# Inter- and intra-patient variability of facial nerve response areas in the floor of the 4th ventricle

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Abstract: BACKGROUND: Surgical exposure of intrinsic brainstem lesions through the floor of the 4 ventricle requires precise identification of facial nerve (CN VII) fibers to avoid damage. OBJECTIVE: To assess the shape, size, and variability of the area where the facial nerve can be stimulated electrophysiologically on the surface of the rhomboid fossa. METHODS: Over a period of 18 months, 20 patients were operated on for various brainstem and/or cerebellar lesions. Facial nerve fibers were stimulated to yield compound muscle action potentials (CMAP) in the target muscles. Using the sites of CMAP yield a detailed functional map of the rhomboid fossa was constructed for each patient. RESULTS: Lesions resected included 14 gliomas, 5 cavernomas, and 1 epidermoid cyst. Of 40 response areas mapped, 19 reached the median sulcus. The distance from the obex to the caudal border of the response area ranged from 8-27 mm (median 17 mm). The rostrocaudal length of the response area ranged from 2-15 mm (median 5 mm). CONCLUSION: Facial nerve response areas showed large variability in size and position, even in patients with significant distance between the facial colliculus and underlying pathological lesion. Lesions located close to the facial colliculus markedly distorted the response area. This is the first documentation of variability in CN VII response area in the rhomboid fossa. Knowledge of this remarkable variability may facilitate the assessment of safe entry zones to the brainstem and may contribute to improved outcome following neurosurgical interventions within this sensitive area of the brain.

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**Title:**

# Inter- and intra-patient variability of facial nerve response areas in the floor of the 4th ventricle.

**Running Title:** Spatial variability of CN VII in rhomboid fossa

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**Keywords:** Brainstem mapping; CN VII; rhomboid fossa; facial colliculus

**Abbreviations:** CN cranial nerve; BSM brainstem mapping; RA CN VII response area; EMG Electromyogram; CMAP compound muscle action potential.

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**Abstract**

**Introduction:** Surgical exposure of intrinsic brainstem lesions through the floor of the 4th ventricle requires precise identification of facial nerve (CN VII) fibers to avoid damage. Shape, size and variability of the area where the facial nerve can be stimulated electrophysiologically on the surface of the rhomboid fossa have not yet been systematically assessed.

**Methods:** Over a period of 18 months, 20 patients were operated on for various brainstem and/or cerebellar lesions. Facial nerve fibers were stimulated to yield compound muscle action potentials (CMAP) in the target muscles. Using the sites of CMAP yield a detailed functional map of the rhomboid fossa was constructed for each patient.

**Results:** Lesions resected were 14 gliomas, 5 cavernomas, and 1 epidermoid cyst. Of 40 response areas mapped, 19 reached the median sulcus. Over all patients, the distance from the obex to the caudal border of the response area ranged 8-27 mm (median 17 mm). The rostrocaudal length of the response area ranged 2-15 mm (median 5 mm).

**Conclusions:** Facial nerve response areas showed large variability in size and position even in patients with significant distance between facial colliculus and underlying pathological lesion. Lesions located close to the facial colliculus markedly distorted the response area. This is the first documentation of variability in CN VII response area in the rhomboid fossa. Knowledge of this remarkable variability may facilitate the assessment of safe entry zones to the brainstem and may contribute to improved outcome following neurosurgical interventions within this sensitive area of the brain.

## INTRODUCTION

Due to the complex and dense anatomy of the brainstem, surgery of brainstem lesions constitutes a challenge for the neurosurgeon and the operating team. Most of the dorsally located pontine and pontomedullary lesions can best be approached via the floor of the 4th ventricle, anatomically also referred to as “rhomboid fossa”. While performing such procedures, one has to bear in mind that intrinsic fibers of the facial nerve (CN VII) form a loop that virtually reaches the surface of the rhomboid fossa at the facial colliculus. Two safe entry zones that spare the facial nerve fibers have been proposed to expose intraaxial brainstem lesions, one rostral and one caudal to the CN VII fiber area.[1-5] Among the brainstem structures with various functions that are under permanent risk of being damaged by surgical manipulation, the facial nerve fibers play a key role for at least two reasons. One is their central location within the rhomboid fossa rendering them particularly vulnerable; the other is the fact that these fibers can relatively easily and precisely be assessed by direct electric stimulation during surgery. To avoid unintended and, in worst case, permanent loss of facial nerve function, exact knowledge of the location of the facial colliculus is indispensable in each individual patient. While magnetic resonance imaging (MRI) provides valuable information on the exact location and extent of the brainstem lesion, electrophysiological brainstem mapping (BSM) provides the functional identification of certain structures such as cranial nerve nuclei and facial nerve fibers on the surface of the brainstem.[1-3, 6] According to the available literature including anatomical textbooks,[7] one might expect that the facial colliculus is rather a symmetrical and homogeneous anatomical area within the rhomboid fossa. The exact intra- and inter-individual variability, as well as the size, shape and location of

the electrophysiological CN VII response area (RA) in the rhomboid fossa have not yet been systematically studied.

The goal of this clinical investigation was, therefore, to exactly assess these parameters in patients who underwent surgery via the rhomboid fossa or in whom the rhomboid fossa had to be widely exposed.

## PATIENTS AND METHODS

### Patient population

We included 20 individuals who underwent surgery by the senior author (H.B.) during an 18-month period (2008-2009) for removal of a brainstem or cerebellar lesion that required BSM of the rhomboid fossa to ensure intraoperative control of the facial colliculus. This study was carried out in accordance with the guidelines of Good Clinical Practice and Swiss regulatory authorities' requirements. Patients were included only with their written informed consent. The study was approved by the independent Ethics Committee of the Kanton Zürich (Projekt E-55/2008). We excluded those patients in which BSM was impossible due to local hemorrhage or in which the lesion had significantly compromised identification of the most important anatomical landmarks of the rhomboid fossa used in this study. Clinical status of CN VII function was assessed with the House-Brackmann Scale (I: normal function; VI: complete loss of function).

### Anesthesia

Following the standard protocol for neurosurgical interventions, anesthesia was induced with intravenous application of the sedative drug Propofol (4 to 8 mg/kg/min), the opioid analgesic Remifentanil (1 - 2 µg/kg/min) and the skeletal muscle relaxant Atracurium (0.5 mg/kg). After intubation, the neuromuscular blocking

drug, Atracurium, was omitted because of its interference with electrophysiological monitoring and mapping.

**Intraoperative neurophysiological monitoring**

Following our standard protocol for neurosurgical interventions affecting the brainstem,[8] we recorded motor evoked potentials (MEP) to monitor the pyramidal tract,[9] somatosensory evoked potentials (SEP) to monitor the medial lemniscus pathway, and auditory evoked potentials (AEP) to monitor mechanical pressure on brainstem nuclei in general.[10]

**Placement of recording electrodes for BSM**

Bipolar electrodes (Xomed, Paired EMG Electrodes, 18 mm) were inserted into M. rectus lateralis for CN VI (N. abducens), and M. orbicularis oculi, M. nasalis and M. orbicularis **oris** for CN VII (N. facialis) to record the bilateral facial muscle electromyogram (EMG).

The CN VI and CN VII were chosen for the following reasons; 1) their close proximity to the dorsal surface of the brainstem makes them susceptible to injury by the surgical approach; 2) these CN are clinically most important for facial and optomotoric functions; 3) the selectivity of the response can be documented; 4) assessment of the response areas allows for selecting so-called “safe entry zones” to the brainstem.[3-5, 11]

**Surgical approach**

All lesions were removed via a median suboccipital craniotomy with the patient placed either in the sitting or in the prone concord position. The craniotomy extended from the transverse sinus superiorly to the foramen magnum. Depending on the size

and the caudal extension of the lesion, a C1 laminectomy was added. To expose the floor of the fourth ventricle and both lateral recesses, the telovelar or trans cerebello-medullary fissure dissection was used, taking care of the posterior inferior cerebellar artery and its branches.[12-13]

**Brainstem Mapping**

After exposing the rhomboid fossa, paper rulers with a millimeter scale were placed on its surface to establish a reference frame with respect to the obex and the median sulcus. The rulers had width of about 3 mm and a length up to 50 mm. One longitudinal ruler was placed adjacent to the median sulcus with its starting point at the obex to determine rostro-caudal distances. A second horizontal ruler was placed orthogonal to the median sulcus, usually rostral to the suspected facial colliculus area, to measure laterality.

Once that an optimal exposure of the floor or the fourth ventricle was obtained, brainstem nerve fibers and nuclei were stimulated using a monopolar stimulation electrode (Xomed, Standard Monopolar Stimulator Probe, tip width 0.58 mm) as cathode with an electrical reference placed on the ipsilateral shoulder. Monopolar constant current stimulation was used with pulse width 200 μs and stimulation frequency 3 Hz. The stimulation current was chosen at the minimum threshold capable of eliciting CMAP through CN VII, usually 0.05 mA, to minimize current spread. The same minimum current was applied at all stimulation sites in one patient. While this procedure was robust in eliciting CN VII responses, the intensity was too small to observe CN VI responses in all but very few stimulation sites.

During stimulation, EMG was transformed into an acoustic feedback to the surgeon, who constantly remained in contact with the neuromonitoring team. If

stimulation resulted in a compound muscle action potential (CMAP) in the EMG, this indicated the vicinity of facial nerve fibers or nuclei. Stimulation was performed on sites on a regular grid to determine the areas where CMAP as response to stimulation was positive and where CMAP response was negative. Stimulation was always performed sequentially first on one and then, after slightly displacing the longitudinal measurement ruler, on the contralateral side.

**Recording of CMAP and video**

After the reference frame was established by the rulers, video frames were captured from the surgery microscope (Pentero, Zeiss, Germany), which provides a pixel resolution of 96 dpi. During stimulation, both EMG and simultaneous frame-grabbing from the video of the microscope were recorded using the ISIS&OSIRIS Intra-Operative Monitoring system (Inomed, Germany).

**Data analysis**

After surgery, a video frame was selected for each region of the rhomboid fossa where CMAP had been elicited during stimulation. Using Adobe Photoshop and Adobe Illustrator, a coordinate frame was established on the basis of the paper rulers. Then, the sites of stimulation were marked in this coordinate frame and color-coded whether CMAP were elicited or not. In this way, the areas of CMAP response in the rhomboid fossa were constructed for each patient in detail. Finally, CN VII response areas (RA) were depicted in a schematic map with respect to obex and median sulcus (**Figure 1**).

To characterize RA, we first determined the distances of the medial limit of RA to the median sulcus (Lx) and the distance of the caudal limit to obex (Ly). We then measured the mediolateral extent of RA (Ex) and the rostrocaudal extent (Ey).

Furthermore, a centroid C of RA was documented by reading out the coordinates Cx and Cy of the centroid for irregular shapes given by Adobe Illustrator. We choose this approach because it is independent of observer bias and reasonably precise within our measurement accuracy.

## RESULTS

The lesion type and location as well as WHO grade are presented for all patients (N = 20, 9 female, age 33 ± 19 y, median 29 y, range [6-66] y) in **Table 1** together with the clinical assessment of pre- and postoperative CN VII function.

### Response area in illustrative patients

The lesion of Patient 12 is illustrated in-video frames taken during (**Figure 2**). On **Panels A and B the** vertical ruler is parallel to the median sulcus. A coordinate frame on the left half of the rhomboid fossa was established by the rulers (**Figure 2A)**. Then stimulation was applied to elicit CMAP responses in the target muscles of CN VII. Red marks on the video frame indicate where stimulation elicited CMAP and black circles denote stimulation sites, where no CMAP could be elicited. Analogously, **Figure 3** shows the lesions of patient-16.

We defined the limits of the left RA (**Figure 2A**) on a schematic map (**Figure 1**) to contain all red marks, i.e. responsive stimulation sites. The caudal limit of RA was found at Ly = 20 mm from obex. The rostrocaudal extend of RA was Ey = 6 mm. The medial limit of RA was Lx = 1 mm from the medial sulcus and the mediolateral extent Ex = 5 mm. The centroid of the RA had the coordinates Cx = 3.4 mm and Cy = 22.8 mm. Analogously, the values were determined in the right part of the rhomboid fossa (Lx = 0, Ly = 22, Ex = 3, Ey = 4, Cx = 1.8, Cy = 24.2). Left and right RA are shown in **Figure 2C**. To quantify the asymmetry between left and right RA, we calculated the

ratio REy between left and right rostrocaudal extent Ey. For easier comparison over patients, the larger length is always divided by the smaller value so that the ratio is larger than 1. For this patient, the length of the right response area exceeds the length of the left response area by 50%, so that 1.5 in patient 12 is the index for the asymmetry. Analogously, we determined the mediolateral extent Ex and the ratio REx. Values for all patients are listed in Table 2.

**All response areas of all patients**

In all patients the CN VII fibers could be identified. Electrical stimulation of facial nerve fibers was followed by CMAP responses of the ipsilateral facial muscles. The CMAP responses were limited to the side and site of stimulation. Due to the vicinity of the CN VI nucleus, in some cases also responses of the lateral rectus muscle were obtained.

**Grouping of patients**

To structure the large variability of CN VII response areas, patients were divided in to three groups:

Group1: Rhomboid fossa not directly involved by the lesion (N = 5).

Group2: Rhomboid fossa involved, lesion remote from RA (N = 10).

Group3: Rhomboid fossa involved at the level of RA (N = 5).

To compare RA over the patient groups, the maps for all patients were overlaid in composite drawings (**Figure 4**). In this figure, RA were aligned with respect to their individual size and rostrocaudal distance from the obex and the mediolateral distance with respect to the median sulcus. The panels A, B, and C of **Figure 4** show composite schematic maps for the three groups of patients. Each patient is color

coded and numbered. Dotted lines represent the border of the pathologic lesion when applicable (Group2 and Group3). Dashed lines depict the entry to the lesion as chosen by the surgeon. To focus more on the location of the response areas than their extent, the position of the centroids is shown in **Figure 5**. Here it becomes evident that in Group1 left and right centroids are at the same rostrocaudal height in a range between 14-23 mm from obex. In Group2, left and right centroids still are at the same rostrocaudal height, but the range is much larger. Finally, in Group3 the rostrocaudal height clearly differs between left and right centroids.

**Table 2** lists rostrocaudal and mediolateral dimensions of the rhomboid fossa and the RA for each side of each patient. There is a large variability in left and right Ly, the distances from the caudal limit of the response area to the obex. In the description of the range and the median of the lengths, left and right measurements were pooled. Range and median of lengths are illustrated for the three groups in the three panels of **Figures 4** and **5**. To capture the asymmetry between extensions Ex and Ey of left and right CN VII response areas, we computed REx and REy, the ratios between left and right Ex and Ey. The largest asymmetry appeared in Group3.

## DISCUSSION

### Brainstem anatomy

The topographical relationships between the location of cranial motor nuclei and anatomical landmarks of the rhomboid fossa have been investigated in regular brains post mortem by several authors.[4, 14-17] In a study based on 40 brainstems of patients who died of non-brain diseases, Bogucki et al.[15] investigated the visibility of the different landmarks. The obex and the median sulcus were well identifiable in all specimens, but the facial colliculus was only poorly visible in 38% and the medullary striae were even invisible in 30% of the analyzed brainstems.[15] The high variability of these structures renders them unreliable as landmarks for brainstem nuclei identification.

### Space-occupying lesions

The presence of brainstem lesions that distort the brainstem even increases the unreliability of anatomical landmarks.[1, 3, 18-20] Depending on the location of the tumor, motor nuclei of cranial nerves can be displaced in different directions.[20] The direction of the nuclei displacement can only be estimated; usually, upper pontine tumors displace them rather caudally and lower medullary tumors tend to displace them rostrally. However, it is impossible to define their exact location merely relying on anatomical landmarks of the rhomboid fossa.

### Brainstem mapping (BSM)

Modern technical tools such as MRI and BSM have remarkably contributed to enabling reasonably brainstem surgery by decreasing the risk of postoperative morbidity. BSM is an intraoperative neurophysiologic procedure that localizes and

identifies superficial and deep cranial motor nuclei and fibers in the rhomboid fossa. It was introduced in the early 1990s.[1, 3, 6] Strauss et al. investigated a series of 10 patients with intrinsic or adjacent brainstem lesions. They stimulated the facial colliculus and hypoglossal trigonum before entering the brainstem. They found selective EMG responses in 90% of the patients in the corresponding facial and tongue muscles. The results of their investigation led to an adaptation of the surgical approach in 33% of the patients with EMG responses. In the group of Morota and co-workers, BSM played a crucial role for tumor resection in 83% of patients.[19] The usefulness of BSM for determining safe entry zones to the brainstem was further emphasized in recent reports.[5, 11]

The importance of BSM is also quite obvious in pediatric patients suffering from brainstem tumors where the prognosis is directly related to the radicality of tumor resection.[21] An attempt of radical tumor resection, however, may increase postoperative morbidity due to damage of functional brainstem tissue. Considering that clear tumor demarcation is often lacking in brainstem gliomas, the decision making process with tendency either towards radicality or merely partial resection can be very difficult. Brainstem mapping helps to a certain degree solving this problem by allowing a more radical intrusion as long as no specific signs demand for an abruption.

Although it is difficult to assess the prognostic value of BSM, some studies have shown a high correlation between monitored intraoperative events and postoperative neurological deficits.[22-23] Glasker and colleagues investigated a series of 21 patients.[22-23] They found a high number of true positive (17 times) and true negative events (40 times) supporting the reliability of BSM in rhomboid fossa surgery.

**Variability of CN VII response areas in the present study**

According to our results, the variability of CN VII response areas falls into four categories:

1) Variability between patients in distance from obex Ly and Cy.

2) Variability between patients in distance from the median sulcus Lx and Cx.

3) Variability between patients in length of response area Ey.

4) Variability within patients between left and right response area in localization and extent.

**Variability between patients in distance from obex**

For the variability in Ly we found a range of 8-27 mm over the whole patient group. This can be compared to the range of 13.3-18.3 reported by Strauss et al.[4] and 11-18 mm reported by Lang et al.[14] in anatomical studies of healthy brainstems. Our finding of 8 mm in patient 16 can be explained by a lesion rostral to the response area. The maximal value of Cy = 30.4 mm occurred in patient 10, who had a lesion caudal to the response area. These explanations are in line with the illustrations of Morota et al.[20]

**Distance from the median sulcus and the stimulation method**

Of the 40 CN VII response areas, 21 touched the median sulcus while 19 had a distance Lx to the median sulcus of up to 3 mm. Patient 16 illustrates the limits of our 2-dimensional mapping procedure, because the lesion caused a 3-dimensional distortion of the rhomboid fossa (Figure 3E).

We can base an estimate for the spatial resolution of our mapping procedure on those findings where the CN VII response area extended to the median sulcus and the median sulcus was very shallow. Since the CN VII response area was found to

be lateral of the medial sulcus by more than 0.3 mm,[4] we can take 0.3 mm as a lower limit of the spatial resolution achieved by our mapping procedure.

The spatial resolution of the mapping depends mainly on the stimulation electrode and stimulation intensity. As current spreads away from the electrode, lower stimulation intensities lead to more accurate localization of the nerve. Therefore, the stimulation current was chosen at the minimum threshold capable of eliciting CMAP, usually 0.05 mA. This threshold is lower than the one reported by other authors,[5, 11] perhaps because our fine tip electrode produces higher electric fields than a wider electrode. From a theoretical point of view, stimulation with a bipolar probe would induce even less current spread and thus improve spatial resolution. In our experience, however, the wider tip of a bipolar stimulation probe and the higher stimulation current required for bipolar stimulation outweighed the advantages. Furthermore, in our study, monopolar stimulation seemed to be more robust in eliciting CMAP responses.

**Variability between patients in extent of response area**

For the variability in Ey we found a range of 2-9 mm in Group1, where the lesion did not directly involve the rhomboid fossa. The rostrocaudal length of the response areas showed a minimum of 2 mm in patient 4. This value is smaller than the 6 mm reported in the 6 specimens by Strauss et al.[4] This raises the general question of how CN VII response areas are related to anatomical CN VII fiber areas.

In our study we aim to delineate the anatomical extension of the CN VII fiber area by mapping the sites of functional CN VII response. To relate the extensions of the response area to the extensions of the fiber areas, the following considerations are of interest. CN VII fibers come as close as 0.2 mm to the ependyma during the ascending course of CN VII medial to the nucleus of CN VI and lateral to the median

sulcus.[4] Since the stimulation current was chosen at minimal intensity where CN VII responses could be elicited and since we observed CN VI responses only occasionally, we assume that our CN VII response area is restricted to the region of the most superficial fiber course.

Can the CN VII response area be smaller than the CN VII fiber area? If the response area is smaller than the fiber area, the fibers may run most superficially only in a restricted area, which is smaller than the area defined to be the facial colliculus by Strauss et al.[4] This possibility constitutes a qualitative difference between physiological response area and anatomical fiber area. This difference also has implication for the surgical approach, because the region of most superficial fiber course is of primary interest in order to reduce morbidity by the surgical procedure.

**Variability within patients between left and right response area**

As illustrated in **Figure 2**, a high variability may occur also between left and right response area in the same patient. The index REy in **Table 2** captures the asymmetry in rostrocaudal length of the response area. The observed large asymmetries are at variance with an anatomical study on healthy brainstems, which report a symmetric distribution of structures in the left and right rhomboid fossa.[15] This variability is most striking in patients of Group1 where the lesion did not distort the brainstem. In some patients of Group3 the asymmetry can be attributed to the proximity of the lesion, e.g. in patient 16, where the lesion has widened the CN VII fiber bundle in mediolateral direction (**Figure 3E)**.

## CONCLUSIONS

The facial nerve response area within the rhomboid fossa showed an unexpectedly high variability in size and position even in patients with significant distance between facial colliculus and underlying pathological lesion. Lesions located close to the facial colliculus markedly distorted the response area. For these reasons, brainstem mapping is strongly recommended for surgery involving the rhomboid fossa. This is the first documentation of variability in CN VII response area in the rhomboid fossa. Knowledge of such remarkable variability as found in this study may facilitate the assessment of safe entry zones to the brainstem and may contribute in the future to an improved outcome following neurosurgical interventions within this sensitive area of the brain.

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## Figure Legends

**Figure 1. Geometric definition of CN VII response area**. The CN VII response area for patient 12 (RA, green) is depicted schematically with respect to obex and median sulcus (vertical line). Given are the distances of the medial limit of RA to the median sulcus (Lx) the distance of the caudal limit to obex (Ly). The inset shows the mediolateral extent of RA (Ex) and the rostrocaudal extent (Ey). Furthermore, a centroid of RA was derived, whose coordinates are given as Cx and Cy.

**Figure 2. Lesion, BSM and RA of Patient 12 (Group2).** Brainstem mapping on **A** left and **B** right part of the rhomboid fossa. **C** Schematic map of left and right CN VII response areas (RA).

**Figure 3. Lesion, BSM and RA of Patient 16 (Group3). A** sagittal, **B** coronal and **C** axial MRI images of the lesion. Brainstem mapping on **D** left and **E** right part of the rhomboid fossa. **F** Schematic map of left and right CN VII response areas (RA).

**Figure 4. Location and extent of CN VII response areas. A** For the five patients of Group1 where the rhomboid fossa was not directly involved by the lesion, RAs are overlaid. In contrast to textbook knowledge, RAs are highly variable between patients and also asymmetric between left and right side within the same patient. **B** In the ten patients of Group2 the lesion involved the rhomboid fossa, but remote from RA. The limit of the lesion is indicated by dotted lines for some patients, the dashed lines delineate the entry to the lesion as chosen by the surgeon. In comparison to

Group1, a larger variability of centroids appears in rostrocaudal direction. **C** For the five patients of Group3 where the rhomboid fossa was involved at the level of RA, the asymmetry between left and right side was enhanced.

**Figure 5. Location of centroids of CN VII response areas. A** Group1, the median rostro-caudal distance of centroids to the obex is Cy = 19.6 mm; centroids are rather symmetrically distributed around the median. **B** Group2, the distances Cy show a larger spread. **C** Group3, the location of centroids is asymmetric between left and right side.

**Table 1. Lesions and clinical status of patients.**

| Patient No. | initial | age | sex | Histology | Location | House-Brackmann pre | House-Brackmann post |
|---|---|---|---|---|---|---|---|
| 1) Rhomboid fossa not directly involved by the lesion (N=5) | | | | | | | |
| 1 | EH | 74 | m | recurrent ependymoma, II | 4th ventricle | 1 | 1 |
| 2 | SH | 44 | m | epidermoid cyst | 4th ventricle | 1 | 1 |
| 3 | BF | 12 | m | pilocytic astrocytoma, I | midbrain tectum | 1 | 1 |
| 4 | KN | 37 | f | atypical plexus papilloma, II | 4th ventricle | 1 | 1 |
| 5 | ZS | 16 | f | pilocytic astrocytoma, I | lt. paravermian | 1 | 1 |
| 2) Rhomboid fossa involved, lesion remote from CN VII response area (N=10) | | | | | | | |
| 6 | CB | 30 | m | cavernous malformation | dorsal pons to superior cerebellar peduncle | 1 | 1 |
| 7 | SB | 54 | f | ependymoma, II | dorsal medulla, 4th ventricle to C2/3 | 1 | 1 |
| 8 | FJ | 22 | f | cavernous malformation | dorsal pons to brachium pontis | 1 | 1 |
| 9 | SH | 43 | m | glioblastoma, IV | rt. dorsolateral medulla | 1 | 1 |
| 10 | MW | 61 | m | ependymoma, II | rt. dorsolateral medulla, 4th ventricle | 1 | 1 |
| 11 | GK | 9 | m | medulloblastoma, IV | rt. paravermian, dorsal medulla, rt. brachium pontis | 1 | 1 |
| 12 | SV | 52 | f | atypical ependymoma, II | dorsal medulla, 4th ventricle | 1 | 1 |
| 13 | DM | 28 | m | pilocytic astrocytoma, I | midbrain tectum to dorsal pons | 1 | 1 |
| 14 | ZT | 28 | m | glioblastoma, IV | intraaxial medulla | 1 | 1 |
| 15 | AH | 66 | f | atypical plexus papilloma, II | rt. dorsal medulla, 4th ventricle | 1 | 1 |
| 3) Rhomboid fossa involved at level of CN VII response area (N=5) | | | | | | | |
| 16 | VJ | 47 | f | cavernous malformation | intraaxial pons | 4 | 4 |
| 17 | SS | 6 | f | glioblastoma, IV | intraaxial pons | 1 | 1 |
| 18 | FG | 15 | f | fibrillary astrocytoma, II | midbrain tectum to dorsal pons | 1 | 1 |
| 19 | RA | 50 | m | cavernous malformation | intraaxial pons | 4 | 5 |
| 20 | MU | 19 | m | cavernous malformation | rt. dorsal pons, exophytic | 1 | 1 |

**Table 2. Anatomical distances in mm.** Ly caudal limit of CN VII response area (RA); Lx medial limit of RA; Ex and Ey denote the mediolateral and rostrocaudal extent of RA; Cx and Cy are the coordinates of the centroid. The ratio RE of left and right Ey quantifies intra-individual asymmetry; width and length of rhomboid fossa.

| **Patient** | | | | **CN VII response area** | | | | | | | | | | | | | | **Rhomboid fossa** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No. | initals | age | sex | Ly left | Ly right | Lx left | Lx right | Cy left | Cy right | Cx left | Cx right | Ey left | Ey right | Ex left | Ex right | REy | REx | width | length |
| 1) Rhomboid fossa not directly involved | | | | | | | | | | | | | | | | | | | |
| 1 | EH | 74 | m | 18 | 17 | 0 | 1 | 20.0 | 20.5 | 2.0 | 3.0 | 4 | 7 | 4 | 4 | 1.8 | 1.0 | | 40 |
| 2 | SH | 44 | m | 16 | 15 | 0 | 0 | 19.7 | 19.4 | 2.7 | 1.2 | 7 | 9 | 6 | 2 | 1.3 | 3.0 | 24 | 50 |
| 3 | BF | 12 | m | 13 | 12 | 2 | 1 | 15.0 | 14.4 | 3.7 | 1.8 | 3 | 5 | 3 | 1 | 1.7 | 3.0 | 20 | 40 |
| 4 | KN | 37 | f | 17 | 17 | 2 | 3 | 18.1 | 18.5 | 3.1 | 3.5 | 2 | 3 | 2 | 2 | 1.5 | 1.0 | | |
| 5 | ZS | 16 | f | 19 | 20 | 0 | 0 | 21.5 | 21.6 | 1.1 | 1.4 | 5 | 4 | 2 | 2 | 1.3 | 1.0 | | 45 |
| | | | min | | 12 | | 0 | | 14.4 | | 1.1 | | 2 | | 1 | 1.3 | 1.0 | 20 | 40 |
| | | | median | | 17 | | 0.5 | | 19.6 | | 2.4 | | 4.5 | | 2 | 1.5 | 1.0 | 22 | 42.5 |
| | | | max | | 20 | | 3 | | 21.6 | | 3.7 | | 9 | | 6 | 1.8 | 3.0 | 24 | 50 |
| 2) Rhomboid fossa involved, lesion remote from CN VII response area | | | | | | | | | | | | | | | | | | | |
| 6 | CB | 30 | m | 18 | 17 | 3 | 0 | 20.4 | 20.0 | 4.9 | 2.2 | 3 | 4 | 3 | 4 | 1.3 | 1.3 | 19 | 38 |
| 7 | SB | 54 | f | 19 | 17 | 0 | 0 | 21.5 | 20.8 | 3.1 | 3.1 | 4 | 5 | 6 | 6 | 1.3 | 1.0 | 22 | 45 |
| 8 | FJ | 22 | f | 14 | 15 | 1 | 1 | 15.6 | 16.0 | 1.7 | 1.8 | 4 | 3 | 2 | 2 | 1.3 | 1.0 | | 37 |
| 9 | SH | 43 | m | 22 | 23 | 2 | 1 | 25.6 | 26.7 | 4.4 | 2.4 | 7 | 7 | 5 | 4 | 1.0 | 1.3 | | 52 |
| 10 | MW | 61 | m | 25 | 24 | 0 | 0 | 29.3 | 30.4 | 1.5 | 1.2 | 8 | 9 | 3 | 3 | 1.1 | 1.0 | 22 | 50 |
| 11 | GK | 9 | m | 13 | 10 | 0 | 0 | 16.2 | 15.4 | 0.8 | 1.2 | 6 | 10 | 1 | 2 | 1.7 | 2.0 | | 40 |
| 12 | SV | 52 | f | 20 | 22 | 1 | 0 | 22.8 | 24.2 | 3.4 | 1.8 | 6 | 4 | 5 | 3 | 1.5 | 1.7 | | 40 |
| 13 | DM | 28 | m | 16 | 14 | 1 | 0 | 16.6 | 15.5 | 1.3 | 0.5 | 2 | 3 | 1 | 1 | 1.5 | 1.0 | | |
| 14 | ZT | 28 | m | 23 | 23 | 0 | 0 | 24.9 | 25.0 | 1.0 | 1.4 | 4 | 4 | 2 | 3 | 1.0 | 1.5 | | 50 |
| 15 | AH | 66 | f | 25 | 27 | 0 | 1 | 26.6 | 28.0 | 0.9 | 1.8 | 3 | 2 | 2 | 2 | 1.5 | 1.0 | 14 | 50 |
| | | | min | | 10 | | 0 | | 15.4 | | 0.5 | | 2 | | 1 | 1.0 | 1.0 | 14 | 37 |
| | | | median | | 19.5 | | 0 | | 22.2 | | 1.8 | | 4 | | 3 | 1.3 | 1.1 | 20.5 | 45 |
| | | | max | | 27 | | 3 | | 30.4 | | 4.9 | | 10 | | 6 | 1.7 | 2.0 | 22 | 52 |
| 3) Rhomboid fossa involved at the level of CN VII response area | | | | | | | | | | | | | | | | | | | |
| 16 | VJ | 47 | f | 8 | 17 | 0 | 4 | 12.5 | 20.5 | 0.3 | 7.9 | 9 | 7 | 1 | 8 | 1.3 | 8.0 | 23 | 40 |
| 17 | SS | 6 | f | 17 | 9 | 1 | 1 | 19.7 | 16.3 | 4.0 | 3.0 | 5 | 15 | 6 | 4 | 3.0 | 1.5 | 20 | 36 |
| 18 | FG | 15 | f | 9 | 10 | 0 | 0 | 11.8 | 12.7 | 1.6 | 2.7 | 5 | 6 | 3 | 5 | 1.2 | 1.7 | | 33 |
| 19 | RA | 50 | m | 14 | 14 | 0 | 0 | 16.5 | 17.8 | 2.0 | 3.0 | 5 | 7 | 4 | 6 | 1.4 | 1.5 | | 50 |
| 20 | MU | 19 | m | 16 | 16 | 1 | 1 | 18.0 | 17.0 | 1.9 | 1.5 | 4 | 2 | 2 | 1 | 2.0 | 2.0 | | 40 |
| | | | min | | 8 | | 0 | | 11.8 | | 0.3 | | 2 | | 1 | 1.2 | 1.5 | 20 | 33 |
| | | | median | | 14 | | 0.5 | | 16.8 | | 2.4 | | 5.5 | | 4 | 1.4 | 1.7 | 21.5 | 40 |
| | | | max | | 17 | | 4 | | 20.5 | | 7.9 | | 15 | | 8 | 3.0 | 8.0 | 23 | 50 |
| All Patients | | | | | | | | | | | | | | | | | | | |
| | | | min | | 8 | | 0 | | 11.8 | | 0.3 | | 2 | | 1 | 1.0 | 1.0 | 14 | 33 |
| | | | median | | 17 | | 0 | | 19.7 | | 1.9 | | 4.8 | | 3 | 1.4 | 1.3 | 21.3 | 41.3 |
| | | | max | | 27 | | 4 | | 30.4 | | 7.9 | | 15 | | 8 | 3.0 | 8.0 | 24 | 52 |

**Figure 1**

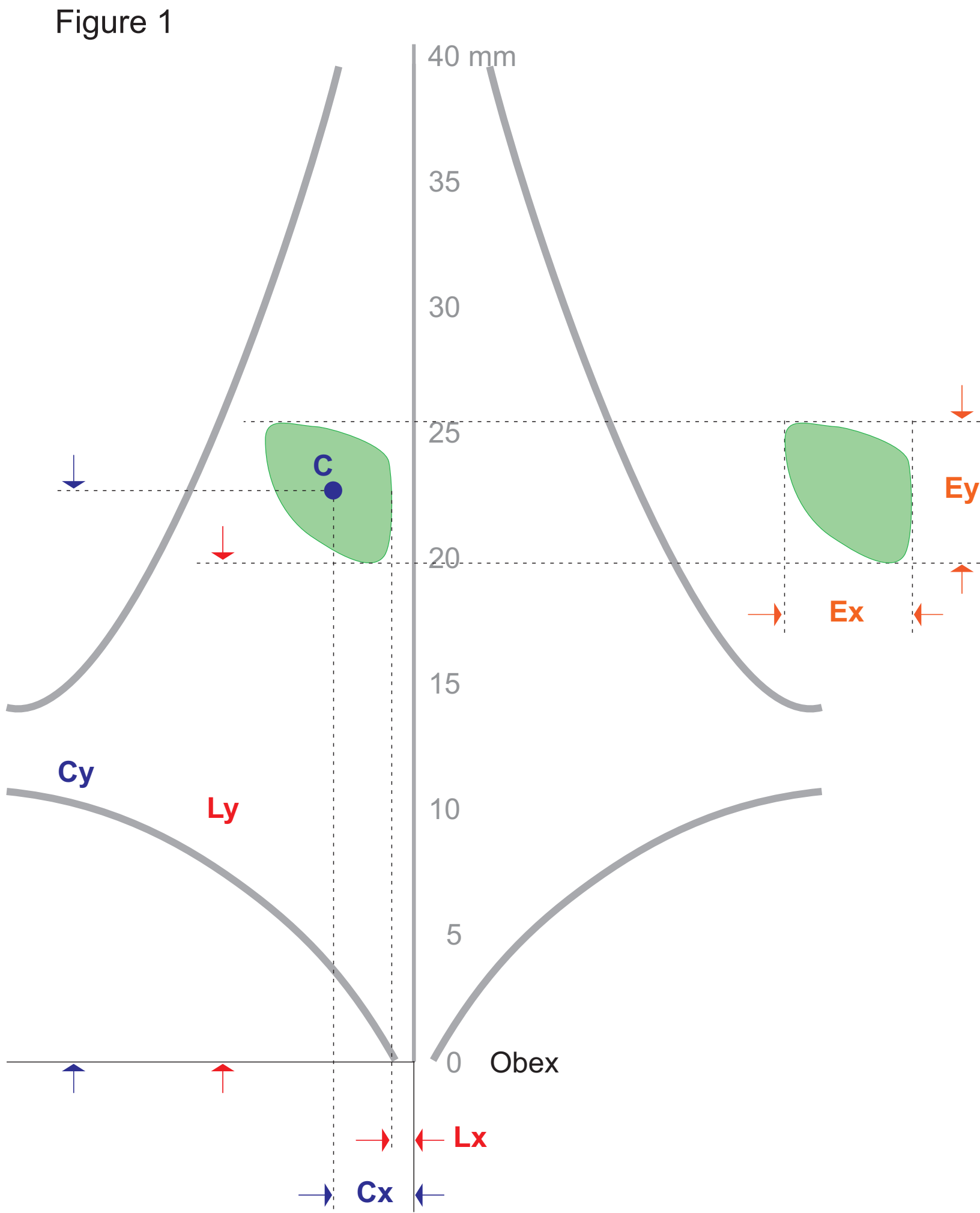

**Figure 2**
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Figure 2 Group2 Patient12 SV52

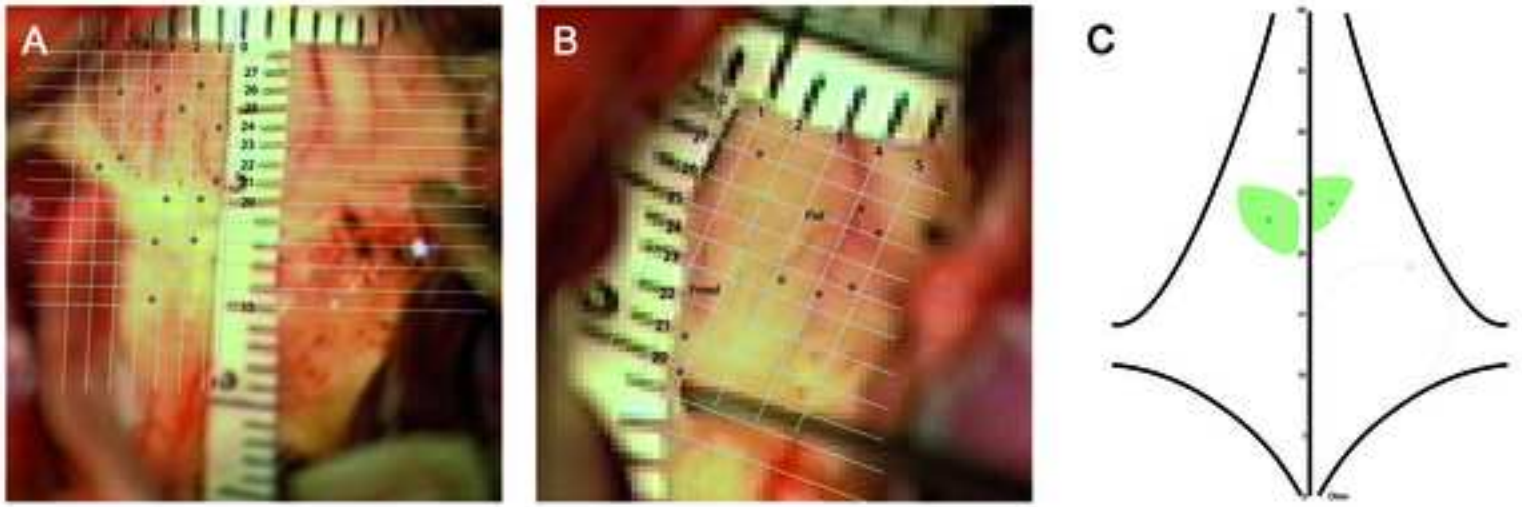

**Figure 3**

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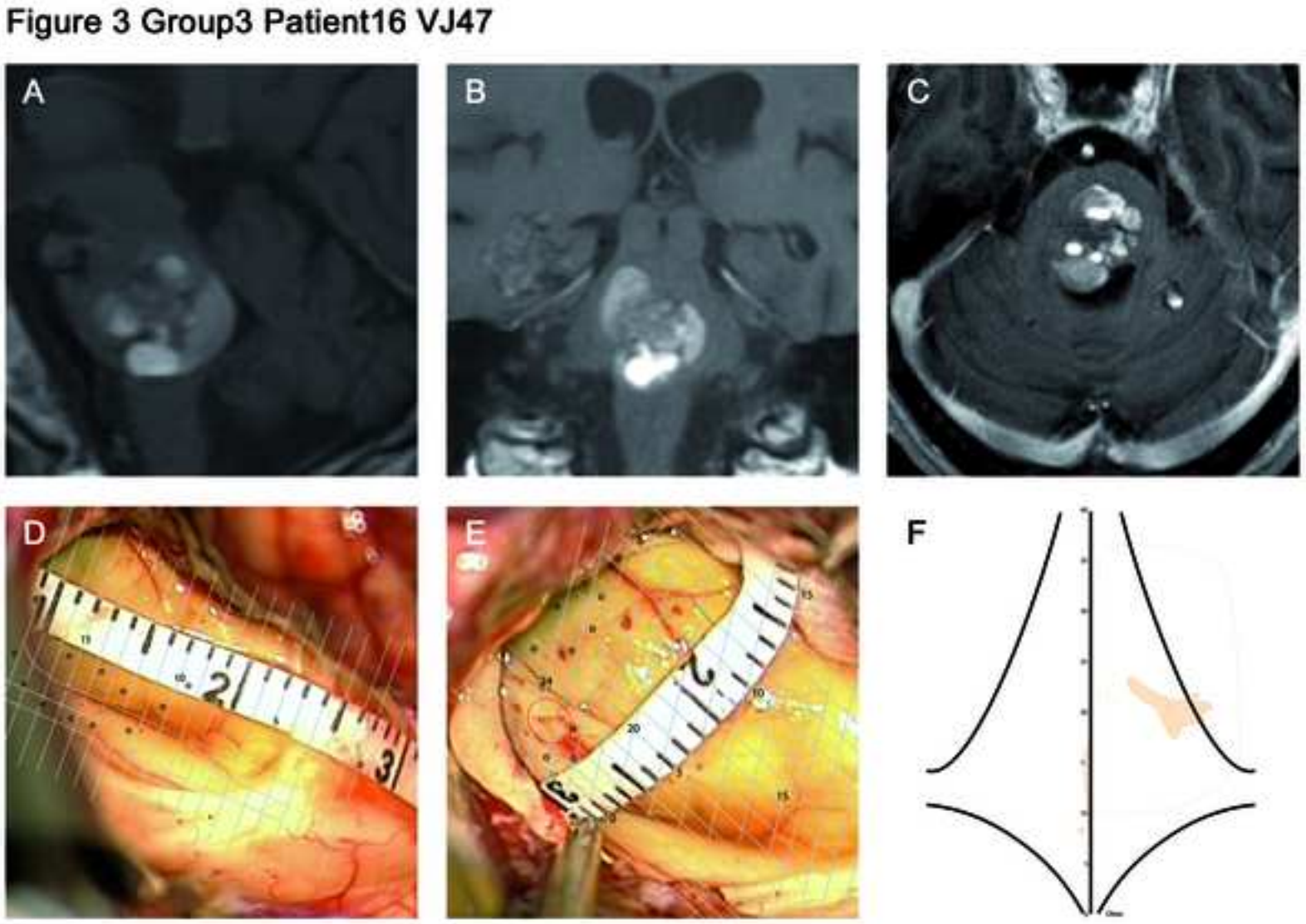

Figure 4A

# Figure 4a

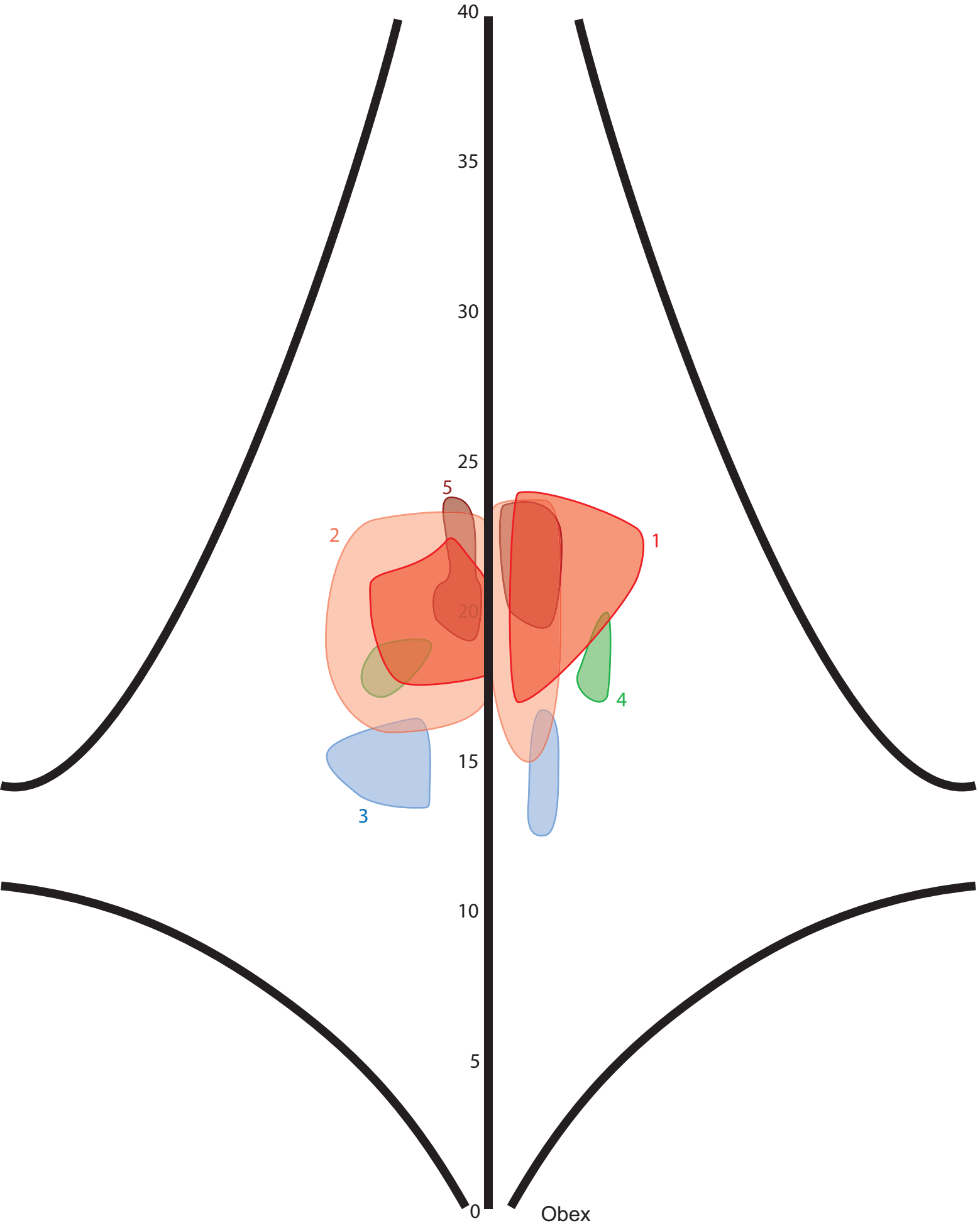

Figure 4b

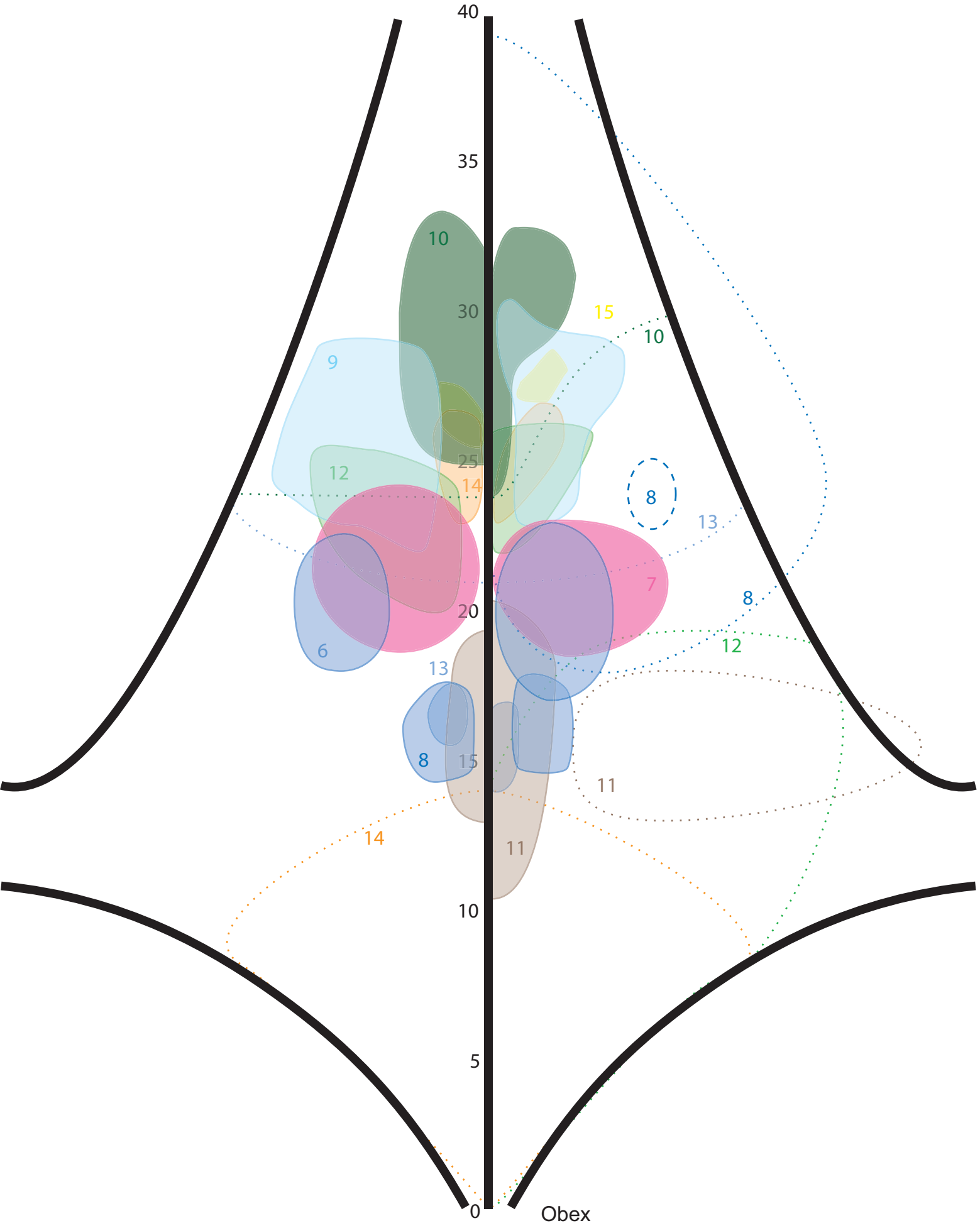
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Figure 4c

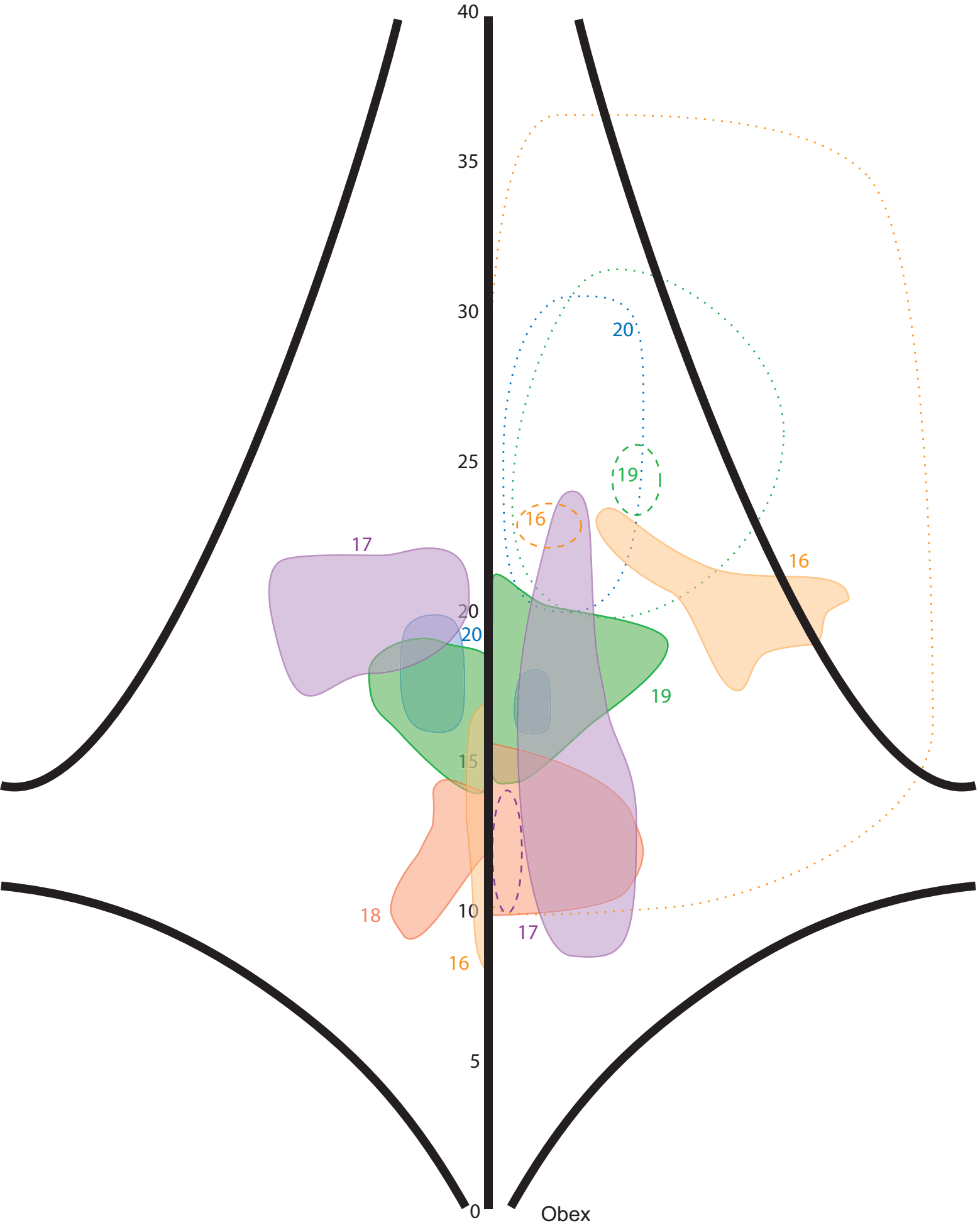

**Figure 5**

Figure 5
Centroids