

METHODS AND SYSTEMS FOR ASSESSING THE PRESENCE OF TRAUMATIC BRAIN INJURY

1. STATEMENT OF CORRESPONDING APPLICATIONS

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This application is based on Australian patent application no. 2023902472, the entire contents of which are incorporated herein by reference.

2. FIELD OF THE TECHNOLOGY

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The technology relates to the field of assessment of brain health, and in particular to the assessment of the presence of traumatic brain injury (TBI), for example mild TBI (mTBI) which is known colloquially as concussion.

3. BACKGROUND TO THE TECHNOLOGY

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The human eye is a complex and delicate organ used to perceive the world around us. The eye captures light and forms an image on the retina. This generates electrical signals which are transmitted to the brain and interpreted as visual information. Scientists and medical professionals have come to understand the importance of tracking eye movement in diagnosing and treating various medical conditions. In particular, the movement of the eye has been found to be a useful indicator of brain pathology, including the presence of certain medical conditions.

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One example of a medical condition that the movement of the eye may be used to assess is traumatic brain injury, including mild traumatic brain injury (mTBI). Mild traumatic brain injury is a complex neurobehavioral phenomenon caused by deformation of the brain tissue from mechanical forces from direct impacts to the skull or indirect forces such as acceleration/deceleration. It may cause a range of symptoms, including headaches, dizziness, fatigue, depression, anxiety, irritability, loss of consciousness and impaired cognitive function, which can last between days and years as microstructural damage to axons and neurometabolic changes result in brain network disruption. The impact of a concussion can affect the brain's ability to control eye movements, leading to symptoms such as double vision, blurred vision, and problems with coordination.

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Despite increased knowledge of the biomechanics and pathophysiology of concussion, no standardised biomarkers exist (either clinical or serological). The diagnosis of a concussion may be based on a combination of self-reported symptoms, and physical and neurological examinations. Self-reported symptoms may not be fully disclosed to a physician and are subjective. One classic method of examination is a physician asking the patient to look at their finger as they move it around and watch how the patient's eyes track the movement. Such methods can be subjective and prone to error, and may ideally require a clinical environment suitable for careful tests.

There are many situations where a quick, accurate assessment of the likelihood of a concussion may be required away from clinical environments. Such situations include during play of a contact or combat sport, for example football (NFL, soccer, Australian rules), rugby, boxing, martial arts, etc., or at the scene of an injury, for example a road vehicle accident.

Brain imaging methods such as CT and MRI scans require expensive, bulky equipment that is not portable and rarely of sufficient sensitivity to diagnose mTBI, and therefore not suitable for in situ diagnoses as required in the above situations.

One existing system is Oculogica's EyeBox. This system relies on vergence (a measure of how well both eyes work together in synchrony) to determine the likelihood of concussion, yielding a sensitivity and specificity of 80.4% and 66.1% in detecting mTBI (Samadani, U., Spinner, R. J., Dynkowski, G., Kirelik, S., Schaaf, T., Wall, S. P., & Huang, P. (2022), *Eye tracking for classification of concussion in adults and pediatrics*, Frontiers in neurology, 13. doi:10.3389/fneur.2022.1039955). This sensitivity may be insufficient for use as a diagnostic tool for immediate judgements as to whether the patient can proceed with high mTBI-risk activities such as contact sports. Further, the operational protocol that the EyeBox uses (vergence) requires a large desktop with a stable platform. The inaccuracy of readings and physicality of the Eyebox makes it unsuitable to be used on sportsgrounds and field settings to provide an indication of concussion around the time of injury.

A system from Neuroalign uses vergence, saccades, and reaction times, with a frame rate of only 100Hz. A frame rate of only 100 Hz is likely to miss more subtle fixational eye events (such as microsaccades and other fixation measures described later in the context of forms of the technology).

Smooth pursuit analysis is an existing area of research in mTBI. Michael Kelly (no commercial device available) developed a portable device displaying a 10-second smooth pursuit figure-eight protocol which has been used in 849 athletes (aged 12-18) and 98 mTBI patients. The mTBI patients showed grossly skewed pursuit movements based on z-scores from normative data (Kelly, M. (2017), *Technical Report of the Use of a Novel Eye Tracking System to Measure Impairment Associated with Mild Traumatic Brain Injury*, Cureus, 9(5), e1251. doi:10.7759/cureus.1251). Likewise, both the Neuroflex (Saccade Analytics) and Righteye Vision System utilise smooth pursuit (with unreported sensitivities to mTBI detection), but only measure amplitude of error. The RightEye does not account for calibration error which is a significant confounder in smooth pursuit accuracy. Maruta et al. from EyeSync (NeuroSync) also rely on smooth pursuit error in their protocols (Maruta, J., Heaton, K. J., Kryskow, E. M., Maule, A. L., & Ghajar, J. (2013), *Dynamic visuomotor synchronization: quantification of predictive timing*, Behav Res Methods, 45(1), 289-300. doi:10.3758/s13428-012-0248-3; Maruta, J., Heaton, K. J., Maule, A. L., & Ghajar, J. (2014), *Predictive visual tracking: specificity in mild traumatic brain injury and sleep deprivation*, Mil Med, 179(6), 619-625. doi:10.7205/MILMED-D-13-00420; Maruta, J., Spielman, L. A., Rajashekar, U., & Ghajar, J. (2018), *Association of Visual Tracking Metrics With Post-concussion Symptomatology*, Frontiers in neurology, 9. doi:10.3389/fneur.2018.00611; Maruta, J., Suh, M., Niogi, S. N., Mukherjee, P., & Ghajar, J. (2010), *Visual tracking synchronization as a metric for concussion screening*, J Head Trauma Rehabil, 25(4), 293-305. doi:10.1097/HTR.0b013e3181e67936). The inventors believe this measure can be improved using the measures described in this specification.

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The RightEye Vision System uses an estimate of fixation stability using a measure known as bivariate contour ellipse area (BCEA), which measures the dispersion of eye tracking coordinates over an ellipsoid area on a graph, specifically how many fall within 68% of the distribution (Snegireva, N., Derman, W., Patricios, J., & Welman, K. (2021), *Eye tracking to assess concussions: an intra-rater reliability study with healthy youth and adult athletes of selected contact and collision team sports*, Experimental Brain Research, 239(11), 3289-3302. doi:10.1007/s00221-021-06205-6). Their fixation protocol only presented the stimulus for two seconds and required the participants to move their head at the same time while trying to fixate. Such a short stimulus presentation would not elicit many eye movements that could be beneficially analysed. In another study, the RightEye's protocol displayed a target for 7 seconds (BCEA as outcome measure), proving a significant difference between concussed and non-concussed subjects which improved when combined with a statistical model including eye vergence (Hunfalvay, M., Murray, N. P., & Carrick, F. R. (2021), *Fixation stability as a biomarker for differentiating mild traumatic brain injury from age matched controls in pediatrics*, Brain Inj, 35(2), 209-214,

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doi:10.1080/02699052.2020.1865566). However, this still only yielded a sensitivity of 65% and specificity of 70% in mTBI diagnosis. Leonard and colleagues specifically investigated fixational eye movements in mTBI as well. This group used a 30Hz scanning laser ophthalmoscope (a large desktop machine used in clinic) which tracked fixational events at 480 Hz. Their fixation measures were

5 evaluated in a direction histogram, specifically examining BCEA, fixational saccade velocity, acceleration, amplitude, and drifts. It was only their measures of fixational saccade peak velocity, acceleration, and amplitude during these fixation tasks that proved significant between recently concussed and healthy patients during their test protocol (Leonard, B. T., Kontos, A. P., Marchetti, G. F., Zhang, M., Eagle, S. R., Reecher, H. M., ... Rossi, E. A. (2021), *Fixational eye movements following concussion*, J Vis, 21(13), 11.

10 doi:10.1167/jov.21.13.11).

Cifu and colleagues used another large desktop application (EyeLink II at 500 frames per second) in a military population with a history of TBI (at least 8.5 months post-injury) (Cifu, D. X., Wares, J. R., Hoke, K. W., Wetzel, P. A., Gitchel, G., & Carne, W. (2015), *Differential eye movements in mild traumatic brain*

15 *injury versus normal controls*, J Head Trauma Rehabil, 30(1), 21-28.

doi:10.1097/htr.000000000000036). Their fixation measures included position variance, root mean square of the eye's velocity, along with the mean and absolute mean velocity of the eyes during fixation. They also included BCEA as a further measure of the geographical distribution of eye tracking coordinates. This did not yield any significant results using this method.

20 In a pilot study of 9 acutely concussed patients and 9 healthy controls, using the Nintendo® Wii device and a 120 Hz head-mounted eye tracking system, the researchers measured "the percentage of time that gaze was fixed on the centre of the game screen (Percentage Time on Centre) and the number of gaze deviations (eye movements) made away from the centre of the screen during play (Gaze

25 Deviations)", which demonstrated a significant difference between groups for both measures (Murray, N. G., Ambati, V. N., Contreras, M. M., Salvatore, A. P., & Reed-Jones, R. J. (2014), *Assessment of oculomotor control and balance post-concussion: a preliminary study for a novel approach to concussion management*, Brain Inj, 28(4), 496-503. doi:10.3109/02699052.2014.887144).

30 Another study recently evaluated 86 concussion patients within 50 days of injury using an integrated virtual reality headset and eye tracker (HTC Vive with 250Hz eye tracker), measuring "the number of saccades generated, the size and speed of the micro saccades, the area covered and the ratio of vertical-to-horizontal direction component of the fixational eye movements" (Mortazavi, M., Thirunagari, P.,

Sarva, S., & Pita, M. (2022), *Microsaccadic Fixational Eye Movements as an Oculomotor Marker for Concussion*, *Neurology*, 98(1 Supplement 1), S5-S5. doi:10.1212/01.wnl.0000801776.06317.1f). Their group found a higher average microsaccade magnitude in their concussed patient cohort. Additionally, microsaccades and drifts covered a more vertical area during fixation.

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There is a need for more tools that allow the evaluation of medical conditions through eye movement in a way that is more convenient, objective, and/or accurate than certain existing diagnostic tools.

4. OBJECT OF THE TECHNOLOGY

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It is an object of the technology to provide an improved method, system and/or device for assessing the health of a patient's brain, for example assessing the presence of traumatic brain injury (TBI) in the patient. Alternatively, it is an object of the technology to at least provide the public with a useful choice.

15 5. SUMMARY OF THE TECHNOLOGY

According to one aspect of the technology there is provided a method of assessing the health of a patient's brain. In certain forms, the method may comprise assessing the presence of traumatic brain injury (TBI) in the patient, for example mild traumatic brain injury (mTBI). The method may comprise
20 analysing data representative of the movement of an eye of the patient.

According to one aspect of the technology there is provided a computer-implemented method of assessing the presence of TBI in a patient, the method comprising:

- receiving eye data representative of movement of an eye of the patient;
- 25 analysing the eye data to determine an indication of the presence of TBI in the patient; and
- outputting the indication.

In certain forms, the eye data representative of the movement of the eye may comprise eye data representative of fixational eye movements of the eye, i.e. the movement of the eye during a fixational
30 task. More particularly, the eye data may be representative of the movement of the eye when the patient is gazing at a fixed target. The fixed target may be displayed at an eccentric position relative to the patient. In some forms, the eye data may be representative of the movement of the eye when the patient gazes at multiple fixed targets appearing sequentially, for example at random time intervals

and/or for random durations. The multiple fixed targets may be displayed at different locations in the eye's field of view.

Additionally, or alternatively, the eye data representative of the movement of the eye may comprise eye data representative of smooth pursuit eye movements of the eye, i.e. the movement of the eye during a smooth pursuit task. More particularly, the eye data may be representative of the movement of the eye when the patient is gazing at a moving target. The moving target may trace a shape, for example repeatedly tracing the shape.

In certain forms, the method may comprise determining a direction of gaze by detecting the position of the iris of the eye. Detecting the position of the iris may comprise applying an object detection algorithm to the eye data representative of the movement of the eye, for example a one-shot object detector such as a YOLO (You Only Look Once) v7 real time object detector. From this, the curvature of the iris may be calculated and from this the pupil position may be accurately estimated even when the pupil is occluded by the eyelids.

In certain forms, the method may comprise classifying the eye data representative of the movement of the eye using a transformer model, for example a bi-directional transformer model.

In certain forms, the method further comprises receiving target data representative of position of a target when the eye data representative of movement of the eye is captured. The method may further comprise analysing the target data to determine an indication of the presence of TBI in the patient.

In certain forms, the step of analysing the eye data, and optionally the target data, may comprise determining one or more measures of the movement of the eye and determining the indication of the presence of TBI in the patient based on the one or more measures.

In certain forms, the one or more measures may comprise:

- a) a measure of an average error between a position of a fixed target and a position of the patient's gaze during a fixational task. For example, the measure of the average error may be a root-mean-square error (RMSE);
- b) a measure of the frequency of microsaccades during a fixational task;

- c) a measure of one or more characteristics of one or more square-wave jerks (SWJs) during a fixational task; and
- d) a measure of a smooth pursuit breakdown in following a moving target. For example, the measure of the smooth pursuit breakdown may be a time before the breakdown occurs in a smooth pursuit task. The breakdown may occur when the accuracy of the eye to follow the moving target falls below a threshold.

In certain forms, the step of analysing the data may comprise determining any combination of one or more of measures a), b), c) and d).

In certain forms, the step of analysing the data may comprise determining any combination of two or more of the measures a), b), c) and d) and the step of determining the indication may comprise combining the two or more measures. For example, the two or more measures may be combined as a weighted average.

In certain forms, determining the indication may comprise comparing the one or more measures and/or a combination of two or more of the measures to one or more predetermined thresholds. In some forms, the one or more predetermined thresholds may be determined from like measures determined from other patients. In other forms, the one or more predetermined thresholds may be determined from like measures determined from the patient at one or more earlier times.

In some forms, the one or more measures may comprise a measure of the fluidity of eye movement in following a moving target. In some forms, the measure of the fluidity may be determined in combination with measure d).

In certain forms, the method comprises outputting the indication as a quantitative and/or qualitative assessment of the risk of the patient having TBI.

In certain forms of the technology, the method further comprises controlling a display screen to display a target to the patient. In some forms, the display screen may be controlled to display a fixed target. The fixed target may be displayed at an eccentric position relative to the patient. In some forms, the display screen may be controlled to display multiple fixed targets appearing sequentially, for example at random time intervals and/or for random durations. The multiple fixed targets may be displayed at

different locations in the eye's field of view. In some forms, the display screen may be controlled to display a moving target. The moving target may trace a shape, for example repeatedly trace the shape. The method may further comprise generating the data representative of the position of the target.

- 5 In certain forms, the method further comprises controlling a camera to capture images of the eye when the eye is gazing at the target. The method may further comprise generating the data representative of movement of the eye from the images captured by the camera.

- According to one aspect of the technology there is provided a computer-implemented method of
10 assessing the presence of TBI in a patient. The method may comprise receiving eye data representative of fixational eye movements of an eye of the patient during a fixational task when the patient is gazing at a fixed target. The method may further comprise determining one or more measures of the movement of the eye from the eye data. The one or more measures may comprise a measure of one or more characteristics of one or more square-wave jerks (SWJs). The method may further comprise
15 determining the indication of the presence of TBI in the patient based on the one or more measures. The method may further comprise outputting the indication.

- In certain forms, the one or more characteristics may comprise atypical characteristics of the one or more SWJs. The inventors have identified that the SWJ(s) of patients experiencing TBI may be
20 morphodiverse in the sense of containing atypical movements resulting in a shape that is different from what would be expected in the patient when healthy. For example, this morphodiversity may be presented in the occurrence of different types or sequences of movements, or in measures such as duration, shape, amplitude and/or velocity. A SWJ exhibiting these atypical traits may be considered malformed in comparison with a typical SWJ, and may be referred to herein as a "malformed" SWJ.
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- In certain forms, at least one of the one or more SWJs may comprise two or more phases. In examples, at least one of the SWJs may comprise three or more phases. A SWJ having two phases may be referred to as biphasic, and a SWJ having more than one phase may be referred to as polyphasic.
- 30 Reference to a phase of a SWJ should be understood to mean a distinct event within the SWJ comprising a movement or sequence of movements which may be distinguished from other events within the SWJ. By way of example, a typical SWJ of a healthy patient comprises a primary saccadic deflection away from the target, a coast portion, and an accurate saccadic restitution back to the target – which collectively

are considered a single phase (i.e., monophasic SWJ). Events that deviate from this form may be considered as additional phases, whether this be additional events (e.g., additional deflections or restitutions), or combinations thereof.

5 In certain forms, determining the one or more measures may comprise classification of each of the two or more phases. In examples, the phases may be classified as two or more of: Primary Saccadic Deflection, Subsequent Saccadic Deflection, Saccadic Restitution, Gradual Restitution, Saccadic Spike, and Coast phase.

10 In certain forms, determining the one or more measures may comprise quantification of one or more characteristics of each of the two or more phases.

In certain forms, the one or more characteristics of a Primary Saccadic Deflection and/or a Subsequent Saccadic Deflection may comprise one or more of: Saccadic Deflection Count, Saccadic Velocity, Saccadic
15 Amplitude, and Peak Deflection.

In certain forms, the one or more characteristics of a Saccadic Restitution and/or a Gradual Restitution may comprise one or more of: Saccadic or Gradual Restitution Count, Saccadic or Gradual Velocity, Saccadic or Gradual Amplitude, Peak Deflection, and classification (e.g., Accurate, Hypermetric, or
20 Hypometric).

In certain forms, the one or more characteristics of a Saccadic Spike may comprise one or more of: Saccadic Spike Count, and Saccadic Amplitude.

25 In certain forms, the one or more characteristics of a Coast phase may comprise one or more of: duration, fibrillation, and slope (e.g., is the angle flat, positive towards restitution, or negative away from restitution).

In certain forms, an indication of variability of fixational stability between SWJ events may be
30 determined. In certain forms, one or more characteristics of variability of fixational stability between SWJ events may comprise one or more of: fibrillation, and drift (e.g., persistent movement away from the target).

In certain forms, determining the indication of the presence of TBI in the patient may be based at least in part on an accumulated total of SWJ occurrences. In examples, a biphasic or polyphasic SWJ may be counted as a single SWJ occurrence. In other examples, each phase of a biphasic or polyphasic SWJ may be counted as a SWJ occurrence.

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In certain forms, a SWJ having higher number of phases may be attributed a higher weighting. In certain forms, a hierarchical weighting may be applied based at least in part on complexity of the SWJ. In certain forms, weighting may be based at least in part on the number of phases of the SWJ. For example, a higher weighting may be attributed to a SWJ having a higher number of phases.

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By way of example, a hierarchical weighting may be applied in which:

1. A typical SWJ is given weighting W_1 ;
2. Malformed SWJ is given weighting W_2 ;
3. Polyphasic SWJ[2] (i.e., determined as having two phases) is given weighting W_3 ;
- 15 4. Polyphasic SWJ[3] is given weighting W_4 ;
5. Polyphasic SWJ[4] is given weighting W_5 ; and
6. Polyphasic SWJ[n] is given weighting W_{n+1} ,

where $W_1 < W_2 < W_3 \dots < W_{n+1}$.

- 20 In certain forms, weightings may be adjusted based on one or more measures of one or more characteristics of an associated phase. For example, a weighting may be biased based on a characteristic such as the amplitude of peak deflection.

By way of example, an algorithm implementing this weighting may comprise:

- 25 Indication of the presence of TBI = (Typical SWJ_{total} * W_1) + (Malformed SWJ_{total} * W_2) +
(Polyphasic SWJ[2]_{total} * W_3) + ... + (Polyphasic SWJ[n]_{total} * W_{n+1})

In certain forms, each phase of a biphasic or polyphasic SWJ may be counted as a SWJ occurrence.

- 30 By way of example, an algorithm implementing this weighting may comprise:

Indication of the presence of TBI = (Typical SWJ_{total} * W_1) + (Malformed SWJ_{total} * W_2) +
(Polyphasic SWJ[2] phase_{total} * W_3) + ... + (Polyphasic SWJ[n] phase_{total} * W_{n+1})

In certain forms, further eye data may be received, the further eye data representative of fixational eye movements of an eye of the patient during a second fixational task. A determination of a second indication of the presence of TBI in the patient may be based on the further eye data. Progression of neuronal recovery of the patient may be determined based on a comparison of the second indication of the presence of TBI with the previous indication of the presence of TBI in the patient.

According to one aspect of the technology there is provided a system for assessing the presence of TBI in a patient, the system comprising a processor configured to perform the computer-implemented method according to another aspect of the technology.

According to one aspect of the technology there is provided a computer-readable medium having stored thereon instructions for performing a computer-implemented method of assessing the presence of TBI in a patient according to another aspect of the technology.

Further aspects of the technology, which should be considered in all its novel aspects, will become apparent to those skilled in the art upon reading of the following description which provides at least one example of a practical application of the technology.

6. BRIEF DESCRIPTION OF THE DRAWINGS

One or more embodiments of the technology will be described below by way of example only, and without intending to be limiting, with reference to the following drawings, in which:

- Figure 1A is a front view illustration of a human eye;
- Figure 1B is a cross-section of the eye 101 of Figure 1A in a sagittal plane;
- Figure 2A is an illustration of typical eye behaviour exhibiting microsaccades;
- Figure 2B is an illustration of typical eye behaviour exhibiting microtremor;
- Figure 2C is an illustration of typical eye behaviour exhibiting drift;
- Figure 2D is an illustration of typical eye behaviour exhibiting square wave jerks;
- Figure 2E is a plot of exemplary eye behaviour exhibiting a square wave jerk;
- Figure 2F is a plot of exemplary eye behaviour exhibiting a malformed square wave jerk;
- Figure 2G is a plot of exemplary eye behaviour exhibiting a biphasic malformed square wave jerk;

- Figure 2H is a plot of exemplary eye behaviour exhibiting a polyphasic malformed square wave jerk;
- Figure 2I is a plot of exemplary eye behaviour exhibiting a malformed square wave jerk;
- Figure 2J is a plot of exemplary eye behaviour exhibiting a polyphasic malformed square wave jerk;
- 5 Figure 2K is a plot of exemplary eye behaviour exhibiting a malformed square wave jerk;
- Figure 2M is a plot of exemplary eye behaviour exhibiting a Saccadic Spike in a malformed square wave jerk;
- 10 Figure 3 is a schematic illustration of a device and/or system for analysing movement of an eye according to one exemplary form of the technology;
- Figure 4 is a schematic illustration of an eye tracking system according to one exemplary form of the technology;
- Figure 5 is a schematic illustration of an exemplary data analysis system according to one form of the technology;
- 15 Figure 6 is a flow chart of an exemplary outline method for assessing the presence of TBI in a patient according to one form of the technology;
- Figure 7A is an illustration of a display screen showing the motion path of a target according to one form of the technology;
- 20 Figure 7B is another illustration of the display screen of Figure 7A also showing projections of the motion path of the target over time on the X-axis and on the Y-axis;
- Figures 8A-D are illustrations of radial-transformed eye tracking data in a smooth pursuit task according to one form of the technology; and
- Figures 9A-D are illustrations of eye tracking data in a smooth pursuit task according to another form of the technology.
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7. DETAILED DESCRIPTION OF EXEMPLARY FORMS OF THE TECHNOLOGY

7.1. Eye

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Forms of the technology are directed to devices, systems and methods for analysing data representative of movement of an eye, for example in the ability of the eye to follow a target. Some relevant aspects of the anatomy and movement of the eye will now be described. Forms of the technology are primarily

concerned with analysing movement of a human eye although the eyes of other animals may be analysed in other forms.

7.1.1. *Anatomy of the Eye*

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Figure 1A is a front view illustration of a human eye 101, including eyeball 104 and pupil 106. Movement of the eye 101 may be characterised by movement of the eyeball 104 and/or the pupil 106 in two mutually perpendicular axes, for example an axis in the lateral direction relative to the body (i.e. the horizontal direction when the body is standing upright), illustrated as x-axis 107 in Figure 1A, and an axis in the superior-inferior direction relative to the body (i.e. the vertical direction when the body is standing upright), illustrated as y-axis 108 in Figure 1A. These axes are also illustrated on Figure 1B, which is a cross-section of the eye 101 of Figure 1A in a sagittal plane (vertical when the body is standing upright).

7.1.2. *Movement of the Eye*

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Bodies have muscles that control movement of the eyeball 104. In the human eye 101, these are the extraocular muscles and the intrinsic eye muscles. There are six extraocular muscles that control the eye's movement and alignment in the orbit, and a seventh muscle to control a portion of the upper eyelid. The intrinsic eye muscles control movement of the lens and pupil dilation/constriction, which enable the eye to focus on near objects and control how much light enters the eye.

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Multiple different types of eye movement have been characterised, including:

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- Saccades – are rapid, ballistic movements of the eyes that abruptly change the point of fixation. They range in amplitude from, for example, the small movements made while reading to the much larger movements made while gazing around a room. Saccades can be elicited voluntarily, but occur reflexively whenever the eyes are open, even when fixated on a target;
- Microsaccades – are a kind of fixational eye movement. They are small, jerk-like, involuntary microscopic eye movements, similar to miniature versions of voluntary saccades. They typically occur during prolonged visual fixation to prevent fading;
- Prosaccades – a saccade towards a target, generally reflexively generated;
- Antisaccade – a saccade away from a target, generally volitionally generated;

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- Drift – the brain mechanisms behind ocular drifts are not fully known, but these are slower, more gradual movements that take place between microsaccades, during fixation;
- Tremor – small, high-frequency perturbations that take place between microsaccades;
- Fixational eye movements: for example microsaccades, square-wave jerks, tremor, and drift;
- 5 • Fixation – a fixation is composed of slower and minute movements (fixational eye movements) that help the eye align with the target and avoid perceptual fading. The duration may vary between, for example 50-600 ms; and
- Smooth pursuits – these are movements that are much slower tracking movements of the eyes designed to keep a moving stimulus on the fovea. Such movements are under voluntary control
- 10 in the sense that the observer can choose whether or not to track a moving stimulus and occur between saccades.
- Square-wave jerk – a form of fixational eye movement which move away and back from a fixation at approximately equal magnitudes, occurring within 150-500 ms. A further discussion on square-wave jerks is provided below in relation to eye movement dysfunction.

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Figures 2A to 2D are illustrations of typical eye behaviour exhibiting some of the eye movements explained above. Figure 2A illustrates a plot of a co-ordinate of an eye's gaze against time. The two illustrated small changes to the direction of gaze may be characterised as microsaccades. Figure 2B illustrates a plot of the horizontal (x) co-ordinate of an eye's gaze against time. The illustrated small, high-frequency perturbations may be characterised as microtremors. Figure 2C illustrates a plot of the horizontal (x) and vertical (y) co-ordinates of an eye's gaze at different points in time, with the line illustrating the sequential points in the plot. The gradual shift in gaze over time illustrated in this plot may be characterised as drift. The movements illustrated in Figures 2A to 2C are typical fixational eye movements, i.e. small, involuntary eye movements that may occur when a person is attempting to fix their gaze on a target. Figure 2D illustrates a plot of a co-ordinate of an eye's gaze against time. The illustrated abrupt changes to the direction of gaze away from the target for a short time (e.g. a few hundred milliseconds) and subsequently back to the target may be characterised as square wave jerks (SWJs). SWJs commonly occur in the horizontal (sideways) direction and therefore the position of gaze plotted on the vertical axis of Figure 2D may be the horizontal (x) co-ordinate of the eye's gaze, at least for some examples in this application. For completeness, it should be appreciated that discussion of movements being in the horizontal direction is not intended to exclude instances in which the SWJs occur in other directions (e.g., vertical).

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Forms of the technology may be used to analyse any one or more of the types of eye movement described above.

Eye movement dysfunction occurs when there is some abnormality or impairment of normal eye movement, for example saccades and smooth pursuits may be inaccurate with reference to a target, or may be interrupted in motion or irregular in timing. Saccade dysmetria is a motor error resulting in over or under shoot of the eye to the target accompanied by corrective saccades. Certain measures may be used to quantify eye movement dysfunction, for example saccade gain is the ratio of the eye movement to target location, and stimulus delay is the delay in reaction before the onset of the motor command when stimulus in the form of a target is presented in the visual plane.

7.1.2.1. Square-Wave Jerks

Figure 2E-2M illustrate theoretical plots of one-dimensional eye position 1000 (i.e., horizontal co-ordinate of the eye's gaze) against time, relative to fixation target position 1002 to illustrate some more detailed characteristics of square-wave jerks referred to in this specification. Figure 2F-2M illustrate malformed, biphasic, and polyphasic SWJs exhibiting various eye movement behaviours described herein.

As explained above, and shown simply in Figure 2D, a square-wave jerk (SWJ) is a form of fixational eye movement which move away and back from a fixation at approximately equal magnitudes, occurring within 150-500 ms. It is believed that fixational eye movements (including microsaccades such as these, drift and tremor) are to improve visibility by thwarting neural adaptation to unchanging stimuli. In view of the importance of detecting and characterising square-wave jerks to some forms of the technology, the characteristics of square-wave jerks in healthy and unhealthy patients will now be described in more detail.

With reference to Figure 2E, a theoretical plot of one-dimensional eye position 1000 (i.e., horizontal co-ordinate of the eye's gaze) is shown against time, relative to fixation target position 1002. In a healthy patient the SWJ has a clean and accurate single deflection away from the target of fixation 1002 in the horizontal direction of less than three degrees. This initial deflection may be referred to general herein as a Primary Saccadic Deflection ("PSD") 1010.

Following the PSD 1010 is a coast phase 1020 in which the eye position 1000 is maintained. A Peak Deflection ("PD") 1014 may occur between the PSD 1010 and coast phase 1020 (not shown in Figure 2E, but see Figure 2F). Reference to a Peak Deflection 1014 should be understood to mean the initial overshoot of a saccadic movement before return to a coast phase 1020. In a healthy patient, the PD 1014 is small or negligible. In contrast, Figure 2F shows a malformed SWJ having a significant PD 1014 following a slow PSD 1010.

In a healthy patient the coast phase 1020 may last for between approximately 70 ms to 700 ms (on average approximately 200 ms), with only small fibrillation. In contrast, Figure 2F shows a malformed SWJ having a negative sloped coast phase 1020. Following the coast phase 1020, a Saccadic Restitution ("SR") 1030 returns the eye position 1000 to the target 1002 of fixation. In a healthy patient the SR 1030 is accurate.

In an individual who is suffering from mTBI, including those with ongoing symptom burden and those with moderate and severe phenotypes, the brain eye systems managing the square-wave jerks fail to act reliably and certain characteristics of square-wave jerks may be observed to have changed.

It is established that square-wave jerks in some patients suffering with mTBI may be biphasic, meaning they return to the fixation target with a saccade that overshoots and is corrected once again by a third, corrective saccade (different to the canonical 'table top' appearance of a square-wave jerk) – see Figure 2G.

The inventors have identified that the movements may be morphodiverse in additional ways, and in severe cases may contain a polyphasic series of saccadic movements. For example, some mTBI cases may exhibit multiple deflections away from the target with larger peak deflections than a healthy patient and failed attempts at restitution back to the target which can be both hypermetric (overshoot) and hypometric (undershoot). There may also be fibrillations and drift seen in the coast phases. In describing the characteristics of square-wave jerks in detail the inventors have introduced new terms further to the simplicity of describing square-wave jerks as biphasic. In fact, complex polyphasic behaviour has been identified, which contains multi-stage breakdowns in fixational movements which can be classified and quantified.

As will be explained later, in certain forms of the technology, these characteristics may be measured and used to establish the severity of the condition. For example, saccadic movements may be quantified

along with its following coast phase. In addition to, or as an alternative from, the frequency and/or amplitude of SWJs, the complexity of the saccadic restitution failure and saccadic amplitude may be considered in measuring trauma.

5 Some illustrative examples of square-wave jerks in patients with mTBI are shown in Figures 2F to 2K.

In an example of the present technology, a SWJ may be determined as comprising a Primary Saccadic Deflection ("PSD") 1010. Measures of the PSD 1010 may include one or more of: Saccadic Velocity ("SV"), Saccadic Amplitude ("SA") 1012 (noting that a microsaccade is described in the literature as
10 being less than three degrees of eye movement, with a saccade being greater than three degrees), and Peak Deflection ("PD") 1014.

In an example of the present technology, a SWJ may be determined as comprising one or more additional saccadic deflections subsequent to the PSD 1010, referred to herein as Saccadic Deflection n ("SDn") 1016 – i.e., additional 'n' deflections away from the target following the PSD 1010. Measures of
15 the SDn 1016 may include one or more of: Saccadic Deflection Count (n) ("SDC"), Saccadic Velocity ("SV"), Saccadic Amplitude ("SA") 1012, and Peak Deflection ("PD") 1014.

In an example of the present technology, a SWJ may be determined as comprising a Coast phase 1020
20 between movements. Measures of the coast phase 1020 may include one or more of: duration (e.g., expected to be in the order of 100 ms to 400 ms), , and slope (e.g., is the angle flat, positive towards restitution, or negative away from restitution). In examples, fibrillation may be measured using RMS error from a line, with a value over a threshold value for standard deviation (e.g., 1) being indicative of malformation.

25 In an example of the present technology, a SWJ may be determined as comprising one or more attempts at restitution, for example Saccadic Restitution ("SRn") 1030 and Gradual Restitution ("GRn") 1040, where 'n' is the number of attempts at restitution). A Gradual Restitution ("GRn") 1040 may be distinguished from a Saccadic Restitution ("SRn") 1030 by the rate at which restitution occurs. For
30 example, normal microsaccades occur in less than 10 ms, with most of the time spent in the 200ms coast phase before a restitution that is equally fast (such that in a trace they appear to be substantially vertical. A Gradual Restitution may occur over a 50-60ms time frame and be more diagonal or curved relative to vertical. Measures of Saccadic Restitution ("SRn") 1030 and/or Gradual Restitution ("GRn")

1040 may include one or more of: Saccadic/Gradual Restitution Count (n) ("SRC"/"GRC"), Saccadic/Gradual Velocity ("SV"/"GV"), Saccadic Amplitude ("SA"), Peak Deflection ("PD"), and a classification of restitution (e.g., as Accurate, Hypermetric or Hypometric).

- 5 In an example of the present technology, and referring to Figure 2M in particular, a SWJ may be determined as comprising one or more Saccadic Spike ("SS") 1050. Reference to a Saccadic Spike should be understood to mean a malformation in a SWJ in which a saccadic restitution is initiated, but fails and returns back to the deflected state, before then attempting a more typical restitution. Measures of the SS 1050 may include one or more of: Saccadic Spike Count (n) ("SSC"), and Saccadic Amplitude ("SA")
- 10 1012.

7.1.3. Eye Tracking

- Forms of the technology relate to devices, systems and methods for analysing data representative of movement of the eye 101. Such data may be obtained by "tracking" movement of the eye 101. Unless the context clearly indicates otherwise, the term "tracking" is intended to mean the act of identifying the way in which the eye 101 moves over a period of time. By identifying movement of the eye 101, the movements may be able to be characterised and analysed. In certain forms, movement of the eye 101 is tracked by observing movement of the pupil 106. The pupil 106 is the aperture through which light enters the internal parts of the eye 101 and its position is therefore indicative of the direction of the eye's vision.
- 15 20

- The eye may be tracked in its ability to follow a target, which may be a fixed target or a moving target. A fixed target may be an object, or representation on a display screen, that is held in a fixed position relative to the eye's field of view for a certain length of time. A moving target may be an object, or representation on a display screen, which moves relative to the eye's field of view, for example the representation may move on a display screen presented to the eye. The target may be represented by a point-like object or image on a display screen, for example a small image (e.g. a dot). Alternatively, the target may be a larger or more complex object or image. The target may alternatively be termed a visual stimulus.
- 25 30

Eye tracking may comprise measuring, and optionally characterising, any errors in the eye's ability to track the target. For example an error may be a difference in the direction of the eye's gaze compared

to the position of the target. The difference may be represented through any appropriate parameter, for example as a physical distance, a measure equivalent to distance (e.g. pixels on a display screen) or an angle representing an angular difference between the direction of the eye's gaze and the direction of the target from the eye.

5

7.2. Eye Analysis Device / System

A schematic illustration of a device and/or system 200 for analysing movement of an eye according to certain forms of the technology is illustrated in Figure 3. Such devices / systems may otherwise be referred to as eye analysis devices / systems 200.

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Eye analysis system 200 may comprise an eye tracking system 300 and a data analysis system 400. The eye tracking system 300 may be configured to track movement of an eye 101 and to output data representative of the movement of the eye 101. That data may be provided to data analysis system 400, which may analyse the data representative of the movement of the eye 101. The data analysis system 400 may output certain information gained from the analysis process. Although described as separate functional systems in the description below, in some forms, the eye tracking system 300 and the data analysis system 400 may be implemented in the same physical system or systems, e.g. a computer or computing network. In other forms, different physical systems may implement the functions provided by each of the eye tracking system 300 and the data analysis system 400. In some forms, each functional system may be implemented by a plurality of physical systems.

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20

7.2.1. Eye Tracking System

In certain forms of the technology, the eye tracking system 300 may be any assembly of components that is configured to track movement of an eye 101 and to output data representative of the movement of the eye 101. Any suitable eye tracking system 300 may be used, an exemplary form will be described with reference to Figure 4, which is a schematic illustration of an eye tracking system 300 according to one exemplary form of the technology.

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7.2.1.1. Display Screen

In the exemplary form shown in Figure 4, the eye tracking system 300 comprises a display screen 310. The display screen 310 may comprise any device configured to present information visually to a viewer. The information may be in the form of images, for example. The display screen 310 may be controllable to alter the information displayed to the viewer. In particular, the display screen 310 may display a target 303 to the patient. For example, a fixed target or a moving target may be displayed to the viewer. In the case of a moving target, the target 303 may move along a motion path 305. The range of ocular motion may be important in detecting some medical conditions, so in certain forms the display is positioned to occupy a large part of the field of view of the eye 101, for example over 100° of the field of view. In other forms the system may explore eye movement nearer the centre of the field of view, in which case the display screen may be smaller. The target 303 may be moved on the display so the viewer must move their eye significant distances to follow the target's movement (e.g. up, down, left and right).

In certain exemplary forms, the display screen 310 is an electronic display, for example an LCD, LED, OLED screen. In some forms, the display screen 310 may be displayed to the viewer through a virtual reality (VR) or augmented reality (AR) display system while, in other forms, a reflection of the display screen 310 may be displayed to the viewer. The information displayed on the display screen 310 may be controllable by a processor, which may be comprised as part of the display screen 310, or may be configured to control the display screen 310 through a physical or wireless connection. In some forms, the display screen 310 is comprised as part of an electronic device, for example a portable electronic device 350 such as a smartphone, tablet, laptop computer or the like.

In some forms, the display screen 310 may be self-illuminating, for example the display screen 310 may comprise light-emitting elements such as LEDs. In other forms, the display screen 310 may be non-self-illuminating, for example the display screen may display information using electronic ink (e-ink). In such forms, a separate light source may be used to illuminate the display screen. It will be appreciated that the level of illumination should be adequate for the camera settings, e.g. the frame rate, exposure and resolution, so that the images are clear and not blurred.

In some forms, the eye tracking system 300 may comprise multiple display screens.

7.2.1.2. Camera

In certain forms of the technology, the eye tracking system 300 may comprise a camera 320. The camera 320 may comprise any optical device configured to capture and record visual images. A suitable frame rate for the camera 320 may be guided by the Nyquist-Shannon sampling theorem, i.e. that the sampling frequency should be at least twice the frequency of the recorded movement. It is considered
5 that frequencies below approximately 100 Hz carry little information about fixational eye movements, so in certain forms the eye tracking system 300 uses a camera 320 with a minimum frame rate of approximately 200 Hz. For example, in one form, the camera 320 has a frame rate of 240 Hz. This provides a time gap of 4.2 ms between frames and consequently captures eye movements with timeframes longer than this timescale, including, for example, subtle fixational movements such as SWJs
10 and components of polyphasic SWJs which may be as short in duration as approximately 5 ms.

In addition, the resolution of the camera 320 may be sufficiently high to capture the eye movements that are detected and analysed in the analysis method. For example, microsaccades are typically less than 3 degrees of a visual angle. In some forms, the camera may have an accuracy of approximately 0.01
15 visual degrees, for example. In some forms, the camera 320 may be of sufficient resolution, and the camera 320 may be positioned relative to the eye 101, so that the size of the image that captures the eye 101 is at least 500 x 500 pixels, for example.

The captured images may be displayed on a display screen, which in some forms may be the display
20 screen 310 comprised as part of the eye tracking device 200 while in other forms the camera may be configured to transmit the images to another device, which may itself comprise a display screen for displaying the images or a memory for storing the images for display elsewhere. The images may be transmitted through a wired or wireless connection, for example to a display screen located remote from the eye tracking system 300. The images may be displayed on the display screen in real-time, near-
25 real-time, or at a later time compared to when the images are captured by the camera. In some forms, the camera 320 comprises a memory configured to store the visual images. It should be appreciated that, in certain forms, the camera 320 is a digital camera and reference to images may mean the data recorded by the camera as being representative of the image.

30 In certain exemplary forms, the camera 320 may be comprised as part of an electronic device, for example a portable electronic device 350 such as a smartphone, tablet, laptop computer or the like. In such forms, the camera 320 comprises display screen 310, which may be configured to display the images captured by the camera 320.

7.2.1.3. Processor

In certain forms of the technology, the eye tracking system 300 may comprise one or more processors.

5 Although multiple distinct processors may be used, the processors may operate together, or may be considered to operate together as a functional unit. For the purposes of the following discussion, the description will refer to a single processor configured to perform any of the described functions for convenience, although it should be understood that multiple processors may be used in some forms.

10 The processor may be configured to generate data representative of the movement of the eye 101 from the image data captured by the camera 320. The processor may be comprised as part of the same device as the camera, for example portable electronic device 350 in the form shown in Figure 4, or the processor may be located remotely from the camera 320 and receive image data from the camera 320, for example over a wired or wireless communication link.

15 The processor may also control the display screen 310 to present information to the patient, for example a fixed or moving target for the patient to gaze at during eye tracking. The processor may be configured to generate data representative of the position of the target 303. Suitable movement protocols may be provided to the processor, for example from a memory or via a suitable
20 communication link.

The processor may further be configured to output the data representative of the movement of the eye 101. The data may be output by the processor by sending the information over a suitable communication network or by outputting the information via an output device, for example display
25 screen 310. Alternatively, the information may be stored in a memory, for example a memory of portable electronic device 350, for later output. The outputted data representative of the movement of the eye 101 may be an array of data representing the position and/or movement of the eye 101, for example the pupil 106, at a plurality of times. The data may be outputted in any suitable format, for example a CSV file.

30 The processor may further be configured to output data representative of the position of the target 303 (which may include data representative of movement of the target 303 if the target is moving). This data may be contemporaneous to the data representative of the movement of the eye 101, i.e. such that the

target data represents movement of the target 303 when the eye 101 is gazing at it and the eye's movement is captured in the eye movement data. The data may be output by the processor by sending the information over a suitable communication network or by outputting the information via an output device, for example display screen 310. Alternatively, the information may be stored in a memory, for example a memory of portable electronic device 350, for later output. The outputted data representative of the movement of the target 303 may be an array of data representing the position and/or movement of the target 303, at a plurality of times. The data may be outputted in any suitable format, for example a CSV file.

In some forms, the processor may output the data representative of the movement of the eye 101 and the data representative of the movement of the target 303 together, for example in the same data file. The outputted data may be time-stamped so that the position of the eye 101 is recorded relative to the position of the target 303 at each time point.

7.2.2. Data Analysis System

Figure 5 is a schematic illustration of an exemplary data analysis system 400 according to one form of the technology. Data analysis system 400 may comprise a hardware platform 402 that manages the collection and processing of data from eye tracking system 300, for example the data representative of the movement of the eye 101 and the data representative of the movement of the target 303. The hardware platform 402 may comprise a processor 404, memory 406, and other components typically present in such computing devices. The hardware platform 402 may be local to the eye tracking system 300 or it may be remote from the eye tracking system 300 and receive the data over a suitable communications link, such as network 416. In the exemplary form of the technology illustrated, the memory 406 stores information accessible by processor 404, the information including instructions 408 that may be executed by the processor 404 and data 410 that may be retrieved, manipulated, or stored by the processor 404. The memory 406 may be of any suitable means known in the art, capable of storing information in a manner accessible by the processor 404, including a computer-readable medium, or other medium that stores data that may be read with the aid of an electronic device.

The processor 404 may be any suitable device known to a person skilled in the art. Although the processor 404 and memory 406 are illustrated as being within a single unit, it should be appreciated that this is not intended to be limiting, and that the functionality of each as herein described may be

performed by multiple processors and memories, that may or may not be remote from each other or from the processing system 400. The instructions 408 may include any set of instructions suitable for execution by the processor 404. For example, the instructions 408 may be stored as computer code on the computer-readable medium. The instructions may be stored in any suitable computer language or
5 format. Data 410 may be retrieved, stored or modified by processor 404 in accordance with the instructions 410. The data 410 may also be formatted in any suitable computer readable format. Again, while the data is illustrated as being contained at a single location, it should be appreciated that this is not intended to be limiting – the data may be stored in multiple memories or locations. The data 410 may also include a record 412 of control routines for aspects of the system 400.

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The hardware platform 402 may communicate with a display device 414 to display the results of analysing the data. In some forms, the display device 414 may be the display screen 320 that is comprised as part of eye tracking system 300. The hardware platform 402 may communicate over a network 416 with one or more other devices (for example user devices, such as a tablet computer 418a,
15 a personal computer 418b, or a smartphone 418c, or other devices including sensors), or one or more server devices 420 having associated memory 422 for the storage and processing of data collected by the local hardware platform 402. It should be appreciated that the server 420 and memory 422 may take any suitable form known in the art, for example a “cloud-based” distributed server architecture. The network 416 may comprise various configurations and protocols including the Internet, intranets,
20 virtual private networks, wide area networks, local networks, private networks using communication protocols proprietary to one or more companies, whether wired or wireless, or a combination thereof.

Following analysis of the data representative of the movement of the eye 101, the data analysis system 400 may be configured to output certain information gained from the analysis process, examples of
25 which will be described in more detail below. The information may be output by the data analysis system 400 by sending the information over network 416 or by outputting the information via an output device, for example display device 414, tablet computer 418a, personal computer 418b, or smartphone 418c. Alternatively, the information may be stored in a memory, for example one or both memory 406 or 422, for later outputting from the data analysis system 400.

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In certain forms, the hardware platform 402 of data analysis system 400 may comprise a computing device, for example a laptop or PC. In other forms, the hardware platform 402 may comprise a plurality of computing devices configured to operate collectively to perform the data analysis / processing.

7.3. Method of Analysing Eye Tracking Data

In certain forms of the technology, there is provided one or more methods for analysing the eye tracking data, i.e. the data representative of the movement of the eye 101. Unless otherwise stated, it should be understood that the analysis methods may be carried out by a data analysis system 400 such as described above and in relation to Figure 5.

7.3.1. Method of Assessing the Presence of TBI

Certain forms of the technology are directed to methods, systems and devices for assessing the presence of traumatic brain injury (TBI) in a patient. In some forms, the assessment is of the presence of mild traumatic brain injury (mTBI), which may alternatively be referred to as concussion.

Figure 6 is a flow chart of an exemplary outline method 600 for assessing the presence of TBI in a patient. The method 600 may be performed by a data analysis system 400 such as illustrated in Figure 5, although some steps of the method, for example pre-processing steps may be performed by the processor of eye tracking system 300 in some forms. The method may comprise receiving eye data representative of movement of an eye 101 of the patient, analysing the eye data to determine an indication of the presence of TBI in the patient, and outputting the indication. Each of these steps will be explained in more detail below.

7.3.1.1. Target Display

In a first step 601 of an exemplary method according to a form of the technology, a display screen 310 is controlled to display a target 303 to a patient for viewing by the patient's eye 101. In certain forms, one or both of two types of target 303 may be displayed to the eye 101: a fixed target and/or a moving target.

The case of the target 303 being a fixed target may be referred to as a fixational task. That is, a fixed target 303 is displayed on the display screen 310 and the patient is asked to gaze at the fixed target. The display screen 310 may be controlled to display the fixed target at an eccentric position relative to the patient. That is, at a position that is not directly in front of the patient in the line of sight with the eye

looking directly forward. In some forms, an eccentric position may be considered to include angles subtending up to 120° from central fixation. It will be appreciated that the display screen 310 needs to be sufficiently large given its distance from the eye 101 to enable the target 303 to be displayed at such a position.

5

In certain forms, the display screen 310 may be controlled to display multiple fixed targets in sequence, i.e. one displayed after another. Each fixed target may be displayed for a random duration and/or the time interval between displayed each fixed target may be random. The selection of the random duration and/or the random time interval may be constrained to be within a certain maximum and minimum

10 time period. In addition, or alternatively, the multiple fixed targets may be displayed at different locations in the eye's field of view. The selection of the location of display of each fixed target on the display screen 310 may also be selected randomly from the locus of positions on the display screen 310 that possess eccentric co-ordinates relative to the eye 101.

- 15 The case of the target 303 being a moving target may be referred to as a smooth pursuit task. That is, a moving target 303 is displayed on the display screen 310 and the patient is asked to gaze at the moving target and to maintain the gaze at the moving target as it moves around the display screen 310. The display screen 310 may be controlled so that the moving target follows a predetermined path around the screen and, in some forms, the moving target 303 may trace a particular shape, for example a circle
- 20 or oval, and the moving target 303 may repeatedly trace the same shape. In the example of the display screen 310 shown in Figures 7A and 7B, the target 303 may be any icon, for example a dot, and the target follows a motion path 305 on the display screen 310. The motion path 305 may be elliptical, circular, sinusoidal, sawtooth or any other motion path considered suitable to test a patient's eye tracking. The target 303 may move in either a clockwise or anticlockwise direction. In the exemplary
- 25 display screen 210 of Figure 7B, the position of target 303 is shown in successive positions 303a, 303b, 303c, 303d over time along its motion path 305. The same figure also shows projections of that path over time on the X-axis and on the Y-axis. The elliptical motion path 305 of the target 303 in this example may cause the eye to move in both the X direction (corresponding to points 303a and 303c) and the Y direction (corresponding to points 303b and 303d) so as to exercise the eye's range of motion.
- 30 In some examples, motion path 305 may be altered to be flat or off-axis for some testing regimes. Repeated motion of the target 303 along the motion path 305 smoothly exercises the human eye/brain interface. The movements in the X and Y axis independently are sinusoidal in nature in the example shown, but may be modified to be a sawtooth wave or square wave in other examples.

In some forms, the speed and/or amplitude of the motion of the target 303 on the display screen 210 may be altered over time. This increases the cognitive stress and physiological demand on the subject during the smooth pursuit task. Increasing the cognitive stress will increase the severity of any symptoms and, by speeding up the motion, a breakdown point may be able to be determined, as explained later. In some forms, the subject may be tested over a set of trials, and the speed of the motion of the target 303, or the rate of acceleration of the target 303, may be progressively increased in each successive trial.

7.3.1.2. Eye Tracking

At step 602, which may occur simultaneously with step 601, the movement of eye 101 is tracked while performing the fixational and/or smooth pursuit tasks. An eye tracking system 300, such as described above, may be used for this step and the camera 320 may capture images of the eye 101 during the tasks when the eye 101 is gazing at the target 303.

The eye tracking system 300 may generate the data representative of movement of the eye from the images captured by the camera 320. This data may be provided to the data analysis system 400 using any suitable data communication protocol. The data representative of movement of the eye from the images captured by the camera 320 may comprise eye data representative of movement of the eye and target data representative of the position of the target.

In some forms, a calibration step may be performed in which the patient is asked to gaze at a target in one or more locations on the display screen 310. From the data generated in this step, a transformation to transform the co-ordinates of the detected eye position and the actual gaze co-ordinates may be determined. This transformation may be applied to the eye movement data, as explained later.

7.3.1.3. Pre-Processing

At step 603, the data analysis system 400 receives the eye data representative of the movement of the eye 101 during the tasks. The data analysis system 400 may additionally receive target data representative of the position of the target 303 during the tasks (if the data analysis system 400 does

not already have this data), for example this target data may be received from the processor of the eye tracking system 300.

In some forms, the eye data representative of the movement of the eye 101 during the tasks and/or the target data representative of the position of the target 303 during the tasks may need to be pre-processed at step 604 before further analysis can be performed. Examples of such pre-processing will now be described. It should be appreciated that, while the data analysis system 400 is described as performing these pre-processing steps, in other forms, the eye tracking system 300 may perform some of these steps prior to providing the data to the data analysis system 400.

In one exemplary step, the two data sets (i.e. representing the movement of the eye and representing the position / movement of the target) are processed so that they can be easily compared and analysed together. For example, a main extract function may be applied to load the data sets, align and curate them. This function may also facilitate further analysis on each task of the protocol. More precisely, data representative of the position of the target 303 during the eye tracking protocols, which may consist of target locations on the display screen 310 and timings, are saved as annotations which are loaded and sampled to a frame rate that is consistent with that for the data representative of the eye movement.

With regard the eye data representative of the eye movement, pupil-tracking coordinates may be loaded and resampled before being merged with the contemporaneous data representing the position of the target. In certain exemplary forms of the technology, a direction of gaze may be determined by detecting the position of the iris of the eye against the sclera. Detecting the position of the iris may be more resilient to occlusion by the upper eyelid (as may occur when tracking the pupil) and any reflections when compared to detecting the position of the pupil. In comparison with a pupil, which changes size as it dilates, the radius of the iris is substantially fixed. In addition, detecting the outer curvature of the iris, which is larger than the curvature of the pupil, provides superior sampling. Therefore detecting the curvature of the iris in perspective may be used to estimate the orientation of the eyeball in the socket with a good degree of accuracy. For example, in some forms using this method, the orientation of the eye may be determined to a sub-pixel estimate of approximately 0.25% of a pixel, which may be roughly equivalent to using a 2000 x 2000 pixel camera. For an average adult human eye, which has a width of 24 mm, this allows for tracking the centre of the eye at approximately 0.06 degrees. This is lower than the minimum amplitude of typical eye movements and therefore promotes accuracy in the results. For example, the minimum amplitude of a SWJ may be approximately 0.2° to

1.5°. Components of a polyphasic SWJ may be as small as 0.1° and there may also be useful information even below this scale in terms of quantification.

In some forms this may be achieved by applying a pre-filter on the iris to normalise colour and texture and applying an object detection algorithm to the eye data to find the bounding location of the iris, for example a one-shot object detector. In certain forms, an example of a one-shot object detector that may be applied to find the bounding location of the iris is a YOLO (You Only Look Once) v7 real-time object detector. The one-shot object detector may be first trained using an appropriate set of eye data with all iris present accurately labelled. Subsequently, a partial curve detector may be applied in order to estimate the full ellipsoid shape of the iris and consequently the centre of the iris and pupil, even if the pupil is occluded by the eyelids. Determining the centre of the iris and pupil may provide the direction of gaze using established techniques that will be known to the skilled reader. In some forms, the method may comprise applying a secondary tracker which looks for the curvature of the pupil to estimate the diameter of the pupil, which can change size as it dilates.

In some forms, the eye data may be processed to determine the position of one or more corners of the eye 101. Existing eye corner detection techniques may be used to achieve this. If changes in the position of the corner(s) of the eye is detected, a suitable adjustment may be made to the pupil position determined, and hence the determined direction of gaze.

In some forms, blink detection may be performed. In some forms, blink detection is performed in order to remove from further analysis eye data that is captured during a blink. This may avoid the results being affected by any anomalies in eye movement that may occur during a blink. In other forms, blink detection may be used in order to measure blinks, for example time between blinks and/or blink frequency. In some forms, one or more of these may be useful measures to help assess mTBI. In certain forms, blink detection may comprise applying an object detection algorithm to the eye data set, for example a one-shot object detector. In certain forms, an example of a one-shot object detector that may be applied to the eye data set for blink detection is a YOLO (You Only Look Once) v7 detector. Again, the one-shot object detector may be first trained using an appropriate set of eye data with all eyelids present accurately labelled. In some forms, the object detection algorithm may additionally be able to detect the eyelash portion of the eyelid in the image data of the eye 101. Since the position of the eyelid changes over time during a blink, the change in vertical position of the eyelid may be used to

measure the eyelid velocity / blink speed. In other forms, blinks may be detected by detecting the absence of the pupil and assuming that this absence is due to the eyelid being closed during a blink.

In another optional pre-processing step, the co-ordinates of the eye position in the eye movement data
5 may be transformed into gaze co-ordinates by applying any necessary transformation determined from a calibration step.

7.3.1.4. Determination of Measures of Eye Movement

10 At step 604, the data analysis system 400 analyses the data. As will be explained, the analysis may determine the presence of TBI (e.g. mTBI) in the patient.

In certain forms, the analysis may comprise determining one or more measures of the movement of the eye 101 and the indication of the presence of TBI in the patient may be determined based on the one or
15 more measures. In different forms of the technology, the determination may be based on each of the measures on their own. Alternatively, in other forms, the determination may be based on a combination of two or more of the measures. Any combination of two or more of the measures may be used, and forms of the technology are not limited to any particular combinations of the measures. It will be appreciated that the accuracy of the determination may increase if more measures are used in the
20 determination of the condition.

In general, determining the indication of the presence of TBI may be based on comparing each of the measures to one or more threshold values. It may be determined that TBI is present if the respective measure is above or below the respective threshold value. It will be appreciated that TBI is not a
25 condition that is diagnosed in such a binary fashion, but the threshold may be selected in order to give a particular confidence level that the condition is present or absent. In some forms, multiple thresholds may be used for each measure, with the thresholds providing a range of confidence levels as to whether the condition is present. Such information may be conveyed as an output, as described in more detail below.

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The following sections explain the exemplary measures that may be determined from the data, how they may be determined and how they may be used to determine an indication of the presence of TBI. While exemplary methods for determining the measures are explained, it should be understood that the

measures may be able to be determined using other methods in other forms of the technology. For example, in certain forms the data analysis system 400 may implement computer analysis of the eye movement data based on an algorithmic approach, e.g., application of one or more algorithms to: extract features of the eye movement data, classify features of the eye movement data, derive values for measures of the eye movement data, and derive and output an indication of the presence of TBI in the patient.

Further, machine learning methods may be employed in order to analyse the large amount of data that is generated in an eye tracking process and to determine the measures from this data. For example, in certain forms machine learning model(s) may be trained to determine the indication of the presence of TBI in the patient. Such machine learning model(s) may include one or more models of one or more machine learning algorithms (e.g., a deep learning model using an artificial neural network). During training, machine learning algorithm(s) can be trained by providing training data as input using learning techniques generally known in the field of machine learning. In examples the training data may include the eye movement data described herein, with examples from healthy patients and patients experiencing TBI. In examples, the machine learning model(s) may be trained to identify the measures within the eye movement data described herein, from which the indication of the presence of TBI in the patient may be determined. In alternative examples, the machine learning model(s) may be trained to infer the indication of the presence of TBI in the patient directly from the eye movement data.

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7.3.1.5. Microsaccade Frequency

In exemplary forms, the eye data representative of the movement of the eye during a fixational task is analysed to determine a measure of the frequency of microsaccades during the fixational task.

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In certain forms, saccades are filtered from the eye movement data using any suitable form of computational algorithm, such as a Hidden Markov Model (HMM) based on speed and distance which has previously been described (Salvucci, D. D., & Goldberg, J. H, 2000, *Identifying fixations and saccades in eye-tracking protocols*, paper presented at the Proceedings of the 2000 symposium on Eye tracking research, Palm Beach Gardens, Florida, USA, <https://doi.org/10.1145/355017.355028>). This process may cluster saccades into two groups depending on the distance of movement of the eye between the beginning and the end of each saccade: small saccades and large saccades. In some forms, the model may apply two states: one state for fixations and one state for any other eye movement. Alternatively,

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in other forms, the model may apply three states: one state for fixations, one state for clipped values (after high-pass filtering) and one state for any other eye movement.

In some forms, this approach is used to auto-label training data which is fed into a transformer model, i.e. a neural network that learns context and thus meaning by tracking relationships in sequential data. The transformer model may be built by encoding the eye motion per frame as a linear series of vectors. These movements may be labelled into different classes as part of the training data. The different classes may be, for example, smooth pursuit, fixation, saccades, microsaccades, tremor and square wave jerk (or components thereof). While some training data may be auto-labelled, some manual overrides may be applied to correct for any errors and fine tune the labelling. As more data is collected from patients and labelled, the performance of the transformer model improves. The transformer model may be able to perform much better than traditional heuristic methods as it may be trained with a huge amount of training data from where it can take the context of the series of motions prior and after. In addition, the model may be able to accommodate secondary effects like the current pupil position which may be important as, with enough data, certain parts of the ocular range of motion may impact performance.

The mean and standard deviation of the states may be initialised using percentiles of the input data. Information from the annotations from the target position data may be used to further classify the saccades, for example corrective saccades may be identified if they immediately precede the onset of the target being displayed. The smallest saccades, for example saccades having an amplitude that is below a predetermined threshold, may be classified as microsaccades and/or microsaccadic intrusions and can occur in either the horizontal or vertical meridian. The saccade is the eye's voluntary act of looking towards the target based on human reaction times while a microsaccade is an involuntary fixational movement which may typically be of a similar velocity but can be an order of magnitude lower in amplitude in movement, e.g. from 0.2° to 1.5° , and is not subject to reaction times. Both of these measures may be used in the analysis in some forms.

In certain forms, the frequency of the occurrence of microsaccades when the target is shown to the patient during the fixational task may be determined. Where multiple fixed targets are presented to the patient to gaze at, the microsaccade frequency may be calculated as an average value of the microsaccade frequencies for the plurality of individual targets.

In some forms, a positive diagnosis of the presence of TBI may be made if the frequency of microsaccades exceeds a certain threshold value. In some forms, a diagnosis of mild TBI (i.e. mTBI or concussion) may be made if the frequency of microsaccades exceeds a first, lower threshold value but is lower than a second, higher threshold value. In such forms, a diagnosis of moderate or severe TBI may be made if the frequency of microsaccades exceeds the second, higher threshold value. In certain forms, the thresholds may be absolute values of microsaccade frequency determined through experimental observation of previous patients. In other forms, the thresholds may be calculated from a control value of microsaccade frequency that is experimentally determined to be a “normal” value. For example, the thresholds may be a certain percentage above the control value. The percentages may again be determined through experimental observation of previous patients.

7.3.1.6. Error Between Gaze and Target

In exemplary forms, the eye data representative of the movement of the eye during a fixational task and the target data are analysed to determine a measure of an average error between a position of a fixed target and a position of the patient’s gaze during a fixational task. For example, the measure of the average error may be a root-mean-square error (RMSE) between the patient’s gaze and the position of the target, which may also be referred to as the root-mean-square deviation (RMSD). In other forms, any other statistical measure of the error between the position of a fixed target and the position of the patient’s gaze during a fixational task may be used. Where multiple fixed targets are presented to the patient to gaze at, the measure of the average error may be calculated as an average value of the errors for the plurality of individual targets.

The error between the position of the fixed target and the position of the patient’s gaze may be represented by any appropriate parameter, for example as a physical distance, a measure equivalent to distance (e.g. pixels on a display screen) or an angle representing an angular difference between the direction of the eye’s gaze and the direction of the target from the eye.

The measure of average error may be skewed if there is a calibration error in the eye tracking system that measures the direction of the gaze of the eye. To address such a possibility, in some forms, a best-fit line may be identified over the participant’s median gaze position. It is assumed that the median gaze position is directed at the target and the gaze data is adjusted accordingly. This approach

may be able to correct for cases where the user and the device may have moved relative to each other post-calibration.

In some forms, a positive diagnosis of the presence of TBI may be made if the measure of the average error between the position of the fixed target and the position of the patient's gaze exceeds a certain threshold value. In some forms, a diagnosis of mild TBI (i.e. mTBI or concussion) may be made if the measure of the average error exceeds a first, lower threshold value but is lower than a second, higher threshold value. In such forms, a diagnosis of moderate or severe TBI may be made if the measure of the average error exceeds the second, higher threshold value. In certain forms, the thresholds may be absolute values of the average error determined through experimental observation of previous patients. It will be appreciated that such absolute values may depend on the particular setup of the apparatus being used, e.g. the size of the display screen 310 and the distance of the display screen from the eye 101. In other forms, the thresholds may be calculated from a control value of average error that is experimentally determined to be a "normal" value. For example, the thresholds may be a certain percentage above the control value. The percentages may again be determined through experimental observation of previous patients.

7.3.1.7. Square-Wave Jerk

Square-wave jerks were selected as a strong candidate for an eye movement measure to correlate to mTBI due to their involuntary nature and correlation to various neurological pathologies. They are considered to result as a failure of cortical cells to suppress saccades during a fixational event.

In exemplary forms, the eye data representative of the movement of the eye during a fixational task is analysed to determine a measure of one or more characteristics of square-wave jerks (SWJs) during the fixational task. For ease of understanding, reference to analysis of a SWJ in this section should be understood to be inclusive of various forms of SWJ described herein, including typical SWJ, malformed SWJ, biphasic SWJ, and polyphasic SWJ.

In certain forms, determining the one or more measures may comprise classification of each of the two or more phases. In examples, the phases may be classified as two or more of: Primary Saccadic Deflection, Subsequent Saccadic Deflection, Saccadic Restitution, Gradual Restitution, Saccadic Spike, and Coast phase.

In certain forms, determining the one or more measures may comprise quantification of one or more characteristics of each of the two or more phases.

- 5 In certain forms, determining the measure of the frequency and/or amplitude of SWJs may rely on identifying saccades using the method explained above and, for each pair of saccades, identifying any one or more of: 1) a magnitude index, i.e. a measure comparing the magnitude of the two saccades in the pair; 2) the angle between both saccade vectors; and 3) the inter-saccades interval (ISI), i.e. the time between the saccades in the pair.

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In eye movement data, the angle between saccades is between 0° and 180° , focusing on the horizontal meridian and taking into account the saccade amplitude.

- 15 In certain forms, a model may be fitted to the dataset of pairs or sequences of saccades (identified as SWJs), for example to cluster their features with diagonal covariance matrices so no correlation between features is captured. The model may be a model fitted using a machine learning approach from suitable patient training data, a Bayesian Gaussian mixture model (GMM), an ex-Gaussian model, or a Gamma distribution model of intersaccadic intervals can be used to classify eye movement. In examples in which a GMM is used, the GMM component with the mean closest to 180° may be considered to be the SWJ cluster. Certain characteristics of the cluster may be determined, for example the mean and variance, and these may be used later to identify SWJs. The other components may not be used in some forms.

- 25 Subsequently, at the time of detection, a Hidden Markov Model (HMM) with two components may be used to assign pairs of saccades to either a SWJ state or an "other" state. The HMM may use Gaussian distributions for the observations (pairs of saccades). The SWJ state may be initialised with the mean and variance of the SWJ component from the GMM. The "other" state may be initialised with the mean and variance of the whole training dataset.

- 30 The transition matrix may be set to force a SWJ state to be followed by a "other" state. The "other" state may transition to the SWJ state or itself with probability 0.5. This way, a saccade in a pair being part of a SWJ cannot be identified as being part of another saccade occurring immediately afterwards.

In certain forms, detecting the SWJ may then comprise running the Viterbi algorithm using this HMM to get the most likely sequence of states.

In certain forms, all eye movement classification may be performed using a bi-directional attention-based transformer model. This is able to provide one unified model for classifying eye movements over time. To train the transformer, sample eye data may be encoded into a sequence of movement vectors which are labelled into different classes such as smooth pursuit, fixation, saccades, micro saccades, tremor and square wave jerk. This labelling may use all of the described processes for automation. There may be a subsequent process where an expert can reclassify any labels as required. The transformer trained on this labelled data may be able to utilise the context of the series of motions forward and back in time. In addition, the model may accommodate different types of eyes and secondary effects like the current pupil position which can be important as, with enough data, certain parts of the ocular range of motion may impact performance. This model can be more accurate than an expert human while performing more computationally efficiently and robustly than the statistical models used to perform the auto labelling for the training data. This model may also be retrained as new data is collected, further increasing the accuracy of classification.

It has been explained how SWJs may be identified and consequently, in certain forms, the frequency of the occurrence of SWJs when the target is shown to the patient during the fixational task, and/or the measurements made of the defined components of the SWJs, may be used as a corollary to injury. Where a series of fixed targets are presented to the patient to gaze at, the SWJ frequency and/or amplitude may be calculated as an average value of the SWJ frequencies / amplitudes for the plurality of individual targets while the frequency of SWJ errors are cumulative.

In some forms, a positive diagnosis of the presence of TBI may be made if the frequency and/or amplitude of SWJs measures exceeds a certain threshold value. In some forms, a diagnosis of mild TBI (i.e. mTBI or concussion) may be made if the frequency and/or measures of SWJs exceeds a first, lower threshold value but is lower than a second, higher threshold value. In such forms, a diagnosis of moderate or severe TBI may be made if the frequency and/or amplitude of SWJs exceeds the second, higher threshold value. In certain forms, the thresholds may be absolute values of SWJ and failure frequency and measures determined through experimental observation of previous patients. In other forms, the thresholds may be calculated from a control value of SWJ frequency that is experimentally determined to be a "normal" value. For example, the thresholds may be a certain percentage above the

control value. The percentages may again be determined through experimental observation of previous patients.

In certain forms, determining the indication of the presence of TBI in the patient may be based at least in part on an accumulated total of SWJ occurrences. In examples, a biphasic or polyphasic SWJ may be counted as a single SWJ occurrence. In other examples, each phase of a biphasic or polyphasic SWJ may be counted as a SWJ occurrence.

In certain forms, a SWJ having higher number of phases may be attributed a higher weighting. In certain forms, a hierarchical weighting may be applied based at least in part on complexity of the SWJ. In certain forms, weighting may be based at least in part on the number of phases of the SWJ. For example, a higher weighting may be attributed to a SWJ having a higher number of phases.

By way of example, a hierarchical weighting may be applied in which:

1. A typical SWJ is given weighting W_1 ;
 2. Malformed SWJ is given weighting W_2 ;
 3. Polyphasic SWJ[2] (i.e., determined as having two phases) is given weighting W_3 ;
 4. Polyphasic SWJ[3] is given weighting W_4 ;
 5. Polyphasic SWJ[4] is given weighting W_5 ; and
 6. Polyphasic SWJ[n] is given weighting W_{n+1} ,
- where $W_1 < W_2 < W_3 \dots < W_{n+1}$.

In certain forms, weightings may be adjusted based on one or more measures of one or more characteristics of an associated phase. For example, a weighting may be biased based on a characteristic such as the amplitude of peak deflection.

By way of example, an algorithm implementing this weighting may comprise:

$$\begin{aligned} \text{Indication of the presence of TBI} = & (\text{Typical SWJ}_{\text{total}} * W_1) + (\text{Malformed SWJ}_{\text{total}} * W_2) + \\ & (\text{Polyphasic SWJ}[2]_{\text{total}} * W_3) + \dots + (\text{Polyphasic SWJ}[n]_{\text{total}} * W_{n+1}) \end{aligned}$$

In an example implementing this algorithm (in which $W_1 = 1$, $W_2 = 2$, $W_3 = 3$, $W_{n+1} = n+1$), during fixation it may be determined that there were two healthy SWJ's, four malformed SWJ's, two polyphasic[2] SWJ's and one polyphasic[4] SWJ. A rating for the indication of the presence of TBI would therefore be calculated as: $(2*1) + (4*2) + (2*3) + (1*5) = 2 + 8 + 6 + 5 = 21$.

By way of further example, in which each phase is counted as an occurrence, an algorithm implementing this weighting may comprise:

$$\begin{aligned} \text{Indication of the presence of TBI} = & (\text{Typical SWJ}_{\text{total}} * W_1) + (\text{Malformed SWJ}_{\text{total}} * W_2) + \\ 5 \quad & (\text{Polyphasic SWJ}[2] \text{ phase}_{\text{total}} * W_3) + \dots + (\text{Polyphasic SWJ}[n] \text{ phase}_{\text{total}} * W_{n+1}) \end{aligned}$$

In this example, the $\text{phase}_{\text{total}}$ is the number of phases determined within the SWJ.

In an example (in which $W_1 = 1$, $W_2 = 2$, $W_3 = 3$, $W_{n+1} = n+1$), during fixation it may be determined that
 10 there were two healthy SWJ's, four malformed SWJ's, two polyphasic[2] SWJ's and one polyphasic[4] SWJ. A rating for the indication of the presence of TBI would therefore be calculated as: $(2*1) + (4*2) + ([2*2]*3) + ([1*4]*5) = 2 + 8 + 12 + 20 = 42$.

The greater the total (i.e., rating), the more symptomatic the patient is of TBI. As noted above, the rating
 15 may indicate relative severity based on comparison to experimentally determined data.

It should be appreciated that there are alternative ways of composing the metric, and the examples provided herein are not intended to be limiting to all forms of the present technology.

20 **7.3.1.8. Breakdown in Following a Moving Target**

In exemplary forms, the eye data representative of the movement of the eye during a smooth pursuit task and target data is analysed to determine a measure of a smooth pursuit breakdown in following a moving target.

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In certain forms, the detection of the change in gaze dynamics during the accelerating phase of a smooth pursuit task is treated as a changepoint detection ("breakdown point") problem. This method may comprise analysing the data collected during a smooth pursuit task and identifying a change in the accuracy of the patient's gaze during smooth pursuit using rank statistics and dynamic programming
 30 (storing calculated values iteratively for subsequent analysis) to search for a changepoint, for example the optimal unique changepoint. Exemplary suitable algorithms are mentioned below. The breakdown point may be determined via one or more of those algorithms (or any other suitable algorithm), which uses rank statistics to find a unique break point per individual. In some forms, the algorithm essentially

graphs all of the distribution of errors as a function of time and then finds a point in the graph where this is broken into two states. In some forms, the measure of the breakdown may be a time before the breakdown occurs in a smooth pursuit task. The breakdown may occur when the accuracy of the eye to follow the moving target falls below a threshold. More particularly, the method may comprise

5 identifying a change in the distribution of errors between the detected position of the eye's gaze and the position of a moving target on a display screen 310. In some forms, the errors may be computed from the eye movement and target movement data as the Euclidean distance between the position of the target on the display screen 310 and the position of the patient's gaze on the display screen 310 at each time point. In other forms, the errors may be calculated as some other measure of distance

10 between the target position and the gaze position, or as an angular error between these positions.

In some forms, the velocity of eye movement during the smooth pursuit task may also be calculated. The velocity may be calculated as a distance measurement per unit time or as an angular measurement per unit time. Calculating the eye movement velocity may allow a measure of the fluidity of the user's

15 eye movement to be calculated, i.e. a measure indicative of how the speed of the eye movement is maintained and the direction changes evenly. This may be useful as an additional measure to calculate in addition to the error between the target position and gaze position since it is possible for a patient's gaze to track smoothly or with short jerks and still achieve a low Euclidean error (i.e. accuracy and lag analysis). However smoother motion with even velocity (i.e. higher fluidity) is indicative of better

20 performance. In some forms, one or more filters may be applied to the eye data to reduce the level of noise in the eye data for the smooth pursuit task so that the smoothness of the motion may be assessed. In some forms, a linear quadratic estimation may be applied, for example a Kalman filter.

In certain forms, an algorithm to detect the breakdown in the eye's ability to follow the moving target

25 may be applied. The algorithm may also be referred to as a changepoint detection algorithm. In certain forms, an exemplary algorithm may rely on rank statistics, as described in Lung-Yut-Fong, A., Lévy-Leduc, C., & Cappé, O, 2015, *Homogeneity and change-point detection tests for multivariate data using rank statistics*, Journal de la Société Française de Statistique, 156(4), 133-162. The exemplary algorithm may also use dynamic programming, i.e. storing calculated values iteratively for subsequent analysis, to

30 search for an optimal unique changepoint. In certain forms, the changepoint detection algorithm may be implemented in the Ruptures Python package (Truong, C., Oudre, L., & Vayatis, N., 2020, *Selective review of offline change point detection methods*, Signal Processing, 167, 107299).

Figures 8A-D are illustrations of radial-transformed eye tracking data in a smooth pursuit task according to one form of the technology. These figures show eye tracking data in a smooth pursuit task in which the target 303 moves on a display screen 310 in a circular path. The charts plot the radius of the target and gaze against the angular location of the target / gaze, with the angular location radially transformed so that the target is always at angle 0°. The black dot 810 represents the position of the target 303 on the display screen 310 in these charts. The blue dots 820 represent the position of the eye's gaze on the display screen 310. Because of the radial transformation, the co-ordinates of the blue dots 820 in the charts represent the error from the target black dot 810. Figure 8A shows eye tracking data during a fixation phase of the task before the target 303 begins moving. Figure 8B shows eye tracking data during a slow phase of the smooth pursuit when the target 303 moves in a circular path with constant speed. Figure 8C shows eye tracking data during an acceleration phase of the smooth pursuit when the target 303 moves in a circular path but with accelerating speed. The data shown in Figure 8C is before the patient is determined to have reached the breakdown point. Figure 8D shows eye tracking data during the acceleration phase of the smooth pursuit when the target 303 moves in a circular path with accelerating speed, and after the patient is determined to have reached the breakdown point.

Figures 9A-D are illustrations of eye tracking data in a smooth pursuit task according to another form of the technology. These figures show eye tracking data in a smooth pursuit task in which the target 303 moves on a display screen 310 in a circular path. The charts plot the horizontal (x) and vertical (y) co-ordinates of the target and gaze on the display screen 310. The black dot or line 910 represents the position of the target 303 on the display screen 310 in these charts. The blue dots 920 represent the position of the eye's gaze on the display screen 310. The red dot / line 930 represents the regression of the blue dots 920 indicating the time-averaged position of the patient's gaze, which can be used in the event of suboptimal calibration of the eye tracker, for example. Figure 9A shows eye tracking data during a fixation phase of the task before the target 303 begins moving. Figure 9B shows eye tracking data during a slow phase of the smooth pursuit when the target 303 moves in a circular path with constant speed. Figure 9C shows eye tracking data during an acceleration phase of the smooth pursuit when the target 303 moves in a circular path but with accelerating speed. The data shown in Figure 9C is before the patient is determined to have reached the breakdown point. Figure 9D shows eye tracking data during the acceleration phase of the smooth pursuit when the target 303 moves in a circular path with accelerating speed, and after the patient is determined to have reached the breakdown point.

In some forms, a quantified value relating to the breakdown point may be used to determine the presence of TBI or even other neurological conditions (non-exhaustively including neuromuscular junction disorders, diseases specifically affecting the extraocular muscles like orbital myositis or thyroid eye disease, and neurodegenerative disorders). For example, in some forms, the measure of the breakdown may be a time before the breakdown occurs in a smooth pursuit task. A positive diagnosis of the presence of TBI may be made if this time is below a certain threshold value. In some forms, a diagnosis of mild TBI (i.e. mTBI or concussion) may be made if the time before the breakdown is below a first, higher threshold value but is higher than a second, lower threshold value. In such forms, a diagnosis of moderate or severe TBI may be made if the time before the breakdown is also below both the second, lower threshold value. In certain forms, the thresholds may be absolute values of time before the breakdown determined through experimental observation of previous patients. In other forms, the thresholds may be calculated from a control value of time before the breakdown that is experimentally determined to be a "normal" value. For example, the thresholds may be a certain percentage below the control value. The percentages may again be determined through experimental observation of previous patients.

7.3.1.9. Combination of Measures

Each of a number of measures that may be used individually to determine the presence of TBI has been explained above. In certain forms, the step 605 of analysing the data may comprise determining any combination of two or more of the previously described measures. These two or more measures may be combined in order to determine the indication of the presence of TBI.

For example, in certain form, the two or more measures may be combined as a weighted average. This may allow more weight to be applied to some of the measures. For example, in one example the weighted average may be calculated as the sum of any two or more of the above measures, each weighted by a factor and where the factors sum to 1. In one example, the three measures may be, in order of the greatest weighting to the least weighting, the measure of the one or more characteristics of SWJs during a fixational task, the measure of the frequency of microsaccades during the fixational task, and the measure of a smooth pursuit breakdown in following a moving target.

7.3.1.10. Reference Measures for Individual Patients

It has been described above how one or more measures may be determined from eye tracking data and those measures may be used to determine the presence of TBI in a patient. In certain forms, determining the indication may comprise comparing any of the measures and/or any combination of two or more of the measures to one or more predetermined thresholds. In certain forms, the measures may provide the indication of the presence of TBI without any prior testing of the patient in question. For example, the one or more predetermined thresholds may be determined from measures determined from other patients. The measures may either be absolute values which may indicate the presence or absence (or severity) of TBI in the patient, or the measures may be values that may be compared to "normal" values determined from experimental observations of previous patients in order to make the determination.

In other forms, the one or more predetermined thresholds may be determined from measures determined from the patient at one or more earlier times. For example, in some forms, an individual patient may have these measures calculated one or more times and these measures are considered to be reference values in order to establish a baseline of the measures as applied to that patient. These provide a point of comparison for future analysis of that patient. When an assessment is made at a future point in time, the same measures may be determined (using the above-described methods) and are compared to the reference measures for the same patient. If a change in any one or more of the measures (or in a combination of the measures, for example a weighted average) is determined to differ from the equivalent reference values by more than a certain threshold difference (which may be an absolute or percentage difference), then this may indicate that TBI is present in the patient. Again, different threshold may be used to determine whether the diagnosis is mild TBI or more severe TBI.

It is noted that patient suffering from a chronic condition may display an elevated baseline (e.g., containing malformed and potentially polyphasic SWJs) for a significant amount of time post-injury (e.g., 6 months or more). For example, a healthy patient may have a score in the range of 0-5 using the algorithm:

$$\text{Indication of the presence of TBI} = (\text{Typical SWJ}_{\text{total}} * W_1) + (\text{Malformed SWJ}_{\text{total}} * W_2) + (\text{Polyphasic SWJ}[2]_{\text{total}} * W_3) + \dots + (\text{Polyphasic SWJ}[n]_{\text{total}} * W_{n+1})$$

$$\text{where } W_1 = 1, W_2 = 2, W_3 = 3, W_{n+1} = n+1).$$

In contrast, a score in the order of 15-20 would not be uncommon in a patient still experiencing moderate symptoms.

In one exemplary form, repeated testing of the patient (i.e., subsequently collecting eye data representative of the movement of the eye during a fixational task at a later point of time) allow for a determination of the change in the indication of the presence of TBI over time. This change may be used as an indication of neuronal recovery.

It is envisaged that ongoing assessment of patients may be particularly useful for people who are at high risk of brain trauma, for example individuals participating in contact sports.

7.3.1.11. Indication Output

Referring again to Figure 6, exemplary methods according to the technology may comprise step 606 where an indication of the presence of TBI in the patient is output from the data analysis system 400. The indication may be output as a quantitative and/or qualitative assessment of the risk of the patient having TBI. For example, in some forms, the output indication may be a simple binary output of a positive or negative diagnosis of TBI, or mTBI. In other forms, the output indication may be an indication of the determined risk of the presence of TBI, or mTBI. Such a risk factor may be determined based on the amount that the one or more measures are above/below the respective thresholds, as determined from earlier experimental observations. The risk factor may be expressed quantitatively (e.g. "there is an 80% likelihood of the presence of TBI") or qualitatively (e.g. "it is highly likely that the patient has TBI"). In other forms, the output indication may provide a qualitative description of the severity indicated, e.g. "no TBI detected", "mild TBI detected", "moderate TBI detected", "severe TBI detected", and the like. The determination of these bands may be based on how the measures compare to a plurality of thresholds, as determined from earlier experimental observations.

7.3.1.12. Exemplary application

The table below demonstrates exemplary data from real-world testing of rugby players (and one civilian injury) of the combined SWJs and malformed SWJs during a 20 second fixation. Many of these patients have been tested before and after injury. The score (i.e., indication of the presence of TBI) is calculated using the algorithm:

Indication of the presence of TBI = (Count_{Typical SWJ} Typical SWJ * W₁) + (Count_{Malformed SWJ} Malformed SWJ * W₂) + (Count_{Polyphasic SWJ[2]} Polyphasic SWJ[2] * W₃) + ... + (Count_{Polyphasic SWJ[n]} Polyphasic SWJ[n] * W_{n+1})

5

where W₁ = 1, W₂ = 2, W₃ = 3, W_{n+} = n+1.

Patient	Description	Baseline score, pre-injury	Within 48 hours of injury	2 weeks post-injury	6 weeks post-injury	6 months post-injury
1	Adolescent rugby player	2 (2 SWJ * W ₁)	8 (3 SWJ * W ₁ , + 1 malformed SWJ * W ₂ , + 1 polyphasic SWJ[2] * W ₃)	5 (1 polyphasic SWJ[2] * W ₃ , + 1 malformed SWJ * W ₂)	4 (1 SWJ * W ₁ , + 1 polyphasic SWJ[2] * W ₃)	2 (2 SWJ * W ₁)
2	Adolescent rugby player	1 (1 SWJ * W ₁)	33 (17 SWJ * W ₁ , + 1 malformed SWJ * W ₂ , + 3 polyphasic SWJ[2] * W ₃ , + 1 Polyphasic SJW[4] * W ₅)	11 (6 SWJ * W ₁ , + 1 malformed SWJ * W ₂ , + 1 polyphasic SWJ[2] * W ₃)	7 (3 SWJ * W ₁ , + 2 malformed SWJ * W ₂)	2 (2 SWJ * W ₁)
3	Adolescent rugby player	0	31 10 SWJ * W ₁ , + 1 malformed SWJ * W ₂ , + 3 polyphasic SWJ[2] * W ₃ , + 1 polyphasic SWJ[3] * W ₄ , + 1 polyphasic SWJ[5] * W ₆)	22 (10 SWJ * W ₁ , + 2 polyphasic SWJ[2] * W ₃ , + 1 polyphasic SWJ[5] * W ₆)	Not available	15 (15 SWJ * W ₁)

4	Adolescent rugby player	Not available	12 (8 SWJ * W ₁ , + 2 malformed SWJ * W ₂)	Not available	2 (2 SWJ * W ₁)	Not available
5	Civilian, Aged 32	Not available	23 (15 SWJ * W ₁ , + 2 polyphasic SWJ[3] * W ₄)	Not available	3 (3 SWJ * W ₁)	Not available

It is noted that during the first two weeks of injury, eye movement dysfunction may transiently worsen before improving due to the inherent pathophysiology of traumatic brain injury; physical injury to brain tissue is followed by a neurometabolic cascade of ‘secondary’ insult (e.g., as described in Giza CC, Hovda DA. *The new neurometabolic cascade of concussion*. Neurosurgery. 2014 Oct;75 Suppl 4(0 4):S24-33. doi: 10.1227/NEU.0000000000000505. PMID: 25232881; PMCID: PMC4479139).

It may also be observed that in addition to the total score reverting to baseline over time, the complexity of the underlying SWJ events also reduces with recovery.

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For completeness, while the above example is provided with respect to the identified algorithm and weighting scheme, it should be appreciated that this is not intended to limit alternative approaches of the present disclosure described herein.

15 **7.4. Other Remarks**

Unless the context clearly requires otherwise, throughout the description and the claims, the words “comprise”, “comprising”, and the like, are to be construed in an inclusive sense as opposed to an exclusive or exhaustive sense, that is to say, in the sense of “including, but not limited to”.

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The entire disclosures of all applications, patents and publications cited above and below, if any, are herein incorporated by reference.

Reference to any prior art in this specification is not, and should not be taken as, an acknowledgement or any form of suggestion that that prior art forms part of the common general knowledge in the field of endeavour in any country in the world.

- 5 The technology may also be said broadly to consist in the parts, elements and features referred to or indicated in the specification of the application, individually or collectively, in any or all combinations of two or more of said parts, elements or features.

- Where in the foregoing description reference has been made to integers or components having known
10 equivalents thereof, those integers are herein incorporated as if individually set forth.

- It should be noted that various changes and modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications may be made without departing from the spirit and scope of the technology and without diminishing its
15 attendant advantages. It is therefore intended that such changes and modifications be included within the present technology.

8. CLAIMS

1. A computer-implemented method of assessing the presence of TBI in a patient, the method comprising:
 - 5 receiving eye data representative of fixational eye movements of an eye of the patient during a fixational task when the patient is gazing at a fixed target;
 - determining one or more measures of the movement of the eye from the eye data, wherein the one or more measures comprise a measure of one or more characteristics of one or more square-wave jerks (SWJs);
 - 10 determining the indication of the presence of TBI in the patient based on the one or more measures; and
 - outputting the indication.
2. A computer-implemented method as claimed in claim 1, wherein the one or more
15 characteristics comprise atypical characteristics of the one or more SWJs.
3. A computer-implemented method as claimed in any one of claims 1-2, wherein at least one of the one or more SWJs comprises two or more phases.
- 20 4. A computer-implemented method as claimed in claim 3, wherein determining the one or more measures comprises classification of each of the two or more phases.
5. A computer-implemented method as claimed in claim 4, wherein potential classifications of each of the phases comprises two or more of: Primary Saccadic Deflection, Subsequent Saccadic
25 Deflection, Saccadic Restitution, Gradual Restitution, Saccadic Spike, and Coast phase.
6. A computer-implemented method as claimed in any one of claims 3-5, wherein determining the one or more measures comprises quantification of one or more characteristics of each of the two or more phases.
- 30 7. A computer-implemented method as claimed in any one of claims 1-6, wherein determining the indication of the presence of TBI in the patient is based at least in part on an accumulated total of SWJ instances.

8. A computer-implemented method as claimed in claim 7, wherein a hierarchical weighting may be applied based at least in part on complexity of each of the one or more SWJs.
9. A computer-implemented method as claimed in claim 8, wherein the weighting is based at least
5 in part on a number of phases of each of the one or more SWJs.
10. A computer-implemented method as claimed in claim 9, wherein the weighting is adjusted based on the one or more measures of the one or more characteristics of an associated phase.
- 10 11. A computer-implemented method as claimed in any one of claims 1-10, wherein the method further comprises:
receiving target data representative of position of the fixed target when the eye data
representative of fixational eye movements of the eye is captured; and
determining the one or more measures of the movement of the eye from the target
15 data.
12. A computer-implemented method as claimed in any one of claims 1-11, wherein the one or more measures further comprise a measure of an average error between a position of the fixed target and a position of the patient's gaze during the fixational task.
20
13. A computer-implemented method as claimed in any one of claims 1-12, wherein the one or more measures further comprise a measure of the frequency of microsaccades during the fixational task.
- 25 14. A computer-implemented method as claimed in any one of claims 1-13, wherein the method further comprises receiving eye data representative of smooth pursuit eye movements of the eye of the patient during a smooth pursuit task when the patient is gazing at a moving target.
- 30 15. A computer-implemented method as claimed in claim 14, wherein the one or more measures further comprise a measure of a smooth pursuit breakdown in following the moving target.
16. A computer-implemented method as claimed in claim 15, wherein the measure of the smooth pursuit breakdown is a time before the breakdown occurs in the smooth pursuit task.

17. A computer-implemented method as claimed in any one of claims 1-16, wherein the step of determining the indication comprises combining two or more of the measures.
18. A computer-implemented method as claimed in any one of claims 1-17, wherein determining
5 the indication comprises comparing the one or more measures and/or a combination of two or more of the measures to one or more predetermined thresholds.
19. A computer-implemented method as claimed in claim 18, wherein the method comprises
10 determining the one or more predetermined thresholds from like measures determined from other patients.
20. A computer-implemented method as claimed in claim 19, wherein the method comprises
15 determining the one or more predetermined thresholds from like measures determined from the patient at one or more earlier times.
21. A computer-implemented method as claimed in any one of claims 1-20, wherein the method
further comprises controlling a display screen to display the fixed target to the patient.
22. A computer-implemented method as claimed in claim 21, wherein the method comprises
20 controlling the display screen to display the fixed target at an eccentric position relative to the patient.
23. A computer-implemented method as claimed in any one of claims 1-22, wherein the method
25 comprises determining a direction of gaze by detecting the position of the iris of the eye.
24. A computer-implemented method as claimed in claim 23, wherein determining the direction of
gaze by detecting the position of the iris of the eye comprises applying an object detection
algorithm to the eye data representative of the movement of the eye.
25. A computer-implemented method as claimed in any one of claims 1-24, wherein the method
30 comprises classifying the eye data representative of the movement of the eye using a transformer model.
26. A computer implemented method as claimed in any one of claims 1-25, including:
35 receiving further eye data representative of fixational eye movements of an eye of the patient during a second fixational task;

determining a second indication of the presence of TBI in the patient based on the further eye data; and

determining progression of neuronal recovery of the patient on a comparison of the second indication of the presence of TBI with the previous indication of the presence of TBI in the patient.

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27. A system for assessing the presence of TBI in a patient, the system comprising a processor configured to perform the computer-implemented method according to any one of claims 1-26.

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28. A computer-readable medium having stored thereon instructions for performing a computer-implemented method of assessing the presence of TBI in a patient according to any one of claims 1-26.