

# Incidence of Malignant Tumors of the Skin by Anatomic Subsite, Gender and Age

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**Objective:** To analyze the clinico-pathological data of the skin lesions, especially malignant tumors, this study being the first step in a future immunohistochemical and molecular analysis.

**Methods:** The 3582 cases of benign, malignant, premalignant and tumor-like lesions of the skin, diagnosed during January 2006–December 2010 in the Pathology Department of the County Emergency Clinical Hospital of Târgu Mureș, surgically specimens, were revised and grouped based on histopathological forms.

**Results:** Epithelial tumors represented 37.32% of all skin tumors. The mesenchymal tumors (30.29%) were followed by melanocytic tumors (12.45%) and lymphomas (0.39%). Synchronous tumors represented 10.24% of cases. 63.5% of epithelial tumors were malignant, in contrast to 4.52% from mesenchymal tumors. Squamous cell carcinomas (SCC) and basal cell carcinomas (BCC) were predominant, both of them affecting the upper half of the face. SCC especially occurred in males (60.98%), but BCC were more frequent in females (50.84%). The average age was 71.30±11.92 years in SCC, and 68.15±11.29 years in BCC respectively. Regarding cutaneous melanomas, females (58.09%) were more affected than males (41.09%). The average age was 61.04±14.35 years. The trunk was the most common location in males, and the lower limb in females. Regarding lymphomas, only Mycosis fungoides was diagnosed.

**Conclusions:** Most tumors of the skin are malignant epithelial tumors, but mesenchymal tumors are rather benign type. Melanomas are mostly related to the sun exposure, the trunk and lower limb being more involved. In a significant percentage of cases synchronous tumors can develop. Further immunohistochemical and molecular studies are necessary to elucidate the differences between single and synchronous tumors and gender-related characteristics.

**Keywords:** skin lesions, malignant tumors, histological types

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## Introduction

The skin is not only the largest organ of the body, but also one of the most affected by the process of malignancy.

Epithelial tumors of the skin are a group of lesions derived from the proliferation of epidermal and adnexal keratinocytes. These tumors account for approximately 90% or more of all skin malignancies, of which basal cell carcinomas represent 70% exceed by squamous cell carcinomas [1]. Risk factors for the development of squamous cell carcinomas in Caucasians is chronic sun exposure, while in darkly pigmented individuals it is chronic scarring and areas of inflammation [2]. Basal cell carcinoma appears more frequently in Caucasians, one of the explanation being the degree of pigmentation [3]. The development of this tumor is correlated with acute and intermittent sun exposure [4]. Other possible risk factors include: immunosuppression, scars, radiotherapy, genetic disorders like xeroderma pigmentation and albinism [3].

Mesenchymal tumors are more rarely observed, but the prognosis is more unfavorable. Melanocytic skin tumors are a large variety of benign and malignant neoplasms with different clinical, morphological and genetics profiles. The incidence of melanoma has increased significantly worldwide over the last several decades [5]. The major risk factor is considered to be sun exposure [6]. The skin is the

second most common site of extranodal lymphoma. These tumors involve the skin as a primary or secondary tumor. They may be either B-cell or T-cell lymphomas [7]. The most common forms of T-cell lymphomas are mycosis fungoides and Sezary syndrome [8]. Cutaneous follicle centre lymphoma, cutaneous marginal zone B-cell lymphomas and cutaneous diffuse large B-cell lymphoma are the B-cell lymphoma's subtypes [9].

The purpose of this study was to analyze the clinico-pathological data of skin lesions and to perform a detailed statistical analysis regarding the primary malignant tumors of the skin. The clinical relevance consists in the histological reevaluation of a very large number of cases (3582 cases), this step being mandatory for the next one, a complex immunohistochemical and molecular analysis of these malignant tumors.

## Methods

In our study we performed a retrospective statistical clinico-pathological analysis of a significant number of benign, malignant and premalignant tumors of the skin, focusing on the malignant tumors. The 3582 cases of skin tumors and tumor-like lesions included in study, were reexamined and reevaluated. The tumors were divided according to their origin in the following categories: I. epithelial tumors (epidermal tumors, Merkel-cell carcinomas and tumors of the epidermal appendages); II. tumors of the mesenchymal tissue (tumors of connective and adipose tissue, vascular,

muscular and nerve tumors); III. melanocytic tumors; IV. lymphoid tumors; V. synchronous tumors.

For each case the following parameters have been analysed: gender and age of patients, localization of tumor and histological type. The degree of differentiation was analysed only in malignant epithelial tumors, namely in squamous cell carcinomas.

This data-linkage study was conducted using data obtained from histopathological forms of the Department of Pathology of the County Emergency Clinical Hospital of Târgu Mureș, Romania. Patients diagnosed between January 2006 – December 2010 were enrolled in the study. Dewaxed paraffin-embedded tissues were used.

The statistical analysis was performed using Graph Pad In Stat 3. The data was collected with Microsoft Excel. We used the chi square test, contingency tables and the Mann-Whitney. P values below 0.05 were considered to be statistically significant, with a 95% confidence interval.

## Results

### Distribution of cases

From the 3582 cases, 50.69% were benign tumors, 28.30% malignant tumors, 0.89% premalignant lesions, 0.55% tumor-like lesions, 10.24% synchronous tumors and 9.29% were cysts. According to their origin, the following lesions have been identified: 1337 epithelial lesions, 1085 mesenchymal tumors, 446 melanocytic tumors, 14 lymphocytic tumors, 367 synchronous tumors and 333 cases were cysts.

From the 1337 epithelial tumors, one case was Merkel-cell carcinoma, diagnosed on the head of a 67 year-old man. More than 60% of epidermal tumors were malignant. On the opposite, only 8% of appendage tumors were malignant ( $p < 0.0001$ ). The distribution of cases is presented in Table I.

In the group of mesenchymal tumors (Table II), we noted that most of the tumors originated from connective and adipose tissue (65.25%). One important aspect was the significantly ( $p < 0.0001$ ) small proportion of malignant cases (4.51%), compared to the number of epithelial tumors (63.32%).

From the 446 melanocytic tumors, 23.54% were malignant melanomas and 76.46% nevi. Thirteen lymphomas and one lymphocytoma were identified.

The following cysts have been diagnosed: epidermal (286), trichilemmal (31), sebaceous (9), serous (4), dermoid (3). The 367 synchronous tumors will be analyzed in a future paper.

### Malignant epithelial tumors

#### 1. Malignant epidermal tumors

From the 840 cases (Table I), 305 were squamous cell carcinomas (SCC) and 535 basal cell carcinomas (BCC). SCC especially occurs in males (60.98%) but BCC were more frequently diagnosed in females (50.84%), with a

significant difference between the two types ( $p = 0.001$ ).

The average age was  $71.30 \pm 11.92$  years (range 23–98) in SCC, and  $68.15 \pm 11.29$  years (range 20–100) in BCC ( $p = 0.34$ ).

47.86% of SCCs and 79.62% of BCCs were located on the head and neck (Table III). For both types the upper half of the face's skin was predominantly involved. The lip (28.52%), penis (9.50%), upper limb (5.90%), lower limb (3.27%), trunk (2.95%), and perineal region (0.65%) were affected by SCC. BCC was most frequently located on trunk (11.58%), lip (2.24%), lower limb (2.24%) and upper limb (1.49%). There was no statistically significant difference between the localization of SCC and BCC ( $p = 0.62$ ).

Most of the SCCs were moderately differentiated (45.57%), followed by well (32.45%) and poorly differentiated carcinomas (21.96%). 68% of the BCC were solid type, 17% were adenoid carcinomas and 7% were superficial-type carcinomas.

#### 2. Malignant appendage tumors

From the 6 cases, 3 were trichilemmal carcinomas, two cases presented eccrine- and one sebaceous differentiation. All of them involved the skin of the head and were diagnosed in patients older than 59 years old.

### Malignant mesenchymal tumors

From the 49 cases (Table II), more than 50% occurred from connective tissue, followed by muscular (24.49%) and vascular (22.45%) origin. Only one malignant schwannoma was diagnosed in a 89 year-old woman, on head. In the adipose tissue only benign tumors have been occurring.

#### 1. Malignant connective tissue tumors

Thirteen females and 12 males with an average age of 52 years were enrolled in study. The tumors were located on the trunk (41%), lower limb (25%), head and neck (21%) and upper limb (13%). Fibrosarcomas, fibromyxosarcomas, epitheloid sarcomas, undifferentiated pleomorphic sarcomas, dermatofibrosarcomas and malignant fibrous histiocytomas were diagnosed.

#### 2. Malignant vascular tumors

From the 11 cases, 8 were Kaposi's sarcoma and 3 hemangiosarcomas. Regarding Kaposi's sarcoma, males (87%) were more affected than females (13%). The average age was 64.6 years (range 30–88). The lower limb (74%) was the common site, followed by the head (13%) and upper limb (13%). Hemangiosarcomas involved the lower limbs and were diagnosed in males older than 58 years.

#### 3. Malignant tumors of muscular tissue

Both leiomyosarcomas and rhabdomyosarcomas have been diagnosed in 9 males and 3 females around 62 years old. The tumors were located on lower limb (54.54%), trunk (36.36%) and upper limb (9.09%).

**Table I.** The distribution of epithelial tumors reveals the preponderance of malignant cases in group of epidermal tumors

Tumor type	Benign tumors	Malignant tumors	Premalignant lesions	Total
Epidermal tumors	389 (29.11%)	840 (62.87%)	32 (2.39%)	1261 (94.38%)
Apendage tumors	69 (5.16%)	6 (0.44%)	–	75 (5.61%)
Total	458 (34.28%)	846 (63.32%)	32 (2.39%)	1336 (100%)

**Table II.** The distribution of mesenchymal tumors depending on their origin reveals the preponderance of connective and adipose benign tumors

Tumor origin	Benign tumors	Malignant tumors	Tumor-like lesions	Total
Connective and adipose tissue	708 (65.25%)	25 (2.30%)	7 (0.64%)	740 (68.20%)
Vascular	273 (25.16%)	11 (1.01%)	–	284 (26.17%)
Muscular	13 (1.19%)	12 (1.10%)	–	25 (2.30%)
Nerve	22 (2.02%)	1 (0.09%)	13 (1.19%)	36 (3.31%)
Total	1016 (93.64%)	49 (4.51%)	20 (1.84%)	1085 (100%)

### Malignant melanomas

One hundred and five patients with melanomas were enrolled in our study. 58.09% were females and 41.09% males. The mean age was  $61.04 \pm 14.35$  years (range 17–89 years), without significant differences between males and females ( $p=0.40$ ).

The lower limb was the common localization (36.19%) followed by the trunk (28.57%), head and neck (14.28%), and upper limb (11.42%). In 9.52% of cases the affected region was not specified (9.52%). In males, melanomas especially occurred on the trunk (40.90%) and lower limb (25.00%) but the most common localization in females was the lower limb (44.26%) followed by the trunk (19.67%), with a statistically significant difference ( $p=0.02$ ).

### Lymphomas

Thirteen cases of mycosis fungoides were diagnosed. Males (54%) were more affected than females (46%), the mean age being 54.92 years (range 25–84).

### Discussion

The number of publications about the skin cancer is increasing in both the medical and non-medical literature. Epithelial tumors, e.g. BCC, are among the most frequent skin tumors and have a high chance of cure if detected in an early phase of development. Similar to our results, there are authors who revealed that SCC is diagnosed in

the elderly and it is twice more common in males than females, probable due to a greater lifetime sun exposure in men with outdoor occupations, their face, scalp, neck and dorsum of the hands being more involved [10].

BCC seems to be the most common cancer in humans and its incidence is increasing. Our study supports previous findings that the main location of this tumor is the head and neck region. Most patients are men over 50 years of age [11]. Our study revealed that BCC especially affects females around 65 years.

The incidence of melanoma has increased significantly worldwide over the last several decades. Paek et al [5] reported that the mean age of diagnosis is 52 years, which is 10 to 15 years younger than other more common cancers (e.g. breast, lung, and colon). They also noted that the most common locations in men are the back, while in women the lower extremities and the trunk [5].

Regarding mesenchymal tumors, for malignant connective tissue and nerve tumors the most common localization was the head, but vascular and muscular tumors especially occurred on the lower limb. In malignant connective tissue females outnumbered males, but vascular and muscular tumors affected mostly the males. From vascular tumors, Kaposi's sarcoma is strongly associated with Human Immunodeficiency Virus infection (HIV) [12]. Previous studies showed that a highly active antiretroviral therapy and chemotherapy improve the quality of life of these patients [13]. None of our cases were HIV-related.

In our study, mycosis fungoides, a subtype of T-cell lymphoma, was the predominant entity. Some authors revealed that this lymphoma occurs more frequently in females (M:F ratio 3:4), the mean age being 43.1 years. Other studies revealed the preponderance of cases in males (M:F ratio 2:1) with the mean age of 55 years [14,15]. Our study revealed that males were more affected than females, the mean age being 54.9 years.

In our paper we presented the statistical results regarding clinico-pathological aspects of skin tumors, this step being the base of a comprehensive study regarding the an-

**Table III.** The distribution of squamous cell and basal cell carcinomas depending on localization

Localization	Squamous cell carcinoma	Basal cell carcinoma
Head and neck	146 (47.86%)	426 (79.62%)
Lip	87 (28.52%)	12 (2.24%)
Upper limb	9 (2.95%)	8 (1.49%)
Lower limb	18 (5.90%)	12 (2.24%)
Trunk	10 (3.27%)	62 (11.58%)
Perineal region	2 (0.65%)	–
Penis	29 (9.50)	–
Unspecified	4 (1.31%)	15 (2.80%)
Total	305	535

giogenesis and lymphangiogenesis of skin tumors, in the next stage being performed immunohistochemical stains (VEGF-A, CD31, CD105, Podoplanin, D2-40, Maspin) and molecular analyses (c-Kit mutations) on a large number of cases.

### Conclusion

In our paper we presented the statistical results regarding clinico-pathological aspects of skin tumors, this step being the base of a comprehensive study regarding angiogenesis and lymphangiogenesis of skin tumors, in the next stage being performed immunohistochemical stains (VEGF-A, CD31, CD105, Podoplanin, D2-40, Maspin) and molecular analyses (c-Kit mutations) on a large number of cases.

In terms of incidence, malignant skin epithelial tumors are predominant, followed by benign mesenchymal tumors and malignant melanomas.

SCC especially occurs in males and BCC are more frequent in females, both of them being especially located on the upper half of the face.

Malignant mesenchymal tumors occur especially in the connective tissue, but the adipose tissue is not involved in the malignant process.

Melanoma affects both genders, but it is the most common on women's lower limb and men's trunk.

Given the relatively high frequency of skin tumours, large studies are necessary to elucidate the best therapeutic management, depending on the tumor type and stage.

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