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Midline and Paramedian Supracerebellar Infratentorial Approach to The Pineal Region : A Comparative Clinical Study in 112 Patients

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Manuscript

Title

Midline and paramedian supracerebellar infratentorial approach to the pineal region: a comparative clinical study in 112 patients.

Abstract

Objective

The midline supracerebellar infratentorial (SCIT) approach and its paramedian development are commonly used for dealing with pineal lesions. However, comparative clinical studies are lacking. We aim to establish the better performance of the paramedian SCIT approach in terms of clinical safety in surgically treated pineal cysts and pineal region tumors. Procedural functionality and effectiveness have been also analyzed.

Methods

A comparative analysis of clinical, radiological, pathological, surgical features, and outcome was performed between 55 midline and 57 paramedian SCIT approaches that were exclusively performed in 112 patients (57 pineal cysts and 55 tumors of the pineal region) operated in sitting position by a single surgeon. Information was retrieved from hospital records and microsurgical videos.

Results

The paramedian SCIT approach linked with less postoperative complications (OR:0.40) and less approach-related complications (OR: 0.28) than the midline SCIT approach. The SCIT paramedian approach was achieved in a shorter time, by a smaller bone flap and less complex procedural steps than the midline approach. The SCIT paramedian approach did not require the opening of the falx cerebelli, midline cerebellar retraction, section of the midline cerebellar draining veins, nor wide opening of the dura. Gross total resection, size of the lesion, microsurgical time for removal, histopathological diagnosis and postoperative outcome were statistically similar in both groups.

Conclusion

The SCIT approach represents a safer and more functional approach for the removal of cysts and tumors of the pineal region than the classic midline approach, while maintaining the same effectiveness.

Key words:

Microneurosurgery, Pineal cysts, Pineal tumors, Sitting position, Supracerebellar infratentorial approach

Introduction

The pineal region, also called posterior incisural space or quadrigeminal cistern is a deeply located surgical area where different type of cysts and tumors may develop. The supracerebellar infratentorial (SCIT) approach and the occipital interhemispheric approach are the most common approaches to this region in the Department of Neurosurgery, Helsinki University Hospital (HUH).¹⁻⁵ The SCIT approach is performed in around 90% of all surgically treated pineal tumors, as well as in almost 100% of pineal cysts operated in HUH.^{1,2} The SCIT approach, initially introduced in HUH as a midline approach, has been progressively modified to a more sophisticated and less invasive paramedian approach.³ Thus, the paramedian SCIT approach resulted from a development of the midline approach. During last years, the paramedian SCIT approach became the standard approach to the pineal region in HUH. Our previous publication on the microsurgical management of cysts and tumors of the pineal region already gave us some clues about the benefits of the paramedian SCIT approach.^{1,2} However, no comparative clinical study has been performed so far between both SCIT approaches.⁶⁻¹⁴ We aim to compare the differences of these two approaches in terms of clinical safety and procedural outcome. We hypothesized that the paramedian SCIT approach could have a better surgical performance than the midline SCIT approach in patients with pineal cysts and pineal region neoplasms undergoing surgery in sitting position. Overall, the surgical performance was evaluated in terms of clinical safety. Procedural functionality and effectiveness were also analyzed.

Material and Methods

Population study and design

This project, which has been approved by the Ethics Committee of HUH, is a retrospective case-control study to evaluate the safety, functionality, and effectiveness of the paramedian SCIT approach versus the midline SCIT in all patients who were surgically treated for pineal region neoplasms and cysts in the Department of Neurosurgery, HUH, between 1997 and 2015. We included only the patients operated in sitting position by the same neurosurgeon (JH) that underwent exclusively SCIT approach, aiming to obtain uniform comparative samples and excluding confounding variables (Figure 1). This report followed STROBE guidelines.

Patient information was retrieved from hospital records to compare the safety and the effectiveness of the SCIT approaches. Information of 61 (16 midline and 45 paramedian approaches) digitalized surgical videos was used to compare the functionality of the procedures. Mortality of the patients was retrieved from the Finnish population registry in July 2018. Radiological information of the pineal tumors and cysts was acquired from IMPAX 6.7.0.4511 (Agfa, Mortsel, Belgium). The extent of surgical resection was evaluated in the postoperative MRI studies. Quantitatively,

gross total resection was defined as the absence of residual lesion; subtotal resection as more than 95% of tumor removal; and partial resection as less than 95% of removal of the tumor. The different steps of the surgical procedure, whose duration was noted from the operative videos, were defined as follows: a. “the skin-muscle incision”, i.e. the time from the skin incision up to the beginning of the craniotomy; b. “the craniotomy”, i.e. the time employed for the craniotomy itself and before the opening of the dura mater; c. “the dura opening and access to the pineal region” that ends when the pineal lesion is reached; e. “the microsurgical removal”, i.e. the time employed for the microsurgical resection of the lesion; and f. “the dura closure”, i.e. the time while the microsurgical closure of the dura is performed.

Analysis of the data

We performed a comparative analysis between the midline and the paramedian SCIT approaches: a) the procedural safety was measured by a matched comparison between the pre- and postoperative functional status of the patients measured by the modified Rankin scale (mRS), postoperative complications, and the approach-related complications; b) the functionality of the procedures was studied in terms of the time spent during the procedural steps and the minor procedural invasiveness during the approach. This invasiveness was studied by comparison of the size of the bone flap, transverse sinus exposure, opening of the falx cerebelli, opening size of the dura, cerebellar retraction, preservation of the bridging veins, and exposure of the deep venous system, and the lateral opening of the quadrigeminal cistern; c) the effectiveness of the approaches was evaluated in terms of time of microsurgical removal, extent of surgical resection, last mRS, and the 5-year survival rate evaluation; while controlling for the histopathological diagnosis, preoperative hydrocephalus, and dimensions of the pineal region lesions. The main criteria to define a better performance of the approach were strictly related with the postoperative neurological impairment represented by the pre- and immediate postoperative mRS difference, or the approach-related complications, in this order of priority. The procedural functionality and effectiveness were evaluated as secondary variables of performance. Table 1 summarizes the qualitative differences regarding the complexity of the procedural steps between the two approaches in the Department of Neurosurgery, HUH. Surgical videos of the midline¹⁵ (<http://surgicalneurologyint.com/video/gallery/pineal-tumor-5/>) and paramedian SCIT approaches^{3,16} (<http://surgicalneurologyint.com/video/gallery/paramedian-suboccipital-approach>) are open access sources available on previous publications.

Statistical methods

RStudio version 1.2.5001-3 was used for the statistical analysis, that was independently performed by two coauthors (JC and SB). Dichotomic variables were compared using Fisher exact test; and continuous variables were compared using Mann Whitney/Wilcoxon test. Survival rates were compared using log-rank Cox test. Chi-square test was utilized to compare the histopathological diagnosis, and the functional status of the patients by a categorization of the mRS. The

differences between the pre- and immediate postoperative functional status of the patients were compared using the Paired samples t-test. The Odds ratio between the complications of the midline and paramedian approaches was calculated by the Fisher exact method. Additionally, multivariate analysis was performed using a linear regression model, and univariate analysis using Spearman rank correlation. Multiple regression was used for the identification of predictors for postoperative complications and approach related complications. For pediatric patients and those who underwent the SCIT paramedian approach, independent multiple regression models were fitted as well. Uni- and multifactorial survival analysis was determined by Cox survival model. Missing data was not extrapolated, and only available data was analyzed. The raw p-value cutoff for significance was set at 0.05 and p-adjustment was performed with Benjamini–Hochberg with significance level $\alpha=0.1$.

Results

During the study period, 137 patients (60 pineal cysts and 76 pineal tumors) were operated. Of them, 14 patients underwent different surgical approaches, and two patients were not operated in sitting position. Two more patients were operated by a different surgeon. Six patients (3 midline and 3 paramedian SCIT approaches) underwent multiple approaches and were excluded from the study. Finally, 112 patients were classified as 55 midline and 57 paramedian SCIT approaches.

The distribution of the SCIT approaches in the Department of Neurosurgery, HUH, between 1997 and 2015 is illustrated in the figure 2. A descriptive analysis of the population study is presented in Table 2. No statistical difference regarding the demographic variables, clinical presentation, the size of the lesions, the histopathological diagnosis, preoperative mRS, and the 5-year survival rate was observed between the two approaches.

Table 3 compares the surgical differences between the two approaches. The paramedian approach was performed in about half of the time spent for the midline approach. This difference was statistically significant for the microsurgical stage, namely the time for the dura opening and access to the pineal region.

However, only two macrosurgical videos regarding the skin muscle incision and craniotomy of the midline SCIT approach were available. Midline skin muscle incision and craniotomy were performed in an average time of 305 ± 35 and 550 ± 156 seconds, respectively; while the average paramedian skin muscle incision and craniotomy times were 158 ± 54 and 296 ± 130 , respectively. The time for the microsurgical removal of the pineal cysts and tumors tended to be shorter in the paramedian approach, but without statistical significance. The extent of surgical resection was similar in the two approaches. Dura closure time was mostly unavailable for the study.

Regarding the invasiveness of the procedures, the bone flap of all the series was significantly smaller in the paramedian SCIT approach. Moreover, as shown in the Figures 3, 4, and 5, the dura opening dimensions were also smaller in the paramedian group. In addition, the opening of the falx cerebelli was almost always required in the midline approach, but never performed in the paramedian approach. Usually, a bilateral opening of the dura was performed in the midline approach. The exposure of both transverse sinuses and of the sinus confluens in the midline approach induced a more profuse bleeding that required a careful hemostasis. The midline SCIT approach was associated with higher rates of coagulated and sectioned midline bridging cerebellar veins. The exposure and the dissection of the deep venous system in the midline approach was higher than in the paramedian approach. The dura closure performed under the microscope demonstrated partial or semi-hermetic closures (Figure 5) in the midline approach, particularly after the opening of the midline falx cerebelli. However, many paramedian approach videos were not available for this stage.

The postoperative complications after the SCIT approaches are summarized in Table 4. Information was unavailable in one patient who underwent a paramedian SCIT approach. Thus, only 111 patients were analyzed here. The approach-related complications were significantly higher in the midline approach, with bacterial meningitis as the most frequent complication. Moreover, wound infections in the midline approach group were more serious with two patients undergoing surgical removal of the bone flap. Conservatively treated pseudomeningocele was considered a minor complication, and was not included as an approach related complication. Shunt-related infections were excluded from the analysis. However, two patients with preliminary shunt surgery that underwent a midline approach many days later developed shunt infections after the approach. In regard to the functional status of the patients, the data analysis showed a discrete trend towards better immediate post-operative mRS with the midline approach, without statistical significance. However, this association was related with the different preoperative functional status of the patients in the two groups (Table 5). The postoperative functional status of the patients was statistically superior than the preoperative functional status of the patients in each of the two approaches and for all the population study as well (paired samples t-test, $p < 0.001$) (Figure 6). The multifactorial analysis of postoperative complications and approach related complications found no association with other variables. Various surgical independent variables (such as histopathology, age, preoperative mRS and volume of the pineal lesion), and surgical dependent variables (such as extent of resection, dura opening dimensions, and number of sectioned veins) were significantly associated with overall mortality at the univariate analysis. However, only WHO grade-histopathology remained significant in multiple survival regression.

Table 6 describes the characteristics of the pediatric population (age ≤ 21 years).^{17,18} No significant difference was observed between the two approaches regarding the demographic features and the clinical outcomes.

Discussion

We present the results of a comparative clinical analysis between the midline and the paramedian SCIT approaches for the management of pineal region cysts and neoplasms. The superior safety and better functionality of the SCIT paramedian approach versus the classic midline approach was associated with a similar effectiveness in the management of the pineal region lesions (Figure 7). A limitation of the project is represented by the fact that it is a retrospective single-center and single-surgeon study, which affects the generalizability of the study. Moreover, information retrieved from surgical videos of the midline SCIT approach was limited to 16 of 61 cases. Still, the statistical analysis with non-parametric tests was strong and we believe it accurately represents our population study. Surgically treated pineal region lesions are very rare and it always represents an inherent limitation for clinical studies in the topic.

Procedural functionality. A single-layer lateral skin muscle incision of the paramedian approach replaced the long midline incision of the midline approach. One burr-hole craniotomies were commonly performed with both the SCIT approaches. Few instruments were always used. The paramedian procedure seems to be a simplified approach since no bilateral suboccipital skin-muscle retraction is required. Thus, a lateral craniotomy does not involve the sinus confluens, but the ipsilateral transverse sinus. The opening of the falx cerebelli, the midline approach with dissection and coagulation of the midline bridging veins, the exposure and dissection of the deep venous system, and some degree of cerebellar retraction in the midline were rather demanding procedures during the midline approach. As observed in the Figure 4, a lateral recess approach to the quadrigeminal cistern reduced the risk of injury of the deep venous system around the vein of Galen. The time for every stage of the paramedian approach was shorter compared to the midline approach. However, since the macrosurgical videos of the skin-muscle incision and craniotomy were unavailable in most of the midline approaches, only the microsurgical stage of the craniotomy became available for the statistical analysis. The microsurgical resection time was quite similar in the two approaches, but, on average, shorter in the paramedian approach.

Procedural safety. The significant difference observed in the approach-related complications between the midline and paramedian approaches denotes the safety of the paramedian procedure. A less traumatic opening of the suboccipital skin and muscles may probably result in a reduced inflammatory reaction that decrease the risk of wound infection and/or dehiscence. Moreover, the preservation of the falx cerebelli allows a better closure of the dura mater, thus lessening the risk of pseudomeningoceles, cerebrospinal fluid leak and consequent meningitis. The preservation of the bridging veins and the deep venous system around the vein of Galen might reduce vascular complications as well.

Certainly, the introduction of new generation hemostatic agents and dura replacement materials along the years would have reduced the risks of cerebrospinal fluid leak. However, the dura closure was a standard microscopic procedure usually performed by the same surgeon or by other neurosurgeons under formal protocols and guidance. No significant difference between the matched pre- and postoperative functional status of the patients following the two approaches was observed.

Effectiveness of the SCIT approaches. The paramedian approach resulted as effective as the midline approach for the removal of pineal region cysts and tumors, since no statistical difference existed between the histology type, lesion size, extent in the surgical resection, microsurgical time for the removal of the lesions, and long term postoperative outcome between the two approaches. As abovementioned, the paramedian approach in HUH followed the midline approach development in concordance with the experience of the surgeon. However, this development was not at the expense of patient safety.

The pineal region might be surgically accessed by anterior and posterior approaches.¹⁹ The posterior approaches are frequently used in microneurosurgery and, among them, the SCIT approach is the most common route to the pineal region in HUH, followed by the occipital interhemispheric approach. The main advantages and disadvantages of both approaches are described in Table 7.²⁰

The SCIT approach is a classic approach introduced by Krause and later developed by Stein for accessing the pineal region.^{21,22} The paramedian SCIT, a variant of the midline approach, was initially proposed by Yasargil for the management of the superior cerebellar artery aneurysms.²³ Later, Van den Bergh, Ogata, and Yonekawa published their series on the surgical management of pineal tumors, the upper brainstem and peduncular lesions by utilizing the SCIT paramedian approach.^{14,24} Nevertheless, no clinical comparative study exists in the literature to evaluate the pros and cons of the paramedian SCIT compared with the classic midline SCIT approach.^{3,6-14,16} Thus, besides the surgical experience of skilled neurosurgeons presented in clinical series, a clear evidence about the differences of the two variants is lacking.

The SCIT approach may be performed in different surgical positions.²⁰ However, the sitting position offers the great advantage of the gravity effect on posterior fossa structures, while a particular attention needs to be paid in order to avoid the risk of venous air embolism.^{20,22} In our previous publications, we discussed the modified sitting praying position developed for pineal region surgery in HUH. In our series the risk of severe venous air embolism that affects hemodynamically the patient was null.^{5,25-28} The ergonomic position of the patient, the use of antigravity trousers, optimal anesthetic considerations, and a proper team work were considered essential variables for a correct management of pineal region surgery in sitting position.^{5,25}

Pineal region lesions frequently associate hydrocephalus. Our previous publications on the management of pineal cysts and pineal region tumors detailed the management of the associated hydrocephalus in HUH.^{1,2} Of 60 pineal cysts, 35% presented with hydrocephalus. Only one patient underwent a shunt surgery in another center. One patient underwent stereotactic aspiration of the cyst, while all the other patients underwent a microsurgical removal of the cyst with opening of the posterior third ventricle as primary treatment. 70% of 76 pineal region tumors presented with hydrocephalus. 24 patients underwent preliminary shunt surgery, and two patients endoscopic procedures. Most of the adjuvant surgeries for hydrocephalus were performed between 1997 and 2007. During the last 10 years of the study, the microsurgical resection of the tumor with opening of the third ventricle represented always the treatment of choice. The patients who received a preliminary shunt surgery underwent, on average, more than two shunt-related surgeries during the follow up. Few of these patients underwent between 5 to 10 shunt-related surgeries, and some others underwent permanent shunt removal. On the other hand, all patients (except one) who underwent primary microsurgical resection solved the hydrocephalus and did not require subsequent therapy for the hydrocephalus. Of the two preliminary endoscopic ventriculostomies, one underwent stereotactic biopsy followed by shunt surgery for persistent hydrocephalus. Comparative studies to evaluate the clinical and economic pros and cons of adjuvants therapies for the management of hydrocephalus in pineal region surgery should be performed, particularly in centers with high prevalence of non-radiosensitive lesions.

Conclusion

The SCIT paramedian approach has a better surgical performance than the midline SCIT in patients undergoing pineal region surgery in sitting praying position. The SCIT approach represents a safer and more functional approach for the removal of cysts and tumors of the pineal region than the classic midline approach. Overall, the SCIT paramedian approach maintains the same effectiveness than the midline approach.

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Figure Legends

Figure 1. Sitting praying position for the supracerebellar infratentorial approach to the pineal region in the Department of Neurosurgery, HUH.

Figure 2. Distribution of the SCIT approaches in the Department of Neurosurgery, HUH, between 1997 and 2015.

Figure 3. Comparative images obtained from different patients illustrating the microsurgical differences between the midline (left column) and the paramedian (right column) SCIT approaches. Skin incision for the midline (A1) and the paramedian SCIT approaches (A2). Bilateral craniotomy with exposure of both transverse sinuses and the confluence of sinuses (B1). Right paramedian approach with ipsilateral transverse sinus exposure (B2). Bilateral opening of the dura with exposure of midline bridging veins (C1). Unilateral small opening of the dura without opening of the falx cerebelli (C2).

Figure 4. Comparative images obtained from different patients illustrating the microsurgical differences between the midline (left column) and the paramedian (right column) SCIT approaches. A1. Midline opening of the quadrigeminal cistern with retraction of the culmen and quadrangular lobules. A2. Opening of the right lateral recess of the quadrigeminal cistern. B1. Exposure and dissection of the deep venous system before reaching the pineal region tumor. B2. Lateral access to the pineal region with limited exposure of the deep venous system. Microsurgical removal of a pineal tumor by midline (C1) and paramedian (C2) SCIT approaches. Complete microsurgical removal and opening of the third ventricle by the midline (D1) and paramedian (D2) approaches.

Figure 5. Comparative images obtained from different patients illustrating the craniotomy closure differences between the midline (left column) and the paramedian (right column) SCIT approaches. Semi-hermetic (A1) and hermetic (A2) closure of the dura mater under the microscope. Cranial fixation with titanium clamp systems of midline (B1) and paramedian (B2) SCIT approaches.

Figure 6. Functional outcome trajectories and histopathology of 112 patients with surgically treated pineal cysts and pineal region neoplasms undergoing the midline and paramedian SCIT approaches.

Figure 7. Procedural performance of the paramedian versus the midline SCIT approach in 112 patients with surgically treated pineal cysts and pineal region neoplasms. In green, significant superior performance. In yellow, absence of statistical significance.

Table 1. Descriptive analysis of the procedural steps in SCIT approaches.

	Midline	Paramedian
Skin and muscle incision	The injection of 20 cm ³ of a solution of ropivacaine and Xylocaine 1% with epinephrine along the incision line.	
	Strong retraction of the soft tissues with muscle retractors	
	Midline long skin incision	Paramedian skin incision with less inferior extension
	Bilateral detachment of suboccipital muscles	Unilateral detachment of suboccipital muscles
Craniotomy	Bilateral opening	Unilateral opening
	Single burr-hole above the sinun confluens	Single burr-hole, 1 cm above the level of the transverse sinus and around 2 cm from the midline.
	The use of long flexible dissectors to detach the dura and the sinuses from the inner surface of the bone	
Dura opening and access	Bilateral opening or unilateral opening	Unilateral opening
	Approach between the tentorium and the midline superior surface of the cerebellum	Approach between the tentorium and the lateral superior surface of the cerebellum
	Retractor-less approach. However, culmen and quadrangular lobules retraction with microinstruments	Gravity effect and small retraction with microinstruments if required
	Midline superior opening of the quadrigeminal cistern	Lateral recess opening of the quadrigeminal cistern
	Microsurgical removal under culmen and quadrangular lobes retraction	Microsurgical removal with small retraction if required

Table 2. Descriptive analysis of the population study, for categorical variables absolute number (percentage), for numeric variables, median [interquartile range]

	All N=112	Midline N=55	Paramedian N=57	p-value	Adjusted p-value
Age	30.0 [19.8;40.5]	29.0 [17.0;39.0]	32.0 [20.0;46.0]	0.169	0.618
Sex: F	71 (63.4%)	35 (63.6%)	36 (63.2%)	1.000	1
Histology:				0.914	1
GCT	11 (9.82%)	6 (10.9%)	5 (8.77%)		
Glioma	14 (12.5%)	6 (10.9%)	8 (14.0%)		
Meningioma	4 (3.57%)	1 (1.82%)	3 (5.26%)		
Other	7 (6.25%)	3 (5.45%)	4 (7.02%)		
Pineal cyst	57 (50.9%)	30 (54.5%)	27 (47.4%)		
PPT	19 (17.0%)	9 (16.4%)	10 (17.5%)		
WHO grade	2.00 [1.00;2.50]	2.50 [2.00;2.88]	2.00 [1.00;2.50]	0.077	0.425
Preoperative hydrocephalus in MRI	49 (43.8%)	26 (47.3%)	23 (40.4%)	0.584	1
Preoperative mRS	3.00 [2.00;4.00]	3.00 [2.00;3.00]	3.00 [2.00;4.00]	0.768	1
Anteroposterior tumour	20.0 [17.0;28.0]	20.0 [17.3;28.0]	20.6 [16.2;26.7]	0.895	1

meas. [mm]					
Craniocaudal tumour meas. [mm]	16.6 [12.0;20.5]	15.0 [11.5;20.0]	17.0 [13.0;21.4]	0.385	1
Transverse tumour meas. [mm]	17.0 [13.6;23.4]	16.6 [13.4;22.5]	17.2 [13.9;23.4]	0.824	1
Volume [mm ³]	24960 [12225;61025]	21870 [11875;64173]	26384 [13254;58081]	0.747	1
Follow-up [months]	144 [78.8;204]	193 [148;218]	85.0 [61.0;109]	<0.001	<0.001
5-year survival	95 (91.3%)	50 (90.9%)	45 (91.8%)	1.000	1

mRS, modified Rankin scale

Table 3. Differences in approaches, for categorical variables absolute number (percentage), for numeric variables, median [interquartile range]

	All N=112	Midline N=55	Paramedian N=57	p-value	Adjusted p-value	Total number
Number of exposed transverse sinuses	1.00 [1.00;2.00]	2.00 [2.00;2.00]	1.00 [1.00;1.00]	<0.001	<0.001	61
Significant sinus tearing	10 (16.4%)	10 (62.5%)	0 (0.00%)	<0.001	<0.001	61
Time of dura opening and access	465 [308;650]	930 [748;1275]	420 [300;540]	<0.001	<0.001	55
Time of microsurgical removal [s]	1260 [780;2160]	1470 [750;1890]	1260 [780;2280]	0.799	0.799	61
Cranio-caudal bone flap meas. [mm]	40.0 [36.0;45.0]	40.0 [38.0;45.8]	38.0 [35.0;42.8]	0.024	0.0324	93
Transverse bone flap meas. [mm]	35.0 [31.0;40.0]	40.0 [35.0;42.0]	32.0 [28.0;35.2]	<0.001	0.0324	97
Bone flap area [mm ²]	1068 [881;1347]	1257 [1076;1450]	935 [815;1092]	<0.001	<0.001	93
Dura opening transverse dimension [mm] [#]	20.6 [18.3;23.9]	23.3 [21.7;25.6]	19.0 [18.0;22.9]	0.001	<0.001	59
Opening of the falx cerebelli	14 (23%)	14 (88%)	0	<0.001	<0.001	61
Dural opening: bilateral unilateral	12 (19.7%) 49 (80.3%)	12 (75.0%) 4 (25.0%)	0 (0.00%) 45 (100%)	<0.001	<0.001	61
Quadrigeminal cistern opening: lateral recess midline	50 (82.0%) 11 (18.0%)	5 (31.2%) 11 (68.8%)	45 (100%) 0 (0.00%)	<0.001	<0.001	61
Number of sacrificed veins	1.00 [0.00;2.00]	2.00 [1.00;3.00]	0.00 [0.00;1.00]	<0.001	<0.001	61
Number of sacrificed lateral veins	0.00 [0.00;1.00]	0.00 [0.00;1.00]	0.00 [0.00;1.00]	0.454	0.519	61
Number of sacrificed midline veins	0.00 [0.00;1.00]	2.00 [1.00;3.00]	0.00 [0.00;0.00]	<0.001	<0.001	61
Exposition of deep venous structures	21 (34.4%)	15 (93.8%)	6 (13.3%)	<0.001	<0.001	61
Dissection of deep venous structures	15 (24.6%)	13 (81.2%)	2 (4.44%)	<0.001	<0.001	61
Gross total resection	98 (87.5%)	49 (89.1%)	49 (86.0%)	0.777	0.799	112
Dural closure: Semi-hermetic watertight	4 (23.5%) 7 (41.2%)	1 (11.1%) 3 (33.3%)	3 (37.5%) 4 (50.0%)	0.211	0.26	17

wide open	6 (35.3%)	5 (55.6%)	1 (12.5%)			
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The bone flap area was calculated as $3.1416 \times [(\text{cranio-caudal bone flap measurement}/2 \times \text{transverse bone flap measurement}/2)^2]$; meas., measures.

The dura opening transverse dimension was indirectly measured from the operative videos using as a reference the transverse diameter of the bone flap.

A semi-hermetic closure was defined as the evidence of a minor cerebrospinal fluid leak after the closure of the dura mater.

Table 4. Differences in outcomes and complications, for categorical variables absolute number (percentage), for numeric variables, median [interquartile range], OR – odds ratio [95% confidence interval]

	All N=111	Midline N=55	Paramedian N=56	OR	p-value	Adjusted p-value
Complication	27 (24.3%)	18 (32.7%)	9 (16.1%)	0.40 [0.14;1.06]	0.048	0.0968
Approach related complication	16 (14.4%)	12 (21.8%)	4 (7.14%)	0.28 [0.06;1.01]	0.033	0.0876
CSF leak	4 (3.60%)	3 (5.45%)	1 (1.79%)	0.32 [0.01;4.11]	0.364	0.582
Meningitis	9 (8.11%)	8 (14.5%)	1 (1.79%)	0.11 [0.00;0.86]	0.016	0.0876
Wound infection	6 (5.41%)	4 (7.27%)	2 (3.57%)	0.48 [0.04;3.48]	0.438	0.584
Pseudomeningocele #	5 (4.50%)	5 (9.09%)	0 (0.00%)	0.00 [0.00;1.03]	0.027	0.0876
Other postoperative complications &	12 (10.8%)	6 (10.9%)	6 (10.7%)	0.98 [0.24;3.94]	1.000	1
Last available mRS	0.00 [0.00;1.00]	0.00 [0.00;1.00]	0.00 [0.00;1.00]	0.95 [0.77;1.16]	0.658	0.752

One patient required spinal puncture.

& Such as small hematoma in the surgical site, perilesional ischemia, aseptic meningitis, epidural hematoma, and tension pneumocephalus. mRS, modified Rankin scale.

Table 5. Categorization of the pre- and postoperative functional status in mRS for the population study. For categorical variables absolute number (percentage).

	All N=112	Midline N=55	Paramedian N=57	P value
Preoperative mRS (0-2, ≥3), nai:2	50 (45%), 60 (55%)	26 (48%), 28 (52%)	24 (43%), 32 (57%)	0.58
Immediate postoperative mRS (0-2, ≥3), nai:2	95 (86%), 15 (14%)	49 (91%), 5 (9%)	46 (82%), 10 (18%)	0.19
Last mRS (0-2, ≥3), nai:1	93 (84%), 18 (16%)	46 (84%), 9 (16%)	47 (84%), 9 (16%)	0.97

mRS, modified Rankin scale; nai, non-available information.

Table 6. Characteristic of the pediatric subpopulation in the study, for categorical variables absolute number (percentage), for numeric variables, median [interquartile range]

	All N=35	Midline N=20	Paramedian N=15	p-value	Adjusted p-value
Age	16.0 [11.0;18.5]	15.5 [12.0;17.0]	16.0 [10.5;20.0]	0.322	0.765
Sex: F	26 (74.3%)	15 (75.0%)	11 (73.3%)	1.000	1

Histology:				0.688	0.896
GCT	6 (17.1%)	4 (20.0%)	2 (13.3%)		
Glioma	3 (8.57%)	1 (5.00%)	2 (13.3%)		
Other	2 (5.71%)	2 (10.0%)	0 (0.00%)		
Pineal cyst	19 (54.3%)	11 (55.0%)	8 (53.3%)		
PPT	5 (14.3%)	2 (10.0%)	3 (20.0%)		
WHO grade	2.00 [1.00;4.00]	4.00 [2.00;4.00]	1.00 [1.00;1.50]	0.015	0.192
Preoperative hydrocephalus in MRI	16 (45.7%)	10 (50.0%)	6 (40.0%)	0.807	0.896
Preoperative mRS	2.00 [2.00;3.00]	2.00 [2.00;3.00]	2.00 [1.50;3.00]	0.353	0.765
Immediate mRS	1.00 [1.00;1.75]	1.00 [0.00;1.00]	1.00 [1.00;2.00]	0.099	0.443
Last mRS	0.00 [0.00;0.00]	0.00 [0.00;0.25]	0.00 [0.00;0.00]	0.327	0.765
Anteroposterior tumour meas. [mm]	23.6 [17.1;29.0]	24.0 [17.3;30.0]	23.3 [17.2;28.0]	0.827	0.896
Craniocaudal tumour meas. [mm]	17.0 [12.0;24.0]	15.0 [12.0;25.0]	17.0 [13.1;21.8]	0.605	0.896
Transverse tumour meas. [mm]	18.5 [13.2;23.6]	19.0 [15.2;25.5]	18.0 [13.2;22.1]	0.677	0.896
Volume [mm ³]	29283 [11886;76627]	35117 [11461;86237]	26021 [13964;58921]	0.739	0.896
Follow-up [months]	148 [81.5;206]	168 [147;209]	86.0 [73.0;175]	0.102	0.443
5-year survival	31 (91.2%)	17 (85.0%)	14 (100%)	1.000	1

mRS, modified Rankin scale

Table 7. Advantages and disadvantages for posterior surgical approaches to the pineal region. (Adapted from Yamamoto 2001)

Approach	Advantages	Disadvantages Weighted compared
Infratentorial supracerebellar approach	<ol style="list-style-type: none"> 1. Basically midline and easy orientation 2. Extra-axial route with reduced risk of neurovascular injuries 3. Beneath the deep venous system 4. Minimal damage to delicate nervous structures 5. No morbidity related to parietal or occipital lobe 	<ol style="list-style-type: none"> 1. Narrow operative field 2. May sacrifice lateral bridging vein and/or precentral cerebellar vein 3. May split upper vermis 4. Poor visualization of supratentorial structures 5. Difficult to reach paramedian lesions in the third ventricle 6. Inadequate view of the posterior floor of the third ventricle
Occipital transtentorial approach	<ol style="list-style-type: none"> 1. Wide operative field 2. No veins crossing from occipital lobe into superior sagittal sinus 3. Easy visualization of deep venous structure 4. Largely extra-axial above the tentorium 5. Good visualization of ipsilateral dorsal and lateral extension of the midbrain 	<ol style="list-style-type: none"> 1. Risk of damage to occipital lobe or internal occipital vein 2. Risk of damage to deep venous structure 3. Variation in anatomy of the tentorial notch 4. Poor visualization of contralateral half of quadrigeminal region and ipsilateral thalamus 5. May need to split splenium
Posterior transcallosal approach	<ol style="list-style-type: none"> 1. Irrelevant to ventricular size 2. Largely extra-axial above tentorium 3. No disruption of hemispheric tissue 4. Shorter transit to the diencephalic roof 5. Ability to develop exposure of the entire third ventricular cavity 	<ol style="list-style-type: none"> 1. Damage of parietal bridging veins 2. Excessive parietal lobe retraction 3. Poor landmark identification 4. Split corpus callosum 5. Risk of damage to deep venous structures 6. Poor visualization of the pineal and quadrigeminal regions

Figure 1. Sitting praying position for the supracerebellar infratentorial approach to the pineal region in the Department of Neurosurgery, HUH.

Figure 2. Distribution of the SCIT approaches in the Department of Neurosurgery, HUH, between 1997 and 2015.

Figure 3. Comparative images obtained from different patients illustrating the microsurgical differences between the midline (left column) and the paramedian (right column) SCIT approaches. Skin incision for the midline (A1) and the paramedian SCIT approaches (A2). Bilateral craniotomy with exposition of both transverse sinuses and the confluence of sinuses (B1). Right paramedian approach with ipsilateral transverse sinus exposition (B2). Bilateral opening of the dura with exposition of midline bridging veins (C1). Unilateral small opening of the dura without opening of the falx cerebelli (C2).

A1	A2
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B1

B2

C1

C2

D1

D2

Figure 4. Comparative images obtained from different patients illustrating the microsurgical differences between the midline (left column) and the paramedian (right column) SCIT approaches. A1. Midline opening of the quadrigeminal cistern with retraction of the culmen and quadrangular lobules. A2. Opening of the right lateral recess of the quadrigeminal cistern. B1. Exposition and dissection of the deep venous system before reaching the pineal region tumor. B2. Lateral access to the pineal region with limited exposition of the deep venous system. Microsurgical removal of a pineal tumor by midline (C1) and paramedian (C2) SCIT approaches. Complete microsurgical removal and opening of the third ventricle by midline (D1) and paramedian (D2) approaches.

Figure 5. Comparative images obtained from different patients illustrating the craniotomy closure differences between the midline (left column) and the paramedian (right column) SCIT approaches. Semi-hermetic (A1) and hermetic (A2) closure of the dura mater under the microscope. Cranial fixation with titanium clamp systems of midline (B1) and paramedian (B2) SCIT approaches.

Figure 6. Functional outcome trajectories and histopathology of 112 patients with surgically treated pineal cysts and pineal region neoplasms undergoing the midline and paramedian SCIT approaches.

Performance	Variable	Paramedian vs midline SCIT approach		
		Superior (p<0.05)	Inferior (p<0.05)	Similar (p>0.05)
Functionality	Time spent during approach	●		
	Unilateral craniotomy	●		
	Cranio-caudal bone flap measurement	●		
	Transverse bone flap measurement	●		
	Area of the bone flap	●		
	Sinus tearing	●		
	Transverse sinus exposure	●		
	Opening of the falx cerebelli	●		
	Unilateral opening of the dura	●		
	Opening size of the dura	●		
	Cerebellar retraction	●		
	Preservation of the bridging veins	●		
	Preservation of the lateral bridging veins			●
	Preservation of the midline bridging veins	●		
	Exposure of the deep venous system	●		
	Dissection of deep venous structures	●		
	Lateral opening of the quadrigeminal cistern	●		
Safety	Preoperative-postoperative difference in the mRS			●
	Postoperative complications	●		
	Approach related complications	●		
	Pseudomeningocele	●		
	Other postoperative complications			●
Effectiveness	Preoperative hydrocephalus			●
	Histopathological diagnosis			●
	Time of microsurgical removal			●
	Dimensions of the lesions			●
	Extent of surgical resection			●
	Last mRS			●
	5-year survival rate			●

Figure 7. Procedural performance of the paramedian versus the midline SCIT approach in 112 patients with surgically treated pineal cysts and pineal region neoplasms. In green, statistical significance of superior performance. In yellow, variables without statistical difference; mRS, modified Rankin Scale.

Figure 1
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Figure 2

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Figure 3A1
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Figure 3C1
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Figure 5A1
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Performance	Variable	Paramedian vs midline SCIT approach		
		Superior (p<0.05)	Inferior (p<0.05)	Similar (p>0.05)
Functionality	Time spent during approach	●		
	Unilateral craniotomy	●		
	Cranio-caudal bone flap measurement	●		
	Transverse bone flap measurement	●		
	Area of the bone flap	●		
	Sinus tearing	●		
	Transverse sinus exposure	●		
	Opening of the falx cerebelli	●		
	Unilateral opening of the dura	●		
	Opening size of the dura	●		
	Cerebellar retraction	●		
	Preservation of the bridging veins	●		
	Preservation of the lateral bridging veins			●
	Preservation of the midline bridging veins	●		
	Exposure of the deep venous system	●		
	Dissection of deep venous structures	●		
	Lateral opening of the quadrigeminal cistern	●		
Safety	Difference on matched pre- and postoperative mRS			●
	Postoperative complications	●		
	Approach related complications	●		
	Pseudomeningocele	●		
	Other postoperative complications			●
Effectiveness	Preoperative hydrocephalus			●
	Histopathological diagnosis			●
	Time of microsurgical removal			●
	Dimensions of the lesions			●
	Extent of surgical resection			●
	Last mRS			●
	5-year survival rate			●