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Eye movement testing in clinical examination

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ABSTRACT

The clinical vision examination routinely includes an evaluation of ocular motor function. In a number of diverse situations, thorough objective recording of eye movements is warranted, using any of a variety of eye-tracking technologies that are available currently to clinicians. Here we review the clinical uses of eye tracking, with both an historical and contemporary view. We also consider several new imaging technologies that are becoming available in clinics and include inbuilt eye-tracking capability. These highly sensitive eye trackers should be useful for evaluating a variety of subtle, but important, oculomotor signs and disorders.

1. Eye movement recording and the clinical examination

Although subjective assessment of oculomotor functioning is a central part of any eye examination (e.g., Pensyl & Benjamin, 2006), objective eye movement recording remains relatively rare in current clinical practice. Like much of the early experimental eye movement research (Wade, 2010), clinicians tend to rely on direct observation of patients' eye movements, probably because the salient characteristics of many abnormalities (e.g., strabismus, nystagmus, inaccurate tracking, etc.) can be assessed qualitatively and, to a limited extent, quantitatively using the naked eye. Objective eye movement recording, facilitated by advances in measurement technology, allows clinicians to achieve more detailed spatial and temporal resolution of oculomotor behavior, make more precise quantitative determinations of eye-movement characteristics such as the response gain (eye velocity/target or head velocity), and generate permanent records. This article will review briefly the history of objective eye tracking in clinical practice, some applications of eye tracking in clinical decision making, and the types of currently available instrumentation for objective eye tracking. Because a number of new retinal imaging technologies such as optical coherence tomography and microperimetry include eye trackers as part of their function, we anticipate that it may be increasingly common for clinicians to have a sensitive eye tracker available for use during eye examinations.

2. Historical aspects of eye movement recording

The objective recording of human eye movements began near the end of the 19th century, initially using awkward mechanical attachments to the eye (e.g., Delabarre, 1898; Huey, 1898) and, subsequently, photographic techniques (Dodge & Cline, 1901; Judd, McAllister, & Steele, 1905). Dodge (1903) recorded the movement of the corneal light reflection as imaged on a moving photographic plate and distinguished the major sub-classes of eye movement that are recognized today: saccades, smooth pursuit, vergence, vestibular, and optokinetic responses. These early photographic eye-movement recordings required precise head stabilization and controlled illumination, making them cumbersome and not always reliable to acquire. Once obtained, the photographic records were time-consuming to process and analyze. These technical considerations relegated early eye-movement recording to the experimental laboratory and kept them, for the most part, out of the clinic. Nevertheless, Huey (1900), Dearborn (1906), Dodge (1907), Buswell (1922) and others (for review see Taylor, 1937) recorded and described the eye movements of accomplished and poor readers photographically. In addition, Diefendorf and Dodge (1908) assessed the eye movements made by a variety of psychiatric patients and documented abnormal pursuit tracking in subjects with schizophrenia, in anticipation of the more recent extensive literature on this topic (for review, see Levy et al., 2010). In their historical reviews of eye-movement research, Wade and Tatler (2005, 2011) include illustrations of some early devices used to record eye movements, along with representative traces.

The application of electrooculography, and specifically electronystagmography, to the recording of eye movements in the middle

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third of the 20th century allowed the relatively easy acquisition of records from clinical patients (Jung & Kornhuber, 1964). Because electronystagmography relies on ac amplification to detect *changes* in the amplitude of the corneo-retinal potential, it is useful primarily for detecting and documenting relatively large and rapid eye movements, such as saccades and various types of nystagmus. This, as well as some earlier recording techniques (Jung, 1977), was used clinically by otolaryngologists and neurologists to assess patients' eye movements in response to natural and artificial vestibular stimulation, and as a result of various brainstem, cerebellar and cortical abnormalities. Jung and Kornhuber (1964) summarized many of the clinical applications of electronystagmography in otolaryngology and neurology. The encyclopedic text by Leigh and Zee (2006) elaborates on the clinical diagnostic applications of eye movement recording in neurological patients, using a range of more modern eye-movement recoding techniques, such as dc electrooculography (made possible by advances in electronic amplification that allowed more stable recording of eye position), limbal tracking, video-oculography, and the magnetic search coil (see, e.g., Collewijn, 1999; Eggert, 2007). Jacobson and Shepard (2008) and Wuyts et al. (2007) review specifically the methods and applications of eye movement recording in otolaryngology. The newer techniques for measuring eye movements are appropriate for assessing slow eye movements, such as vergence, in addition to rapid movements like nystagmus and saccades. In addition, some of these newer techniques provide substantially finer spatial resolution and the capability to record changes in eye torsion, as well as changes in horizontal and vertical eye position. One clinical application of recording torsional eye position is during a combination of bodily rotation and translation, to evaluate utricular functioning (Wuyts et al., 2003).

3. Current clinical applications of eye-movement recording

As discussed briefly in the section above, objective eye-movement recordings are an important adjunct in diagnosing, documenting, and managing a variety of neurological abnormalities, including peripheral and central vestibular imbalances, and brainstem, cerebellar and cortical lesions and malformations that result in saccadic intrusions and oscillations, slow saccades, inaccurate and imprecise pursuit, various forms of acquired nystagmus, etc. Various clinical applications of eye-movement recording are summarized in Leigh and Zee (2006) and Jacobson and Shepard (2008). To give an example, the eye movement recording illustrated in Fig. 1 reveals a continuous train of square wave jerks in a patient who was diagnosed subsequently with paraneoplastic cerebellar degeneration, a cerebellar disease secondary to cancer, in this case a tumor of the lung. Note that the entire vertical axis in the Figure corresponds to just 1 deg. Although these eye movements are large enough to produce disturbing oscillopsia in this patient, they are too small to be resolved by direct observation of the eyes in a clinical examination. It is likely that this patient's horizontal saccades would be visible using direct ophthalmoscopy, which is estimated to detect eye movements with an amplitude of 0.15–0.2 deg (Herishanu & Sharpe, 1981) and eye velocities faster than approximately 4 deg/s (West, Sheppard, & King, 2012). In some patients, oscillopsia occurs in conjunction with eye movements that are smaller than ophthalmoscopy can detect (Sharpe & Fletcher, 1986).

Objective eye-movement recording is of value in patients with nystagmus for a number of reasons. *First*, frequently it is important to ascertain whether a patient's nystagmus has been present since infancy, and therefore can be presumed to represent a stable neurological situation, or is an acquired condition. When the patient's history is vague or unclear, the clinician can examine the recorded waveform characteristics of the nystagmus, which typically differ between the acquired and infantile varieties (Dell'Osso & Daroff, 2009). *Second*, in the absence of associated conditions that reduce visual functioning, such as albinism or optic nerve hypoplasia, the expected visual acuity in patients with infantile nystagmus is related to the duration and variability of the foveation periods, the brief intervals in the nystagmus waveform when the target of interest is imaged with low velocity on or near the fovea (Dell'Osso & Jacobs, 2002; Felius et al., 2011). Consequently, in patients with repeatable and prolonged foveation periods, therapeutic intervention would not be expected to produce an appreciable improvement in visual acuity. On the other hand, treatment to reduce the nystagmus might be expected to result in improved visual acuity

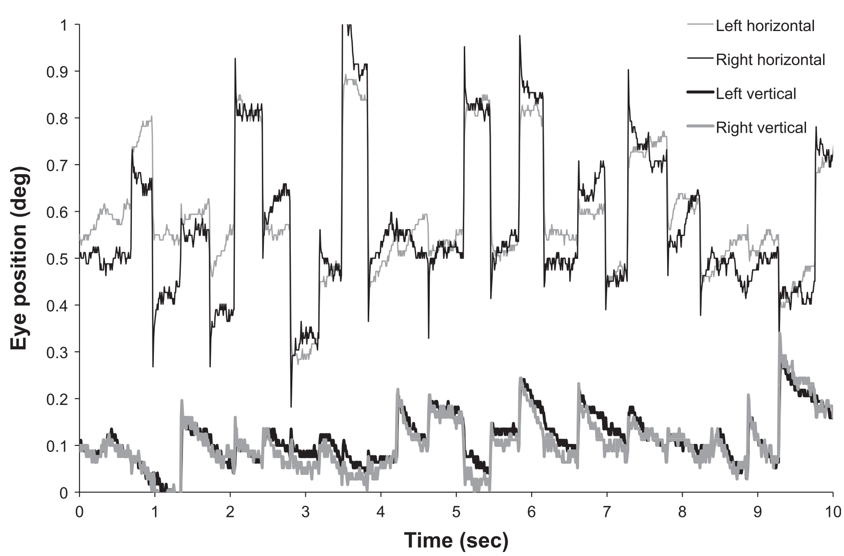

Fig. 1. Binocular eye movement trace recorded with a dual Purkinje image eye tracker. The patient was attempting steady fixation of a laser spot, but produced a series of uncontrolled square wave jerks throughout the recording. Square wave jerks may be caused by a variety of neurological conditions (Leigh & Zee, 2006). In this case, the root cause was discovered to be an operable tumor in the patient's left lung, which resulted in paraneoplastic cerebellar degeneration. With technical improvements and more widespread availability of eye tracking technology in the clinic, screening for such oculomotor abnormalities could become routine (Averbuch-Heller et al., 1999; van Broekhoven et al., 2007). Upward deflections of the trace correspond to rightward and upward eye movements. The position of the trace with respect to the y axis scale is arbitrary.

in patients whose foveation periods are brief and/or exhibit substantial position variability from beat to beat (e.g., Abplanalp & Bedell, 1987; Hertle et al., 2003). Indeed, metrics based on eye-movement parameters have been used as a principle outcome measure to assess the efficacy of surgical and pharmacological interventions for nystagmus (e.g., Hertle et al., 2004a, 2004b, 2003; McLean et al., 2007). It is important to recognize that neither the aspects of the nystagmus waveform that distinguish between the infantile and acquired forms, nor the duration or position variability of the foveation periods in infantile nystagmus waveforms can be assessed accurately by eye. Indeed, only relatively recently did simultaneous eye-movement recordings in the horizontal, vertical, and torsional directions reveal that a torsional component typically accompanies the horizontal eye movements of patients with infantile nystagmus (Averbuch-Heller et al., 2002; Bedell et al., 2008). A *third* clinical use of objective eye movement recordings in patients with nystagmus is to ascertain whether or not a small angle strabismus is present. Although large and moderate angles of strabismus may be detected by direct clinical observation, a small angle of strabismus can be difficult to distinguish when it is superimposed on the ongoing eye movements of patients with nystagmus. Finally, although nystagmus with an amplitude of 1 deg or more is visible by clinical observation, extended periods of eye-movement recording can be useful to document if the direction of the nystagmus fast phase changes over time. A periodic change in the direction of the fast phase influences the choice of a possible surgical intervention in patients with infantile nystagmus (Gradstein et al., 1997; Hertle et al., 2003) and provides diagnostic information in patients with acquired nystagmus (Leigh & Zee, 2006; Shallo-Hoffmann & Riordan-Eva, 2001). The documentation of tiny amplitudes of *acquired* nystagmus, which may not be readily visible even in a careful clinical examination, can provide an explanation for worrisome symptoms, such as blur and oscillopsia. Patients with a small amplitude of acquired nystagmus may report that oscillopsia is more noticeable for distant than for near targets, which presumably is a manifestation of the perceptual phenomenon of size constancy (Holway & Boring, 1941).

The objective evaluation of eye movement behavior also is valuable clinically in patients with bilateral central field loss. Most patients with bilateral central field loss view a visual target using one or more peripheral preferred retinal locations (PRLs) instead of the non-seeing fovea (Crossland, Engel, & Legge, 2011; Fletcher & Schuchard, 1997; Whittaker, Budd, & Cummings, 1988). It can be difficult to train patients with central field loss to make the best use of their residual non-foveal vision if the location of the PRL is uncertain, or if the location varies during the performance of a visual task or between tasks (Lei & Schuchard, 1997; Timberlake et al., 2006). Indeed, some patients with bilateral central field loss spontaneously adopt PRLs that are non-optimal for specific visuomotor tasks, such as reading (Fletcher & Schuchard, 1997; Timberlake et al., 1987). Objective recording of a patient's fixation behavior using a scanning laser ophthalmoscope (SLO) or a similar device provides the clinician with precise information about the location and extent of the PRL as well as the spatial relationship between the PRL and the region of visual-field loss. By evaluating fixation behavior objectively and providing feedback, patients may be induced to shift the PRL to a more effective retinal location (Nilsson, Frennesson, & Nilsson, 2003; Tarita-Nistor et al., 2009). Reading speed has been reported to be related to the unsteadiness of fixation with respect to the PRL (Crossland, Dunbar, & Rubin, 2009). Training that improves the oculomotor performance of patients with central field loss therefore has the potential to improve reading performance (Seiple, Grant, & Szlyk, 2011). Commercially available microperimeters, such as the Nidek MP-1, compensate for patients' unsteady fixational eye movements and allow clinicians to assess visual sensitivity by presenting perimetric targets repeatably at known retinal locations (Crossland, Jackson, & Seiple, 2012; Rohrschneider, Bültmann, & Springer, 2008).

Following some of the early workers who recorded reading eye movements (see Taylor, 1937 for review), a number of clinics continue to measure and assess the eye movements of patients with reading difficulties. Although a causal relationship between eye movement characteristics and inefficient reading is contentious (e.g., Rayner, 1998; Tinker, 1936), interventions such as visual training have been reported by some investigators to improve the characteristics of reading eye movements and increase reading speed (e.g., Ciuffreda & Tannen, 1995; Scheiman & Wick, 2008).

Abnormalities of pursuit, vergence and saccadic eye movements have been documented in a number of other patient groups. For example, as noted above, pursuit gain is reduced in patients with schizophrenia, as well as in their psychiatrically normal first-degree relatives (Calkins, Iacono, & Ones, 2008; Holzman, Proctor, & Hughes, 1973). A reduction of pursuit gain, a decrease in vergence velocity, and an increase in the trial-to-trial variability of both types of eye movements have been reported to occur in patients with mild traumatic brain injuries (Maruta et al., 2010; Thiagarajan, Ciuffreda, & Ludlam, 2011). Prolongation of the saccadic latency and an increase in the number of errors on anti-saccade tasks, in which the patient is instructed to look in the *opposite* direction of a peripherally presented stimulus, have been reported in patients with Parkinson's disease and patients with dementia (e.g., Hood et al., 2007; Mossiman et al., 2005). Nevertheless, the eye-movement responses made by the above groups of patients and matched samples of normal subjects exhibit enough overlap that none of the reported oculomotor abnormalities can as yet be considered to be definitively diagnostic. This situation may improve as researchers in these areas devise more sensitive metrics and more specific testing paradigms for identifiable classes of patients.

4. Current instrumentation for clinical eye-movement recording

Although the technology required to assess saccade accuracy, pursuit gain, and fixation stability is not available currently to most clinicians, specialty clinics often have devices that are dedicated to particular kinds of eye-movement testing, such as videooculography for the evaluation of vestibular function (Jacobson & Shepard, 2008), or limbal trackers like the VisaGraph for recording eye movements during reading (Quaid & Simpson, 2013). Electrooculography and electronystagmography remain in widespread clinical use for the evaluation of large saccadic and vestibular mediated eye movements. Video processing hardware and software have developed rapidly in the last two decades and have become common in research applications. It is likely that video-based systems will be employed more frequently in the clinic as their performance continues to improve and as prices continue to fall. Several recent publications provide tabular comparisons between the properties of different eye-tracking techniques (e.g., Eggert, 2007; Jacobson et al., 2008; Leigh & Zee, 2006).

Because the actual performance of a clinical eye-tracking instrument may or may not match the manufacturer's stated specifications, it is worthwhile to evaluate performance in comparison to the current "gold standard" methods for eye-movement recording, such as the scleral search coil (Collewijn, van der Mark, & Jansen, 1975; Robinson, 1963) and dual-Purkinje image tracker (Crane & Steele, 1985). Like the scleral search coil and dual-Purkinje image tracker, electrooculography and limbal tracking systems produce continuous signals of eye position that can be sampled at arbitrarily high rates. Most current video eye trackers provide discrete temporal samples, corresponding to very high frame rates, such as 500 or 1000 Hz. On the other hand, SLOs typically have a frame rate of 30 or 60 Hz, which can provide information about successive eye positions but does not adequately represent changes in eye velocity. However, off-line analysis of adaptive optics SLO video signals (see Section 5) permits the extraction of eye-movement samples at many times the original frame rate, e.g., 300–900 Hz.

van der Geest and Frens (2002) compared saccadic eye movements measured simultaneously using scleral search coils and a video based eye tracker (EyeLink) in 4 normal subjects and found good agreement over a ±20 deg range of eye rotations. Nevertheless, they concluded that the video method should not be relied upon for the assessment of eye movements that are less than 1 deg in amplitude. Houben, Goumans, and van der Steen (2006) compared recordings made with scleral search coils and a Chronos eye tracker, using Chronos-supplied software to compute horizontal, vertical, and torsional eye position off line from recorded video signals. They found good agreement between the search-coil and video systems for a variety of large eye movements (saccades, optokinetic nystagmus and vestibulo-ocular responses) but the noise level of the eye-position signals from the video system was considerably greater during steady fixation. Crossland and Rubin (2002) compared the eye positions during normal fixation with an EyeLink system and a scanning laser ophthalmoscope and determined that the variability of fixation positions was approximately twofold larger using the EyeLink tracker.

Because the vertical positions of the two eyes normally are tightly yoked (Riggs & Niehl, 1960; van Rijn, van der Steen, & Collewijn, 1994), a recording of vertical *vergence* during fixation is a revealing indicator of the noise level and susceptibility to drift of a binocular eye tracking device. Fig. 2 shows the difference in recorded vertical eye position (vertical vergence) during 8 s of steady fixation, as measured with a dual Purkinje image tracker and a video-based EyeLink II. The trace obtained with the video-based system indicates approximately 0.5 deg of spurious vertical vergence drift during the 8 s of recording, as well as considerably larger sample-to-sample noise than the dual-Purkinje tracker. These results are in qualitative agreement with the studies cited above, which concluded that video-based systems are useful primarily for assessing eye rotations of approximately 0.5 deg and larger.

Video-based eye-tracking systems are still evolving and the comparisons cited above may not reflect the capabilities of the most recent version of each system. Although video eye-trackers do not yet achieve the same precision of horizontal and vertical eye-movement resolution as retinal-image-based trackers, video systems have the advantage of being lightweight and optionally head mounted, which makes them ideal for vestibular testing and for tracking the eyes during natural, head-free behavior. For many applications, the relevant features of eye movements are large enough that resolution of a few arc min is not required to make accurate clinical judgments.

Even so, it is clear that one cannot assume that the values of accuracy and precision measured by the manufacturer or in a research lab with an artificial eye provide a realistic representation of an eye tracker's performance when it measures actual eye movements. Dynamic variation in pupil size and shape, lid position, and tear film all may contribute to the noise of the eye-position estimates determined using a video-based eye tracker. Some of these noise sources influence the precision of other types of eye trackers as well. Given that small eye movements themselves typically follow a "random walk" of drifts interrupted by microsaccades, it can be difficult to distinguish tracker noise from the actual rotations of the eye.

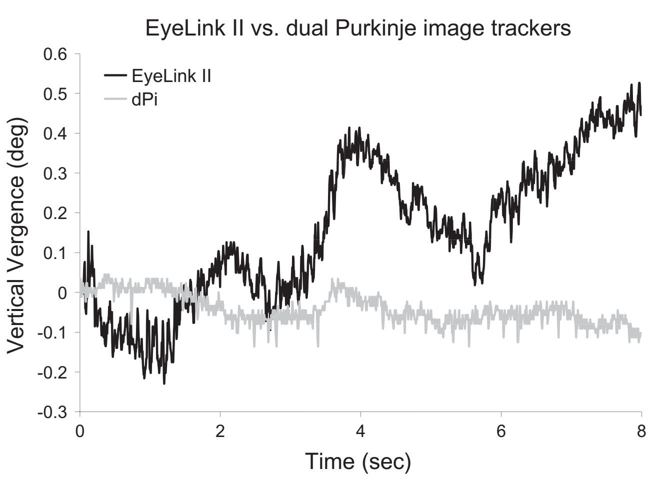

Fig. 2. Comparison of head mounted video (EyeLink II) and dual Purkinje image (dPi) records of vertical vergence (left–right vertical eye position) during 8 s of steady fixation. The two records were made in separate runs. The head was stabilized with a mouth bite in both cases. Because vertical eye position is tightly yoked, the expected standard deviation of vertical vergence during steady fixation is on the order of 2–4 arc min (Riggs & Niehl, 1960; van Rijn, van der Steen, & Collewijn, 1994). The comparison of left- and right-eye vertical position during steady fixation is therefore a useful check on a binocular eye tracker's level of noise and drift.

5. Future directions of clinical eye-movement recording

The eye trackers discussed above generally are stand-alone devices with the sole or primary function of recording eye movements. Other types of clinical devices, such as SLOs, optical coherence tomographers (OCTs), and refractive surgery systems, also may include the capability to track eye position as a way to improve their performance. In particular, as the precision of these devices improves, uncompensated motion of the eye or the retinal image becomes an increasingly important source of noise and inaccuracy. Achieving the best quality image in a retinal scanner or the optimal implementation of a surgical refractive correction requires the detection and appropriate compensation of eye motions during small as well as large eye movements.

SLOs have been used as eye tracking systems throughout their development (Lakshminarayanan et al., 1992; Mulligan, 1997; Ott & Daunicht, 1992; Ott & Eckmiller, 1989; Schuchard & Raasch, 1992; Stetter, Sendtner, & Timberlake, 1996). Recent developments in SLO technology, in particular the inclusion of adaptive optics (AO) to correct for higher-order aberrations of the eye, allow for much higher-resolution imaging of the retina, with a wide range of current and potential clinical applications (Godara et al., 2010) At the same time, the small rotations of the eye that occur during "steady" fixation become a limiting factor in the ability of these AO-SLO systems to obtain stable, high contrast images. Obtaining the best quality images requires averaging over time; therefore, eye motion must be corrected with high precision (Huang et al., 2011; Stevenson & Roorda, 2005). Currently, real-time AO-SLO correction for spontaneous eye movements is sufficient to register successive images on the scale of a single cone diameter (Yang et al., 2010), but only during the periods of fixational drift. AO-SLOs with integrated eye-tracking systems have been developed as well, to allow for relative image stabilization even during large eye movements (Ferguson et al., 2010). Off-line image processing of AO-SLO video yields high-frame-rate records of horizontal and vertical eye movements with a precision on the order of a few arc sec, which is higher than either scleral search coils or dual-Purkinje trackers and in excess of the precision needed in any clinical application. These high frame rates are achieved by sampling only a few lines of the video signal at one time (Stevenson, Roorda, & Kumar, 2010). The precision of the torsional signals extracted from AO-SLO video is on the order of 5–10 min of arc, which is nominally poorer than can be achieved using search-coil recording. An important benefit when eye movements are extracted from AO-SLO video is that the absolute position and orientation of a target's image can be visualized directly on the retina (Raghunandan et al., 2008; Stevenson, Roorda, & Kumar, 2010). This capability would make a binocular version of the AO-SLO particularly useful for the examination of patients with small angles of strabismus.

Like SLOs, as the optical resolution of OCT devices improves, the quality of the resulting images becomes limited by motion that results from eye movements. Some commercial OCT devices incorporate a SLO to track eye movements and thereby improve the registration of neighboring retinal areas in volumetric scans (Chin et al., 2012). The combination of AO scanning laser ophthalmoscopy and OCT, with a correction for eye movement, provides high-resolution volumetric imaging with the highest possible image fidelity (Zawadzki et al., 2011).

At present, the extraction of eye-movement information from both standard- and AO-SLO devices requires special purpose, custom software. Therefore, at this point these technologies remain essentially a research tool. The importance of precise eye tracking for optimizing SLO and OCT image quality suggests that the requisite software will be bundled with these devices in the future as they become deployed more widely in clinics. The signals of eye movement that are extracted as part of the image-registration process therefore are potentially available to users.

Current laser refractive surgery systems generally employ video-based tracking systems that follow features of the iris to compensate for horizontal, vertical, and torsional movements of the eye during the application of the optical correction (Chernyak, 2005; Narváez et al., 2012). The existing systems reduce, but do not eliminate errors in the applied refractive correction. Improved tracking of and compensation for eye movements is necessary during wavefront-guided refractive surgery, to ensure that the correction for higher order optical aberrations is located appropriately on the eye.

The current rapid rate of technological improvement all but ensures that sophisticated retinal imaging and refractive surgical systems, with sophisticated integrated eye-tracking capabilities, will be deployed more and more commonly in the clinic. It is worth bearing in mind that, in addition to their principal role as an imaging or surgical device, these instruments have the capability to be used as a clinical eye tracker. The manufacturers of these instruments should be encouraged to provide appropriate interfaces to allow for eye-movement signals to be sampled, stored, and visualized so that this additional functional capability can be used to the best clinical advantage.

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