# Incidence, Survival and Risk of Subsequent Primaries in Ocular Melanoma: Analysis of the Surveillance, Epidemiology and End Results Data

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## BACKGROUND AND PURPOSE

Ocular melanomas (OM) are rare but comprise the greatest number of melanomas (3.8%) after skin melanomas (94.8%). In the U.S. an average of 6.8 new cases per million are diagnosed each year, with higher rates among males (7.1/million) than females (5.5/million). Most cases are diagnosed in European-Americans (95.2%) and in the choroid (65%) and ciliary body of the eye (15%). Principle treatment historically involved amputation of the eye (enucleation), but eye-sparing treatments, such as brachytherapy radiation are now being used, especially on smaller tumors.

Our purpose here is to describe the incidence and survival of this rare cancer and to investigate the risk of developing subsequent cancers following diagnosis of a 1st primary ocular melanoma.

## METHODS

Using SEER*STAT© software, we analyzed age-adjusted incidence (IR) rates of malignant ocular melanoma (OM) from 1973-2007 by sex, race (European American-EA, African American-AA, Other/Unknown-Oth/Unk), stage and year of diagnosis group (1973-1984, 1985-1996, 1997-2007). A graph of incidence rates stratified by year of diagnosis and sex, charts of race and primary site percentages and a chart of incidence rates stratified by stage and sex were created in MS Excel© from incidence data generated using SEER*STAT. Median age at diagnosis by sex and race were calculated by generating a caselisting dataset of ocular melanomas in SEER*STAT, which was loaded into SAS© to calculate median age. SAS© was also used to perform log-rank tests and graphs comparing survival differences by sex and race of *1st primary* OMs. 5-year relative survival rates (1998-2008) by treatment were generated in SEER*STAT and graphed in Excel. Standardized Incidence Ratios (SIR) and excess risk rates were generated in SEER*STAT© of 1st primary OMs to evaluate risk of developing a subsequent cancer. Median time in months was calculated from development of 1st primary OM to next eligible cancer. Cancers diagnosed within two months following the 1st primary OM were considered concurrent diagnoses and were excluded as a "next eligible cancer" (designated "latency" cancer in SEER*STAT.)

## RESULTS AND CONCLUSIONS

From 1973-2008, there were 4,999 new OM diagnosed with Incidence rate (IR) = 6.2 per million. Males (IR: 7.1, CI: 6.9-7.4; 52%) had significantly greater IR than females (IR: 5.5, CI: 5.3-5.7; 48%) and were diagnosed at younger age (male median age=61 vs. female median age=64.) Both sexes were primarily diagnosed at local stage. European-Americans (EA) (IR: 7.3, CI: 7.1-7.5, 97% (including Hispanic)) had significantly greater incidence than African-Americans (AA) (IR: 0.5, CI: 0.3-0.7, 1%) and were diagnosed at older age (median=63) than AA (median age=53.5) or Other race (median age=55). All race categories were diagnosed primarily at local stage. When accounting for Hispanic (Hisp) ethnicity, EAs comprised 95.2%, AAs=0.6%, Hisp=2.1% and Other=2.1% of incident OMs. IRs significantly decreased over time (1973-1984: 6.9, CI: 6.5-7.2; 1985-1996 & 1997-2008: 6.0, CI: 5.7-6.3).

Males and females had similar survival (p=0.2326) for 1st primary OM (N=4,425), as did EAs and AAs (p=0.8221). 5-year survival was similar across year of diagnosis groups, with slightly better survival for cases diagnosed in the most recent period, 1997-2008 (p=0.0855). 5-year relative survival was best for those receiving local resection, which probably reflects attempts within the last 10 years to perform vision-sparing surgery but could also be an indication of earlier diagnosis of smaller tumors. 5-year relative survival was statistically significantly better for those receiving radioactive implants or radioisotopes than those receiving no radiation. Those receiving beam radiation also had better survival than those with no radiation but this was not statistically significant.

Risk of SubCa was significantly higher in OM patients (SIR: 1.15, CI: 1.06, 1.24) than the general population, with greatest risk in females (SIR: 1.20, CI: 1.06, 1.36) and no increased risk in children (ages <20). Of 607 cases with a SubCa, only n=7 were in non-European-Americans. The top SubCa sites in males were prostate (32%), lung (14%), colon (9%) and bladder (9%), while the top sites in females were female breast (23%), skin melanoma (10%), lung (9%) and colon (8%). However, in each sex, the highest statistically significant risk of subsequent cancer following ocular melanoma was another ocular melanoma (males: SIR=20.04, 95%CI=8.65-39.49, n=8), (females: SIR=16.20, 95%CI=5.26-37.81, n=5) and skin melanoma (males: SIR=2.60, 95%CI=1.73-3.75, n=28), (females: SIR=4.83, 95%CI=3.19-7.03, n=27).

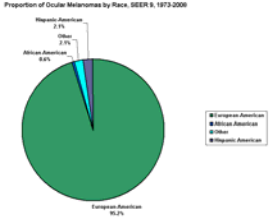
Conclusions: Incidence rates of OM are highest in Males and European-Americans but survival is similar by sex and race. Females have greater risk of SubCas. Each sex has highest statistically significant risk of ocular and skin melanoma SubCa.

## INCIDENCE

**FREQUENCY AND INCIDENCE RATES OF MALIGNANT MELANOMA BY SITE SEER 9, 1973 - 2008**

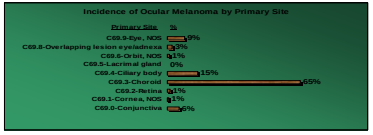
| Site | N | % | Rate | Lower CI | Upper CI |
|---|---|---|---|---|---|
| All Sites | 131,723 | 100.0% | 163.0 | 162.1 | 163.9 |
| Melanoma of the Skin | 124,869 | 94.8% | 154.4 | 153.6 | 155.3 |
| **Eye and Orbit** | **4,999** | **3.8%** | **6.2** | **6.1** | **6.4** |
| Vulva | 598 | 0.5% | 0.8 | 0.7 | 0.8 |
| Nose, Nasal Cavity and Middle Ear | 367 | 0.3% | 0.5 | 0.4 | 0.5 |
| Vagina | 172 | 0.1% | 0.2 | 0.2 | 0.3 |
| Anus, Anal Canal and Anorectum | 144 | 0.1% | 0.2 | 0.2 | 0.2 |
| Rectum and Rectosigmoid Junction | 111 | 0.1% | 0.1 | 0.1 | 0.2 |
| Gum and Other Mouth | 92 | 0.1% | 0.1 | 0.1 | 0.1 |
| Penis | 41 | 0.0% | 0.1 | 0.0 | 0.1 |
| Other Urinary Organs | 35 | 0.0% | 0.0 | 0.0 | 0.1 |
| All other | 295 | 0.2% | 0.4 | 0.3 | 0.4 |

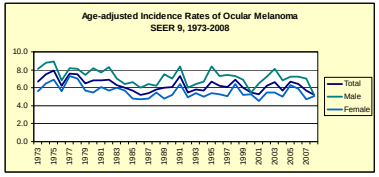
Rates are per 1,000,000 and age-adjusted to the 2000 US Std Population (19 age groups-Census P25-1130) standard; Confidence intervals (Tiwari mod) are 95% for rates.

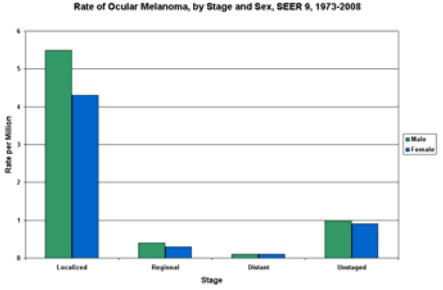



**Median Age at Diagnosis by Sex and Race of Ocular Melanoma SEER 9, 1973-2008**

| | Median Age | 95% CI |
|---|---|---|
| Sex | | |
| Male | 61 | (60 , 62) |
| Female | 64 | (63 , 65) |
| Race | | |
| White | 63 | (62 , 64) |
| Black | 53.5 | (47 , 64) |
| Other | 55 | (51 , 57) |




## SUBSEQUENT CANCER RISK

**Top 5 Subsequent Cancers following a 1st Primary Ocular Melanoma Diagnosis by Sex and Site, SEER 9, 1973-2008**

| Males | n | % | % | n | Females |
|---|---|---|---|---|---|
| All Sites | 346 | 100% | 100% | 261 | All Sites |
| Prostate | 110 | 32% | 23% | 59 | Female Breast |
| Lung and Bronchus | 50 | 14% | 10% | 27 | Melanoma of the Skin |
| Colon excluding Rectum | 30 | 9% | 9% | 24 | Lung and Bronchus |
| Urinary Bladder | 30 | 9% | 8% | 22 | Colon excluding Rectum |
| Melanoma of the Skin | 28 | 8% | 7% | 18 | Corpus and Uterus, NOS |

**Top 3 Subsequent Highest Risk* Cancers following a 1st Primary Ocular Melanoma Diagnosis by Sex and Site, SEER 9, 1973-2008**

| | Observed | Expected | SIR | 95% CI | Excess Risk |
|---|---|---|---|---|---|
| **Males** | | | | | |
| All Sites | 346 | 311.92 | 1.11 | (1.00, 1.23) | 18.43 |
| Eye and Orbit - Melanoma | 8 | 0.40 | 20.04 | (8.65, 39.49) | 4.11 |
| Melanoma of the Skin | 28 | 10.78 | 2.60 | (1.73, 3.75) | 9.31 |
| Kidney | 15 | 7.72 | 1.94 | (1.09, 3.20) | 3.94 |
| **Females** | | | | | |
| All Sites | 261 | 217.09 | 1.20 | (1.06, 1.36) | 24.77 |
| Eye and Orbit - Melanoma | 5 | 0.31 | 16.20 | (5.26, 37.81) | 2.65 |
| Melanoma of the Skin | 27 | 5.59 | 4.83 | (3.19, 7.03) | 12.08 |
| Soft Tissue including Heart | 4 | 0.93 | 4.29 | (1.17, 10.98) | 1.73 |

*Statistically significant sites. Excess risk is per 10,000.

**Median Time in Months from 1st Primary Ocular Melanoma to Next Subsequent* Cancer, SEER 9, 1973-2008**

| Sex | N | Median |
|---|---|---|
| Female | 261 | 72.0 |
| Male | 346 | 72.5 |
| Total | 607 | 72.0 |

*Note: Cancers diagnosed within 2 month latency period following 1st primary are not eligible.

## SURVIVAL