Correlation Between Largest Basal Diameter, Gene Expression Profile, and Survival of Patients With Posterior Uveal Melanoma Evaluated by FNAB

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OBJECTIVE Discuss the potential correlation between largest basal diameter, gene expression profile, and metastasis-free survival of patients with posterior uveal melanoma evaluated by fine needle biopsy.

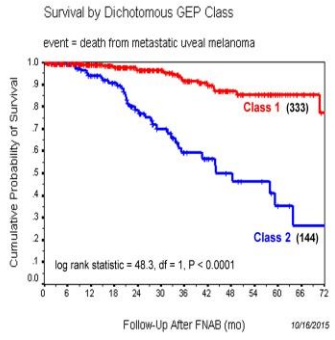
PURPOSE Peer-reviewed publications have shown that gene expression profile (GEP) is the most robust prognostic test for posterior uveal melanomas. However, largest basal diameter (LBD) has been shown to further increase the prognostic accuracy of GEP in smaller tumors. This study aims to evaluate the correlation of LBD, GEP and metastasis-free survival of patients with PUM.

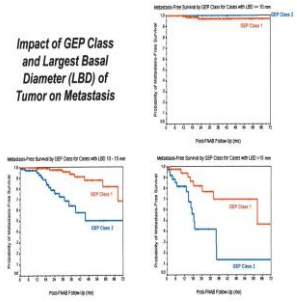
METHODS This is a retrospective study of 482 consecutive patients with PUMs evaluated by FNAB prior to treatment. Tumor features were evaluated at baseline and recorded. Aspirates were submitted to both cytology and GEP testing. Tumors were classified by GEP as Class 1A (very low metastatic risk), 1B (low metastatic risk), or 2 (high metastatic risk). Cumulative probability of metastasis-free survival was evaluated according to GEP classification and further by GEP in each different tumor size category LDB ≤ 10 mm, LBD > 10 mm but ≤ 15 mm and LBD >15 mm.

RESULTS Of the 482 patients studied, 5 were excluded because of failed GEP. Three hundred and thirty-three patients had a Class 1 tumor, 135 (28.0%) were classified prior to the Class 1 A and B separation, 123 (25.5%) were classified as class 1A and 75 (15.6%) were class 1 B. One hundred forty-four patients (29.9%) had a class 2 tumor. The overall cumulative survival probability of all 482 patients was 62% at 72 months. The cumulative survival of Class 1 tumor patients was 77% and of Class 2 patients was 26% at 72 months ($p < 0.0001$). The cumulative survival by GEP in the different LBD size categories showed limited negative predictive value among the smaller tumors and better discrimination in medium and larger tumors. Only 10 patients with GEP Class 1 tumor developed metastasis during the available follow-up interval, four of these had tumors with LBD ≤ 12 mm. In contrast, 43 patients with GEP class 2 tumor developed metastasis and all of them had LBD ≥ 12 mm.

CONCLUSION While GEP remains a robust prognostic test for patients with PUM, clinicians can further increase their prognostic accuracy by including tumor LBD to the test result.

TAKE HOME MESSAGE Factoring in tumor largest basal diameter, clinicians can further improve the prognostic accuracy of Gene Expression Profile (GEP) testing for patients with Posterior Uveal Melanoma.





HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

Outcomes of Chorioretinal Biopsy Using 27-Gauge Microincision Vitrectomy

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OBJECTIVE To describe early experience and outcomes of chorioretinal biopsy using 27-gauge (g) microincision vitrectomy instrumentation for various choroidal and retinal lesions

PURPOSE To describe the characteristics, clinical outcomes, effectiveness in establishing a definitive pathologic diagnosis, intra-operative and post-operative complications of choroidal and retinal biopsies performed using a 27-g microincision vitrectomy system (Alcon Constellation, Fort Worth, TX) for choroidal melanomas and indeterminate choroidal and retinal lesions.

METHODS Interventional, retrospective, non-comparative case series of consecutive patients who underwent 27-g vitrectomy assisted choroidal or sub-retinal biopsy between 12/2014 and 1/2016. Clinical and lesion characteristics, adequacy of specimen for diagnostic outcomes (cytopathology, histology, gene expression profiling (GEP) for metastasis prognosis), visual acuity (VA, logMAR) outcomes, complications including vitreous hemorrhage (VH), subretinal hemorrhage (SRH), increased serous retinal detachment (RD), rhegmatogenous RD and need for additional surgeries were reviewed. 18 eyes of 18 patients were included of which 16 underwent choroidal biopsy and 2 underwent sub-retinal biopsy.

RESULTS Mean age was 63.2±13.1 years, and follow-up was 4±3.3 months (range 0.5-13). Preop VA was 0.5±0.6, unchanged at final follow-up (0.7±0.84, p=0.07). Indications were choroidal melanoma (CM) (n=10), indeterminate choroidal (n=4) and subretinal lesions (n=3). Mean lesion height (mm) was 3.53 ± 1.42 (range 0.80-6.75) and largest diameter (mm) was 8.90±3.04 (range 3-15.5). Mean number of passes required in the lesion were 1.76±0.83 (range 1-4). A pathologic diagnosis was obtained in 16/18 (88.9%) eyes (CM (n=11), lymphoma (n=2), hemangioma (n=1) and lung adenocarcinoma (n=1)). GEP data was obtained in all 11 melanomas. 8/18 eyes had a serous RD preop, which increased in 2 eyes, decreased in 2 and was unchanged in 4 postop. VH following biopsy was noted in 13/18 (72.2%) eyes but was severe enough to warrant a concurrent limited vitrectomy in 6 eyes. Severe VH was noted from tumors with greater lesion height (4.08±1.68 vs. 2.76±1.43mm, p=0.04). Post-operative RD was noted in 2/18 eyes (11.1%).

CONCLUSION 27-g vitrectomy-assisted biopsy established a definitive diagnosis in 88.9% and genetic information in all cases. Post biopsy VH occurs frequently, specially with greater lesion height, but can be cleared in same surgery. Although repeat surgery was required for RRD in 11%, the breaks were not related to biopsy site. This technique allows adequate sampling across a wide range of lesion sizes.

TAKE HOME MESSAGE Microincisional vitrectomy instruments can be used to obtain diagnostic tissue for pathologic diagnosis for retinal and choroidal disease.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

Retinal Astrocytic Hamartoma Arises Within Nerve Fiber Layer and Demonstrates Optically Empty Spaces on Spectral Domain Optical Coherence Tomography

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OBJECTIVE Precise OCT retinal location of retinal astrocytic hamartoma and features with correlation of age, visual acuity, tumor size and location to presence and size of intralesional optically empty spaces.

PURPOSE To evaluate the specific spectral domain optical coherence tomography features of retinal astrocytic hamartoma and evaluate for relationship of features with tumor size and location.

METHODS There were 47 tumors in 42 patients with clinically confirmed RAH were imaged with fundus photography and spectral domain OCT included in the study. Each patient had a macular raster scan and a center crossline scan over the epicenter of each tumor.

RESULTS Of 42 patients with retinal astrocytic hamartoma, 86% were unilateral. Systemic tuberous sclerosis complex was present in 8 patients. The largest tumor demonstrated mean basal diameter of 3 mm and mean thickness of 1.9 mm located 3 and 1.8 mm to the foveola and optic nerve, respectively. Related features included subretinal fluid (n=9, 19%), cystoid retinal edema (n=6, 13%), retinal traction

(n=11, 23%), intralesional cavities (n=28, 60%), and intralesional calcification (n=29, 62%). By SD-OCT, the tumor epicenter was always in the nerve fiber layer, with all other layers appearing thinned. Majority (n=43,91%) showed optically empty spaces (OES) correlating with intralesional calcification or cavitation with mean diameter of 327 um. Subgroup analysis showed correlation of OES number with OES size (p=0.01) and macular tumor location (p=0.03). OES size correlated with tumor basal diameter (p<0.01), tumor thickness (p<0.01), calcification (p=0.01), and logMAR visual acuity (p=0.02).

CONCLUSION Retinal astrocytic hamartoma arose in the nerve fiber layer in every case and demonstrated “moth-eaten OES in 91% of cases, related to intrinsic calcification or cavitation. Macular tumors have greater OES number, while larger calcified lesions with poor vision have larger OES size.

TAKE HOME MESSAGE Retinal astrocytic hamartoma arises from the nerve fiber layer and characteristically show optically empty spaces or "moth eaten" appearance on SD-OCT, which correlate with tumor features and vision.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

Prognostic Choroidal Melanoma Biopsy After Proton Beam Radiotherapy

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OBJECTIVE Attendees will learn that biopsy of choroidal melanoma after proton beam radiotherapy provides meaningful prognostic information while avoiding concerns regarding tumor seeding and metastasis.

PURPOSE Metastasis from choroidal melanoma occurs almost exclusively in patients whose tumor shows monosomy 3. Biopsy can cause tumor seeding and there is a risk that if metastasis develops patients and relatives may attribute this to the biopsy. We performed this audit to determine whether genetic analysis on biopsy samples obtained after proton beam radiotherapy reliably predicts survival.

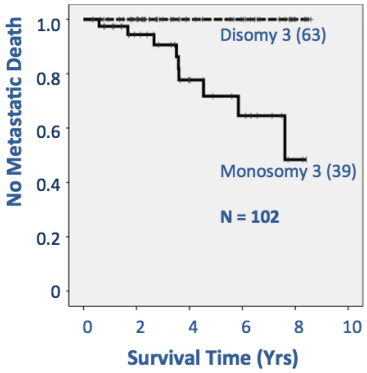
METHODS Patients attending our center were included if they were resident in England or Wales and had trans-retinal biopsy after proton beam radiotherapy. Patients received 56 Gy over 4 days. Trans-retinal biopsy was performed by the pars plana approach with a vitreous cutter, without vitrectomy, laser or tamponade. Chromosome 3 status was determined by multiplex ligation-dependent probe amplification or microsatellite analysis. All patients were flagged at the National Health Service Cancer Registry, which automatically informed us of the date and cause of any deaths. Ethical Committee Approval was not required because this was an audit of our routine practice.

RESULTS The 102 patients, 55 male and 47 female, had a mean age of 57 years (range, 25 – 82). The tumors had a mean diameter of 12.0 mm (range, 5.4 – 19.3) and a median thickness of 3.5 mm (range, 0.9 – 10.3). Genetic studies showed monosomy 3 in 39

patients and disomy 3 in 63. Biopsy was performed on the last day of radiotherapy in 70 patients, between 1 and 7 days in 28 patients and between 8 and 31 days in 4. The median follow-up was 3.6 years (range, 0.3 – 8.6). By the study close, 12 patients had died, 9 from metastatic disease. The actuarial rates of metastatic death at 7 years were 0% in patients with disomy 3 and 35% in patients with monosomy 3.

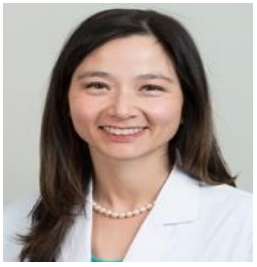
CONCLUSION MLPA/MSA on choroidal melanoma biopsy samples obtained after proton beam radiotherapy reliably predict metastatic risk. Further studies are required to determine whether similar results are achieved with other forms of radiotherapy and other method of genetic analysis.

TAKE HOME MESSAGE If you want to reliably predict survival after proton beam radiotherapy of choroidal melanoma you need to perform genetic analysis on the tumor, which can safely be biopsied after the radiotherapy.



HUMAN RESEARCH This study involves human research.
IRB Approval Status: Exempt from approval

Visual Benefit of Iodine-125 Brachytherapy With Vitrectomy and Silicone Oil for Large Choroidal Melanoma: 1-to-1 Matched Case-Control Series



- Tara A. McCannel, MD, PhD
- Colin A. McCannel, MD

OBJECTIVE To determine the effect on vision of large choroidal melanoma treated with iodine-125 brachytherapy with vitrectomy and silicone oil 1000 centistokes in a 1-to1 matched case-control series.

PURPOSE Radiation treatment for large tumors is controversial due to high risk of local treatment failure and poor visual outcome. Having initially reported the iodine-125 radiation-attenuating effect and clinical benefit of silicone oil 1000 centistokes, we wanted to further elucidate the potential advantage of this technique for vision in larger sized melanoma.

METHODS Patients diagnosed with a choroidal melanoma and for whom a 23 mm diameter iodine-125 plaque was constructed (largest size at our center) were included if there was at least one year follow-up. A one-to-one matched case-control comparison was performed to determine the effect of vitrectomy and silicone oil 1000 centistokes on visual acuity, ocular complications and metastatic outcome. Cases who underwent 23 mm diameter iodine-125 plaque with vitrectomy and silicone oil 1000 centistokes were

matched to control patients who underwent plaque alone, with respect to tumor size and duration of follow-up.

RESULTS 20 cases and 20 controls with choroidal melanoma treated with a 23 mm plaque were identified with average follow-up of 20.9 months. Average tumor height of cases was 7.8 mm (3.0 to 12.1 mm) and in controls, 7.9 mm (3.2 to 11.0 mm) (P=0.85). Average tumor greatest basal diameter of cases was 16.4 mm (14.0 to 20.9 mm) and in controls, 17.5 mm (14.0 to 21.3 mm) (P=0.05). Excluding patients with NLP vision, the final LogMAR vision was 0.83 in case patients and 2.06 in control patients (P=0.0064); the change from pre-treatment to last follow-up LogMAR vision in cases was 0.70 and 1.62 in controls (P=0.019). Of good vision results, 65% of cases and 25% of controls achieved vision >20/200 (P=0.025). Of poor vision results, 35% of cases and 80% of controls achieved vision <20/200 (P=0.0053), and 5% of cases and 35% of controls achieved LP or NLP vision (P=0.044). 39 of the 40 eyes (98%) achieved local tumor control at last follow-up. Metastasis was not statistically different between groups.

CONCLUSION Iodine-125 for the treatment of mostly large choroidal melanoma is effective at achieving local tumor control at our center. Furthermore, combining brachytherapy with vitrectomy and silicone oil 1000 centistokes for radiation attenuation significantly improves vision over plaque alone. This report describes further evidence of visual advantage of radiation attenuation in eyes with uveal melanoma.

TAKE HOME MESSAGE Shielding non-tumor ocular tissue with silicone oil 1000 cs as a vitreous substitute significantly improves vision in larger-sized choroidal melanoma undergoing brachytherapy for local tumor control.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board