Diploma Thesis

Distance to the Base of Skull (DTBOS): Significance of the new predictor regarding perioperative surgical complications of carotid body tumor resections- a retrospective analysis

DTBOS

submitted by

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For the Academic Degree of

Doctor of Medicine

(Dr. med. univ.)

At the

Medical University of Graz

Department of Surgery – Division of Vascular Surgery

under the supervision of

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Graz, 03.11.2021

Declaration

I declare that, this thesis has been written by me and, to the best of my knowledge and belief, this thesis is authentic except where acknowledgements are made in the text. It does not include any material for which any other university degree or diploma has been awarded.

Graz, 03.11.2021 *Filip Ivanjko eh.*

Acknowledgements

I would like to thank my supervisor, PD Dr. Peter Konstantiniuk, for his constant support, his numerous revisions and his valuable contributions. Furthermore, I pay my acknowledgments to my second supervisor Univ.- Prof.in Dr.in med. Tina Ulrike Cohnert. I also want to acknowledge the great support and love I received from my mother, my father and brother. Finally, I am grateful for my partner, who encouraged me and supported me whenever I needed her.

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1 LIST OF ABBREVATIONS

BMI .... Body-Mass-Index
CBS .... carotid body tumor surgery
CBT .... carotid body tumor
CCA .... common carotid artery
cm .... centimeter
CN IX .... glossopharyngeal nerve
CN X .... vagal nerve
CN XII .... hypoglossal nerve
CRF .... case report form
CRFs .... case report forms
CT .... computed tomography
DTBOS .... distance to the base of skull
ECA .... external carotid artery
HNPGL .... head and neck paraganglioma
ICA .... internal carotid artery
kg .... kilogram
MEDOCS .... electronic data system of the University Hospital of Graz
mm .... milimeter
MRI .... Magentic Resonance Imaging
PACS .... Picture Archiving and Communication System
PGL .... paraganglioma
RLN .... recurrent laryngeal nerve
SDH .... succinate dehydrogenase
SDHx .... succinate dehydrogenase complex
SE .... standard error
SLN .... superior laryngeal nerve
STA .... superior thyroid artery
y .... years

2 LIST OF TABLES

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5 ABSTRACT IN GERMAN

Glomustumore sind seltene neuroendokrine Neoplasmen, die sich an der Karotisgabel lokalisieren. Das therapeutische Mittel der Wahl ist die Tumor-exstirpation. Die häufigste Komplikation bei der Entfernung des Tumors sind Hirnnervenverletzungen.

Ziel- Die Absicht dieser Diplomarbeit ist es herauszufinden, ob der neue Prädiktor DTBOS (distance to the base of skull) eine bessere Aussagekraft hinsichtlich perioperativer chirurgischer Komplikationen, speziell Hirnnervenverletzungen, besitzt als die Shamblin Klassifikation. Weiters wurden weiteren Variablen, wie morphologische Parameter, bezüglich der Aussagekraft von perioperativen chirurgischen Komplikationen analysiert. Durch aussagekräftige Parameter können PatientInnen vor ihrer Karotisglomustumorresektion besser aufgeklärt werden und ChirurgInnen nötige Vorkehrungen treffen.

Design/Methoden- Bei dieser Diplomarbeit handelt es sich um eine retrospektive Studie, die Daten von den Jahren 2004 bis 2019 erhoben hat. Es wurden die Datensätze von allen PatientInnen analysiert, die an der Medizinischen Universität Graz elektiv wegen eines Karotisglomustumors operiert worden sind und deren Datensätze komplett waren. Durch stattgefundene Bildgebung konnten tumorspezifische Parameter, wie DTBOS und Durchmesser, evaluiert werden. In einer logistischen Regressionanalyse wurde der Einfluss von DTBOS, Shamblin-Klassifikation und anderer Parameter auf das Risiko einer Hirnnervenverletzung berechnet. Univariat signifikante Parameter wurden in einem multivariaten Modell analysiert.

Resultate- Es wurden insgesamt 93 Fälle erhoben, von denen 47 in die Studie eingeschlossen und 46 aus der Studie ausgeschlossen wurden. 42 Fälle sind ausgeschlossen worden, weil keine auswertbare Bildgebung vorhanden war. 2 wurden ausgeschlossen, weil es sich um Zufallsbefunde handelte, 1 Fall wurde ausgeschlossen, weil es sich um ein Paragangliom des Nervus vagus handelte, und 1 Datensatz wurde ausgeschlossen, weil keine Operation stattfand.

In der univariaten Analyse waren Körpergewicht (p=0.046), DTBOS (p=0.009), kraniokaudaler Durchmesser des Tumors (p=0.027), Tumorvolumen (p=0.036) signifikant. Die univariat signifikanten Parameter wurden multivariat analysiert. Dabei zeigte sich, dass alle univariat signifikanten Parameter im multivariaten

Modell ihre Signifikanz verloren außer DTBOS (p=0.046). Dies führt zur Schlussfolgerung, dass DTBOS der aktuell beste Parameter zur präoperativen Risikoabschätzung einer Hirnnervenverletzung ist.
Klinischer Nutzen- Durch die Ergebnisse dieser Studie kann durch ein wenig aufwendiges Ausmessen von DTBOS in der Bildgebung (CT, MRT) ein statistisch signifikanter Parameter ermittelt werden. Dieser relevante Parameter hilft den ChirurgInnen nicht nur, PatientInnen präziser aufklären zu können, sondern auch bei Operationen eventuell nötige Vorkehrungen im Vorfeld treffen zu können.
Limitationen- Aufgrund des äußerst seltenen Auftretens eines Karotisglomus-tumors werden an der Medizinischen Universität Graz durchschnittlich 3 Karotisglomustumorresektionen pro Jahr durchgeführt. Zusätzlich konnten Datensätze nicht eingeschlossen werden, da die dazugehörige Bildgebung technisch bedingt nicht akquirierbar war.

6 ABSTRACT

Carotid body tumors (CBTs) are rare neuroendocrine neoplasms located at the carotid bifurcation. Therapeutic gold standard is the tumor resection. The most frequent complication in patients undergoing carotid body tumor resections are injuries of the cranial nerves.

Goal- The primary aim of this study is to investigate the impact of the newly developed DTBOS (distance to the base of skull), regarding prediction of perioperative cranial nerve (CN) injuries compared to the Shamblin classification. Correspondingly, this work also reflects on the significance of variables, including morphological parameters. Relevant parameters aid in the preoperative information and consent of a patient before their carotid body tumor resection as well as support the surgical team in deciding upon precautionary measures.

Design/Methodology- The dissertation analyzes data from 2004 to 2019 in a retrospective study. Patients undergoing elective surgery for carotid body tumor at Graz Medical University and presenting complete medical data records were analyzed. By medical imaging (Magnetic Resonance Tomography or Computed Tomography), tumor-specific parameters such as DTBOS and diameter were determined. The significance of DTBOS, Shamblin Classification and other parameters was analyzed with univariate logistic regression analysis. Univariately significant parameters were analyzed in a multivariate model.

Results- There was a total of 93 cases, 47 cases were included and 46 had to be excluded from the study. Forty-two cases were excluded because of a lack of medical imaging, two were excluded as a result of incidental findings, one was excluded because the paraganglioma location was not located at the carotid bifurcation, and one case was excluded since the patient did not undergo surgery. In the univariate analysis four univariately significant parameters were detected; body weight (p=0.046), DTBOS (p=0.009), craniocaudal tumor diameter (p=0.027) and volume of tumor (p=0.036). In the multivariate calculation only DTBOS (p=0.046) remained significant. In conclusion, DTBOS is currently the best parameter regarding preoperative risk assessment of CN injuries.

Clinical values and benefits- The established results of this dissertation reveal, that the parameter DTBOS supports surgeons and patients to grow a deeper

understanding for the respective medical issue and can aid in taking preoperative precautions.

Limitations – On the basis of the infrequent appearance of a carotid body tumor, the surgical cadre of the Medical University of Graz perform on average three carotid body tumor resections per year. Additionally, a relevant number of data had to be excluded from this degree dissertation, as the medical imaging could not be retrieved.

7 INTRODUCTION

Paragangliomas are neoplasms that consist of cells from the endocrine and nervous system, and are generally benign and slow-growing. Ninety percent of paragangliomas are pheochromocytomas, 8.5% are located in the abdomen, 1.2% in the thorax, and 0.3% are located in the head and neck. (1,2)

HNPGL (head and neck paraganglioma) are divided in four groups: carotid body PGL (paraganglioma), vagal PGL, middle ear PGL and laryngeal PGL. Sixty percent of HNPGL are CBTs (carotid body tumors) and were first described by von Haller in 1743. (1-4)

Risk factors for developing HNPGL are chronic hypoxia, living at high altitude and germ line mutations in the SDHx (succinate dehydrogenase complex). (5,6)

In the literature women are affected by CBTs 1.9 times to 3 times as often as men. (7-10)

CBTs clinically present themselves as a slow growing mass in the neck. CBTs are often asymptomatic due to a slow growing mass in the neck, but CBTs can clinically present symptoms caused by local invasion and pressure on the adjacent tissue. The most common symptoms of CBTs are pain, dysphagia, hoarseness, swallowing difficulty, stridor, Horner syndrome, bradycardia, unconsciousness, recurrent infections of the upper airways and cerebrovascular complications. (9,10)

CBTs are often found incidentally during a medical imaging like Doppler ultrasound; however, symptomatic CBTs are suspected clinically and the diagnosis is ensured by Doppler ultrasound, CT with contrast agent or MRA. (9,10)

Tumor resection is the gold standard. (10)

In 1971 the Shamblin classification was introduced by Shamblin et al. (7) and is still used to grade CBTs up until now.

A frequent complication after CBT resections patients prevalently suffer from cranial nerve (CN) injuries due to perioperative surgical complications. In order to assess the risk of a CN injury a new predictive parameter was introduced in 2015 by Kim et al. (8) namely DTBOS (distance to the base of skull).

DTBOS is measured by using CT or MRI and it is the Distance from the base of the skull to the most superior portion of the CBT. (8)

Since CNs, arteries and veins were often injured during CBT resections,

Shamblin et al. (7) reviewed 96 CBTs from 90 patients, who underwent CBT resection at the Mayo Clinic, from 1931 to 1967.Their revision revealed that not only the tumor size was variable but also the relationship of the CBT and the carotid artery wall. To analyze the relationship of the CBT and carotid artery wall in depth, Shamblin et al. (1) divided CBTs in three groups. The excision of group 1 tumors (26%) is self-explanatory for their characteristics: small and minimally attached to carotid vessels. The usually larger group 2 tumors (46.5%) which partially surround the carotid artery are moderately attached to the adventitia (carotid artery). The carotid arteries were circumferentially embedded in group 3 tumors (27.6 %) and had a strong relationship with the tumor. (7)
Over a period of 10 years (2004 - 2014) a pilot study was carried out at the University of Los Angeles, which included 16 multinational institutions and analyzed a total of 356 CBTs in 332 patients,Kim et al's (8) study ascertained that there is a correlation between increased risk of CN injuries and specific tumor parameters like DTBOS and tumor volume. Kim et al (8) pointed out that the smaller the DTBOS the higher the risk of a CN injury, i.e. for every 1 cm decrease of DTBOS the risk of a CN injury increases by 151%. In summary, the determination of DTBOS, tumor volume and Shamblin classification is important because a combination of these 3 parameters has a higher validity than only one of these. (8)
Up until now the Shamblin classification has been used to grade CBTs. In order to optimally inform patients before surgery, the Department of Surgery - Division of Vascular Surgery- at the Medical University of Graz applies the Shamblin classification to assess the risk of perioperative surgical complications. The evaluation of the risk not only helps surgeons to provide more specific information to patients, but it is also essential for surgical risk management.

8 MATERIAL AND METHODS

8.1 Design

This work is a retrospective study. The clinical data of patients were obtained from medical reports (MEDOCS). Data from 1987-2011 were collected by Dr. Fruhmann (11) and published in 2013 with focus on genetic analysis of SDH mutations. In this work her data is reviewed and additionally, patient's clinical data from 2012-2019 was acquired and evaluated together.

8.2 Trial procedure

After approval by the ethics committee of the Medical University of Graz (13.2) clinical data of patients with carotid body tumor resection between 2012 and 2019 were added to the dataset. If accessible, preoperative images of all carotid body tumors were measured on screen. Potentially influencing factors were acquired by MEDOCS and PACS. Only cases with complete records were included for this work.

8.3 Criteria

8.3.1 Inclusion criteria

There were following inclusion criteria for this work:

- Existence of CBT
- Surgery at Medical University of Graz
- Access to complete medical reports
- Access to preoperative three-dimensional cross section images of the neck
- Age 1-100
- Surgery between 1987 and 2019

8.3.2 Exclusion criteria

There were following exclusion criteria for this work:

- Incomplete patients’ data
- Missing access to preoperative three-dimensional section images of the neck
- Vagal paraganglioma
- Incidental finding
- No CBT resection

8.4 Collected Data

According to the study protocol the collected data were documented on Case report forms (CRFs).

8.4.1 Physical properties

Following data were gathered from patient records:

- Age [y]
- Weight [kg]
- Height [cm]

Following data was calculated from the gathered data:

- Body-Mass-Index (BMI)

8.4.2 Tumor characteristics

Following data was gathered:

- DTBOS [mm]
- Shamblin classification
- Craniocaudal diameter of the carotid body tumor [mm]
- Transversal diameter of the carotid body tumor [mm]
- Sagittal diameter of the carotid body tumor [mm]

Following data was calculated by the gathered data:

- Tumor volume [mm^3]

8.4.3 Surgical aspects

Following data was gathered:

- Laterality
- Duration of surgery
- Preoperative embolization

8.4.4 Vascular surgical interventions

Following data was gathered:

- Resection and reinsertion of ICA
- Saphenous interposition ICA
- Ligation CCA
- Ligation STA
- Ligation ECA

8.4.5 Cranial nerve injuries

Following data was gathered:

- Glossopharyngeal nerve injury
- Vagal nerve injury
- Hypoglossal nerve injury
- Superior laryngeal nerve injury
- Recurrent laryngeal nerve injury

8.5 Statistical evaluation

The p-value is the probability of receiving the observed results assuming that the null hypothesis is correct. (12) p-values under 0.05 were considered significant. The mean is the expected value of a collection of data. It is the sum of all values divided by the number of values. (13)

$$\bar{x} = \frac{x_{1+}x_{2+\cdots+}x_n}{n} \qquad \text{Eq. 1}$$

$\bar{x}$…mean, x_1…first element, x_2…second element, x_n…nth element, n…number of elements

The 95 % confidence interval for mean is an interval, which consist of a lower and an upper bound, that contains the mean with a 95 % certainty. (14)

$$CI = \bar{x} \pm z_c \frac{s}{\sqrt{n}} \qquad \textit{Eq. 2}$$

CI…confidence interval, $\bar{x}$…mean, z_c…value for confidence level, s… standard deviation, n…number of elements

To obtain the values for the 5% trimmed mean the lowest and highest 5% of values of the data collection are excluded and the mean is calculated by using the remaining 90% of values. (15)
The median is the middle value of a data set, which means that 50% of the values are higher and smaller than the median, respectively. (16)

The variance is a dispersion parameter and is the mean square deviation of a random value from the mean. (17)

$$\sigma^2 = \frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{n} \quad \text{Eq. 3}$$

σ^2...variance, x_i... i^{th} element, n...number of samples

The standard deviation is calculated by the square root of the variance and describes how spread out the data is. (18)

$$\sigma = \sqrt{\sigma^2} \quad \text{Eq. 4}$$

σ...standard deviation, σ^2...variance

The standard error (SE) is the estimated standard deviation of a sampling distribution. (19-21)

$$SE = \frac{\sigma}{\sqrt{n}} \quad \text{Eq. 5}$$

SE...standard error, σ...standard deviation, n...number of elements

Minimum and maximum are the lowest value and highest value of a data set, respectively. The range is calculated by subtracting the minimum from the maximum.

The interquartile range is the difference between third quartile and first quartile, i.e. the interquartile range consists of the middle 50% of the values of the data set. (22)

$$IQR = Q_3 - Q_1 \quad \text{Eq. 6}$$

IQR...interquartile range, Q_3...third quartile, Q_1...first quartile

The skewness provides information about the asymmetry of a distribution curve. If there is a shift in the distribution curve it is skewed. Possible values of the skewness can be undefined, zero, negative or positive. (23,24)

$$S = \frac{1}{n}\sum_{i=1}^{n}\left(\frac{x_i - \bar{x}}{\sigma}\right)^3 \qquad \text{Eq. 7}$$

S…skewness, n…number of elements, x_i…i^{th} element, $\bar{x}$…mean, σ…standard error

Kurtosis is a measure of steepness of a distribution function. A higher kurtosis means that values are further apart from its mean, vice versa a smaller kurtosis means that the values are more focused around their mean. (25)

$$K = \frac{1}{n}\sum_{i=1}^{n}\left(\frac{x_i - \bar{x}}{\sigma}\right)^4 \qquad \text{Eq. 8}$$

K…kurtosis, n…number of elements, x_i…i^{th} element, $\bar{x}$…mean, σ…standard error

8.6 Boxplot

A boxplot is a graphical depiction of data. The maximum and minimum value are imaged by the upper and lower whisker, respectively. Outliers are exceptions and are represented by circles. The median is shown as a thick line in the box. The box contains 50% of the values. (26,27)

8.7 Formulas

The BMI was calculated by using the following formula:

$$BMI = \frac{weight}{height^2} \qquad Eq.\ 9$$

BMI…Body-Mass-Index, weight [kg], height [m]

The tumor volume was calculated by using Kim et al.'s (8) formula to an ellipsoid approximation model:

$$V = \frac{4}{3}\pi abc \qquad Eq.\ 10$$

V…volume, a…$\frac{vertical\ diameter}{2}$, b… $\frac{transversal\ diameter}{2}$, c… $\frac{sagittal\ diameter}{2}$

8.8 Analytic procedure

The influence of all collected parameters from *8.4.1 Physical properties, 8.4.2 Tumor characteristics* and *8.4.3 Surgical aspects* on CN injuries was analyzed univariately in a logistic regression model. Univariately significant parameters were further analyzed multivariately. Furthermore, univariately significant parameters were categorized. DTBOS was divided in cm steps, and the risk of a CN injury was calculated for each cm. To prove the relation between sagittal and transversal diameters the Spearmen correlation coefficient was determined. To exclude a systemic bias concerning the inclusion-exclusion process, gender and age of both included and excluded patients were compared using Fishers's exact test and Student's t-test.

8.9 Data protection

8.9.1 Case Report Form (CRF)

The CRFs are only accessible for authorized people and are locked at the Department of Surgery- Division of Vascular Surgery.

8.9.2 Data protection

In order to ensure anonymity, all cases were provided with an identification number. All data is stored in the database which is stored on the server space of the Medical University of Graz. There is no direct relation to the patients.

8.9.3 Data safety

CRFs and the elaborated data are only accessible for people with authorization.

9 RESULTS

9.1 Inclusion process

Over the period from 1987 to 2019, there were 93 CBT resections carried out in 81 patients at the Medical University of Graz. Among these, 48 cases (43 patients) could be included. The cause of exclusion was mainly the missing access to imaging such as CT or MRI (42 cases). Two incidental findings discovered during surgery were not included for the respective study, and another patient did not undergo surgery due to her age of over 80 years. The last cause for exclusion was a histologically diagnosed vagal paraganglioma.

9.2 Physical properties

9.2.1 Age

The mean age of the 48 cases, at time of CBT resection, was 55.6 years (± 2.5 SE). The lower bound of the 95% confidence interval for mean was 50.6 years, the upper 60.6 years. (Table 1)

The mean age of the 45 excluded cases was 54.6 years (± 2.3 SE) and the lower bound of the 95% confidence interval for mean was 50.0 years while the upper was 59.3 years. (Table 1)

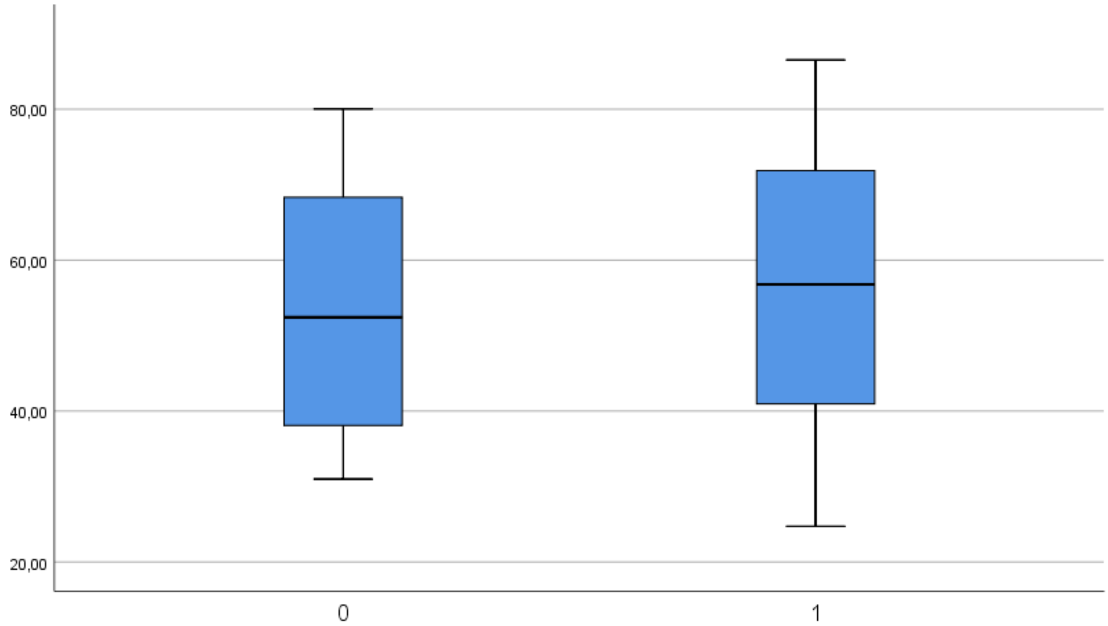
Mean age of included and excluded cases did not differ significantly ($p = 0.80$).

Image 1 represents the age of the patients that underwent CBT resection (Boxplot 1, Image 3) versus that did not undergo CBT resection (Boxplot 0, Image 3).

Table 1: Statistical evaluation of patients' age

Age		Included cases (n=48)	Standard Error (n=48)	Excluded cases (n=45)	Standard Error (n=45)
Mean		55.6	2.5	54.6	2.3
95% Confidence Interval for Mean	Lower Bound	50.6		50.0	
	Upper Bound	60.6		59.3	
5% Trimmed Mean		55.8		54.5	
Median		56.8		52.4	
Variance		299.0		240.1	
Standard Deviation		17.3		15.5	
Minimum		24.7		31.0	
Maximum		86.5		80.0	
Range		61.8		49.0	
Interquartile Range		32.5		31.3	
Skewness		-0.184	0.343	0.030	0.354
Kurtosis		-1.12	0.674	-1.37	0.695

Image 1: Boxplot Age



9.2.2 Gender

Out of the 43 patients who underwent surgery, 14 were male, which accounts for 32.6 %, and 29 were female, which are 67.4%. (Table 2)

In this study women have a nearly 2 times higher prevalence than men (female to male ratio of 2.07:1). There was no significant difference between the excluded and included cases (Fisher's exact test, p=0.462)

Table 2: Assessment of patients' gender

	Absolute frequency (incluced cases)	Relative frequency [%] (included cases)	Absolute frequency (excluded cases)	Relative frequency [%] (exluded cases)
Male	14	32.6	9	23.7%
Female	29	67.4	29	76.3%

Image 2: Gender distribution of included cases

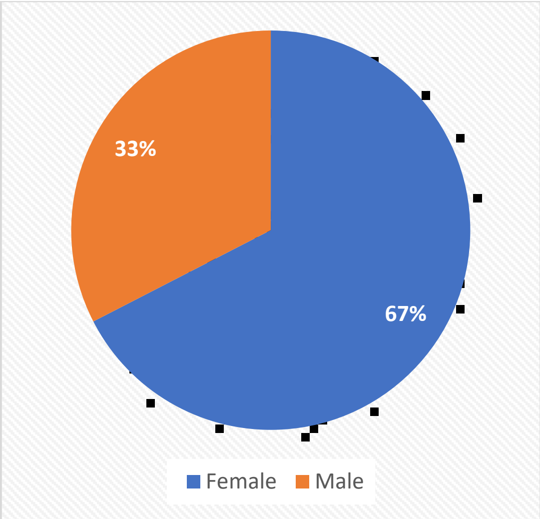
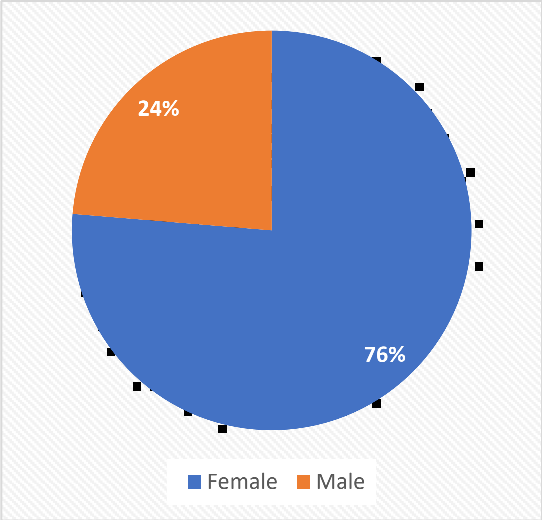


Image 3: Gender distribution of excluded cases



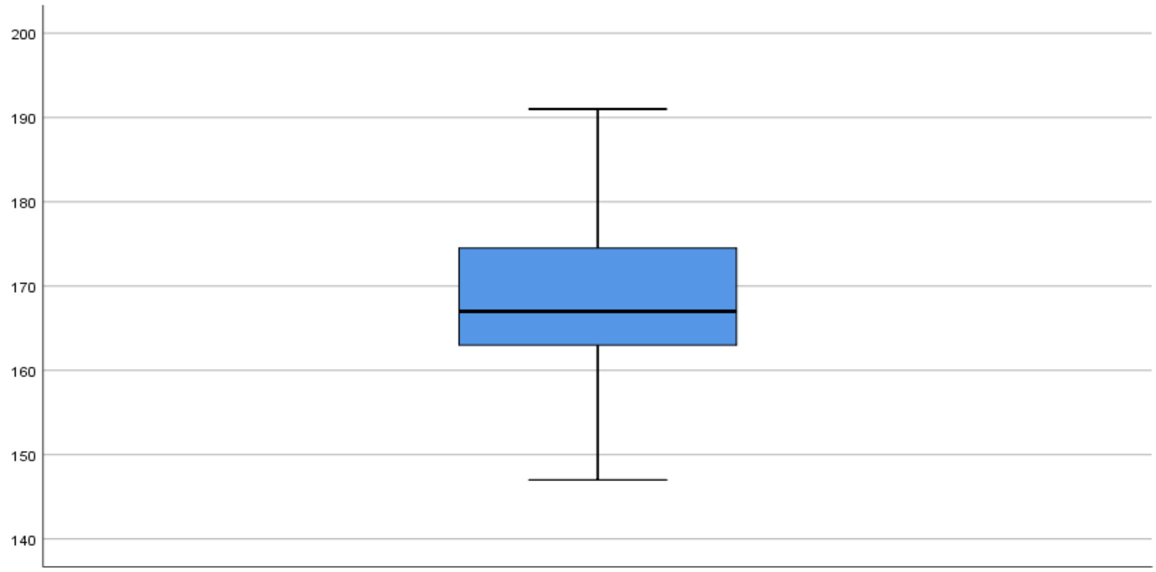
9.2.3 Height

Data was available from 47 cases. The mean height was 169 cm (±1.3 SE), the lower bound of the 95 % confidence interval for mean was 166 cm while the upper bound was 171 cm. (Table 3)

Table 3: Statistical evaluation of patients' height

Height		Statistic [cm]	Standard Error [cm]
Mean		168.5	1.35
95% Confidence Interval for Mean	Lower Bound	165.7	
	Upper Bound	171.2	
5% Trimmed Mean		168.4	
Median		167.0	
Variance		85.0	
Standard Deviation		9.22	
Minimum		147.0	
Maximum		191.0	
Range		44.0	
Interquartile Range		12.0	
Skewness		0.145	0.347
Kurtosis		-0.073	0.681

Image 2: Boxplot Height



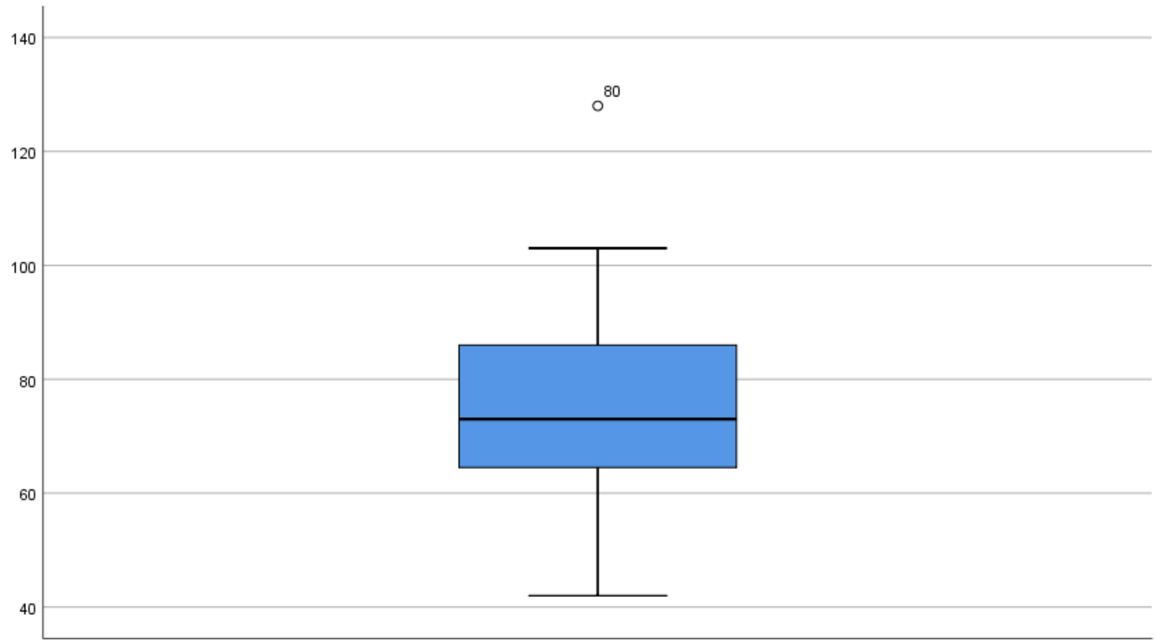
9.2.4 Weight

Data was available from 47 cases. The mean weight was 75.5 kg (±2.3 SE), the lower bound of the 95% confidence interval for mean was 71.0 kg and the upper bound was 80.1 kg. (Table 4)

Table 4: Statistical evaluation of patients' weight

Weight		Statistic [kg]	Standard Error [kg]
Mean		75.5	2.25
95% Confidence Interval for Mean	Lower Bound	71.0	
	Upper Bound	80.0	
5% Trimmed Mean		75.0	
Median		73.0	
Variance		239.0	
Standard Deviation		15.5	
Minimum		42.0	
Maximum		128.0	
Range		86.0	
Interquartile Range		23.0	
Skewness		0.669	0.347
Kurtosis		1.68	0.681

Image 3: Boxplot Weight



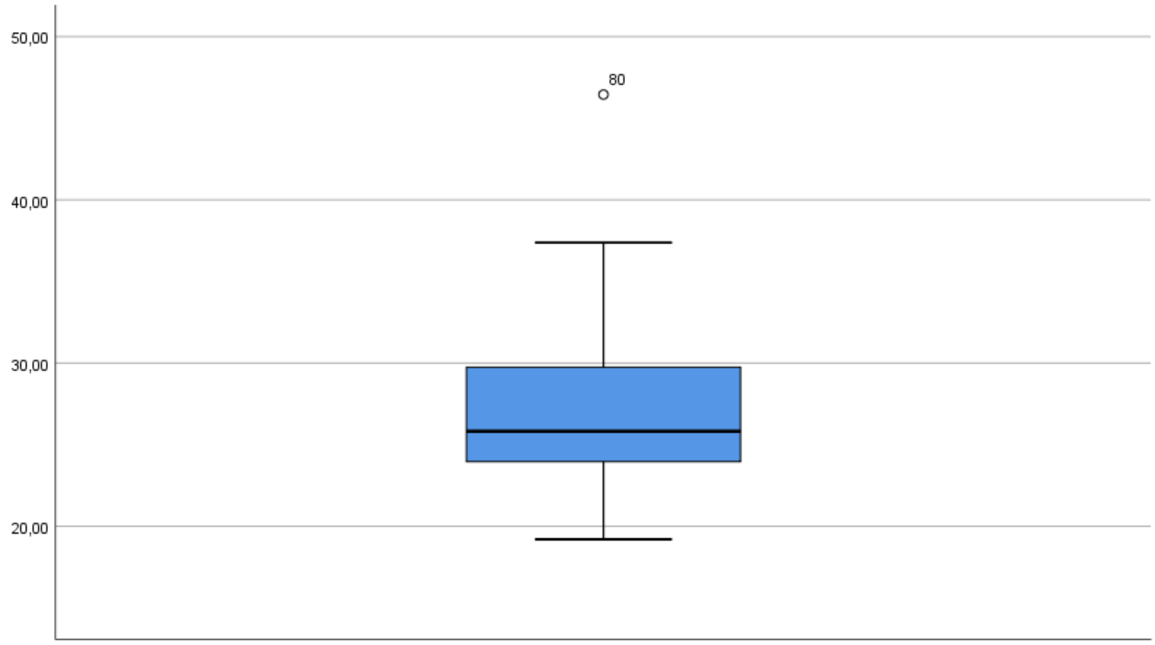
9.2.5 BMI

Data from 47 cases was gathered to calculate the BMI. The mean BMI was 26.6 kg/m² (±0.8 SE), the lower bound of the 95 % confidence interval for mean was 25.1 kg/m² while the upper bound was 28.1 kg/m². (Table 5)

Table 5: Statistical evaluation of patients' BMI

BMI		Statistic [kg/m²]	Standard Error [kg/m²]
Mean		26.6	0.759
95% Confidence Interval for Mean	Lower Bound	25.1	
	Upper Bound	28.1	
5% Trimmed Mean		26.2	
Median		25.8	
Variance		27.1	
Standard Deviation		5.21	
Minimum		19.2	
Maximum		46.5	
Range		27.3	
Interquartile Range		5.95	
Skewness		1.34	0.347
Kurtosis		3.42	0.681

Image 4: Boxplot BMI



9.3 Tumor characteristics

9.3.1 DTBOS

Data were available from 48 cases. The mean Distance to the Base of Skull was 43.2 mm (± 8.8 SE), the 95% confidence interval for mean had a lower bound of 39.9 mm and an upper bound of 46.5 mm. (Table 6)

Table 6: Evaluation of DTBOS

DTBOS		Statistic [mm]	Standard Error [mm]
Mean		43.2	8.81
95% Confidence Interval for Mean	Lower Bound	39.9	
	Upper Bound	46.5	
5% Trimmed Mean		44.0	
Median		43.5	
Variance		129.0	
Standard Deviation		11.4	
Minimum		8.0	
Maximum		65.0	
Range		57.0	
Interquartile Range		14.0	
Skewness		-0.993	0.343
Kurtosis		1.94	0.674

9.3.2 Shamblin Classification

It was possible to grade all 48 CBTs according to the Shamblin classification. 12 CBTs were classified Shamblin 1 (25.0%), 18 were Shamblin 2 (37.5%) and 18 were graded Shamblin 3 (37.5%). (Table 7)

Table 7: Summary of the Shamblin Classification

Shamblin Score	Absolute Frequency	Relative Frequency [%]
1	12	25,0
2	18	37,5
3	18	37,5

9.3.3 Tumor Diameter

Image 5: Frontal section

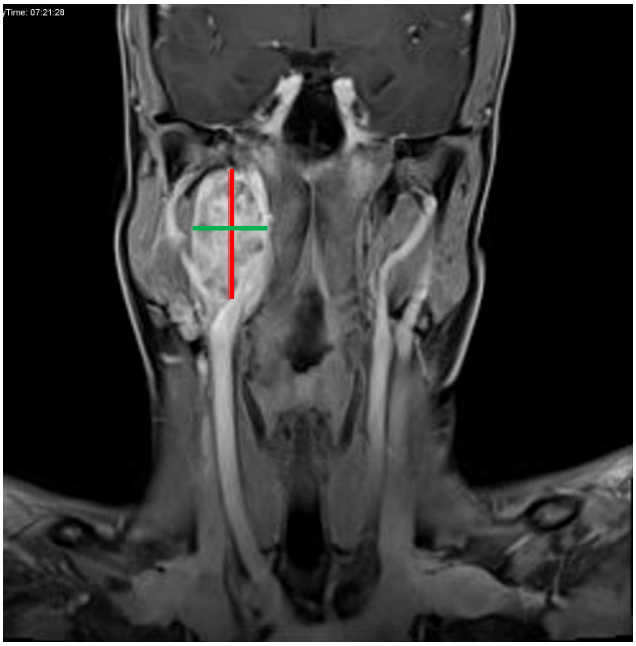


Image 6: Sagittal section

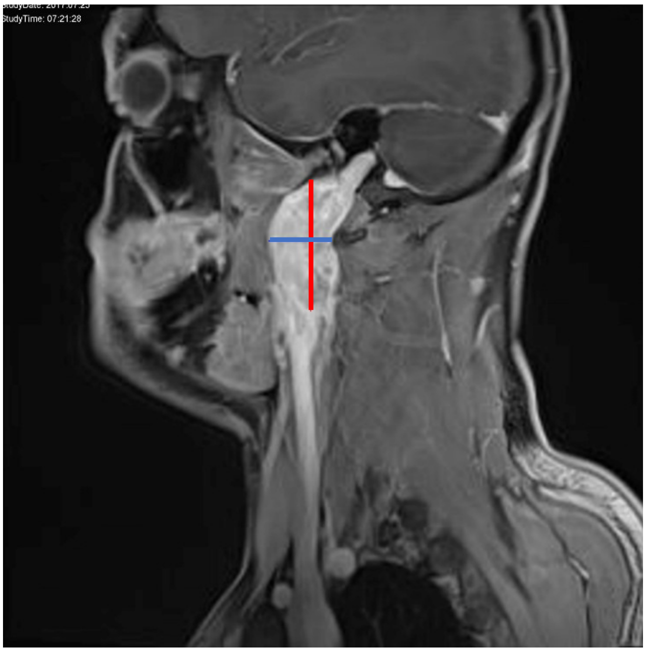


Image 7: Transverse section

MRI was used as imaging modality for Images 5-7.
Image 5 shows the craniocaudal diameter (red) and transversal diameter (green).
Image 6 depicts the craniocaudal diameter (red) and sagittal diameter (blue). Image 7 displays the transversal diameter (green) and sagittal diameter (green).

The craniocaudal, transversal and sagittal diameter could be measured in 48 CBTs.

9.3.3.1 Craniocaudal tumor diameter

The mean craniocaudal diameter was 30.8 mm (± 1.7 SE), the lower bound of the 95% confidence interval for mean was 27.4 mm whilst the upper bound was 34.2 mm. (Table 8)

Table 8: Evaluation of the craniocaudal diameter

Craniocaudal Tumor Diameter		Statistic [mm]	Standard Error [mm]
Mean		30.8	1.68
95% Confidence Interval for Mean	Lower Bound	27.4	
	Upper Bound	34.2	
5% Trimmed Mean		30.7	
Median		30.0	
Variance		135.0	
Standard Deviation		11.6	
Minimum		10.0	
Maximum		56.0	
Range		46.0	
Interquartile Range		17.0	
Skewness		0.131	0.343
Kurtosis		-0.589	0.674

9.3.3.2 Transversal tumor diameter

The mean transversal diameter was 21.1 mm (± 1.2 SE), the 95% confidence interval for mean had a lower bound of 18.8 mm and an upper bound of 23.8 mm. (Table 9)

Table 9: Assessment of the transversal diameter

Transversal Tumor Diameter		Statistic [mm]	Standard Error [mm]
Mean		21.3	1.23
95% Confidence Interval for Mean	Lower Bound	18.8	
	Upper Bound	23.8	
5% Trimmed Mean		21.3	
Median		22.0	
Variance		72.7	
Standard Deviation		8.53	
Minimum		4.0	
Maximum		42.0	
Range		38.0	
Interquartile Range		13.0	
Skewness		-0.23	0.343
Kurtosis		-0.368	0.674

9.3.3.3 Sagittal tumor diameter

The mean sagittal diameter was 20.9 mm (± 1.3 SE). The lower bound of the 95% confidence interval for mean was 18.2 mm while the upper bound was 23.8 mm and the 5% trimmed mean was 21.3 mm. (Table 10)

Table 10: Evaluation of the sagittal diameter

Sagittal Tumor Diameter		Statistic [mm]	Standard Error [mm]
Mean		20.9	1.32
95% Confidence Interval for Mean	Lower Bound	18.2	
	Upper Bound	23.5	
5% Trimmed Mean		20.8	
Median		20.5	
Variance		84.0	
Standard Deviation		9.16	
Minimum		5.0	
Maximum		41.0	
Range		36.0	
Interquartile Range		15.0	
Skewness		0.114	0.343
Kurtosis		-0.631	0.674

9.3.4 Tumor volume

48 cases were available to calculate the tumor volume. The mean tumor volume was 9889.3 mm^3 (± 1295.5 SE). The 95% confidence interval for mean had a lower bound of 7283.1 mm^3 and an upper bound of 12495.4 mm^3. (Table 11)

Table 11: Assessment of tumor volume

Volume		Statistic [mm^3]	Standard Error [mm^3]
Mean		9889	1295
95% Confidence Interval for Mean	Lower Bound	7283	
	Upper Bound	12495	
5% Trimmed Mean		9139	
Median		7555	
Variance		80555311	
Standard Deviation		8975	
Minimum		105	
Maximum		36047	
Range		35943	
Interquartile Range		11389.	
Skewness		1.13	0.343
Kurtosis		0.804	0.674

9.4 Surgical aspects

Unilateral CBT resection was performed in 38 patients whereas bilateral in five, totalling 48 CBT resections.

9.4.1 Laterality

Left sided CBT resection was performed in 22 cases (45.8%), right sided CBT resection in 26 (54.2%) (Table 12)

Table 12: Summary of the laterality

	Absolute frequency	Relative frequency [%]
left	22	45,8
right	26	54,2
total	48	100,0

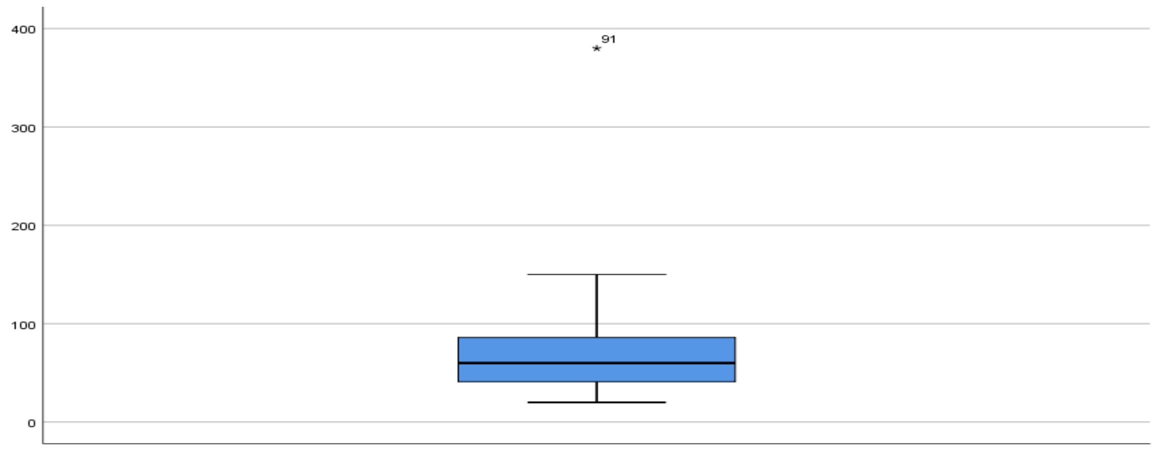
9.4.2 Operative Time

Forty-two out of 48 surgeries were analyzed to evaluate the duration of the operation. In six cases CBS (carotid body tumor surgery) was combined with another surgical intervention thus the pure CBS duration could not be determined. The mean operative time was 72.1 min (±8.8 SE), the lower bound of the 95% confidence interval for mean was 54.3 min and the upper bound was 89.9 min. The minimum surgery duration was 20 min whereas the maximum surgery duration was 380 min thus a range of 360 min was calculated. (Table 13) (Image 10) Due to intraoperative complications one operation took 380 minutes.

Table 13: Assessment of the operative time

Operative Time		Statistic [min]	Standard Error [min]
Mean		72.1	8.81
95% Confidence Interval for Mean	Lower Bound	54.3	
	Upper Bound	89.9	
5% Trimmed Mean		64.4	
Median		60.0	
Variance		3257	
Standard Deviation		57.1	
Minimum		20.0	
Maximum		380	
Range		360	
Interquartile Range		46.0	
Skewness		4.05	0.365
Kurtosis		20.9	0.717

Image 8: Boxplot operative time



9.4.3 Preoperative embolization

In nine cases out of 48 a successful preoperative embolization of the ECA (external carotid artery) was performed.

Image 9: Angiography pre embolization

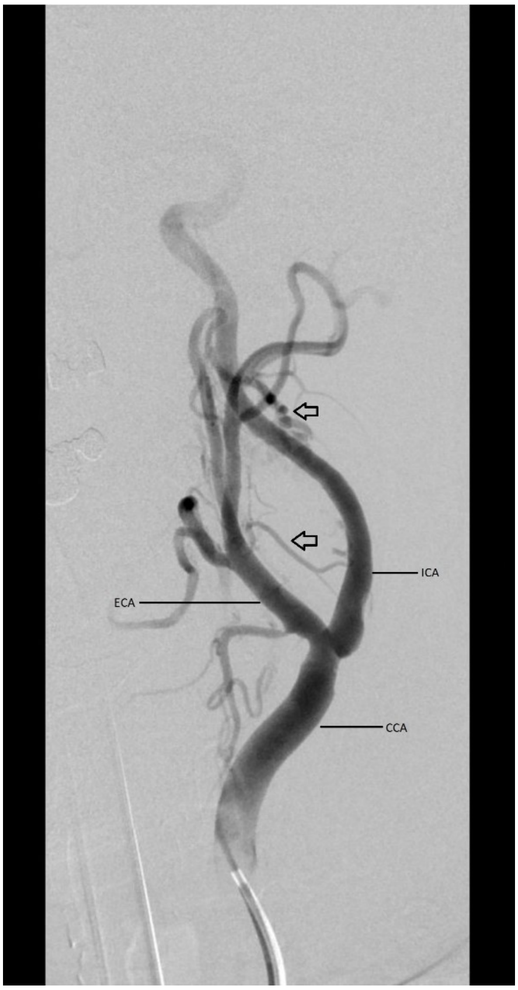


Image 10: Angiography post embolization

Image 9 shows an intraarterial digital subtraction angiography before embolization. The branches of the ECA planned to be embolized are marked with an arrow. Image 10 illustrates an angiography after embolization.

9.5 Vascular surgical interventions

The vascular surgical interventions have been evaluated in 48 CBT resections.

9.5.1 Resection and reinsertion of Internal Carotid Artery (ICA)

The internal carotid artery (ICA) had to be resected and reinserted once in 48 CBT resections. (Table 14)

Table 14: Assessment of resection and reinsertion of ICA

		Absolute frequency	Relative frequency [%]
Resection and reinsertion ICA	Procedure not performed	47	97.9 %
	Procedure performed	1	2.1 %

9.5.2 Saphenous Vein Interposition Internal Carotid Artery (Interposition saphenous vein bypass graft between the common and internal carotid artery)

A saphenous vein interposition was not required during 48 CBT resections.

9.5.3 Ligation Common Carotid Artery (CCA)

The common carotid artery was not ligated in this patient cohort.

9.5.4 Ligation Superior Thyroid Artery (STA)

The superior thyroid artery was ligated in 4 CBT resections. (Table 15)

Table 15: Assessment of superior thyroid artery ligation

		Absolute frequency	Relative frequency [%]
Ligation of superior thyroid artery	Procedure not performed	44	91.7 %
	Procedure performed	4	8.3 %

9.5.5 Ligation External Carotid Artery (ECA)

The ECA was ligated 13 times. (Table 16)

Table 16:Assessment of external carotid artery ligation

		Absolute frequency	Relative frequency [%]
Ligation of external carotid arery	Procedure not performed	35	72.9 %
	Procedure performed	13	27.1 %

9.5.6 Summary of additional vascular surgical interventions

There was a total of 18 additional vascular surgical interventions performed in 48 CBT resections. On average there were 0.375 vascular surgical interventions per CBT resection. The most frequent vascular surgical procedure performed was the ligation of ECA, which was carried out 13 times. The ligation of ECA accounts for 72.2 % of all 18 vascular surgical interventions among 48 CBT resections. During 4 CBT resections the STA had to be ligated, which are 22.2 % of vascular surgical interventions that were carried out. Once the ICA was resected and reinserted, accounting for 5.6 % of vascular surgical interventions executed. (Table 17)

Table 17: Distribution of vascular surgical interventions

		Absolute frequency	Relative frequency [%]
Total of 18 vascular surgical interventions	Ligation ECA	13	72.2 %
	Ligations STA	4	22.2 %
	Resection and reinsertion ICA	1	5.6 %
	Saphenous interposition ICA	0	0 %
	Ligation CCA	0	0 %

9.6 Injuries of cranial nerves and branches

The cranial nerve injuries were evaluated after 48 CBT resections.

9.6.1 Glossopharyngeal nerve (CN IX)

The glossopharyngeal nerve was not injured in 48 CBT resections.

9.6.2 Vagal nerve (CN X)

The vagal nerve was injured 5 times. (Table 18)

Table 18: Assessment of vagal nerve injuries

		Absolute frequency	Relative frequency [%]
CN X	intact	43	89.6 %
	injured	5	10.4 %

9.6.3 Hypoglossal nerve (CN XII)

The hypoglossal nerve (CN XII) was injured 7 times. (Table 19)

Table 19: Assessment of hypoglossal nerve injury

		Absolute frequency	Relative frequency [%]
CN XII	intact	41	85.4 %
	injured	7	14.6 %

9.6.4 Superior laryngeal nerve (SLN)

The superior laryngeal nerve was injured during 1 CBT. (Table 20)

Table 20: Assessment of superior laryngeal nerve injury

		Absolute frequency	Relative frequency [%]
Superior laryngeal nerve	intact	47	97.9%
	injured	1	2.1 %

9.6.5 Recurrent laryngeal nerve (RLN)

The recurrent laryngeal nerve was injured 3 times. (Table 21)

Table 21: Assessment of recurrent laryngeal nerve injury

		Absolute frequency	Relative frequency [%]
Recurrent laryngeal nerve	intact	45	93.8 %
	injured	3	6.2 %

9.6.6 Summary of injuries to cranial nerves and branches

Among 48 CBT resections there was a total of 16 CN injuries, which occurred during 10 CBT resections. On average there were 0.33 CN injuries per surgery. If a CN was injured, there were on average 1.6 CN injuries. (Table 22)
The hypoglossal nerve (CN XII) was the most frequently injured CN. The second most frequent injured CN was the vagal nerve (CN X). The recurrent laryngeal nerve (RLN) was the third most frequent damaged. Followed by superior laryngeal nerve and the glossopharyngeal nerve (CN IX).
Combined injuries to CNs and branches occurred in 4 cases, in 2 cases there were 3 CN injuries in each case, specifically CN X, CN XII and RLN. In the other 2 cases a combination of 2 CN injuries happened, namely CN X and CN XII.

Table 22: Assessment of CBT resections with CN injury

		Absolute frequency	Relative frequency [%]
CBT resections with CN injury	CN intact	38	79.2 %
	CN injured	10	20.8 %

Table 23: Distribution of CN injuries

		Absolute frequency	Relative frequency [%]
	Hypoglossal nerve (CN XII)	7	43.8 %
	Vagal nerve (CN X)	5	31.3 %
	Recurrent laryngeal nerve	3	18.8 %
	Superior laryngeal nerve	1	6.3 %
	Glossopharyngeal nerve	0	0 %
	Total	16	100 %

9.7 Univariate logistic regression analysis

9.7.1 Physical Properties

9.7.1.1 Gender

There is no significant correlation between gender and CN injuries. (p= 0.616)

9.7.1.2 Age

Twenty-one CBTs were resected in patients younger than 55 years,14 without CN injury, and seven CBT resections were associated with CN injury which amounts to a relative frequency of 33.3%. Twenty-seven CBTs were resected in patients older than 55 years. These include 24 CBT resections without CN injury (88.9%) and three CBT resections with CN injury (11.1%). Table 24 demonstrates, that in this study younger people were more likely to suffer from CN injury after CBT resection. Using age as continuous variable, a significant correlation between age and CN injuries (p=0.034) could be proven. Calculating with age groups (threshold 55 years) did not reveal a significant difference (Fisher's exact test, p=0.081).

Table 24: Evaluation of the correlation between CN injuries and age

			CN injury		
			no	yes	total
Age	<55	count	14	7	21
		% of people younger than 55 Y	66.7%	33.3%	100.0%
	>55	count	24	3	27
		% of people older than 55 Y	88.9%	11.1%	100.0%
		count	38	10	48
		Distribution of CN injuries [%]	79.2%	20.8%	100.0%

9.7.1.3 Height

There is no significant correlation between height and CN injuries. (p=0.358)

9.7.1.4 Weight

There is a significant correlation between weight and CN injuries (p= 0.046). Table 25 demonstrates that people who weigh more than 73 kg have approximately 2.5 times higher risk of suffering a CN injury (30.4%) compared to people who weigh less than 73 kg (12.0%).

Table 25: Evaluation of the correlation between CN injuries and weight

			CN injury		
			no	yes	total
Weight	<=73	count	22	3	25
		% of people weighing less than 73 kg	88.0%	12.0%	100.0%
	>73	count	16	7	23
		% of people weighing more than 73 kg	69.6 %	30.4%	100.0%
		count	38	10	48
		Distribution of CN injuries [%]	79,2%	20,8%	100,0%

9.7.1.5 BMI

There is no significant correlation between BMI and CN injuries (p=0.095).

9.7.2 Tumor characteristics

9.7.2.1 DTBOS

There is a significant correlation between DTBOS and CN injuries (p=0.009) Table 26 shows that the smaller the DTBOS the higher the risk of a CN injury.

Table 26:Evaluation of DTBOS categories regarding CN injuries

DTBOS	Absolute Frequency	Relative Frequency [%]	CN injuries	CN injuries [%]
DTBOS <=10	2	4.2	2	100
10<DTBOS<=20	0	0	0	0
20< DTBOS <= 30	1	2.1	1	100
30< DTBOS <= 40	13	27.1	4	30.8
40< DTBOS <= 50	18	37.5	2	11.1
50< DTBOS <= 60	13	27.1	1	7.7
60< DTBOS <= 70	1	2.1	0	0
Total	48	100	10	20.8

9.7.2.2 Shamblin Classification

There is no significant correlation between Shamblin Classification and CN injuries. (p=0.251) After Shamblin 1 CBT resection, in 8.3% of the surgeries a CN injury occurred. A rate of 16.7% of Shamblin 2 CBTs were resected with CN injury. In 33.3% of the Shamblin 3 CBT resection a CN was damaged. (Table 27)
Table 27 reveals that the higher the shamblin score (ranges from 1 to 3), the higher the risk is that a cranial nerve injury occurs during surgery.

Table 27: Evaluation of Shamblin Score and cranial nerve injuries

			Cranial nerve injury	
			no	yes
Shamblin Score	1	quantity	11	1
		Relative frequency [%]	91.7%	8.3%
	2	quantity	15	3
		Relative frequency [%]	83.3%	16.7%
	3	quantity	12	6
		Relative frequency [%]	66,7%	33,3%

9.7.2.3 Tumor Diameter

9.7.2.3.1 Craniocaudal

The craniocaudal diameter showed a significant correlation between CN injury and craniocaudal tumor diameter (p=0.027). Table 28 demonstrates that the size of the craniocaudal diameter is important for the risk assessment of CN injuries, i.e., if the craniocaudal diameter is larger than 30 mm the risk of a CN injury is more than doubled.

Table 28: Evaluation of CN injuries and craniocaudal diameter

			CN injury		
			no	yes	total
Craniocaudal diameter	<=30	count	21	3	24
		% of CBTs <=30 mm	87.5%	12.5%	100.0%
	>30	count	17	7	24
		% of CBTs >30 mm	70.8%	29.2%	100.0%
		count	38	10	48
		Distribution of CN injuries [%]	79.2%	20.8%	100.0%

9.7.2.3.2 Transversal

There was no significant correlation between transversal tumor diameter and CN injury (p=0.083).

9.7.2.3.3 Sagittal

There was no significant correlation between transversal tumor diameter and CN injury (p=0.055).

9.7.2.4 Volume

There is a significant correlation between CN injury and tumor volume ($p=0.036$). Table 29 indicates that patients with CBTs with a volume of more 7500 mm³ have approximately a 2.4 times higher risk of suffering a CN injury.

Table 29: Evaluation of CN injuries and volume

			CN injury		
			no	yes	total
Volume	<=7500	count	21	3	24
		% of CBTs <= 7500 mm³	87.5%	12.5%	100.0%
	>7500	count	17	7	24
		% of CBts >7500 mm³	70.8%	29.2%	100.0%
		count	38	10	48
		Distribution of CN injuries [%]	79.2%	20.8%	100.0%

9.7.3 Surgical aspects

9.7.3.1 Laterality

There is no significant correlation between laterality and CN injuries. (p=0.678)

9.7.3.2 Preoperative embolization

Thirty-nine cases did not undergo preoperative embolization. In 15.4% of the surgical interventions a CN injury occurred.
Nine tumors were preoperatively embolized. In 44.4% of the cases a cranial nerve injury occurred. After preoperative embolization the risk of a CN injury is almost 3 times higher than without, but not significant (p=0.065, Fisher's exact test).

Table 30: Correlation between preoperative embolization and CN injuries

			CN injury		
			no	yes	total
Preoperative embolization	no	Absolute frequency	33	6	39
		Relative frequency	84.6%	15.4%	100,0%
	yes	Absolute frequency	5	4	9
		Relative frequency	55.6%	44.4%	100,0%
total		Absolute frequency	38	10	48
		Distribution of CN injuries [%]	79,2%	20,8%	100,0%

9.8 Multivariate logistic regression analysis

9.8.1 DTBOS, craniocaudal diameter and tumor volume

Table 31 clarifies that out of these three univariately significant variables, only DTBOS (p=0.046) is significant in a multivariate analysis. In other words, craniocaudal diameter (p=0.987) and tumor volume (p=0.989) lose their statistical significance and only DTBOS stays statistically significant. (Table 31)

Table 31: Multivariate analysis of DTBOS, craniocaudal diameter and tumor volume

DTBOS	0.046
Craniocaudal diameter	0.987
Tumor volume	0.989

9.8.2 DTBOS and age

Age also showed statistical correlation with CN injuries. After multivariate analysis with DTBOS age (p=0.080) lost its significance and DTBOS (p= 0.017) remains statistically significant. (Table 32)

Table 32: Multivariate analysis of DTBOS and age

DTBOS	0.017
age	0.080

9.8.3 DTBOS and weight

In a multivariate regression analysis including DTBOS and weight, weight (p= 0.405) lost its statistical significance and DTBOS (p=0.033) remained significant. (Table 33)

Table 33: Multivariate analysis of DTBOS and weight

DTBOS	0.033
weight	0.405

10 DISCUSSION

Head and neck paragangliomas are rare tumors. (1,2) As few centers have experience with these entities, objective identification of parameters to predict complicated treatment is necessary to centralize treatment for high-risk patients and improve the single patients' safety.

The main aim of this diploma thesis was to find out whether the predictive value of DTBOS regarding perioperative surgical complications is superior compared to the Shamblin classification. The perioperative surgical complications especially refer to cranial nerve injuries. A further concern of this diploma thesis was to find other possibly influential parameters.

An exact p-value calculation regarding the influence of parameters, such as physical properties, tumor characteristics and surgical aspects, on CN injuries was implemented in this analysis. Nonetheless, the parameters DTBOS, tumor volume, craniocaudal tumor diameter and weight were found to be univariately significant.

DTBOS was described in 2017 by Kim et al. (8) It has not been validated yet in the literature.

Of our patients 67.4% (29/43) were female. In the study of Kim et al. (8) 72% (257/356) of their patients were female. Reith et al. (10) described a female prevalence of about 75%. These gender distributions are very well comparable with our rate of female patients.

In our data 20.8% (10/48) CBT resections were associated with CN injury, whereas in Kim et al.' study during 24.4 % (87/356) of CBT resections a CN injury occurred. Table 34 compares the distribution of CN injuries between our study and Kim et al.'s study.

Table 34: Comparison of injuries to CNs and branches between our study and Kim et al.'s study

Injuries to CNs and branches	Our Study (%)	Kim et al.'s study (%)
CN VII (facial nerve)	-	7.6% (10/132)
CN IX (glossopharyngeal nerve)	0 % (0/16)	9.1% (12/132)
CN X (vagal nerve)	31.3% (5/16)	29.5% (39/132)
SLN (superior laryngeal nerve)	6.3% (1/16)	14.4% (19/132)
RLN (recurrent laryngeal nerve)	18.8% (3/16)	2.3% (3/132)
CN XI (accessory nerve)	-	3% (4/132)
CN XII (hypoglossal nerve)	43.8% (7/16)	26.5% (35/132)

Body weight marked statistical significance in the univariate analysis ($p = 0.046$). Nevertheless, there was no other study to be found that analyzed the significance of the weight.

The univariate analysis revealed that DTBOS had a statistical significance of $p=0.009$. Kim et al. (8) additionally stated that the smaller the distance between the highest point of the tumor and the base of skull, the higher is the chance of a cranial nerve injury. This diploma thesis describes that DTBOS presents a statistic significance in relation to cranial nerve injuries. Our study did not confirm the 151 % increase in risk of a CN injury per 1 cm decrease in DTBOS.

Table 35 compares two categories of DTBOS and it depicts the nearly 3-fold increase in risk between these categories. (Table 35)

Table 35: Comparison of two DTBOS categories

DTBOS		Absolute Frequency	Relative Frequency [%]	CN injuries	CN injuries [%]
	30< DTBOS <= 40	13	27.1	4	30.8
	40< DTBOS <= 50	18	37.5	2	11.1

The tumor volume also showed a statistical significance (p=0.036), which was not reported by other studies, as it was never investigated as a risk factor in relation to CN injuries. The only additional information related to this was by Kim et al (8), namely the higher loss of blood that is to be expected if the volume of tumor increases.

Additionally, our study revealed that the tumor's craniocaudal diameter exhibits a statistical significance of p=0.027, which was also not underpinned by another study, as it was not a topic for analysis.

In the multivariate analysis of the three tumor specific parameters (DTBOS, volume of tumor and craniocaudal diameter), it was revealed that solely DTBOS (p=0.046) remained significant. In opposition to DTBOS, the craniocaudal diameter (p=0.987) as well as the volume of tumor (p=0.989) lost their significance in the multivariate analysis. As of today, there are no other studies, which have multivariately analyzed DTBOS in relation to other parameters.

To the present day, the Shamblin classification is still valid and being used to provide an overview of how difficult or easy a carotid body tumor is to remove. (7)

As this method is contemporary, Kim's study recommends the application of DTBOS, Shamblin classification and volume of tumor, as through this combination of these three parameters a risk of injuring the CN or bleeding is better predictable. (8)

In our study the following relevant medical parameters were investigated: physical properties, tumor specific parameters, surgical aspects, cranial nerve injuries as well as information about vascular surgical interventions.

The focus of this study mainly aimed at injuries of the CNs and their branches, whereas Kim et al. (8) have documented in greater detail the estimated blood loss in combination with CN injuries. Moreover, this study also focuses on the needed vascular surgical interventions. The overall positive aspects of Kim's et al. (8) study was their amount of data. They worked with the information of 332 patients affected by 356 CBTs and treated at 16 different medical institutions over the period from 2004 to 2014. As of tumor parameters, they were measured by the means of medical imaging such as MRT or CT. In addition to this, Kim's et al. (8) study also made use of ultrasound imaging. The negative acknowledgement of ultrasound imaging is the

fact that the tumor diameter is measured only in a two-dimensional way. Subsequently, Kim et al. (8) assumed that the sagittal diameter corresponded to the transversal diameter, which was true for our data as well ($r=0.861$, $p<0.001$). Nevertheless, we decided to measure all three original diameters and use them for regression analysis.
It is to mention, that in my study, a non-existing imaging such as CT or MRT was criteria for excluding the case from the analysis.
Given that DTBOS remained significant after the conduction of a multivariate analysis, the other univariately significant parameters (weight, craniocaudal diameter and volume of tumor) are negligible predictors for cranial nerve injuries. The results of this study facilitate the information access for patients as surgeons easily reach a good expressiveness of CN injuries by measuring the DTBOS parameter. Thus, surgeons are able to explain the affected person their individual risks after a few easy measuring steps. A further step is the implementation of the data by the departments of vascular surgery, for a better preoperative patient counselling.

The comparative study came to the result that DTBOS and volume of tumor add information to the Shamblin classification in the best way and more than that, the combination of all three parameters positively complete the pre-medical analysis. (2.) Through the study, the conclusion was made that DTBOS was also in fact a predictor for perioperative surgical complications as injuries and bleedings. (8)

DTBOS is clearly a valid predictor that should be implemented in all cases affected by this medical procedure, namely the Carotid body tumor resections. It can increase individual patients' safety by identification of high-risk surgery, and supports the decision for patients in highly specialized centers. One must point out that the number of cases for this study was limited as CBTs are a rare medical entity. Another limitation was that we did not differentiate whether the CN injury was temporary or permanent while Kim et al. (8) categorized the CN injuries in temporary and permanent CN injuries. Nonetheless, our results can reinforce those of Kim's et al. (8) study, as they had 356 CBTs involved and thus serving as a credible analysis base. Upon completion of the predictors implementation and several years have passed, a validity study upon this topic can be conducted. Furthermore, the option of studying DTBOS in connection to other cohorts is available.

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12 TITLES

Long English title

Distance to the Base of Skull (DTBOS): Significance of the new predictor of perioperative surgical complications of carotid body resections- a retrospective analysis

Short English title

DTBOS

Langer deutscher Titel

Distance to the Base of Skull: Bedeutung des neuen Prädiktors bezüglich perioperativer chirurgischer Komplikationen bei Carotisglomustumorresektionen- eine retrospektive Analyse

Kurzer deutscher Titel

DTBOS

13 APPENDIX

13.1 CRF

Distance to the Base of Skull (DTBOS): Significance of the new predictor of perioperative surgical complications of carotid body resections -a retrospective analysis

Patient: **Geburtsdatum:** **ID** (fortlaufende Nummer)**:**

Geschlecht: O männlich O weiblich **Größe:** **Gewicht:**

Telefonnummer: **Aufklärungsdatum:**

Datum der Operation: **Operateur:**

Karotisgabeltumor: **Seite:** O rechts O links

Tumordurchmesser (mm)	
Shamblin Klassifikation	
DTBOS	
SDH-Mutation	

Contralateral voroperiert:

O ja O nein

Blutverlust (ml):

Operationsdauer (min):

Sonstige Komplikationen:

Nervenläsion:

N. Glossopharyngeus (IX)	
N. Vagus (X)	
N. Hypoglossus (XII)	
N. laryngeus superior	
N. laryngeus reccurens	

Gefäßchirurgische Eingriffe:

Resektion und Reinsertion ACI	
Saphenainterponat	
Ligatur ACC	
Ligatur ATS	
Ligatur ACE	
Präoperative Embolisation	
Erfolg der Embolisation	

Abkürzungen:

ACI- Arteria carotis interna, **ACC**- Arteria carotis communis

ATS- Arteria thyroidea superior, **ACE**- Arteria carotis externa

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13.2 Ethics Committee approval

Medizinische Universität Graz
Ethikkommission

Auenbruggerplatz 2, A-8036 Graz
ethikkommission@medunigraz.at
Tel.: +43 / 316 / 385-13928, Fax: -14348

VOTUM

gültig bis 15.04.2021

EK-Nummer:	32-247 ex 19/20
Studientitel:	Distance to the Base of Skull (DTBOS): Significance of the new predictor of perioperative surgical complications of carotid body resections- a retrospective analysis
Prüfer:	PD Dr. Peter Konstantiniuk MUG
Sponsor:	Medizinische Universität Graz, Klinische Abteilung für Gefäßchirurgie
Ansprechpartner:	PD Dr. Peter Konstantiniuk, 8036 Graz, Auenbruggerplatz 29
CRO:	-
Antragsteller:	MUG
Ansprechpartner:	Filip Ivanjko

Die o.a. Studie wurde von der Ethikkommission erstmals im 'expedited Review' am 24.02.2020 behandelt. Die Ethikkommission ist zu folgendem Schluss gekommen:

Es besteht kein Einwand gegen die Durchführung der Studie in der vorliegenden Form.

Kommissionsmitglieder, die für diesen Tagesordnungspunkt als befangen anzusehen waren und daher gemäß Geschäftsordnung an der Entscheidungsfindung und Abstimmung nicht teilgenommen haben: keine

Zur Beurteilung vorliegende Dokumente:

Dokumente eingegangen am 06.02.2020, begutachtet im 'expedited Review' am 24.02.2020

✓ Antragsformular ECS	06.02.2020
Originalprotokoll Studienprotokoll-DTBOS-Version 01-2020 02 04 01	04.02.2020
Case Report Form CRF-DTBOS-VERSION 01-2020 02 02 01	02.02.2020

Dokumente eingegangen am 09.03.2020 (in der nächsten Begutachtung mitbegutachtet)

✓ Antragsformular ECS Unterschriftenseiten	06.03.2020

Dokumente eingegangen am 02.04.2020, begutachtet im 'expedited Review' am 15.04.2020

✓ Originalprotokoll 02-2020 03 09	
✓ Case Report Form 02-2020 03 09	
✓ Sonstiges: E-Mail: Stellungnahme zur Bearbeitungsmitteilung	02.04.2020
✓ Letter of Authorization	27.03.2020

Die Ethikkommission geht - rechtlich unverbindlich - davon aus, dass es sich um keine klinische Prüfung nach AMG bzw. MPG handelt.

Es handelt sich um eine Studie im Rahmen einer Diplomarbeit.

Das Votum der Ethikkommission berührt in keiner Weise die alleinige Verantwortung der Prüferin / des Prüfers / der Prüfer für die ordnungsgemäße Durchführung der Studie unter Einhaltung aller einschlägiger gesetzlicher Bestimmungen und Richtlinien.

Weiters machen wir darauf aufmerksam, dass der Kommission unverzüglich zu melden sind:

Medizinische Universität Graz, Auenbruggerplatz 2, A-8036 Graz. www.medunigraz.at
Rechtsform: Juristische Person öffentlichen Rechts gem. UG 2002, Information: Mitteilungsblatt der Universität. UID: ATU 575 111 79. Bankverbindung: Raiffeisen Landesbank Steiermark IBAN: AT443800000000049510, BIC: RZSTAT2G

- Abweichungen vom Protokoll aus Sicherheitsgründen oder Protokolländerungen

- Änderungen, die das Risiko der Teilnehmer/-innen erhöhen oder die Durchführung der Studie wesentlich beeinflussen

- Mutmaßliche unerwartete schwerwiegende Nebenwirkungen - SUSARs (AMG-Studien ab 1.5.2004) oder schwerwiegende unerwünschte Ereignisse - SAEs (andere Studien)

- Jegliche Information über sonstige Umstände, die die Sicherheit der Teilnehmer/-innen oder die Durchführung der Studie beeinträchtigen können

zusätzliche Auflagen: Die behördlich vorgeschriebenen Maßnahmen hinsichtlich der COVID-19 Pandemie müssen beachtet werden. Der Prüfer und der Sponsor müssen in ihrem jeweiligen Wirkungskreis unter allfälliger Beachtung von Leitlinien gewährleisten, dass keine zur Bekämpfung der Pandemie benötigten Ressourcen gebunden werden bzw. ausreichend Personal vorhanden ist und die TeilnehmerInnen durch ihre Studienteilnahme keiner zusätzlichen Infektionsgefahr ausgesetzt werden.

Dieses Votum gilt für ein Jahr ab dem Datum der Ausstellung. Bei längerer Studiendauer ist rechtzeitig vor Ablauf der Gültigkeit des Votums ein Zwischenbericht vorzulegen (Berichtsformular), um eine etwaige Verlängerung zu erlangen.

Graz, 15. April 2020

Univ.Prof.DI Dr.Josef Haas
Vorsitzender

Univ.Prof.Dr.Hans Dimai
Stv. Vorsitzender

Achtung: Bitte bei allen das Projekt betreffende Schreiben oder telefonischen Anfragen die EK-Nummer angeben!

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Rechtsform: Juristische Person öffentlichen Rechts gem. UG 2002, Information: Mitteilungsblatt der Universität UID: ATU 576 111 79, Bankverbindung: Raiffeisen Landesbank Steiermark IBAN: AT443800000000049510, BIC: RZSTAT2G