



# WHO grade, proliferation index, and progesterone receptor expression are different according to the location of meningioma

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Received: 22 March 2019 / Accepted: 20 September 2019 / Published online: 21 October 2019  
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## Abstract

**Background** Meningiomas may show a different WHO grade and variable biological and clinical behaviors. The aim of the present study is to assess whether WHO grade, proliferation index, progesterone receptor (PR) expression, histological subtype, neuroradiological features, and the recurrence rate differ depending on the tumor location.

**Methods** Three hundred meningiomas operated on from 2006 to 2016 were reviewed. The WHO grade (2007 classification), Ki67-MIB1, progesterone receptor expression, and histological subtype were reexamined and correlated to the meningioma location, classified as medial skull base, lateral skull base, non-skull base, and spinal.

**Results** Non-skull base and lateral skull base meningiomas showed significantly higher rates of atypical WHO II forms (34% and 25.5% respectively) than medial skull base (12.5%) and spinal ones (7%) ( $p = 0.0003$ ) and also higher rates of tumors with Ki67-Li > 4% (42% and 38% vs 22% and 14%) ( $p = 0.0031$ ). The rate of meningiomas with PR expression  $\leq 50\%$  was significantly lower in medial skull base (25%) than in non-skull base (48%) ( $p = 0.009$ ). Meningothelial and transitional meningiomas were more frequent at the skull base (68.5% and 54.5%, respectively), the fibroblastic subtype at the non-skull base (48.5%), and the psammomatous at the spinal canal (50%) ( $p < 0.00001$ ). Medial skull base and spinal meningiomas showed significantly lower size ( $p < 0.00001$ ), lower rates of cases with lost arachnoid interface ( $p = 0.0022$ ), and significantly lower recurrence rates ( $p = 0.0035$ ) than lateral skull base and non-skull base meningiomas.

**Conclusion** Medial skull base meningiomas show lower size, lower rate of atypical forms, lower Ki67-Li values, and significantly higher PR expression than those at the lateral skull base and non-skull base. This corresponds to lesser aggressiveness and lower recurrence rates.

**Keywords** Meningioma · WHO grade · Proliferation index · Progesterone receptor expression · Meningioma location

## Introduction

The location of intracranial meningiomas is a well-known factor correlated to the extent of resection, recurrence, and outcome [34, 36, 42].

Several studies have also shown that the meningioma location, with regard to the skull base versus non-skull base, has an effect on tumor pathology and biology [7, 10, 15, 16, 19, 28, 31, 47, 49, 54].

The WHO grades II and III meningiomas are significantly more numerous in the non-skull base locations [7, 15, 23, 28, 32, 47, 54]; besides, skull base meningiomas show significantly lower values of Ki67-MIB1 [7, 10, 16, 28, 31]. Finally, only one recent study [19, 21] has investigated the progesterone receptor (PR) expression according to the tumor location.

All but one [54] above-cited studies globally consider all skull base versus all non-skull base meningiomas. However, it is known that the group of skull base meningiomas includes tumors with different growth potential and recurrence risk. Thus, it should be useful to investigate whether the different

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This article is part of the Topical Collection on Tumor - Meningioma

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locations correspond to different pathological and biological behaviors.

The aim of the present study is to investigate the WHO grade, Ki67-MIB1, and PR expression in different meningioma locations, separately considering medial and lateral skull base tumors.

## Materials and methods

### Patient population

Three hundred fifty-two patients who underwent neurosurgery for intracranial and spinal tumors diagnosed as meningioma at the neurosurgical clinic of the “Federico II” University of Naples between 2006 and 2016 were reviewed. Two children with neurofibromatosis, three patients with multiple meningiomas, five with post-irradiation meningiomas, and forty-two recurrences were excluded. Thus, 300 consecutive patients with primary intracranial or spinal meningiomas were included in the study. An ethics committee approval was not necessary because this is a retrospective study.

### Analyzed factors

The factors analyzed in the study include location of the meningioma, neuroradiological and surgical features, WHO grade, proliferation index Ki67-MIB1, histological subtype, progesterone receptor (PR) expression, and recurrence rate.

The tumor location was defined from the review of surgical descriptions. Four groups were identified: group 1, or medial skull base, including the olfactory groove, planum ethmoidale-sphenoidale, tuberculum sellae, parasellar, clival-petroclival, and foramen magnum meningiomas; group 2, or lateral skull base, including the middle and lateral sphenoid wings and temporal fossa, speno-orbital meningiomas, and those of the petrous bone and occipital fossa; group 3, or non-skull base, including convexity, parasagittal and falx meningiomas, those of the tentorium, cerebellar convexity, and pineal region, and those of lateral ventricles; group 4, including spinal meningiomas.

The neuroradiological and surgical features were defined from the preoperative MR studies and surgical descriptions. These include tumor size and shape, brain-tumor interface, presence of cystic and necrotic areas, and classifications. The tumor size was determined as the largest tumor diameter. The shape was determined by the ratio between the dural attachment and the tumor height and classified as round ( $\leq 1$ ) or flat ( $> 1$ ). The brain-tumor interface was classified as preserved or lost.

The surgical specimens were reviewed independently by two pathologists (MDBDC and EG), who were blinded to tumor location. The WHO grade was defined according to the 2007

WHO classification [22]. The immunohistochemical studies were performed to evaluate Ki67-MIB1 and PR expression. The specimens were fixed in neutral buffered 10% formalin, embedded in paraffin, and cut into sections of 5- $\mu$ m thickness.

The expression of Ki67-MIB1 was evaluated in all cases by using the monoclonal antibody MIB-1 Immunotech® (DAKO system) (dilution 1:1000, overnight incubation). The streptavidin-biotin system and the diaminobenzidine (DAB) were used for antigen detection and visualization. A specimen of breast carcinoma was used as positive control. Ki67-L.I. count was performed by eye counting, taking the average on five adjacent representative fields of neoplastic cells in a hot spot area. The values of Ki67-L.I. were divided into two groups: group I  $\leq 4\%$  and group II  $> 4\%$ .

The expression of PR was determined in all specimens with monoclonal antibody against the progesterone (DAKO 1:400, overnight incubation). The quantitative evaluation was expressed as percentage of positive nuclei among 100 cells, for a total of 500 cells. The following score was used: (a)  $\leq 50\%$ ; (b)  $> 50\%$ .

In 220 specimens of benign WHO grade I meningiomas, the histological subtype was also evaluated.

### Statistical analysis

WHO grade, Ki67-L.I. values, PR expression and histological subtype, tumor size and shape, brain-tumor interface, presence of cystic and necrotic areas and calcifications, and recurrences were carefully analyzed and stratified in all cases according to the distribution of the tumor location. Data were analyzed by one-way ANOVA test or Fisher’s exact test, and  $p$  value was calculated. A  $p$  value  $\leq 0.05$  was considered statistically significant. All tests were two sided and carried out with GraphPad Prism 5 software (GraphPad Software, La Jolla, CA, USA).

## Results

### Tumor location

Among the 300 meningiomas, 72 (24%) were located at the medial skull base and 39 (13%) at the lateral skull base; 161 (54%) were non-skull base; and 28 (9%) were in the spinal canal. The distribution of the tumor location in each main group is summarized in Table 1.

### Location and neuroradiological and surgical features

The distribution of the tumor size (median diameter) according to the location of the 4 groups of meningiomas was statistically significant (medial skull base vs non-skull base,  $p <$

**Table 1** Meningioma location

Locations	No. of cases
Medial skull base	33
- Olfactory groove, planum ethmoidale-sphenoidale	
- Tuberculum sellae	18
- Parasellar (anterior clinoid and optic canal)	16
- Clivus, petroclival, foramen magnum	5
Total	72 (24%)
Lateral skull base	14
- Middle and lateral sphenoid wings, temporal fossa	
- Spheno-orbital	16
- Petrous bone, occipital fossa	9
Total	39 (13%)
Non-skull base	137
- Cerebral convexity, parasagittal, falx	
- Tentorial, cerebellar convexity, pineal	19
- Lateral ventricles	5
Total	161 (54%)
Spinal	28 (9%)
	300

0.00001; medial skull base vs lateral skull base,  $p < 0.00001$ ) (Table 2).

The rate of cases with preserved brain-tumor interface both at MR images and surgical exploration was significantly higher in the medial skull base and spinal groups than in the non-skull base group ( $p = 0.0022$ ). On the other hand, the tumor shape (round vs flat,  $p = 0.26$ ), the presence of cystic and necrotic areas ( $p = 0.19$ ), and the presence of calcifications ( $p = 0.8$ ) did not show statistically significant differences between the different locations (Table 3).

## Overall pathological data

According to the WHO grade [19], 220 meningiomas (73%) were WHO grade I, 76 (25.5%) atypical or WHO grade II, and 4 (1.5%) anaplastic or WHO grade III (Table 4).

**Table 2** Correlation between tumor location and size

Meningioma location	No. of cases	Size	
		Median diameter (cm)	SD
Medial skull base	72	2.8	0.59
Lateral skull base	39	3.9	0.73
Non-skull base	161	4.6	1.16
Spinal	28	1.7	0.5

Medial skull base vs non-skull base vs lateral skull base vs spinal  $p < 0.00001$

Medial skull base vs non-skull base  $p < 0.00001$

Medial skull base vs lateral skull base  $p < 0.00001$

Lateral skull base vs non-skull base  $p = 0.00007$

The Ki67-L.I. was  $\leq 4\%$  in 198 (66%) and  $> 4\%$  in 102 (34%) meningiomas.

The PR expression showed values of  $\leq 50\%$  in 122 cases (41%) and  $> 50\%$  in 178 (59%).

According to the histological subtype, investigated in the 220 WHO grade I meningiomas (Table 5), 38 (17.5%) were meningothelial, 77 (35%) transitional, 62 (28%) fibrous, 26 (12%) psammomatous, 6 (2.5%) secretory, 3 (1.5%) metaplastic, and 8 (3.5%) microcystic.

## Location and WHO grade

Among the four main groups of tumor locations (Table 4), a significantly higher incidence of atypical and malignant meningiomas was observed in the non-skull base (34% and 2%) and the lateral skull base (25.5% and 2.5%) than in the medial skull base (12.5% and 0) and spinal meningiomas (7% and 0) ( $p = 0.00034$ ) (Fig. 1a).

In the group of medial skull base, the incidence of atypical tumors was higher in parasellar (25%) than in planum ethmoidale (9%) and tuberculum sellae (5.5%) meningiomas, but this difference was not statistically significant ( $p = 0.2973$ ). In the lateral skull base group, no difference of incidence of atypical tumors was evidenced in the different locations. In the non-skull base group, the incidence of atypical tumors was higher in parasagittal, falx, and convexity (36.5%) meningiomas than in other locations, but with no statistical significance.

## Location and Ki67-Li

Non-skull base and lateral skull base meningiomas showed significantly higher rates (42% and 38%, respectively) of tumors with Ki67-L.I.  $> 4\%$  than medial skull base (22%) and spinal ones (14%) ( $p = 0.0031$ ) (Fig. 1b, Table 4).

In medial skull base, the rate of tumors with Ki67-L.I.  $> 4\%$  was almost twice in parasellar (38%) than in planum ethmoidale-sphenoidale (19%) and tuberculum sellae meningiomas (17%).

On the other hand, in the lateral skull base and non-skull base, the values of Ki67-Li in the various locations were rather similar, and the difference was not statistically significant.

## Location and PR expression

Medial skull base meningiomas showed higher rate (75%) of cases with PR expression  $> 50\%$  than the other groups (52% and 61%) ( $p = 0.009$ ) (Table 4, Fig. 1c).

## Location and histological subtype

Medial skull base meningiomas were mainly of transitional (50.5%) and meningothelial (29%) types. In the lateral skull base group, similar rate of meningothelial tumors (28.5%) and

**Table 3** Correlation between tumor location and neuroradiological and surgical features

Meningioma location	No. of cases	Tumor shape		Arachnoid interface		Cystic-necrotic areas		Calcifications	
		Round	Flat	Preserved	Lost	Yes	No	Yes	No
Medial skull base	72	55 (76%)	17 (24%)	61 (85%)	11 (15%)	8 (11%)	64 (89%)	11 (15%)	61 (85%)
Lateral skull base	39	23 (60%)	16 (40%)	30 (77%)	9 (23%)	5 (13%)	34 (87%)	8 (20%)	31 (80%)
Non-skull base	161	112 (70%)	49 (30%)	107 (66%)	54 (34%)	32 (20%)	129 (80%)	28 (17%)	133 (83%)
Spinal	28	18 (64%)	10 (36%)	26 (93%)	2 (7%)	–	28 (100%)	6 (21%)	22 (79%)
Total	300	208 (69%)	92 (31%)	224 (75%)	76 (25%)	45 (15%)	255 (85%)	53 (18%)	247 (82%)
Statistical analysis		$p = 0.26$ not significant		$p = 0.0022$		$p = 0.19$ not significant		$p = 0.8$ not significant	

slightly lower rate of transitional type (36%) were evident. Thus, the transitional subtype was the most common in the skull base, followed by the meningothelial one.

Non-skull base meningiomas were mainly of fibrous (48.5%) and transitional (26%) types, whereas the meningothelial histotype was rare (10%). Among spinal meningiomas, 50% were psammomatous and 31% transitional. Among the more rare subtypes, all 8 microcystic meningiomas were found at the non-skull base locations ( $p < 0.00001$ ).

### Location and recurrence

The recurrence rate of the overall series, after a follow-up of 3 to 13 years, was 13% (39 among 300 patients). The medial skull base and spinal meningiomas showed significantly lower rates

of recurrences (5.5% and 3.6%, respectively) than the lateral skull base (19%) and non-skull base ones (16%) ( $p < 0.035$ ) (Table 6). The higher recurrence rates of the lateral skull base and non-skull base groups reflect the high number of sphenoidal and parasagittal meningiomas, respectively, which recur more frequently than the other locations [8, 24, 25].

### Discussion

This study shows that the medial skull base and spinal meningiomas have lower size, higher rate of cases with preserved brain-tumor interface, lower rate of WHO II and III tumors, significantly lower rate of Ki67-LI, and higher values of PR expression when compared with lateral skull

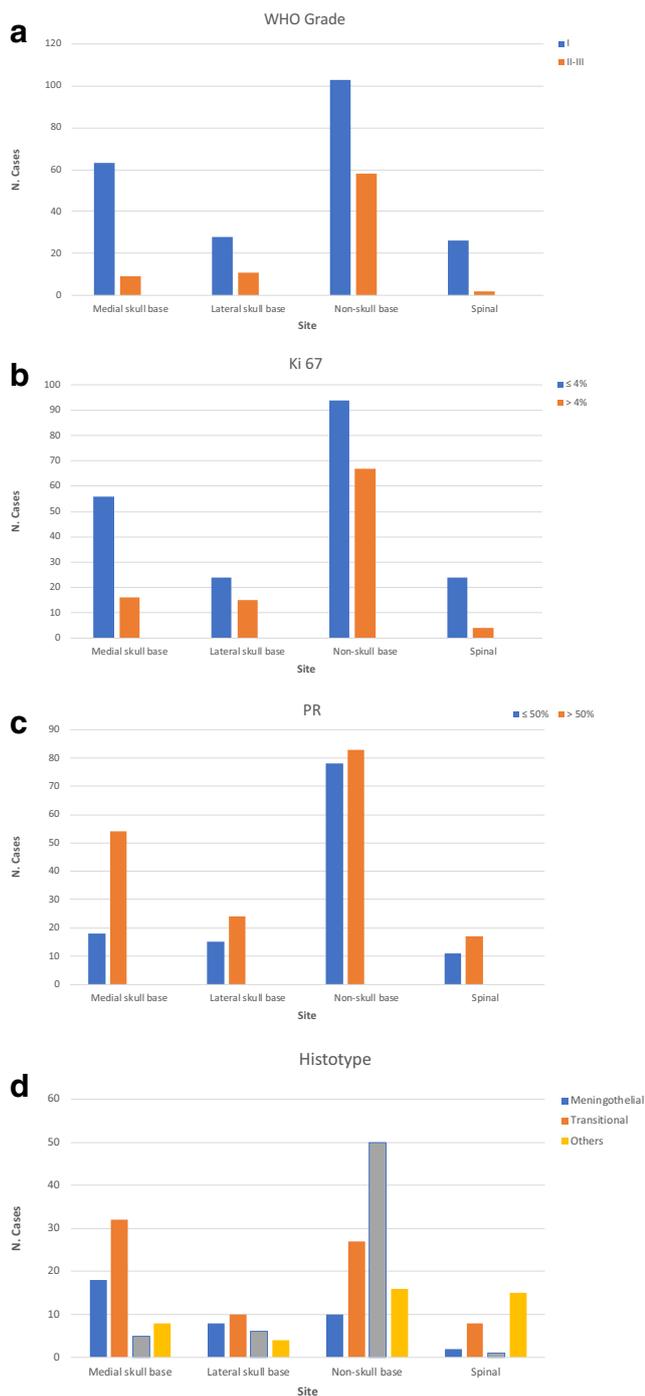
**Table 4** WHO grade, Ki67-MIB1, and PR expression in the 4 groups of meningioma locations

Meningioma location	No. of cases	WHO grade			Ki67		PR expression	
		I	II	III	≤ 4%	> 4%	≤ 50%	> 50%
Medial skull base	72	63 (87.5%)	9 (12.5%)	–	56 (78%)	16 (22%)	18 (25%)	54 (75%)
Lateral skull base	39	28 (72%)	10 (25.5%)	1 (2.5%)	24 (62%)	15 (38%)	15 (38.5%)	24 (61.5%)
Non-skull base	161	103 (64%)	55 (34%)	3 (2%)	94 (58%)	67 (42%)	78 (48%)	83 (52%)
Spinal	28	26 (93%)	2 (7%)	–	24 (86%)	4 (14%)	11 (39%)	17 (61%)
Total	300	220 (73%)	76 (25.5%)	4 (1.5%)	198 (66%)	102 (34%)	122 (41%)	178 (59%)
Statistical analysis		$p = 0.00034$			$p = 0.0031$		$p = 0.009$	

**Table 5** Distribution of histological subtypes according to the location of 220 WHO grade I meningiomas

Meningioma location	No. of cases	Meningothelial	Transitional	Fibrous	Psammatous	Secretory	Metaplastic	Microcystic
Medial skull base	63	18 (29%)	32 (50.5%)	5 (8%)	5 (8%)	1 (1.5%)	2 (3%)	–
Lateral skull base	28	8 (28.5%)	10 (36%)	6 (21.5%)	3 (10.5%)	1 (3.5%)	–	–
Non-skull base	103	10 (10%)	27 (26%)	50 (48.5%)	5 (5%)	2 (2%)	1 (1%)	8 (7.5%)
Spinal	26	2 (7.5%)	8 (31%)	1 (4%)	13 (50%)	2 (7.5%)	–	–
Total	220	38 (17.5%)	77 (35%)	62 (28%)	26 (12%)	6 (2.5%)	3 (1.5%)	8 (3.5%)

Statistical significance  $p < 0.00001$



**Fig. 1** Correlation of the location of meningiomas with **a** WHO grade, **b** Ki67-Li, **c** PR expression, **d** histological subtype

base and particularly with non-skull base meningiomas. The different pathological features between the medial and lateral skull base tumors, particularly concerning the PR expression, are the main and previously unreported findings of this study. In fact, all but one [47] published studies have compared all skull base versus non-skull base meningiomas (Table 7).

**Table 6** Correlation between meningioma location and recurrence

Meningioma location	No. of cases	Recurrence rate
Medial skull base	72	4 (5.5%)
Lateral skull base	39	7 (19%)
Non-skull base	161	27 (16%)
Spinal	28	1 (3.6%)
Total	300	39 (13%)

Statistical significance  $p < 0.035$

### Location, WHO grade, and proliferation index

As for other studies published in the last 2 years [16, 19, 23, 29, 46, 49], we have used the 2007 WHO classification, because all cases were diagnosed before 2016. Several studies published in the last 10 years have reported significantly higher rates of WHO II and III tumors [7, 15, 23, 28, 32, 47, 54] and higher values of Ki67-Li [7, 10, 15, 16, 28, 31, 46] in non-skull base versus skull base meningiomas (Table 7), as in our series. Only two recent studies [19, 49] did not find significant difference for both WHO grade and Ki67-Li between the two groups of meningiomas. However, both these studies include in the group of skull base meningiomas a high rate of lateral skull base tumors, mainly sphenoid wing and petrous, than medial skull base ones. In our study, lateral skull base meningiomas have shown higher rates of WHO II and III tumors and higher values of Ki67-Li than medial ones. This may explain the lack of significant difference in these two reports. Thus, according to our results, skull base meningiomas include locations with different rates of atypical forms and different values of Ki67-Li. This finding has not previously been reported. In our series, spinal meningiomas show rates of atypical tumors and values of Ki67-Li rather similar to those of medial skull base meningiomas and significantly lower than non-skull base ones. Similar results are reported only in the study by Sade et al. [47]. On the other hand, the lower mean value of Ki67-Li of WHO grade I meningiomas, as compared with the intracranial ones, was also confirmed in other studies [2, 17, 24, 25, 35, 43].

### Location and progesterone receptor expression

Only one recent study [19] has focused on the PR expression and meningioma location; it has found significantly higher proportion of positive PR expression in skull base meningiomas than non-skull base ones. Our study shows significantly higher rates of cases with PR expression > 50% and lower rates of cases with PR ≤ 50% in the medial skull base meningiomas as compared with lateral skull base and non-skull base ones. This finding has not previously been reported.

Several studies [33, 41, 44, 45, 53], including our previous report [26], found inverse correlation between PR expression and Ki67-Li in intracranial meningiomas, with tumors with

**Table 7** Reported studies on histopathological features and anatomical location of meningiomas

Authors/year	No. of cases	Time frame	WHO classification	Overall WHO grade		Correlation between pathological features and location			PR expression	Histological subtype
				II	III	Groups of tumor locations	WHO grades II and III vs I	Ki67-Li		
Kasuya et al. 2006 [16]	342	1995–2004	2000	8%	5%	Skull base vs non-skull base		0.305 vs 0.956 ( <i>p</i> = 0.035)		Meningothelial skull base vs non-skull base
Lee et al. 2006 [21]	794	1991–2004	2000	5.9%	2%	Medial skull base vs lateral skull base vs non-skull base				vs 48.5% ( <i>p</i> < 0.001) medial vs lateral skull base 84.9% vs 58.3% ( <i>p</i> = 0.001)
Stade et al. 2007 [47]	794	1991–2004	2000	5.9%	2%	Skull base and spinal vs non-skull base	3.5% and 1.3% vs 12.1% ( <i>p</i> < 0.001)			
McGowern et al. 2010 [31]	216	1965–2001	2000	10%	4%	Skull base vs non-skull base (recurrent)	5% vs 36% ( <i>p</i> = 0.024)	1.35% vs 2.60% ( <i>p</i> = 0.016)		
Kane et al. 2011 [15]	378	2000–2007	2000	16%	2%	Skull base vs non-skull base	12% vs 27% ( <i>p</i> < 0.001)			
Hashimoto et al. 2012 [10]	210	1993–2005	2007			Skull base vs non-skull base		2.09% vs 2.74% ( <i>p</i> = 0.013)		
Zhou et al. 2013 [54]	1737	2005–2010	2007	21.3%	3.3%	Medial skull base vs lateral skull base vs medial non-skull base vs lateral non-skull base	OR 1.72, WALD 4.72 ( <i>p</i> < 0.032) OR 2.80, WALD 9.37 ( <i>p</i> = 0.002) OR 2.89, WALD 22.41 ( <i>p</i> = 0.001)			
Cornelius et al. 2013 [7]	1663	1991–2011	1993–2000	4.6%	0.4%	Skull base vs non-skull base	OR 2.043 ( <i>p</i> = 0.004)	1.97% (SD 1.56) vs 2.24% (SD 1.57) ( <i>p</i> = 0.001)		
Mansouri et al. 2016 [28]	398	1993–2014	2000	19.6%	5.8%	Skull base vs non-skull base	85.3% vs 69.1% ( <i>p</i> = 0.003)	0.041 vs 0.062 ( <i>p</i> = 0.001)		
Savardekar et al. 2018 [49]	582	1995–2016	2007	9%	0	Skull base vs non-skull base	11/28 vs 10/39 ( <i>p</i> = 0.3)	3.06 ± 2.24 vs 4.08 ± 3.9 ( <i>p</i> = 0.244)		
Kuroi et al. 2018 [19]	161	2007–2016	2007	14.7%	4.4%	Skull base vs non-skull base	13.1% vs 21% ( <i>p</i> = 0.2066)	4.2 ± 5.7 vs 4.8 ± 5.6 ( <i>p</i> = 0.5275)	61.5 ± 33.4% vs 42.2 ± 35.7% ( <i>p</i> = 0.0009)	
Magill et al. 2018 [23]	113	1985–2016	2007	18.7%		Skull base vs falx-parasagittal-convexity	OR 1.83 (CI 1.19–2.82) ( <i>p</i> = 0.006)			
Meling et al. 2019 [32]	1148	1990–2010		5%	2%	Skull base vs non-skull base	4.5% vs 9.3% RR 0.5 ( <i>p</i> < 0.001)			
Present study	300	2006–2016	2007	25.3%	1.3%	Lateral skull base vs non-skull base vs medial skull base vs spinal base	<i>p</i> = 0.00034	<i>p</i> = 0.0031	<i>p</i> = 0.009	<i>p</i> < 0.00001

PR progesterone receptor, *ns* not significant, “–” not studied

higher PR expression showing significantly lower Ki67-Li values than those with low or negative PR expression. This correlation is confirmed in groups of different locations, mainly for medial skull base meningiomas. Only two previous studies [2, 43] and our one recent report [25] have focused on the PR status of spinal meningiomas. Both have shown variable and often high positivity in a high rate of cases and no significant correlation with the Ki67-Li.

### Location and histological subtypes

The distribution of the histological subtypes of meningiomas in the different locations has been investigated in two studies [4, 21]. Lee et al. [21] found that the meningothelial subtype was significantly more frequent at the medial skull base and spinal canal than at the lateral skull base and non-skull base locations. On the other hand, Bhat et al. [4] reported no significant differences in the various locations. In our study, most meningothelial meningiomas (68%) were located at the skull base; however, in this location, the transitional type was the most frequent.

### Embryological implications

Several embryological and genetic aspects may be suggested to explain the different pathological findings and PR expression according to the meningioma location. Two previous studies [5, 39] have stated that the meninges are derived from the neural crest in the telencephalon, cephalic mesoderm around the brain stem, and somatic mesoderm in the spinal canal. This should agree with the different pathological features according to the meningioma location in our series. However, other studies [3, 13, 50, 52] do not agree with this different origin and suggest that all cranial and spinal meninges originate from the neural crest.

Several studies on the molecular pathogenesis of meningiomas have attempted to identify different genetic pathways from the cells of origin to diverse meningioma subtype [14, 40]. Kalamarides et al. [14] in a mice model have shown that the biallelic NF2 inactivity resulted in meningioma development at the skull base but not at the convexity. This suggests that meningiomas may develop different abilities to express PR according to their site of origin and genetic differentiation [6].

### Clinical implications

The significant differences of WHO grade, proliferation index, PR expression, tumor size, and arachnoid interface in our study agree with the different behavior and recurrence rate of the various meningioma locations. Medial skull base meningiomas include locations (such as the olfactory groove, tuberculum sellae, anterior clinoid, and foramen magnum) with often more slow course and recurrence rates ranging from 0 to 15% [18, 20, 38, 50]. Besides, the low recurrence rate of spinal meningiomas is well known (0–10% in 15

among 19 reviewed series in our recent study [25]). On the other hand, the reported recurrence rates are higher for lateral skull base (lateral sphenoid wing and particularly sphenoorbital (35–40%)) [29, 30, 48] and for non-skull base meningiomas (mainly parasagittal and falx) (16–24%) [8, 37].

It is well known that positive PR expression is a prognostic factor for better biological behavior and lesser risk of recurrence for intracranial meningiomas [1, 23, 28, 36, 39, 40, 47]. In our study, the group of medial skull base meningiomas shows significantly higher PR expression than lateral skull base and non-skull base.

Some studies have shown that larger tumor size is associated with an increased likelihood of a meningioma being WHO grade II [9, 11] and with increased risk of recurrence [12, 25, 37]. Besides, disruption of the arachnoid layer and irregular tumor margins are also correlated to the recurrence [12, 26, 27, 36, 37, 51]. Our study confirms that non-skull base and lateral skull base meningiomas show larger tumor size, higher rates of cases with lost arachnoid interface, with WHO II and III histology, and higher recurrence risk.

Thus, an inverse correlation between WHO grade and PR expression is also maintained in the various locations and different tumor sizes.

### Conclusion

Medial skull base and spinal meningiomas show significantly lower incidence of atypical WHO II forms, lower rate of cases with Ki67-Li values > 4%, lower medial tumor diameter, lower rate of cases with lost arachnoid interface, and lower rate of recurrence than lateral skull base and non-skull base meningiomas. The rate of meningiomas with negative or weakly positive PR expression is significantly lower in the medial skull base than in the non-skull base group, whereas the incidence in the spinal group is not significantly different.

Further studies will investigate the molecular and genetic characteristics of the various locations and subtypes of meningiomas, and correlate them with the different recurrence risk.

### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** For this retrospective study, no institutional review board approval or patient consent is required per institutional policy.

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