

# Management and Clinico-Pathologic Aspects of Non-Melanoma Skin Cancer of the Head and Neck: A Retrospective Institutional Based Study at the Egyptian National Cancer Institute

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## Abstract

**Background:** Reviewing and analyzing the Clinico-pathologic aspects of non-melanoma skin cancer of the head and neck (NMSCHN), type of management, prognostic factors, and disease-free survival (DFS) in a period of 5 years at the National Cancer Institute—Cairo University—Egypt. **Materials and Methods:** A retrospective study of two hundred patients with NMSCHN was treated at the National Cancer Institute—Cairo University—Egypt from January 2008 to December 2012. The mean follow-up was 6 months (1 - 84 months). **Results:** 117 males and 83 females with 90% ≥ 50 years old. The scalp (27.5%), the periorbital region (13%), the cheek (12.5%) and the nose (12.5%) are the main anatomical sites affected. BCC represented 71.5% with nodular type (79%) predominance; SCC represented 21% with GII (61.1%) the commonest grade. Surgery was the main modality of treatment (93%) with local flaps only (63.9%) and primary closure (14.7%) were the main surgical options following wide local excision. Positive and close margins were detected in 23.5% of excised specimens. No significant association was found between disease-free survival (DFS) and pathology, treatment modality, the occurrence of complications or safety margin status. **Conclusion:** NMSCHN lesions should be surgically excised in specialized high volume centers with readily available peripheral margin control and should be operated by senior experienced surgeons.

## Keywords

Basal Cell Carcinoma, Squamous Cell Carcinoma, Non-Melanoma Skin Cancer

## 1. Introduction

Non-melanoma skin cancer (NMSC) is the most common malignancy among Caucasians. NMSC principally comprises basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), but includes a host of rarer skin tumors [1]. According to The National Cancer Registry in Egypt based on Data of 40,477 patients collected from Tanta Cancer Center retrospectively to form the largest population-based cancer registry in Egypt covering a period of 9 years, skin cancer incidence was calculated as 3.1% of all cancers in both sexes and 3.8% of all cancers in males based on population of Gharbia (as an indicator for rates in Egypt) and based on number of cases of each cancer type there [2]. In the Egyptian population, over 60% of NMSC could be attributed to sun exposure and approximately 45% to skin color [3]. More specifically the incidence of NMSC was addressed at the National Population-Based Cancer Registry Program (2008-2011) as 1.35% of all cancers in males and 1.24% of all cancers in females [4]. In settings such as developing countries where Moh's Micrographic Surgery is not readily available, prediction of NMSC aggressive lesions based on preoperative information (age, immunosuppression status, and location) is critical not only for surgical planning but also for reducing recurrence risk by treating the lesion with sufficiently adequate margins. Several studies have attempted to create a risk scale or model for assessing preoperative risk for aggressive NMSCs [5] [6] [7] [8]. In Egypt, few studies focused on NMSC, mostly with a limited number of patients and not specific to NMSCHN and not addressing many prognostic factors highlighted and evaluated in this study [9] [10] [11] [12]. In other parts of the world, with almost similar climate to Egypt, skin cancer is a common cancer [13], with increasing incidence of SCC and Basosquamous carcinoma (BSC) [14]. This study will focus on Egyptian patients with non-melanoma skin cancer of the head and neck (NMSCHN) who presented, diagnosed and managed at the National Cancer Institute—Cairo University—Egypt.

## 2. Materials and Methods

A retrospective study where all patients' data with non-melanoma skin cancer of the head and neck (NMSCHN) diagnosed, admitted and managed at the National Cancer Institute—Cairo University—Egypt in the period from January 2008 to December 2012 were documented and analyzed regarding patients' characteristics (age and sex), tumor characteristics (anatomical site, T stage and number of lesions), histopathology (type and grade), treatment modality (surgery  $\pm$  adjuvant treatment or no interference), safety margin status (positive, close or negative), type of reconstruction and type of flap used, complications and recurrence(s) during a follow-up period ranging from 1 to 84 months with a mean follow-up of 6 months. Recurrence and Disease-free survival will be correlated statistically with different parameters.

### 2.1. Exclusion Criteria

- Patients with NMSCHN who were managed outside our institute and were

just referred for follow-up or for consultation.

- Patients with Xeroderma pigmentosum.
- Patients with melanoma skin cancer by histopathology.

## 2.2. Statistical Method

Demographic data and survival outcome will be analyzed using SPSS statistical package version 20. Relations between qualitative data will be done using Chi-square test or Fisher's exact test. Moreover, survival analyses will be done using Kaplan Meier's method and Comparison between survival curves will be done using log-rank test. A p-value less than 0.05 will be considered significant.

## 3. Results

Two hundred patients with NMSCHN were involved in this retrospective study in the period from January 2008 to December 2012.

### 3.1. Patients' Characteristics

- **Age:** The age of the patients ranged between 5 and 90 years with the peak incidence in the sixth decade of life. 15.5% of patients were below or equal to the age of 50 while 84.5% were 51 years old or more (**Table 1**).
- **Sex:** Male patients constituted 58.5% (117/200) of cases while females constituted 41.5% (83/200). Male to female ratio was about 1.4:1 (**Table 2**).

### 3.2. Tumor Characteristics

- **Anatomical distribution of lesions:** The main site affected was the scalp 27.5% (55/200), followed by the periorbital region 13% (26/200), while the cheek and nose were equally affected 12.5% (25/200) each. Two patients with BCC showed multiple lesions in different sites 1% (2/200) (**Table 3**).
- **T Stage:** The majority of cases were T1 representing 52% of all cases (104/200) and T4 representing 4% (8/200) with tumor invasion to parotid gland and eye globe (**Table 4**).

**Table 1.** Age distribution of patients with NMSCHN.

Age (years)	Number of patients	Percent (%)
≤50	31	15.5
>50	169	84.5
<b>Total</b>	<b>200</b>	<b>100</b>

**Table 2.** Sex distribution of patients with NMSCHN.

Gender	Number of patients	Percent (%)
Males	117	58.5
Females	83	41.5
<b>Total</b>	<b>200</b>	<b>100</b>

**Table 3.** Anatomical site distribution of NMSCHN lesions.

Site	Number of patients	Percent (%)
Scalp	55	27.5
Cheek	25	12.5
Auricle	6	3
Periorbital	26	13
Forehead	10	5
Upper lip	11	5.5
Lower lip	20	10
Nose	25	12.5
Neck	2	1
Nasolabial	4	2
Temple	6	3
Post-auricular	4	2
Pre-auricular	4	2
Post auricular, scalp, nose	1	0.5
Forehead, nasolabial, lower lip	1	0.5
<b>Total</b>	<b>200</b>	<b>100</b>

**Table 4.** Distribution of NMSCHN lesions according to T stage.

Stage	Number of patients	Percent (%)
T1	104	52
T2	72	36
T3	16	8
T4	8	4
<b>Total</b>	<b>200</b>	<b>100</b>

- **Number of Lesions:** 94% (188/200) of patients presented with a single lesion, 1% (2/200) of patients presented with 2 lesions and 5% (10/200) with multiple lesions. 12 patients presented with two and more lesions where 8 of them BCC (two of them in different sites), 2 SCC and 2 were BSCC patients (**Table 5**).

### 3.3. Tumor Histopathology: (Tables 6-8)

All lesions were pathologically examined preoperatively and postoperatively to confirm the diagnosis and determine the margin status. BCC was detected in 72.5% (145/200) of patients, SCC in and basosquamous were detected in 21% (42/200) and 6% (12/200) of patients, respectively (**Table 6**). The most common type of BCC was the nodular type representing 79% (113/200) of cases (**Table 7**). The most common grade among the fifty four patients with Squamous Cell Car-

cinoma (SCC) and Basosquamous Carcinoma (BSC) was grade II, moderately differentiated tumors represented 61.1% (33/54) of cases (**Table 8**).

**Table 5.** Distribution of patients with NMSCHN according to the number of Lesions per patient.

Number of lesions per patient	Number of patients	Percent (%)
Single	188	94
Two lesions	2	1
Three or more	10	5
<b>Total</b>	<b>200</b>	<b>100</b>

**Table 6.** Tumor histopathology of NMSCHN among the study population.

Tumor Histopathology	Number of patients	Percent (%)
Basal cell carcinoma	143	71.5
Squamous cell carcinoma	42	21
Basosquamous	12	6
Adenocarcinoma	3	1.5
<b>Total</b>	<b>200</b>	<b>100</b>

**Table 7.** Clinico-pathologic types of BCC.

Clinico-pathologic types	Number of patients	Percent (%)
Nodular	113	79
Adenocystic	6	4.2
Superficial spreading	3	2.1
Pigmented	6	4.2
Morpheaform	6	4.2
Micronodular	1	1.4
Infiltrative	3	2.1
Keratotic	4	2.8
Mixed nodular superficial	1	0.7
<b>Total</b>	<b>143</b>	<b>100</b>

**Table 8.** Histopathological Grades of Squamous Cell Carcinoma (SCC) and Basosquamous Carcinoma (BSC).

Grade	Number of patients	Percent (%)
I	14	25.9
II	33	61.1
III	7	12.9
<b>Total</b>	<b>54</b>	<b>100</b>

### 3.4. Treatment Modality: (Table 9)

Surgery was the only treatment modality in 93% (186/200) of patients, surgery followed by post-operative radiotherapy (PORT) in 2% (4/200) of patients, they had positive margins and were not candidates for re-excision because of reconstruction and proximity to the eye. One patient (0.5%) developed metastatic SCC and received adjuvant chemotherapy 3% (6/200) of patients developed local recurrence followed by lung metastasis they underwent surgical excision followed by radiotherapy then chemotherapy. Meanwhile, 3 patients with BCC (1.5%) received no treatment because they were locally advanced, elderly with co-morbidities and beyond treatment.

### 3.5. Safety Margin Status: (Table 10)

Peripheral margin control guided by intraoperative frozen section analysis (IFSA) was not used in all patients but most of them. Postoperative Histopathological examination of all surgically excised specimens was done (except for four patients where SM was not assigned) for histopathological confirmation of tumor type and to detect adequacy of the safety margins where all specimens' margins were oriented by sutures. Margins of surgical excision were negative in 150 (76.5%), positive in 41 (20.9%) and close in 5 (2.6%) of postoperative specimens.

### 3.6. Closure of the Defect and Type of Reconstruction: (Table 11 & Table 12)

Most of the study population underwent reconstruction with local flaps only 126/197 (63.9%), in 14.7% of patients (29/197) primary closure only was successfully achieved. Among patients who underwent surgical excision the method

**Table 9.** Treatment modality in patients with NMSCHN.

Treatment Modality	Number of patients	Percent (%)
Surgery	186	93
Surgery + PORT	4	2
Surgery + chemotherapy	1	0.5
All	6	3
No interference	3	1.5
<b>Total</b>	<b>200</b>	<b>100</b>

**Table 10.** Safety margin status in postoperative pathologically examined specimens.

Margin Status	Number of patients	Percent (%)
Positive	41	20.9
Close	5	2.6
Negative	150	76.5
<b>Total</b>	<b>196</b>	<b>100</b>

of defect closure was not assigned in only one patient 1/197 (0.5%) due to inadequate patient operative documentation. Rotational flaps (**Figures 4-6**) were the most commonly used type of flaps for the reconstruction of post-excision defects in this study (28.3%) followed by advancement flaps (27%) (**Figure 1**) then forehead flaps (12.1%) (**Figure 3**).

### 3.7. Distribution of BCC and SCC in Relation to Different Factors

Regarding sex, number of lesions, treatment modality, occurrence of complications and safety margin status no statistically significance was detected in relation to the histopathological type of NMSCHN either BCC or SCC (after exclusion of other histopathological types) (**Table 13**).

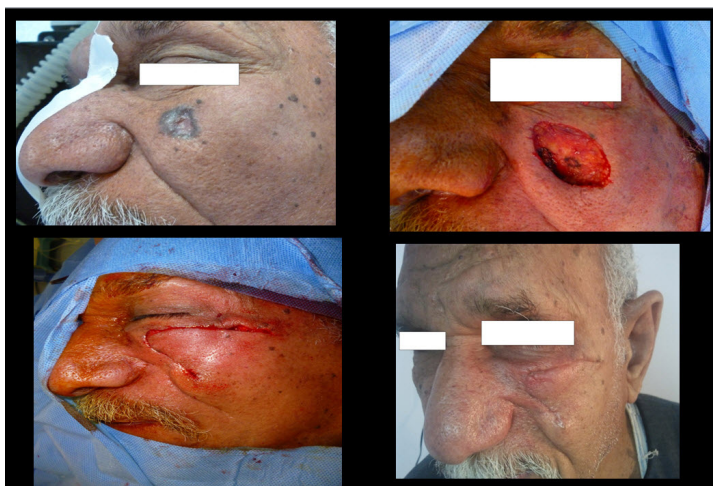
**Table 11.** Methods used for closure of the defects following surgical excision of NMSCHN.

Type of closure	Number of patients	Percent (%)
Primary closure	29	14.7
Secondary intention	5	2.5
Graft ( <b>Figure 7</b> )	19	9.7
Local flap	126	63.9
Free flap	2	1
Graft + local flap	15	7.7
Defect closure was not assigned	1	0.5
<b>Total</b>	<b>197</b>	<b>100</b>

**Table 12.** Types of local flaps used for reconstruction following surgical excision of NMSCHN (**Figures 1-7**).

Type of local flap	Number of patients	Percent (%)
Advancement	38	27
Bilobed ( <b>Figure 2</b> )	3	2.1
Cervicofacial	3	2.1
Forehead	17	12.1
Glabellar	5	3.5
Rhomboid	8	5.7
Random	1	0.7
Estlander flap	2	1.4
Rotational	40	28.3
Transposition	3	2.1
V-Y flap	11	7.8
Nasolabial	4	2.8
Karapandzic flap	6	4.3
<b>Total</b>	<b>141</b>	<b>100</b>





**Figure 1.** Advancement cheek flap for left cheek BCC.



**Figure 2.** Bilobed flap for BCC of the nose.

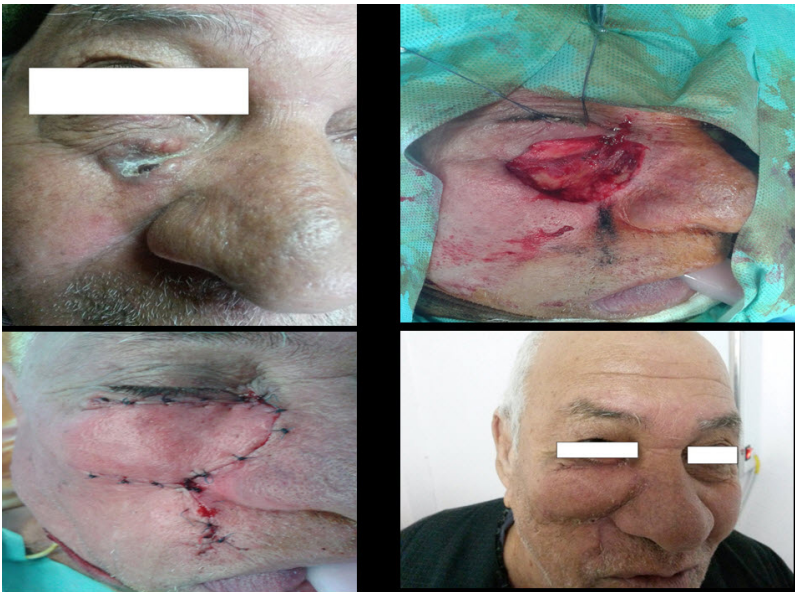


**Figure 3.** Large SCC of the nose with forehead flap to close the defect.





**Figure 4.** SCC of the occipital region with WLE and closure of the defect with rotational scalp flap.



**Figure 5.** BCC below the right lower eye lid WLE was done with rotational flap.



**Figure 6.** Rotational flap for right nasal BCC.



**Figure 7.** Full thickness (Wolfe) graft from the skin of the arm after WLE of BCC of the nose.

**Table 13.** Distribution of BCC and SCC in relation to different factors and its significance.

Factor	BCC	SCC	Total	p-value
Sex				
Male	79	31	110	0.031
Female	64	11	75	
Total	143	42	185	
Number of lesions				
Single	135	41	176	0.395
Multiple	8	1	9	
Total	143	42	185	
Treatment modality				
Surgery	134	39	173	0.481
Surgery plus	6	3	9	
adjuvant therapy				
No interference	3	0	3	
Total	143	42	185	
Complication	3	2	5	0.367
No complication	136	40	176	
Total	139	42	181	
Safety margins				
Positive	31	5	36	0.335
Close	3	1	4	
Negative	105	36	141	
Total	139	42	181	

### 3.8. Recurrence (Locoregional/Distant): (Table 14)

Fifty patients developed loco-regional recurrence. Out of the 50 patients who developed loco-regional recurrences, 45 developed single recurrence and 5 developed repeated recurrences. 9 patients developed regional lymph nodes

**Table 14.** Correlation between different factors and recurrence among NMSCHN patients.

	Recurrence	No recurrence	Total	p-value
Age				
≤50 years	13	18	31	0.18
>50 years	37	132	169	
Total	50	150	200	
Sex				
Male	24	93	117	0.082
Female	26	57	83	
Total	50	147	200	
Number of lesions				
Single	43	145	188	0.007
Multiple	7	5	12	
Total	50	150	200	
T stage				
T1	25	79	104	0.771
T2	19	53	72	
T3	3	13	16	
T4	3	5	8	
Total	50	150	200	
Treatment modality				
Surgery	40	146	186	0.001
Surgery plus adjuvant therapy	10	1	11	
Total	50	147	197	
Pathology				
BCC	30	115	145	0.25
BSC	13	31	44	
Total	43	146	189	
Grade for SCC and BSC				
G I	4	10	14	0.008
G II	10	23	33	
G III	6	1	7	
Total	20	34	54	
Safety margins				
Positive	26	15	41	0.001
Close	2	3	5	
Negative	22	128	150	
Total	50	146	196	
PO complications				
Complications	4	3	7	0.051
No complications	46	143	189	
Total	50	146	196	

metastasis. 6 patients of them were SCC and 3 patients were BSC. Those patients underwent neck dissection. During follow-up 6 SCC, patients developed pulmonary metastasis.

Many independent prognostic factors were found to significantly affect the recurrence rate among patients with NMSCHN. Patients aged more than 50 years old (p-value = 0.18), patients with multiple lesions (p-value = 0.007), patients with high grade of SCC or BSC (p-value = 0.008), patients with positive and close margins (p-value = 0.001), patients subjected to surgery + adjuvant therapy (p-value = 0.001) and patients who showed PO complications (p-value = 0.051), all those, showed significantly higher recurrence rate in relation to the rest of the study population. Other factors as T stage, sex of patients and BCC vs. BSC pathology didn't show a significant increase in recurrence rate among the study population (**Table 14**).

### 3.9. Disease-Free Survival (DFS): (**Table 15**)

Disease free survival ranged from 10.5 to 29.5 months with a median of 20 months. Regarding age, sex, T stage, treatment modality, occurrence of complications, histopathology (BCC vs. SCC) and safety margins; none of those factors showed a statistically significant correlation with Disease-free Survival (DFS).

## 4. Discussion

To our knowledge, this study is by far the largest one in Egypt addressing non-melanoma skin cancer of the head and neck (NMSCHN), regarding the number of patients and the period of follow up which extended up to 84 months. The incidence of non-melanoma skin cancer is still rising worldwide [15], this increase can be, in part, attributed to the increase in the elderly population, in addition, many patients develop more than one non-melanoma skin cancer after the first one [16]. In this study, patients over 50 years old represented 84.5% of the study population (mean 60, 6 years with the peak incidence in the sixth decade) in whom recurrence rate was significantly higher (p-value = 0.18), similarly some studies on NMSC detected a peak incidence in the sixth decade of life [10] [11] [17] [18], others in the seventh decade [8] [9] [13] [19] [20]. Male predominance was observed in this study as well as other studies [9] [11] [14] [19] [21], on the other hand, other studies of NMSC showed female predominance [10] [13] [17] [20]. The male sex predilection of skin cancer in Egypt is explained by the fact that men represent the main workforce (outdoor work) with more risk for UV exposure than women [22]. NMSC most commonly occur in the head and neck region [1] [10] [11] [13] [21] [23] [24] [25], and according to this study the scalp, nose and cheek are the most common anatomic sites for the occurrence of NMSCHN, according to Mahmoud *et al.*, 2006 the cheek and nose [10], according to Rhee *et al.*, 2008 the nose, cheek and eyelids [20], according to Al-Zou *et al.*, 2016 the face (NOS), the eyelids and the ear [13], according

**Table 15.** Correlation between different factors and DFS among NMSCHN patients.

	Number of patients	Median Survival (mo.)	p-value
<b>Age</b>			
≤50 years	31	36	<b>0.177</b>
>50 years	165	20	
<b>Total</b>	<b>196</b>	<b>20</b>	
<b>Sex</b>			
Male	114	12	<b>0.4</b>
Female	82	20	
<b>Total</b>	<b>196</b>	<b>20</b>	
<b>T stage</b>			
T1	102	20	<b>0.112</b>
T2	71	12	
T3	16		
T4	7	48	
<b>Total</b>	<b>196</b>	<b>20</b>	
<b>Treatment modality</b>			
Surgery	185	20	<b>0.398</b>
Surgery plus adjuvant therapy	11	30	
<b>Total</b>	<b>196</b>	<b>20</b>	
<b>Pathology</b>			
BCC	139	20	<b>0.927</b>
SCC	42	30	
<b>Total</b>	<b>181</b>	<b>20</b>	
<b>Safety margins</b>			
Positive	41	12	<b>0.187</b>
Close	5	6	
Negative	149	36	
<b>Total</b>	<b>195</b>	<b>20</b>	
<b>PO complications</b>			
Complications	7	36	<b>0.507</b>
No complications	189	20	
<b>Total</b>	<b>196</b>	<b>20</b>	

to Marconi *et al.*, 2016 the nose and face [26] and according to Zargaran *et al.*, 2013 the nose, the cheek and the scalp [21] are the most common sites for occurrence of NMSCHN, noting that the nose is commonly affected in all the studies. T1 lesions represented the main T stage in this study (52%) while T2 represented 36% of lesions in the study population; this is in agreement with other studies [11] [26]. Nodular type of BCC was by far the most common in this study population (79%) similarly other studies showed nodular type predominance in BCC [9] [10] [18] [27]. Grade II for SCC and BSC was predominant in our study (61.1%) while Mahmoud *et al.*, 2006 reported Grade I predom-



ance (46.6%) [10]. In spite of alternatives to the surgical management of cutaneous malignancies may be preferred under certain circumstances [11], Surgery remains the main line of treatment for NMSC [28], a recent meta-analysis comparing the different treatment modalities for NMSC demonstrated that surgical excision had superior outcomes when compared to cryotherapy, photodynamic therapy, radiotherapy, 5-fluorouracil (5-FU), and imiquimod in terms of complete lesion response, clearance of NMSC, and cumulative recurrence probabilities [29]. 98.5% of our patients were operated upon as a part of the management strategy. It should be noted that head and neck skin cancers are particularly challenging to treat given the difficulty in determining the amount of tissue that should be excised to provide adequate cancer-free margins with the best functional and cosmetic outcome. In this study, we relied mainly on intra-operative frozen section analysis (IFSA) whenever available, unfortunately, it was not used in all our patients due to unavailability and sometimes due to surgeons' reluctance leading to a high rate of positive margins (20.9%) with a significant recurrence rate ( $p = 0.001$ ). Mohs Micrographic Surgery (MMS) is still not available at our institute, which was not considered a big concern by our team relying on a systemic review by Bath-Hextall *et al.*, 2007 where surgical excision was compared to MMS and demonstrated no difference in 30-month recurrence rates in the treatment of BCC [30]. Similarly, no difference was found in the recurrence risk following treatment of recurrent BCC removed by surgical excision versus MMS [31]. A recent meta-analysis by Lansbury *et al.*, 2013 indicated similar results for cutaneous SCC, signifying no difference between recurrence risk of surgical excision and MMS [32]. Although Bartos and Kullova 2018 stated that BCC and SCC had several clinicopathological differences and should be considered separately [33], our study didn't show any significance regarding the distribution of both BCC and SCC in relation to different factors (Table 13).

Since NMSC only very sporadically leads to metastases, one of the most adverse clinical features of disease is local tumor recurrence. This is a relatively frequent matter in a routine dermatologic practice. According to literature data, local recurrence rates range between 2% and 4.3% [34] [35], unfortunately the recurrence rate in this study was high up to 25% due to several factors including the anatomic sites of the lesions, the size (high risk lesions), the positive margins due to unavailability of IFSA and many patients were operated upon by young surgeons and senior residents.

## 5. Conclusion

NMSCHN lesions should be surgically excised in specialized high volume centers with readily available peripheral margin control and should be operated by senior experienced surgeons.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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