

# NOTES ON THE 7<sup>TH</sup> EDITION ON TNM CLASSIFICATION OF SKIN TUMORS

## COMENTARIILE CU PRIVIRE LA CEA DE-A 7-A EDIȚIE A CLASIFICĂRII TNM A TUMORILOR CUTANATE

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### Abstract

#### Keywords:

Skin tumours, TNM classification, Skin carcinoma, malignant melanoma of skin, Merkel cell carcinoma of skin.

In the 7th edition of the TNM classification of malignant tumours some alterations and innovations for skin tumours were introduced including an entirely new classification for Merkel Cell Carcinomas. The changes are shown along with notes on some critical issues. The chapter "cutaneous squamous cell carcinoma and other cutaneous carcinomas" has been newly named and supplied with new definitions. The UICC definitions of the T categories in the 7th edition differ from those in the AJCC Cancer staging manual. The classification of carcinomas of the eyelid has been moved from the ophthalmic tumours chapter to the skin tumours chapter and has undergone some changes in the definition of categories T2 - T4 as compared to the 6th edition. In Malignant Melanoma of skin in addition to tumor ulceration, mitotic rate replaces level of invasion as a primary criterion for defining the subcategory of pT1b. The first staging proposal for Merkel Cell Carcinoma of the skin is based on the analysis of over 4,700 patients using the National Cancer Database as well as extensive review of the literature.

### Rezumat

#### Cuvinte-cheie:

Tumori cutanate, clasificare TNM, carcinom cutanat, melanom cutanat, carcinom cutanat cu celule Merkel.

În cadrul celei de a 7-a ediții privind clasificarea TNM a tumorilor maligne, au fost introduse o serie de modificări și informații noi legate de tumorile cutanate, printre care, în premieră, o clasificare a carcinoamelor cutanate cu celule Merkel. Lucrarea de față prezintă modificările aduse precum și câteva comentarii legate de diferite aspecte importante. Capitolul "carcinoame spino-celulare și alte carcinoame cutanate" a fost redenumit și completat cu definiții noi. În cea de-a 7-a ediție, definițiile UICC ale categoriei T sunt diferite de cele din Manualul AJCC de stadializare a cancerului. Comparativ cu cea de 6-a ediție, clasificarea carcinoamelor pleoapei a fost mutată din capitolul de tumori oftalmice în cel de tumori cutanate și a suferit o serie de modificări în ceea ce privește definirea categoriilor T2-T4. Legat de melanomul cutanat, pe lângă ulcerația cutanată, rata mitotică înlocuiește nivelul de invazie ca prim criteriu de definire a subcategoriilor pT1b. Prima propunere de stadializare a carcinoamelor cutanate cu celule Merkel are la bază analiza a peste 4 700 de pacienți incluși în Baza de Informații Națională a Cancerului, precum și o analiză extensivă a literaturii de specialitate.

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Eficacitate îmbunătățită datorită unui nou ingredient activ

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Repară filmul hidrolipidic

[Glicerină]

Restabilește elasticitatea pielii

[Niacinamidă]

Combate pruritul și reconstruiește bariera cutanată

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**Introduction**

In the 7<sup>th</sup> edition of the UICC TNM classification of malignant tumours, published in 2010, several alterations for tumours of the skin have been introduced<sup>[1]</sup>. The number of entities enrolled in this chapter has been enlarged from two to four. Carcinoma of the skin of eyelid has been moved from the ophthalmic tumours chapter to the skin tumours chapter and Merkel cell carcinoma TNM classification is entirely new. The alterations and new definitions will be introduced in this contribution.

Skin tumours	
UICC 2002 [2]	UICC 2100 [1]
Carcinoma of skin	Carcinoma of skin
	Carcinoma of skin of eyelid
Malignant melanoma of skin	Malignant melanoma of skin
	Merkel cell carcinoma of skin

**Carcinoma of the skin**

The chapter “cutaneous squamous cell carcinoma and other cutaneous carcinomas” has been newly named and supplied with new definitions. A comparison between the definitions of T categories of the 6<sup>th</sup> and 7<sup>th</sup> edition is shown in Table 1.

**Table 1.**

UICC 6 <sup>th</sup> edition 2002 [2]	UICC 7 <sup>th</sup> edition 2010 [1]
<b>T1</b> Tumour 2 cm or less in greatest dimension	<b>T1</b> Tumour 2 cm or less in greatest dimension
<b>T2</b> Tumour more than 2 cm, but no more than 5 cm in greatest dimension	<b>T2</b> Tumour more than 2 cm
<b>T3</b> Tumour more than 5 cm in greatest dimension	<b>T3</b> Tumour with invasion of deep structures, e.g., muscle, bone, cartilage, jaws, and orbit
<b>T4</b> Tumour invades deep extradermal structures as cartilage, skeletal muscle, or bone	<b>T4</b> Tumour with direct or perineural invasion of skull base or axial skeleton

The UICC definitions of the T categories in the 7th edition differ from those in the AJCC Cancer staging manual<sup>[3]</sup>.

The differences between the TNM classifications of UICC and AJCC are shown in Table 2.

**Table 2.**

UICC 7th edition [1]	AJCC 7th edition [3]
<b>T2</b> Tumour more than 2 cm in greatest dimension	<b>T2</b> Tumour more than 2 cm in greatest dimension or tumour any size with two or more high risk features *
<b>T3</b> Tumour invades deep extradermal structures	<b>T3</b> Tumour with invasion of maxilla, mandible, orbit or temporal bone
<b>T4</b> Tumour with direct or perineural invasion of skull base or axial skeleton	<b>T4</b> Tumour with invasion of skeleton (axial or appendicular) or perineural invasion of skull base

\*High-risk features for the primary tumour (T) staging are:

Depth/invasion	<input type="radio"/> > 2 mm thickness <input type="radio"/> Clark level ≥ IV <input type="radio"/> Perineural invasion
Anatomic location	<input type="radio"/> Primary site ear <input type="radio"/> Primary site non-hair bearing lips
Differentiation	<input type="radio"/> Poorly differentiated <input type="radio"/> Undifferentiated

The AJCC TNM classification does focus on tumours of skin of face not really taking into consideration other sites as skin of hands or legs. Additionally the definitions of the N categories between UICC and AJCC differ in that UICC only has a N2 category and AJCC offers subcategories N2a - N2c (not shown in a Table 2). In the UICC TNM classification the high-risk features are considered in stage grouping, cases with high-risk features being located in a stage II.

**Carcinoma of the skin of eyelid**

According to the rules of classification for these tumours there should be histological confirmation of the disease and division of cases by histological type, eg., basal cell, squamous cell, sebaceous carcinoma. Melanoma of the eyelid is classified with skin tumours. The classification of carcinomas of the eyelid has undergone some changes in the definition of categories T2 - T4 as compared to the 6th edition (are shown in a Table 3).

In these definitions some new elements have been introduced. T3/pT3 is depending on the extent of resection and T4/pT4 is defined by resectability. Additionally, some changes in the stage grouping of these tumours have been introduced (not shown in a Table 3).

**Malignant Melanoma of Skin**

According to the rules of classification there should be histological confirmation of the disease. Malignant melanoma of eyelid is classified with skin tumours. The extent of the primary tumor is classified after excision, there is only a pT category. A T category is not a valid category.

For pT melanomas, in addition to tumor ulceration, mitotic rate replaces level of invasion as a primary criterion for defining the subcategory of pT1b. This has been differently used in the first print of the 7th edition of TNM [1]. Data from the AJCC Melanoma Staging Database demonstrated a highly significant correlation with increasing mitotic rate and poorer survival rates<sup>[4]</sup> (Table 4).

Since the feature of mitotic rate was not published in the original 7th edition of the UICC TNM classification, it is recommended to use it for the sake of uniformity<sup>[5]</sup>. The change will appear in subsequent UICC reprinting of the 7th edition. The other definitions of the T-, N- and M categories have not changed from the 6th to the 7th edition. The site of distant metastasis continues to represent the primary component of subcategorizing

**Table 3.**

UICC 6th edition 2002 <sup>[2]</sup>	UICC 7th edition 2010 <sup>[1]</sup>
<b>T1</b> Tumour of any size, not invading the tarsal plate; or at eyelid margin 5 mm or less in greatest dimension	<b>T1</b> Tumour 5 mm or less in greatest dimension not invading the tarsal plate or eyelid margin
<b>T2</b> Tumour invades tarsal plate; or at eyelid margin, more than 5 mm but not more than 10 mm in greatest dimension	- <b>T2a</b> Tumor more than 5 mm, but not 10 mm or less in greatest dimension or any tumour that invades the tarsal plate or the eyelid margin - <b>T2b</b> Tumour more than 10 mm, but more than 20 mm in greatest dimension, or involves full thickness eyelid
<b>T3</b> Tumour involves full eyelid thickness; or at eyelid margin, more than 10 mm in greatest dimension	- <b>T3a</b> Tumour more than 20 mm in greatest dimension or any tumour that invades adjacent ocular or orbital structures or any tumour with perineural invasion - <b>T3b</b> Tumour whose complete resection requires enucleation, exenteration, or bone resection
<b>T4</b> Tumour invades adjacent structures	<b>T4</b> Tumour is not resectable due to extensive invasion of ocular, orbital, craniofacial structures or brain

**Table 4.**

UICC 7th edition <sup>[1]</sup>	AJCC 7th edition <sup>[3]</sup>
<b>pT1</b> - Tumor 1 mm or less in thickness	<b>pT1</b> - Tumour 1 mm or less in thickness
<b>pT1a</b> - Clark level II or III, without ulceration	<b>pT1a</b> - without ulceration and mitosis < 1/mm <sup>2</sup>
<b>pT1b</b> - Clark level IV or V, or with ulceration	<b>pT1b</b> - with ulceration or mitoses ≥ 1/mm <sup>2</sup>

the M category. In contrast to the AJCC<sup>[3]</sup> in the UICC classification isolated tumor cells in regional lymph nodes are classified as pN0(i+) whereas in the AJCC TNM classification these findings are classified as pN1. The findings of tumor cells in a lymph node is considered clinically significant. A lower threshold of clinically insignificant metastasis of regional lymph nodes has not been defined based on evidence.

**Merkel Cell Carcinoma**

This is the first staging proposal for Merkel Cell Carcinoma of the skin. Up till this publication sev-

eral staging proposals have been used, none of which will be mentioned here.

According to the AJCC Cancer staging Manual<sup>[3]</sup> the new staging system is based on the analysis of over 4,700 patients using the National Cancer Database as well as extensive review of the literature. According to the AJCC rules for classification, Merkel Cell carcinoma of the eyelid (C44.1) is not included in this chapter but is classified with carcinomas of the eyelid.

**The definitions of the different T-, N-, and M categories are shown below ( Table 5).**

**Table 5.** TNM Clinical Classification

T - Primary Tumour	
<b>TX</b>	Primary tumour cannot be assessed
<b>T0</b>	No evidence of primary tumour
<b>Tis</b>	Carcinoma in situ
<b>T1</b>	Tumour 2 cm or less in greatest dimension
<b>T2</b>	Tumour more than 2 cm but not more than 5 cm in greatest dimension
<b>T3</b>	Tumour more than 5 cm in greatest dimension
<b>T4</b>	Tumour invades deep extradermal structures, i.e., cartilage, skeletal muscle, fascia or bone
N - Regional Lymph Nodes	
<b>NX</b>	Regional lymph nodes cannot be assessed
<b>N0</b>	No regional lymph node metastasis
<b>N1</b>	Regional lymph node metastasis
<b>N1a</b>	Microscopic metastasis (clinically occult: cN0 + pN1)
<b>N1b</b>	Macroscopic metastasis (clinically apparent: cN1 + pN1)
<b>N2</b>	In transit metastasis

**Note:** In-transit metastasis: a tumor distinct from the primary lesion and located  
 1) between the primary lesion and the draining regional lymph nodes and/or  
 2) distal to the primary lesion

M – Distant Metastasis	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
M1a	Skin, subcutaneous tissues or non-regional lymph node(s)
M1b	Lung
M1c	Other site(s)

**pTNM Pathological Classification**

The pT, pN, and pM categories correspond to the T, N, and M categories.

pN0 Histological examination of a regional lymphadenectomy specimen will ordinarily include 6 or more lymph nodes. If the examined lymph nodes are negative, but the number ordinarily resected is not met, classify as pN0.

**A histopathological Grading is not applicable.**

A new element in stage grouping is the use of a cN0 and pN0 in stage grouping. The N1 category is subdivide in N1a with microscopic metastasis (clinically occult: cN0 + pN1) and N1b with macroscopic metastasis (clinically apparent: cN1 + pN1). Thus, stages I and II are subdivided into IA and IB as well as IIA and IIB, depending on the results of regional lymph node examination cN0 versus pN0, the latter being the more reliable.

**Table Anatomical Stage Grouping**

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IA	T1	pN0	M0
Stage IB	T1	cN0	M0
Stage IIA	T2,T3	pN0	M0
Stage IIB	T2,T3	cN0	M0
Stage IIC	T4	N0	M0
Stage IIIA	Any T	N1a	M0
Stage IIIB	Any T	N1b,N2	M0
Stage IV	Any T	Any N	M1

**Summarizing commentary**

The TNM classification of skin tumours has undergone some changes from the 6<sup>th</sup> to the 7<sup>th</sup> edition. These changes have resulted in some differences between the definitions of the UICC and AJCC TNM classification. They become obvious in the definitions of T categories of squamous cell carcinomas of skin, in meanwhile adapted definitions of pT1 and pT1

categories as well as in the definitions of ITCs in regional lymph nodes (UICC pN0 versus AJCC pN1).

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