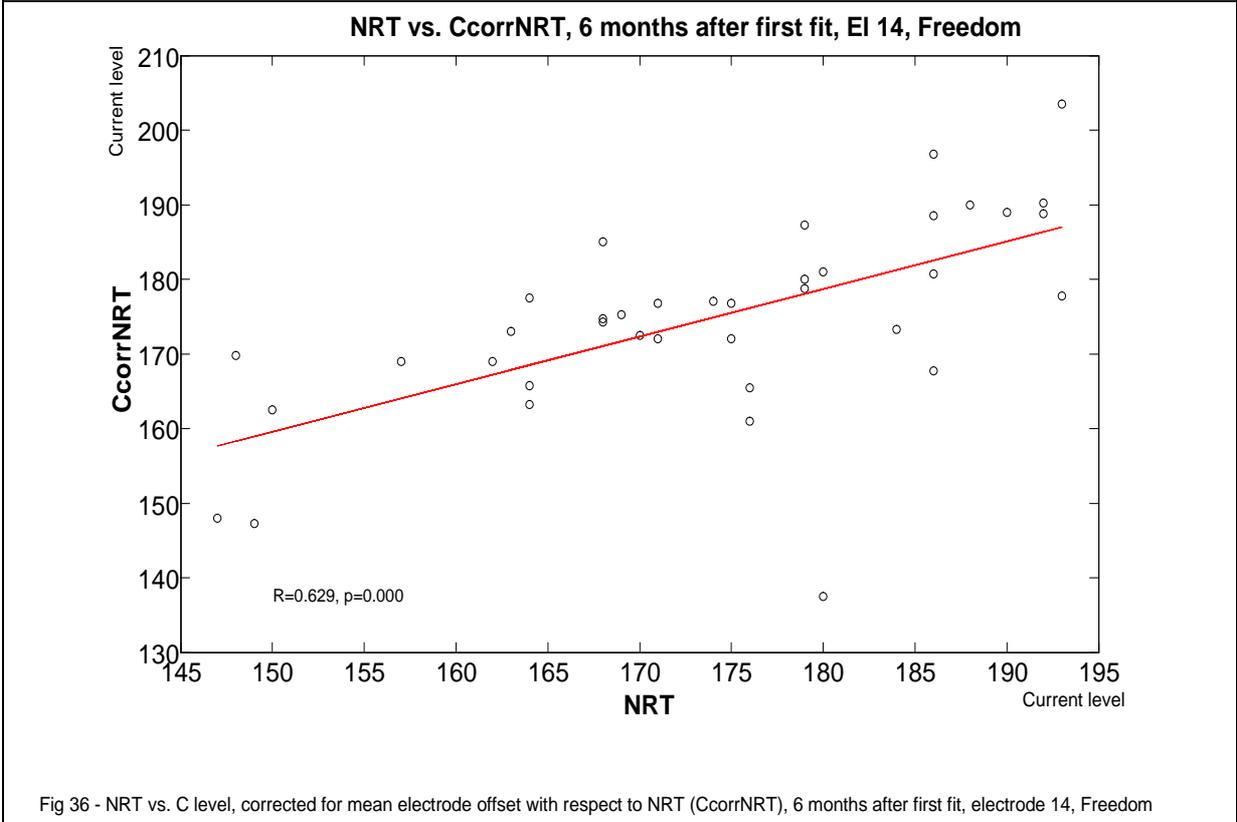


Fig 36 - NRT vs. C level, corrected for mean electrode offset with respect to NRT (CcorrNRT), 6 months after first fit, electrode 14, Freedom

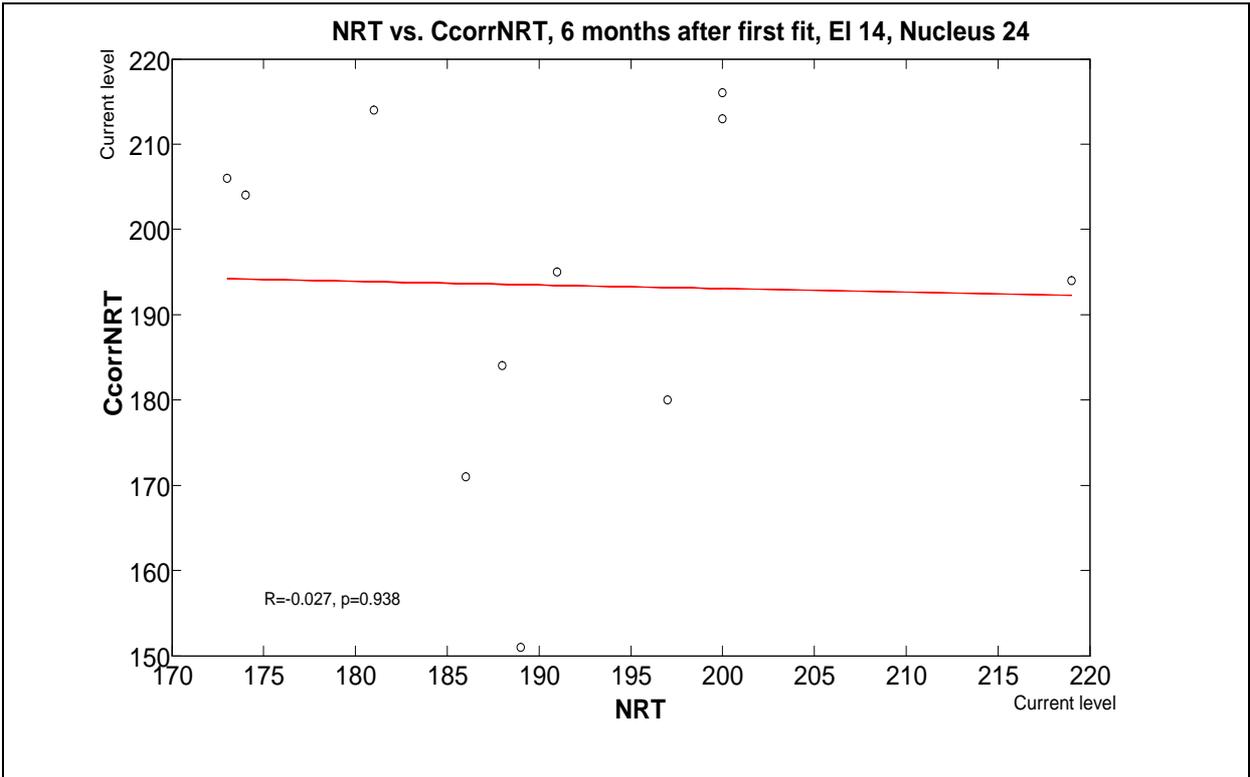


Fig 37 - NRT vs. C level, corrected for mean electrode offset with respect to NRT (CcorrNRT), 6 months after first fit, electrode 14, Nucleus 24

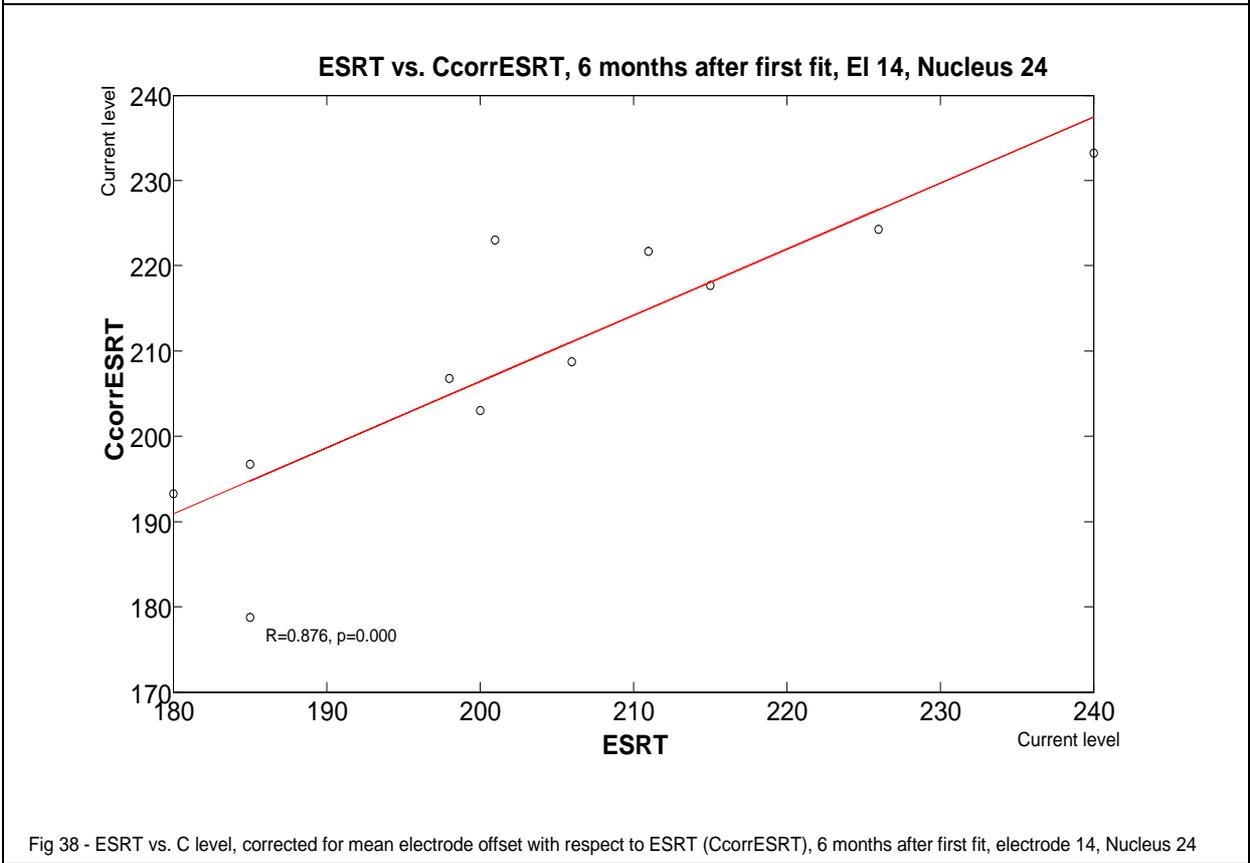


Fig 38 - ESRT vs. C level, corrected for mean electrode offset with respect to ESRT (CcorrESRT), 6 months after first fit, electrode 14, Nucleus 24

## 8. Bibliography

1. Gärtner L, Lenarz T, Joseph G, Büchner A. Clinical use of a system for the automated recording and analysis of electrically evoked compound action potentials (ECAPs) in cochlear implant patients. *Acta Oto-laryngologica*. 2010;130:724-732.
2. Patrick JF, Busby PA, Gibson PJ. The development of the Nucleus Freedom™ Cochlear Implant System. *Trends Amplif*. 2006;10:175-200.
3. Hughes ML, Brown CJ, Abbas PJ, Wolaver AA, Gervais JP. Comparison of EAP thresholds with MAP levels in the nucleus 24 cochlear implant: data from children. *Ear Hear*. 2000;21:164-174.
4. Brown CJ, Hughes ML, Luk B, Abbas PJ, Wolaver AA, Gervais J. The relationship between EAP and EABR thresholds and levels used to program the Nucleus 24 speech processor: data from adults. *Ear Hear*. 2000;21:151-163.
5. Cafarelli Dees D, Dillier N, Lai WK, von Wallenberg E, van Dijk B, Akdas F. Normative findings of electrically evoked compound action potential measurements using the neural response telemetry of the Nucleus CI24M cochlear implant system. *Audiol Neurootol*. 2005;10:105-116.
6. Smoorenburg GF, Willeboer C, JE vD. Speech perception in nucleus CI24M cochlear implant users with processor settings based on electrically evoked compound action potential thresholds. *Audiol Neurootol*. 2002;7:335-347.
7. Holstad BA, Sonneveldt VG, Fears BT, Davidson LS, Aaron RJ, Richter M, et al. Relation of electrically evoked compound action potential thresholds to behavioral T- and C-levels in children with cochlear implants. *Ear Hear*. 2009;30:115-127.
8. Probst R, Grevers G, Iro H. *Hals-Nasen-Ohren-Heilkunde*. 3., korr. und aktualisierte Aufl. ed. Stuttgart: Thieme; 2008. 415 S. p.
9. Allum J, Greisiger R, Probst R. Relationship of intraoperative electrically evoked stapedius reflex thresholds to maximum comfortable loudness levels of children with cochlear implants. *Int J Audiol*. 2002;41:93-99.
10. Caner G, Olgun L, Gültekin G, Balaban M. Optimizing fitting in children using objective measures such as neural response imaging and electrically evoked stapedius reflex threshold. *Otol Neurotol*. 2007;28:637-640.
11. Lorens A, Walkowiak A, Piotrowska A, Skarzynski H, Anderson I. ESRT and MCL correlations in experienced paediatric cochlear implant users. *Cochlear Implants Int*. 2004;5:28-37.
12. Jiang XJ, Yang HJ, Hui L, Yang N. [Electrically evoked stapedius reflex threshold and its clinical contribution of cochlear implantations]. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*. 2007;42:735-738.
13. Lai WK, Dillier N, Weber BP, Lenarz T, Battmer R, Gantz B, et al. TNRT profiles with the nucleus research platform 8 system. *Int J Audiol*. 2009;48:645-654.
14. Diedenhofen, Birk. Cocor: Comparing correlations 2013. Version 0.01-4:[Available from: <http://r.birkdiedenhofen.de/pckg/cocor/>].

15. Clark G. Cochlear implants: Fundamentals and Application. Beyer RT, Physics Do, University B, Providence R, USA, editors. New York: Springer Verlag New York, Inc.; 2003. 868 p
16. Henkin Y, Kaplan-Neeman R, Muchnik C, Kronenberg J, Hildesheimer M. Changes over time in electrical stimulation levels and electrode impedance values in children using the Nucleus 24M cochlear implant. *Int J Pediatr Otorhinolaryngol.* 2003;67:873-880.
17. Thai-Van H, Chanal JM, Coudert C, Veuillet E, Truy E, Collet L. Relationship between NRT measurements and behavioral levels in children with the Nucleus 24 cochlear implant may change over time: preliminary report. *Int J Pediatr Otorhinolaryngol.* 2001;58:153.
18. Potts L, Skinner M, Gotter B, Strube M, Brenner C. Relation between neural response telemetry thresholds, T- and C-levels, and loudness judgments in 12 adult nucleus 24 cochlear implant recipients. *Ear Hear.* 2007;28:495-511.

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## 10. Curriculum Vitae

### Patrizia Maria Savoia von Zürich ZH

21.08.1984	Geboren in Baden AG
1991 - 1996	Primarschule in Zufikon
1996 - 2000	Bezirksschule in Bremgarten
2000 - 2004	Kantonsschule in Wohlen
2005 - 2011	Medizinstudium an den Universitäten Fribourg und Zürich (3.- 6. Studienjahr)
2011	Staatsexamen an der Universität Zürich
Dezember 2011 – Mai 2013	Assistenzärztin Chirurgie, Kantonsspital Baden
Seit Juli 2013	Assistenzärztin an der Klinik für Kinder und Jugendliche, Kantonsspital Baden