

CLINICAL UPDATE

Eye Cancer Patients Favor Genetic Testing

An overwhelming majority of eye cancer patients would favor genetic testing to predict the risk of their tumor metastasizing, even without any interventions that could improve the outcome after such a test showed that they were at high risk, according to a study by UCLA's Jules Stein Eye Institute that was published in the June 2009 issue of *Journal of Genetic Counseling*.

"Our goal was to explore what people with cancer want," says study co-author Tara A. McCannel, M.D., Ph.D., assistant professor of ophthalmology and director of JSEI's Ophthalmic Oncology Center. "We learned that patients want to know their prognosis, good or bad, even when there are no treatments at present for their condition."

Although rare, ocular melanoma is the most common eye cancer to strike adults. The

National Eye Institute reports some 2,000 newly diagnosed cases of the cancer per year.

Interest in Prognostic Findings Nearly Unanimous The JSEI research team surveyed 99 patients who had been diagnosed with ocular melanoma. Half of the patients had undergone localized radiation to shrink the tumor; the rest of the group also underwent radiation, but first had cells from their tumors biopsied. These cells were grown in culture and studied for a missing copy of chromosome 3, the genetic marker most strongly linked to rapid metastatic disease. Patients whose tumors contain the genetic marker have at least a 50 percent chance of death within five years, due to swift spreading of the tumor to the liver and other organs. Aggressive cases can result in blindness and death in as little as a year.

In the UCLA study, all of the patients were



asked to evaluate their interest in receiving genetic testing results related to prognosis. Of the 99 patients, 98 responded that they would have wanted predictive testing at the

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New Approaches for Detection and Prediction of Visual Field Progression in Glaucoma Patients

Recent developments coming out of the Jules Stein Eye Institute and elsewhere have the potential to improve the way glaucoma patients' visual progression is evaluated, which could ultimately influence their care.

The standard of care for evaluating changes over time in glaucoma patients' visual function continues to be through

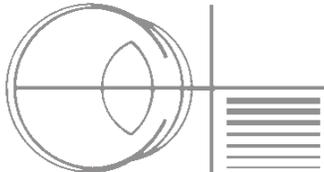
a comparison of results from visual field examinations taken at least annually. However, these tests are imperfect, notes Kouros Nouri-Mahdavi, M.D., M.Sc., assistant professor of ophthalmology in the Jules Stein Eye Institute's Glaucoma Division. "There is a significant amount of 'noise' - long-term fluctuation - in the visual field data gathered over the follow-up

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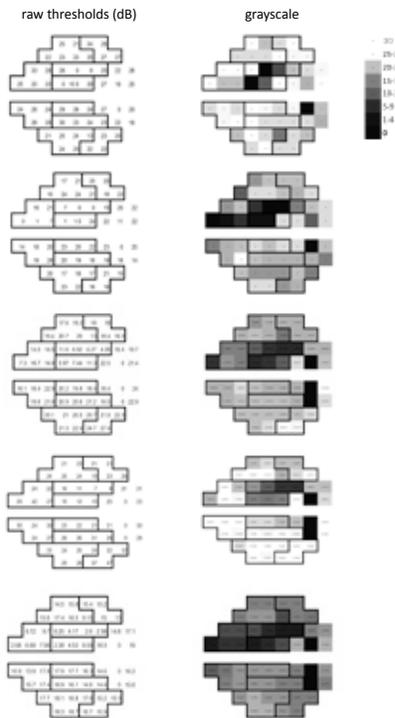
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JULES STEIN EYE INSTITUTE

Example of a prediction algorithm for forecasting the future course of a field series. The visual field status at seven years was predicted using four-year data. The upper and lower limits of prediction represent the 80% confidence interval for prediction.

► **Baseline**
Last
Predicted
Predicted: upper limit
Predicted: lower limit



age, AGIS visual field score, mean intraocular pressure, intraocular pressure fluctuation, and sum of slopes), Dr. Nouri-Mahdavi and colleagues found that a more negative sum of slopes was the strongest predictor of subsequent visual field progression.

“Patients with faster or more extensive deterioration in their visual field in the first four years of follow-up were more likely to have progression at the end of eight years,” Dr. Nouri-Mahdavi says, adding: “The sum of slopes may prove to be a useful tool when combined with other clinical information in order to make an informed decision regarding patient care.”

In a separate study using data from the same AGIS patients, Dr. Nouri-Mahdavi’s group applied an innovative approach to compare three methods for detecting visual field progression (AGIS, PLR, and Glaucoma Change Probability Analysis). In comparing results after four years of follow-up with those after eight years, the researchers found that all methods had a high sustainability rate – i.e., if there was evidence of progression at four years, it was rare for the progression not to be present at eight years. “This means that if visual field progression is detected by any of the commonly used methods based on rigorous criteria, it is unlikely to be due to fluctuation, and likely represents true change,” Dr. Nouri-Mahdavi says.

Other Methods Show Promise “The rates and topography of progression across the visual field do matter as well. Detection of rates of progression in the central areas of the field is paramount because of the more ominous implications with regard to patients’ functional prognosis, Dr. Nouri-Mahdavi explains. Based on ongoing research by our team (see figure above), we may be able soon to forecast the worst- and best-case scenarios with regard to how an individual patient’s field will look a few years down the road if the same rate of progression continues.”

“Based on ongoing research by our team in the Glaucoma Division, we may be able soon to forecast the worst- and best-case scenarios with regard to how an individual patient’s field will look a few years down the road if the same rate of progression continues.”

— DR. NORUI-MAHDABI

period,” Dr. Nouri-Mahdavi explains. “Hence, it can be a difficult task to make a definitive decision regarding the visual field trend in a given patient.”

Because of this, Dr. Nouri-Mahdavi and his colleagues in JSEI’s Glaucoma Division have begun to move away from strict interpretations of the tests as “worse” or “stable” compared to previous tests. “A visual field series may not be getting worse based on defined criteria we commonly use in research or clinically, but there might still be sufficient evidence to make us worry about a downward trend,” he explains.

New Tool Predictive of Progression

Dr. Nouri-Mahdavi’s group recently tested a new statistical tool for analyzing the test results. In a study of 161 patients enrolled in the Advanced Glaucoma Intervention Study (AGIS) who had at least eight years of follow-up, a pointwise linear regression (PLR) analysis, which included a new “sum of slopes” index defined by the JSEI researchers, provided data on the rate of progression. Among six risk factors collected over the first four years of the eight-year follow-up (intervention sequence,



time of their treatment; only one would have declined. Additionally, 98 percent of the respondents stated that supportive counseling should be offered when patients receive their test results.

“We were surprised to see such a unanimous response,” Dr. McCannel says. “We expected some patients would prefer not to know, but the numbers consistently said otherwise.”

“People understand that no good treatment currently exists after their cancer spreads. Everyone wants to know what their risk is for metastasis,” adds co-author Annette Stanton, Ph.D., a UCLA professor of psychology, psychiatry and biobehavioral sciences. “If the risk is low, it’s a huge relief and emotional burden off patients’ shoulders. If the risk is high, it enables patients to plan arrangements for their family and finances and make the most of their time alive.”

The study also measured quality of life and depression symptoms in patients who received genetic test results and compared their rankings to those of untested patients. “Regardless of their test result, all of the patients rated themselves about the same in terms of quality of life and emotional well-being,” Dr. Stanton says. “We hope that these findings reduce clinical resistance and pave the way for prognostic testing to become the standard of care in the management of ocular melanoma.”

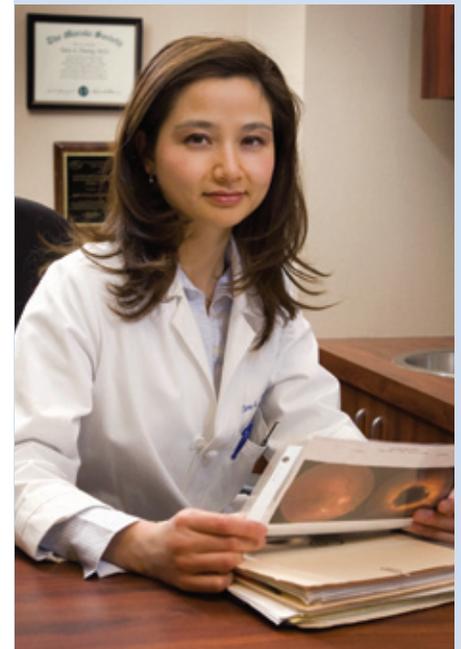
Genetic Testing Controversial Dr. McCannel notes that the issue of genetic testing is a major source of controversy among clinicians. “People want information; they have a lot of things they still want to do in life,” she says. “Knowing their prognosis offers a tool that helps them plan their lives. Our research demonstrates that it’s valuable to give people these details, even if their disease may not presently be treatable.”

The study results emphasize the advantage for patients to be treated in an academic healthcare environment where opportunities ranging from laboratory basic research and genetic testing to psychological research and counseling ensure that patients can receive holistic approaches to treatment in addition to a focus on their disease, Dr. Stanton says.

Tumor biopsy can help researchers search for key genes that play a role in aggressive metastasis, improving clinicians’ ability to provide the best care. The technique of fine-needle aspiration biopsy for collecting cancer cells from the living eye has been utilized at the Jules Stein Eye Institute since 2004 but has been adopted by only a handful of other ophthalmic centers in the nation. “After analyzing the tumor specimens, we grow the biopsied cells in a culture dish and can add drugs to test which ones block cancer growth,” Dr. McCannel explains. “Developing drugs to target these genes will one day result in therapies and a cure.”

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— DR. TARA MCCANNEL



◀ Patient responses to prognostic testing questions, mean depressive symptoms, and mean quality of life scores stratified by cytogenetic test result

Questionnaire item/scale	Response	Response by category					p value ^a
		Total (N=99) % (n)	No testing (n=61) % (n)	Monosomy ^b (n=11) % (n)	Disomy ^b (n=13) % (n)	Inconclusive result (n=14) % (n)	
Patient-reported desire for prognostic information ^b	Yes	94% (93)	93% (57)	91% (10)	100% (13)	93% (13)	0.99
	No	3% (3)	3% (2)	0% (0)	0% (0)	7% (1)	
	No response	3% (3)	3% (2)	9% (1)	0% (0)	0% (0)	
Patient-reported desire for supportive counseling ^b	Yes	91% (90)	92% (56)	91% (10)	84% (11)	93% (13)	0.44
	No	2% (2)	2% (1)	0% (0)	8% (1)	0% (0)	
	No response	7% (7)	7% (4)	9% (1)	8% (1)	7% (1)	
Depressive symptoms (CES-D) ^c		M=7.7 SD=1.6	M=7.6 SD=2	M=3.7 SD=1.2	M=9.7 SD=6.2	M=9.5 SD=6.2	F=1.72 p=0.19
Mental Health Component Summary Score (MOS-SF-36) ^c		M=52.7 SD=2	M=53.9 SD=2.3	M=53.2 SD=2.4	M=47.7 SD=7.9	M=52.0 SD=6.9	F=0.82 p=0.45
Physical Health Component Summary Score (MOS-SF-36) ^c		M=44.9 SD=2.3	M=44.0 SD=3.2	M=45.2 SD=4	M=49.9 SD=6	M=43.8 SD=7.4	F=1.24 p=0.30

^ap<0.01; ^bp value is based only on individuals tested who also responded to the relevant questionnaire item; ^cChi-square test; ^dT test



AARP The Magazine ranks Jules Stein Eye Institute as No. 3 in the country for complex eye-care referrals.



Please recycle

Dr. Kouros Nouri-Mahdavi Joins Faculty



The Jules Stein Eye Institute is pleased to announce the appointment of Kouros Nouri-Mahdavi, M.D., M.Sc., as assistant professor of ophthalmology in the Glaucoma Division.

Dr. Nouri-Mahdavi received his medical training and completed his first residency in ophthalmology in Iran. After fellowships at the Glaucoma Institute of Paris and Yale University, he served as director of the Glaucoma Section at Iran University of Medical Sciences in Tehran. He joined the UCLA Jules Stein Eye Institute in 2002 as visiting assistant professor of ophthalmology in the Glaucoma

Division. During this period, he also obtained his masters degree in clinical research from UCLA. Dr. Nouri-Mahdavi returns to the Institute after completing a second residency in Ophthalmology at University of California, San Diego, where he continued his contribution to clinical research in glaucoma.

Dr. Nouri-Mahdavi's clinical focus is the medical and surgical management of adult and pediatric glaucomas, cataract surgery in glaucoma patients, and complicated cataract surgeries. His research interests include surgical outcomes and new surgical approaches in glaucoma, optic nerve imaging, perimetry, and epidemiology of glaucoma.

Please join us in welcoming Dr. Nouri-Mahdavi back to the Institute. He may be reached at nouri-mahdavi@jsei.ucla.edu, (310) 794-1477. ☎



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