



Impact of AJCC Staging on Ophthalmic Oncology

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Do you speak ocular tumor?

Paul T Finger, MD – Guest Editorial
Ophthalmology 2003;110(1):13-14.

This editorial introduced the concept of AJCC-UICC TNM staging to the ophthalmologic community and, as you will see, it marked the beginning of a revolution in our field.



Evolution of the 6th, 7th and 8th Eye Cancer Staging Systems

AJCC 6th edition = Small group of diverse USA-based subspecialists
A pair (one clinical, one pathology) for each section.

AJCC 7th edition = 45 eye cancers specialists, from 10 countries
3 representatives from the UICC
A peer-review system*

AJCC 8th edition = >50 multispecialty eye cancer specialists
8 clinical plus 2 ophthalmic pathology review committees
1 Data Collection / 1 Editorial Board Representative

Foundational Elements for Collaboration in Ophthalmic Oncology?

Paul T Finger, MD – Guest Editorial

Ophthalmology Retina 2017;1(4):263-265

Now that AJCC eye cancer staging was adopted by most ophthalmic journals, societies and eye cancer specialists, this editorial laid the groundwork for a path forward utilizing the most collaborative consensus tumor staging language for improve both research and clinical care.



Based at Princess Margaret Hospital in Toronto, Ontario, Canada, multicenter, international registries were created to validate the AJCC staging systems and answer questions that required pooled-data.

Each effort was championed by an eye cancer specialist, who formed a committee to select data fields for inquiry. Each center was certified, all data was anonymized, and a writing committee submitted their work for comment and approval from all authors/institutions.

8th Edition, AJCC Chapter 67

Tero Kivelä, E. Rand Simpson, Hans E. Grossniklaus,
Martine J. Jager, Arun D. Singh, José M. Caminal,
Anna C. Pavlick, Emma Kujala, Sarah E. Coupland,
and Paul T. Finger

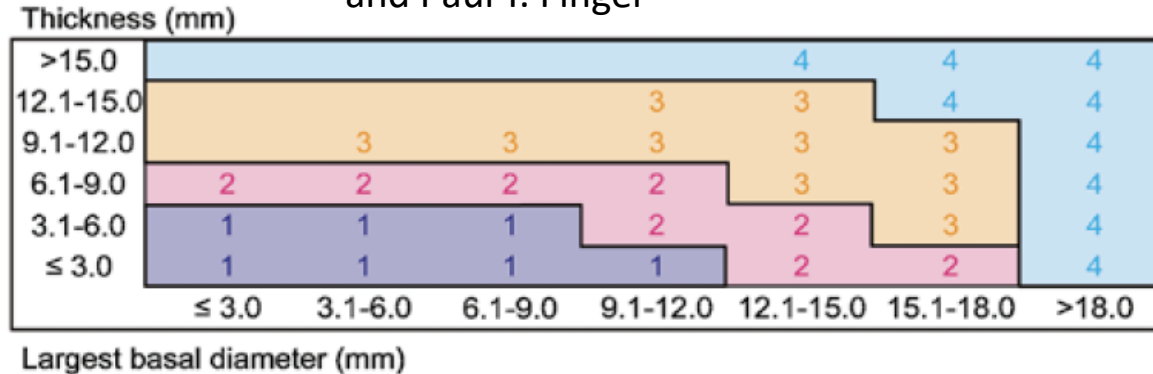


Fig. 67.1 Classification of ciliary body and choroid uveal melanoma based on thickness and diameter



- Validation of the AJCC staging system for choroidal melanoma
- Showed failure of primary local control increased the risk (6.3x H.R.) for metastasis
- Described Stage IV uveal melanoma at presentation and that whole body PET/CT staging was more likely to reveal extrahepatic, occult metastatic melanoma



The AJCC-OOTF was expanded such that this registry included 38 established world-wide retinoblastoma centers from 14 countries: USA, Canada, Finland, China, India, Russian, Jordan, Mexico, Argentina, Hong Kong, Australia, Singapore, Ghana, and Spain.

Ankit Singh Tomar, MD, Paul T. Finger, MD, Brenda Gallie, MD, Ashwin Mallipatna, MBBS, MS, Tero T. Kivelä, MD, Chengyue Zhang, MD, Junyang Zhao, MD, Matthew W. Wilson, MD, Rachel C. Brenna, MD, Michala Burges, BS, Jonathan Kim, MD, Vikas Khetan, MBBS, MS, Suganeswari Ganesan, MS, Andrey Yarovoy, MD, Vera Yarovaya, MD, Elena Kotova, MD, Yacoub A. Yousef, MD, Kalle Nummi, MD, Tatiana L Ushakova, MD, Olga V Yugay, MD, Vladimir G Polyakov, MD, Marco A Ramirez-Ortiz, MD, MPH, Elizabeth Esparza-Aguiar, MD, Guillermo Chantada, MD, Paula Schaiquevich, MD, Adriana Fandino, MD, Jason C. Yam, MD, Winnie W. Lau, MD, Carol P. Lam, MD, Phillipa Sharwood, FRANZCO, Sonia Moorthy, MD, Quah Boon Long, MD, Vera Adobea Essuman, MD, Lorna A. Renner, MD, Ekaterina Semenova, MD, Jaume Català, MD, Genoveva Correa-Llano, MD, Elisa Carreras-Bertran, MD



- Validation of the 8th edition AJCC staging system for Retinoblastoma
- Compared, contrasted it with the prior ocular staging systems (WEH and CHLA)
- Examined socio-economic factors and how they correlate to rates of RB mortality.
- Examined how intraocular retinoblastoma seed distribution affects tumor outcome
- Showed how AJCC RB staging can be used to predict both mortality and globe salvage.
- Showed how cT-categories can be used to predict "high-risk pathologic factors" which are used to determine treatment modality.

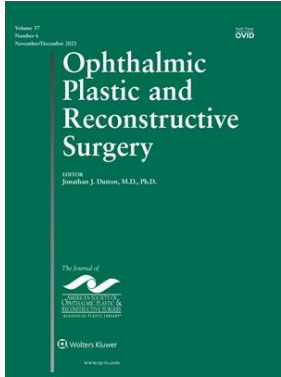


•AJCC 8th edition eliminated the term PAM “~~primary acquired melanosis with atypia~~” in favor of **conjunctival melanoma in situ**. The former term had been mistaken for benign disease.

•AJCC-OOTF pooled registry data validated that AJCC staging could be used to estimate risk of metastatic mortality as well as post-treatment recurrence.

AND

•Esmaeli found “tumor thickness, ulceration and positive lymph node are associated with worse prognosis in patients with conjunctival melanoma: Implications for future AJCC classifications. Am J Surg Pathol 2019;43(12):1701-10.



Jonathan J. Dutton, MD, PhD, FACS

Professor, UNC School of Medicine

Lead on the AJCC Orbital Sarcoma Section

Editor in Chief, Ophthalmic Plastic and Reconstructive Surgery (Wolters Kluwer, THE journal of the American Society of Ophthalmic Plastic and Reconstructive Surgery) require all manuscript submissions concerning malignancies to use the 8th edition, AJCC TNM staging classification.





Sa, Rubin, Ning et al evaluated the prognostic performance of the 8th edition AJCC TNM classification for orbital Sarcoma. JAMA Ophthalmol 2020;138(4):374-381.

In this study, 73 patients with 3 different orbital sarcomas were evaluated. They found that cT3 category and a tumor size of at least 3 cm was significantly associated with a higher risk of local recurrence, lymph node and distant metastasis as well as tumor-related death.

Steffen Heegaard, MD

Professor and Research Director, The University of Copenhagen, Denmark,
headed an international, multicenter, retrospective data-pooling study

“AJCC staging has been fully adopted regarding ocular adnexal lymphoma all over the world – both in the respective national/international societies and in ophthalmological /cancer journals”

“AJCC staging is fully implemented in research and presentations at national and/or international meetings.”

“AJCC staging is used in national/international registries and in prospective trials regarding ocular adnexal lymphoma.”

“AJCC staging is incorporated in the journal instructions for authors for: Acta Ophthalmologica and Ocular Oncology and Pathology (the journal of the International Society of Ophthalmic Oncology).”

The Danish-based OAL International, Multicenter, Retrospective Data-pooling Study yielded 9 peer-review articles all utilizing AJCC - OAL staging

8 papers differentiated OAL by ophthalmic location and 4 by cell-type

Select Conclusions:

- Histopathologic subtype was more important than tumor location to predict mortality
- Treatment with orbital radiation therapy was associated with less subsequent systemic disease for MALT and Follicular subtypes.
- Follicular lymphoma was more common in females; while Mantle-cell type was predominantly found in males.

Bitá Esmaeli, MD, MA, FACS

Professor, Orbital Oncology & Ophthalmic Plastic Surgery Program, Department of Plastic Surgery,

MD Anderson Cancer Center, USA

- Transition from the 7th to the 8th AJCC staging systems resulted in an 80% change in T-category for 167 patients.
- Validated the 8th edition criteria for eyelid carcinoma for metastasis (included: squamous and sebaceous cell carcinoma).
- Validation of AJCC staging for lacrimal gland carcinoma recurrence and metastasis.
- Validation of AJCC staging for orbital Sarcoma

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Bitá Esmaeli, MD, MA, FACS

Dr. Esmaeli is one of the most prolific investigators and supporters of AJCC staging in ophthalmic oncology.

Dr. Esmaeli has led investigations leading to publication of 24 peer-review papers questioning, validating and ultimately improving AJCC staging.

Led AJCC Eyelid Carcinoma staging and co-authored the orbital and conjunctival melanoma staging.

The AJCC eye cancer staging systems were created by consensus of a large, carefully selected portion of the ophthalmic oncology community.

“Made by the community, it was accepted by the community” - Finger

Accepted by the UICC, it was accepted into the mainstream of world cancer care.

As AJCC staging was employed for clinical care, it served as a foundational element for multicenter, international data-pooling registries. Each has provided statistically significant medical evidence answering clinical and research questions.

“Do you speak ocular tumor?” Yes, ophthalmic oncology has embraced a common language that allows us to improve the care of eye cancer patients.

The AJCC - UICC Ophthalmic Oncology Task Force Registry

Validated AJCC - UICC Staging of Uveal Melanoma (Mortality)

Validated AJCC - UICC Staging of Conjunctival Melanoma (Mortality)

Validated AJCC - UICC Staging of Retinoblastoma (Mortality and Globe Salvage)

The MD Anderson Ophthalmic Oncology Registry

Validated AJCC Staging of Lacrimal Gland Carcinoma (Mortality)

Validated AJCC staging for Eyelid and Periocular Squamous Carcinoma (Mortality)

The Denmark-based Ocular Adnexal Lymphoma Registry

Invalidated AJCC Staging in Favor of Histopathologic Type (Mortality)

1) Orbital Lymphoma--An International Multicenter Retrospective Study

Olsen TG, Holm F, Mikkelsen LH, Rasmussen PK, Coupland SE, Esmali B, Finger PT, Graue GF, Grossniklaus HE, Honavar SG, Khong JJ, McKelvie PA, Mulay K, Sjö LD, Vemuganti GK, Thuro BA, Heegaard S. Am J Ophthalmol. 2019 Mar;199:44-57.

2) Conjunctival Lymphoma--An International Multicenter Retrospective Study

Kirkegaard MM, Rasmussen PK, Coupland SE, Esmali B, Finger PT, Graue GF, Grossniklaus HE, Honavar SG, Khong JJ, McKelvie PA, Mulay K, Prause JU, Ralfkiaer E, Sjö LD, Toft PB, Vemuganti GK, Thuro BA, Curtin J, Heegaard S. JAMA Ophthalmol. 2016 Apr;134(4):406-14.

3) Lymphoma of the Eyelid: - An International Multicenter Retrospective Study

Svendsen FH, Rasmussen PK, Coupland SE, Esmali B, Finger PT, Graue GF, Grossniklaus HE, Honavar SG, Khong JJ, McKelvie PA, Mulay K, Ralfkiaer E, Sjö LD, Vemuganti GK, Thuro BA, Curtin J, Heegaard S. Am J Ophthalmol. 2017 May;177:58-68.

4) Lymphoma of the Lacrimal Gland - An International Multicenter Retrospective Study.

Vest SD, Mikkelsen LH, Holm F, Rasmussen PK, Hindso TG, Knudsen MKH, Coupland SE, Esmali B, Finger PT, Graue GF, Grossniklaus HE, Honavar SG, Mulay K, Sjö LD, Sniegowski MC, Vemuganti GK, Thuro BA, Heegaard S. Am J Ophthalmol. 2020 Nov;219:107-120.

5) Clinicopathological features of ocular adnexal **Mantle-Cell Lymphoma** in an international multicenter cohort.

Knudsen MKH, Rasmussen PK, Coupland SE, Esmaeli B, Finger PT, Graue GF, Grossniklaus HE, Khong JJ, McKelvie PA, Mulay K, Ralfkiaer E, Sjö LD, Vemuganti GK, Thuro BA, Curtin J, Heegaard S. JAMA Ophthalmol. 2017;135(12):1367-1374.

6) Ocular adnexal diffuse **Large B-cell lymphoma**: a multicenter international study

Munch-Petersen HD, Rasmussen PK, Coupland SE, Esmaeli B, Finger PT, Graue GF, Grossniklaus HE, Honavar SG, Khong JJ, McKelvie PA, Mulay K, Prause JU, Ralfkiaer E, Sjö LD, Sniegowski MC, Vemuganti GK, Heegaard S. JAMA Ophthalmol. 2015;133(2):165-73.

7) Ocular adnexal **Follicular Lymphoma**: a multicenter international study.

Rasmussen PK, Coupland SE, Finger PT, Graue GF, Grossniklaus HE, Honavar SG, McKelvie P, Mulay K, Prause JU, Ralfkiaer E, Sjö LD, Heegaard S. JAMA Ophthalmol. 2014 Jul;132(7):851-8.

8) International multicentre retrospective cohort study of ocular adnexal **Marginal Zone B-cell Lymphoma**

Hindsø TG, Esmaeli B, Holm F, Mikkelsen LH, Rasmussen PK, Coupland SE, Finger PT, Graue GF, Grossniklaus HE, Honavar SG, Khong JJ, McKelvie PA, Mulay K, Sjö LD, Vemuganti GK, Thuro BA, Heegaard S. Br J Ophthalmol. 2020 Mar;104(3):357-362.

1) Change in **Eyelid Carcinoma** T Category With Use of the 8th Versus 7th Edition of the American Joint Committee on Cancer: Cancer Staging Manual.

Ding S, Sagiv O, Guo Y, Kandl TJ, Thakar SD, Esmaeli B. Ophthalmic Plast Reconstr Surg 2019;35(1):38-41.

2) Prognostic Factors for Local Recurrence, Metastasis and Survival for **Sebaceous Carcinoma of the Eyelid**: Observations in 100 Patients.

Sa HS, Rubin ML, Xu S, Ning J, Tetzlaff M, Sagiv O, Kandl TJ, Esmaeli B. Br J Ophthalmology 2019;103(7):980-984.

3) Validation Study of the AJCC Cancer Staging Manual, Eighth Edition, Staging System for **Eyelid and Periocular Squamous Cell Carcinoma**.

Xu S, Sagiv O, Rubin ML, Sa HS, Tetzlaff M, Nagarajan P, Ning J, Esmaeli B. JAMA Ophthalmology 2019;137:537-542.

4) Greater Tumor Thickness, Ulceration, and Positive Sentinel Lymph Node are Associated With Worse Prognosis in Patients With **Conjunctival Melanoma**: Implications For Future AJCC Classifications.

Esmaeli B, Rubin ML, Xu S, Goepfert RP, Curry JL, Prieto VG, Ning J, Tetzlaff MT. Am J Surg Pathol 2019;43(12):1701-1710.

5) Association of T and N Categories of the American Joint Commission on Cancer, 8th Edition, With Metastasis and Survival in Patients With **Orbital Sarcoma**. Sa HS, Rubin ML, Ning J, Li W, Tetzlaff MT, McGovern SL, Paulino AC, Herzog CE, Gill JB, Esmaeli B. JAMA Ophthalmol 2020;138:374-81.

6) Prognostic factors for local recurrence and survival and impact of local treatments on survival in **Lacrimal Gland Carcinoma**. Ford JR, Rubin ML, Frank SJ, Ning J, Debnam JM, Bell D, El-Naggar A, Ferrarotto R, Esmaeli B. Br J Ophthalmol. 221:105(6):168-74.

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In 1998, Dr. Paul Finger established The Eye Cancer Foundation (ECF), as an educational and supportive resource for eye cancer patients, their families, and physicians. Our mission is three-fold:

- To develop and encourage **international, multicenter, cooperative research** on new diagnostic treatments.
- To provide much needed **support services** for patients and their families.
- To save lives through our **International Fellowship Program** by training doctors in underserved and unserved countries.

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