Diagnosis of Ocular Myasthenia Gravis by Means of Tracking Eye Parameters

Muhammad Azri[1,*], Stephanie Young[2,*], Hazel Lin[2], Clement Tan[2], Zhi Yang[1]
[1]Dept. of Electrical and Computer Engineering, National University of Singapore
[2]Dept. of Ophthalmology, National University Hospital, Singapore
[*] equally contributed to the work

***Abstract*— Ptosis of the eyelids is a common condition with a myriad of causes. Its management depends on the underlying cause, which can be challenging to diagnose in some cases. Current diagnosis methods include serum antibodies, tensilon test, and electromyography (EMG). Each has its own set of limitations such as invasiveness and lack of sensitivity. To overcome these limitations, we have developed a Portable Real-time Infrared Lids, Iris and Blink (PRILIB) monitoring system, with a long-term goal to improve clinical diagnosis of ptosis. In this paper, we present the algorithms to detect and analyze eye parameters and report experimental results. From experiments conducted on normal volunteers and myasthenic patients, we found 1. Partial blinks happen when Ocular Myasthenia Gravis (OMG) patients are tired or engaged in an activity; 2. Blink rate is significantly higher for OMG patients due to failure to blink fully; 3. There are noticeably more fluctuations of palpebral aperture of OMG patients due to rising and falling of the eyelid height. These experimental findings suggest new diagnostic features for OMG patients and have implications for disease management.**

I. INTRODUCTION

Ptosis, otherwise known as drooping of the eyelids, has many congenital and acquired causes, including myasthenia gravis, aponeurotic ptosis and nerve palsies[2][3][4]. Determining the cause of ptosis is essential for optimal individualization of patient management. However, it is sometimes difficult to elicit the cause of the ptosis even with thorough history, examination and work-up. In particular, ptosis caused by ocular myasthenia gravis (OMG) may sometimes be difficult to diagnose when it is the only ophthalmic manifestation[5][6].The hallmark of myasthenia gravis is fluctuating or fatigable weakness, but clinicians know that the symptoms can sometimes be much more subtle and diagnosis problematic.

Currently ophthalmologists and neurologists depend on several investigations to make the diagnosis. They are serum antibodies, tensilon test, and electromyography (EMG). However none are 100 percent accurate in determining the disease and they each have their limitations[5][6][7]. Serum antibodies consist of anti cholinesterase antibodies (Anti-AchR) and anti-skeletal muscle antibodies (Anti-MuSK). Despite Anti-AchR having 70-90 percent sensitivity, negative AChR does not exclude disease and approximately 50 percent of OMG patients are negative for this antibody. Anti-MuSK is detectable in approximately 40 percent of anti-AChR-negative patients, but is usually negative in patients with isolated OMG. The tensilon test using edrophonium has a 80 percent sensitivity, but it is accompanied with potentially life-threatening risks of hypo-tension, bradycardia, arrhythmia, bronchospasm and other cholinergic side effects. EMG consists of repetitive nerve stimulation (RNS) which looks for decremental amplitude with repetitive stimulation (50-90 percent sensitivity) and single fibre EMG which looks for variability between individual muscle fibres within a motor unit (80-95 percent sensitivity). However these tests are invasive and require insertions of electrodes into the extraocular muscles or eyelid muscles. The invasive nature of this test sometimes poses as a deterrent in going for further investigation in our population of patients. In addition, single fibre EMG abnormalities can also be seen in other primary neuropathic and myopathic disorders as a result of abnormal conduction of the impulse in degenerating or reinnervating nerve terminals and newly formed endplates and hence may confuse the results.

In view of the limitations of the tests mentioned above, and the importance of correct diagnosis of the underlying cause of ptosis in patients, we propose to build a new diagnostic tool based on wearable cameras mounted on a glass. As shown in Figure 1, recorded video data is streamed to a laptop for disease diagnosis in pilot study. So far we have built a prototype to assess the lids, pupils, and blinks of subjects in real-time fashion (the recorder hardware is a quick revision of the pupil project [1] and the software is developed by us). To the best of our knowledge, there have been no previous studies looking into the blink pattern and palpebral aperture opening pattern of patients with myasthenic ptosis and normal controls.

II. LITERATURE OVERVIEW

There are many computational algorithms reported in the literature that detect eye parameters. For example, cascade-based feature tracking e.g. Viola and Jones [8] and shape detection e.g. Hough Transform [9] and its variants [10] - [12]. The current challenge is that most of the available algorithms are slow, complex and not robust to changes in illumination conditions.

A. Pupil Detection and Monitoring

Detection of the pupil using cascade-based feature tracking is reasonably fast but it is not as precise as the method

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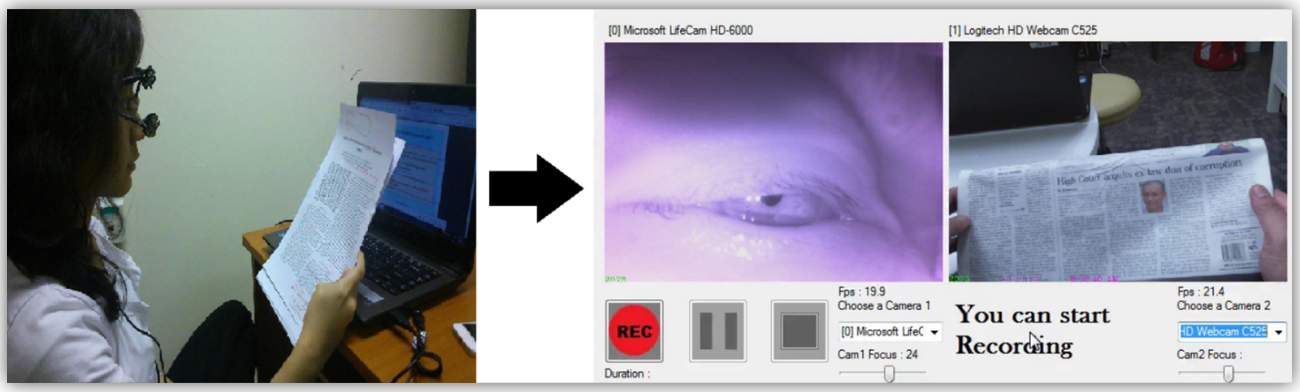

Fig. 1. This figure shows how a recording is done from the volunteer to PC. The picture on the right is an OMG patient recording however the left picture is just an illustration of how it would be like in an experiment. This is to ensure confidentiality of patient.

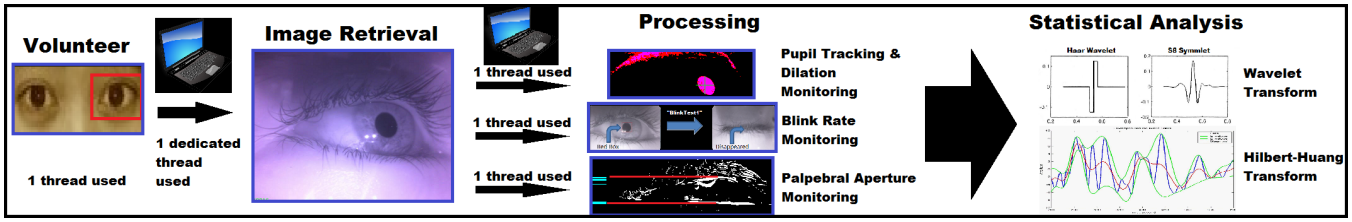

Fig. 2. System Summary. From the left, the user input is taken by the wearable camera and is then linked to a laptop where the image retrieval and different types of processing are each process on an independent thread in parallel. The raw data is then being processed by Wavelet Transform or Hilbert Huang Transform to mine the features that can easily differentiate OMG and normal controls

used in this paper. It also takes a long time - weeks for training using Viola and Jones [8] and at least a day for the more efficient method proposed in [13] - and both do not support multi threading during implementation. Another cascade-based method of detection is using Local Binary Patterns, which takes one to three days to train, depending on the number of samples used [16]. In addition, these previous studies using cascade-based methods did not factor in the time and efforts needed for collection of samples. There is also a chance of failure in creating a good cascade if the samples collected are not good. Furthermore, if more than one cascade is used in real time, the performance in real time is affected. Performance could drop from 30 frames per second (fps) to 20 fps or lesser.

The computational complexity of the pupil detector used in this paper is far less compared to using Hough Transform [9] and its variants [10] - [12]. The number of model parameters for Hough Transform increases due to the elliptical nature of the pupil and the complexity of the search time increases exponentially per increase in parameter [14]. The complexity increases at a rate of $\mathcal{O}\left(A^{m-2}\right)$ per additional parameter, where A is the image space's size and m is the number of parameters. A more efficient variant, Iterative Randomized Hough Transform (IRHT), has been proposed in [15] but it is still not fast enough for real-time application. As a comparison, the method used in this paper has a complexity of $\mathcal{O}(N)$ whereas Hough Transform and its variants have complexities close to $\mathcal{O}(N^3)$. Furthermore all variants of Hough Transform require edge detectors e.g. Canny before implementation hence their performance is highly dependent on the quality of the edge detector.

B. Palpebral Aperture Monitoring

There are a few works currently available in detecting the eyelid height or palpebral aperture. Two notable ones are for fatigue detection in drivers [17] and another using webcam [18]. The method in [17] detects the eyelid's height by getting an initial template from a rough location of the eyes by filtering and the template is retaken when there are notable changes of the eye. The templates found earlier were then used to find the eye region and the palpebral aperture. This method is adaptive but it requires relocating the eye and reinitializing the template every time there are notable changes in the aperture. Changes happen a lot of times due to blinks, eye movements and changing illumination condition, thus this method will prove to be too slow and not robust for real time application. The method mentioned in [18] goes through a lot of computationally expensive stages to accurately and precisely get the location of the eyelids. Hence, this will be too slow for real-time eyelid detection.

There are other similar works that detect the eyelids for performance improvement of iris recognition [19], [20]. These works aim for more accuracy and precision than speed so they cannot work well in real time applications. There are works that detect the eyelids for general purposes like in [21] and [22] but both of them are also not tailored enough

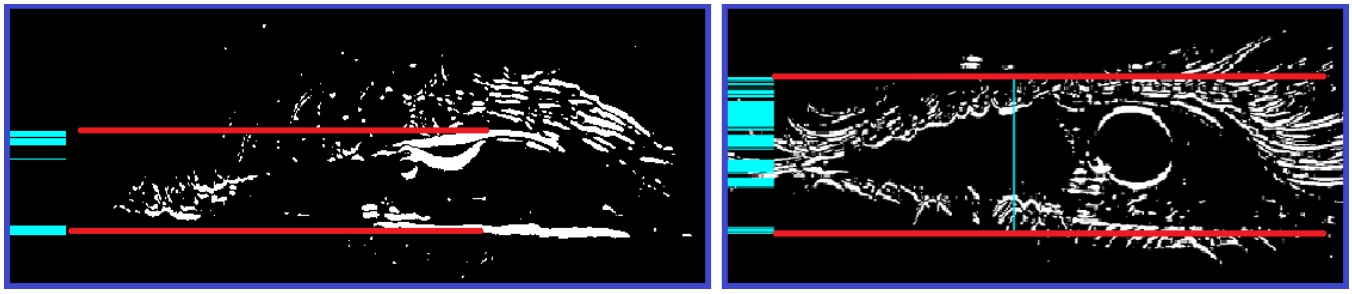

Fig. 3. OMG Vs Normal palpebral aperture. The blue horizontal lines indicates the region where there's a defined minimum threshold of pixels counted horizontally. The red lines marks out the palpebral aperture.

for the experiments in this paper. The work in [22] uses edge detection but it gives unnecessary and unspecific edges, which introduces noise.

Precious information of blinking, eye movements and aperture would be lost due to the fast speed of these activities if these algorithms were used and thus a new method is needed to detect them.

III. The Proposed Method

A. System Summary

The PRILIB system's hardware is purchasable at http://pupil-labs.com/pupil/. In the prototype, we have adopted the hardware and developed algorithms for the targeting applications. Three algorithms to detect blink rate, palpebral aperture, and pupil dilation are running each on different threads, in parallel at 30 fps or the camera's frame rate. The frames captured from the camera are put in a circular buffer in a different thread from all the image processing algorithms so that the image retrieval and its processing can be done in parallel. The algorithms have been tailored to ensure that the prototype works reliably in different illumination conditions, such as in a clinic, at home, and in a classroom. The summary of the system is seen in Figure 2 on the previous page.

B. Blink Detection

The blink detector proposed in this paper uses three algorithms to detect a blink, making it sensitive yet specific. How the detector works is described below.

1. A blink is detected by first detecting the pupil by a cascade-based tracker trained using local binary patterns [16]. The absence of the iris changes a "boolean variable" e.g. "BlinkTest1" to "true" indicating a blink has possibly occurred.

2. The image is then color-thresholded to show only the pupil. The height of the pupil is then determined by counting the Highest Vertical Connected Pixel (HVC). When the height becomes zero, it changes a "boolean variable" e.g. "BlinkTest2" to "true" indicating a blink has possibly occurred.

3. When the palpebral aperture height reaches a certain threshold, a "boolean variable" e.g. "BlinkTest3" changes to "true" indicating a blink has possibly occurred.

4. When "BlinkTest3" and "BlinkTest2" and "BlinkTest1" are all true, a blink is detected.

C. Palpebral Aperture Height detection

The method of eyelid detection in this paper uses a horizontal edge detection by means of contrasting colours. Since eyelids are horizontal, using horizontal edge detection instead of full edge detection ensures only necessary edges are filtered, hence filtering can be done twice as fast. Pupil tracking supplements the eyelid detection by limiting the search to the area around the pupil. The equations for finding the horizontal edges for an image with dimension $640x480$ can be seen below.

Note: j = 0 to j = 474 and i = 0 to i = 640 where i+1 each time j has iterated through a column from top to bottom.

$$R' = R_{i,j} + R_{i,j+1} + R_{i,j+2} \tag{1}$$

$$R'' = R_{i,j+3} + R_{i,j+4} + R_{i,j+5} \tag{2}$$

$$R_C = |R' - R''| \tag{3}$$

G and B can be substituted for R in equations (1) to (3).

$$(R_C, G_C, B_C)_{i,j} = |\sum_{k=0}^{2}(X_i, Y_{j+k}) - \sum_{m=3}^{5}(X_i, Y_{j+m})| \tag{4}$$

$$C_{i,j} = R_{i,j} + G_{i,j} + B_{i,j} \tag{5}$$

In equation (3), R_C refers to the contrast between R' (refer to (1)), the sum of the first three pixels, and R'' (refer to (2)), the sum of the next three pixels. $C_{i,j}$ is then compared to a defined threshold to determine if the point should be accepted as an edge. If it is within threshold, it is accepted, and a white pixel is placed in location $(X_{i,j}, Y_{i,j})$ in a blank image container. The threshold is auto-calibrated by a white pixel limit of 4000 pixels, for example, that can represent edges. Auto-calibration of the threshold ensures that there are enough edges to represent the eyelids in different lighting conditions. The palpebral aperture is then obtained by finding the prominent horizontal features as shown in Figure 3.

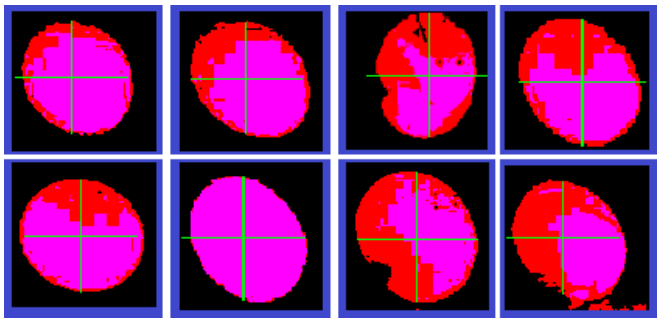

Fig. 4. Pupil and detection and dilation monitoring in action from myasthenic patients to normal controls. The varying orientations are due to the pupil looking in different directions.

D. Pupil Detection

Pupil detection is achieved by executing color thresholding twice in parallel using threading. The color thresholding is auto calibrated using pixel limiting like in the horizontal edge detector described in the previous section. First pixel limiter is used to calibrate the color thresholding so that only the pupil will be detected making it specific while the second is calibrated so that it is sensitive. This is shown in the Figure 4 above where the specific thresholding is pinkish while the sensitive thresholding is red.

The pupil dilation is derived by measuring the highest vertically connected. The algorithm used in monitoring the pupil is hence low computation due to $\mathcal{O}(N)$ complexity, high precision due to sensitive thresholding and accurate due to specific thresholding.

IV. EXPERIMENTS

A pilot test was conducted with 4 OMG patients and 10 normal controls.

A. Experiment Procedure

1) The volunteer wears the PRILIB device and is given a remote controller to press whenever they experience eye fatigue.
2) The volunteer is told to read a newspaper for 20 minutes, followed by a 5 minute break.
3) The volunteer then watches a 90 minute long movie. In this part of the experiment, all lights are turned off to minimise extraneous variables e.g. lighting affecting the volunteer's pupil dilation, eyelid activity and blink rate.

B. Observation

From the experiments, we came up with three observations. They are:

1) OMG vs Normal Blink Rate: OMG patients blink more than normal controls likely due to the poorer quality of their blinks secondary to weaker and more easily fatigable muscles. This could explain the earlier onset of eye fatigue. A possible exception to the above would be OMG patients with smaller eyes as the eyelid movement required for a full blink would be less as seen in asterisk in Table I. From Table I above, calculated average blink rate of the normal controls is 15 while the OMG patients is 20.

TABLE I

BLINK RATES OF NORMALS AND OMG PATIENTS

Condition	Average Blink Rate Per Minute									
Normal	9	12	15	13	19	9	14	23	19	12
OMG	33	22	12*	13*	-	-	-	-	-	-

2) OMG vs Normal Palpebral Aperture Fluctuations: The OMG patients in our study showed significantly more palpebral aperture fluctuations due to more frequent rise and fall of their eyelids, which are seen as spikes in Figure 5. A likely explanation for this would be the fatigable nature of the orbicularis muscle fibres, the need to overcome physiological drooping of the lids to avoid obstruction of their visual axis, as well as the increased blink rate, see Table I. The higher number of spikes, in contrast, is not seen in normal patients, although there is a possibility the spikes may increase with longer periods of activity and decreasing attention spans.

3) OMG vs Normal Blink Percentage: OMG patients were also noted to execute half blinks or lesser when they were focused on their task. This is in comparison to normal controls who blink fully throughout the task. See Figure 6.

V. CONCLUSIONS

In conclusion, we have found from our pilot study that the blink pattern and rate of OMG patients differ significantly from normal subjects: OMG patients have higher blink rate, more significant palpebral aperture fluctuations and exhibit half-blinks or less that are not seen in normal subjects. These observations form the basis for future comparisons for patients with other ptosis mechanisms and hold important clinical implications for ptosis as well as other eyelid movement disorders.

VI. ONGOING WORK

Currently we are increasing the number of OMG patients from different demographic groups and also including the other kinds of ptosis in the experiments to monitor a trend unique to each condition.

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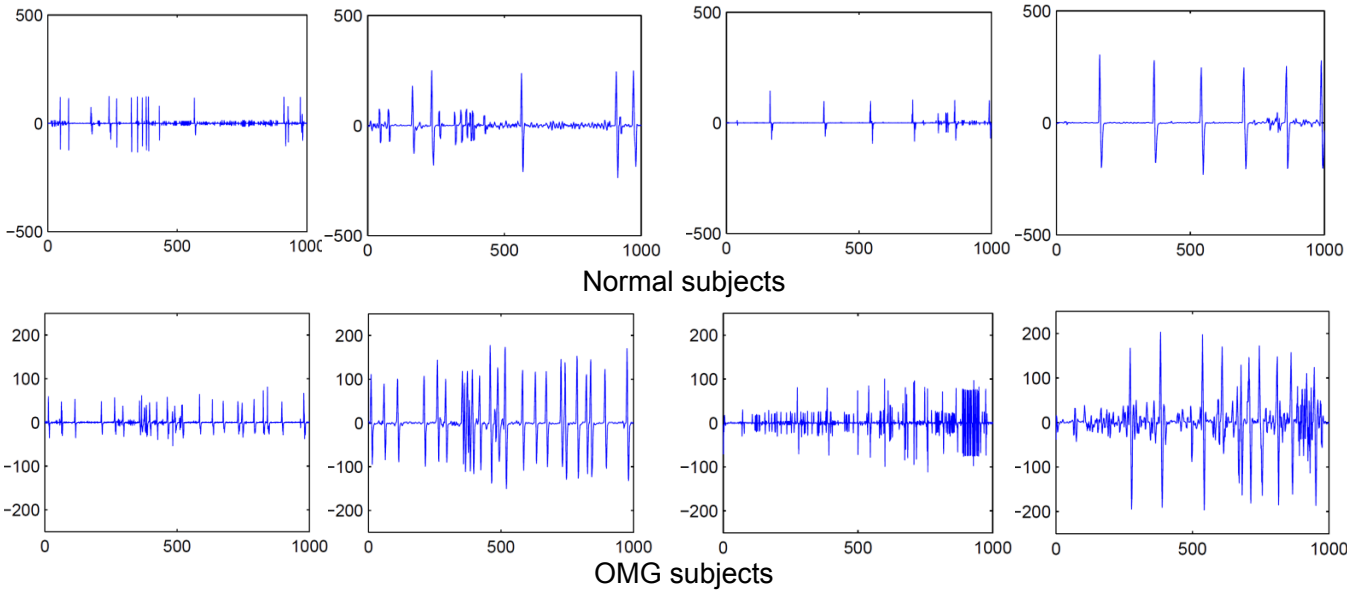

Fig. 5. Normal vs OMG aperture fluctuations processed using haar wavelets up to 6 levels. The first 2 columns represent the 1st and 3rd scales respectively of the 6 levels, comparing a normal subject (top) to an OMG subject (bottom). The last 2 columns show a similar comparison of a different normal subject-OMG subject pair. The OMG subjects exhibit more spikes showing more fluctuations compared to normal subjects.

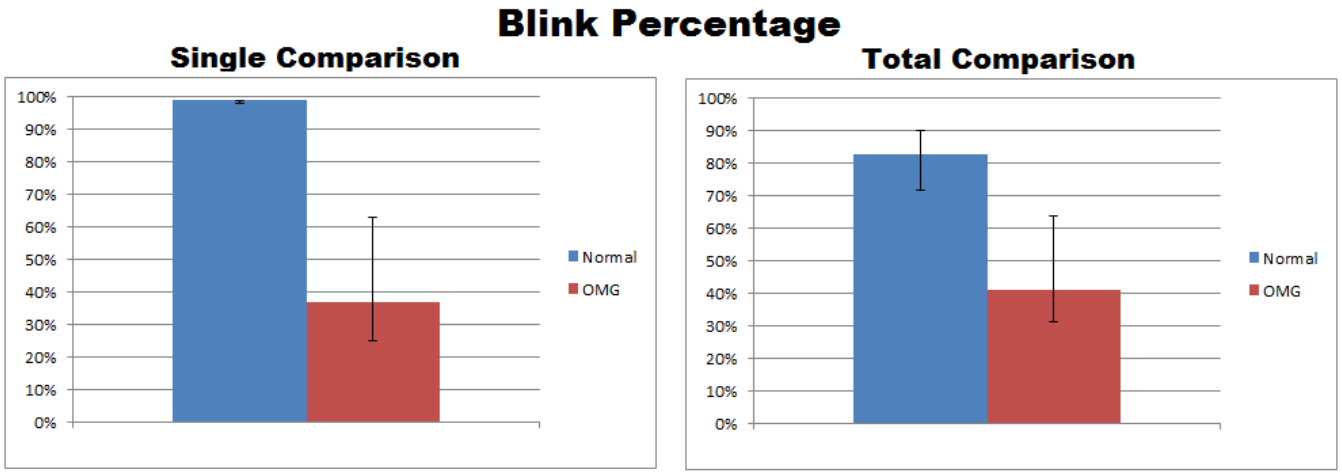

Fig. 6. Normal Vs OMG blink percentage. Comparison of blink percentage of one individual from each group on the left. Comparison of the average of each group on the right.

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