Tear Film Quality Assessment in the Corneal Topographer via Placido's Disk as a Supplement to the Standard Tear Break Up Time Test. A Comprehensive Literature Review

Joshua Davidson

Zachary Boeskool

Vandana Rajaram O.D, Ph.D, FAAO

OPTM 817

Michigan College of Optometry

Ferris State University

Tear Film Quality Assessment in the Corneal Topographer via Placido's Disk as a Supplement to the Standard Tear Break Up Time Test. A Comprehensive Literature Review

Zac Boeskool, Joshua R. Davidson
Optometry Students, Michigan College of Optometry, Ferris State University

KEYWORDS:

Tear Break Up Time (TBUT)

Topographer

Placido's Disk

Aqueous Deficiency

Keratoconjunctivitis Sicca

D.E.W.S

Dry Eye Syndrome

Tear Film Stability

Abstract:

BACKGROUND: Dry Eye Syndrome is a progressive disease of the ocular surface that is increasing in frequency within the United States. Current estimates state that approximately 40% of Americans regularly experience Dry Eye symptoms. To date, most eye care professionals have relied heavily upon archaic testing methods in their diagnosis of the disorder with the advances of modern technology seemingly ignored.

QUESTION: In the 2007 Report of the Diagnostic Methodology Subcommittee of the International Dry Eye Workshop, the authors repeatedly emphasized the necessity of noninvasive techniques to analyze the ocular surface's tear film. They, along with numerous other authors of peer-reviewed literature, frequently stress that tests such as the standard TBUT are not as reliable or repeatable as once thought. This review of peer-reviewed literature and committee reports investigated the potential benefit of incorporation of modern noninvasive techniques into the management of Dry Eye patients in a modern optometric practice.

CONCLUSION: The "gold-standard" test of the modern optometric practice known as the fluorescein TBUT remains the most practical in a modern optometric practice as it provides adequate information for a proper diagnosis. For those practices that specialize in Dry Eye treatment and management, a non-invasive measurement of tear quantity and quality utilizing modern instrumentation is a wise investment. Nowhere would a non-invasive test such as this be more practical than at an academic institution such as the Michigan College of Optometry. As patients change examiners on a regular basis, a noninvasive technique would offer a more standardized data set to compare at each subsequent exam giving greater consistency in patient records to aid in treatment and diagnosis.

Today's Optometrists and eye care practitioners are inundated with educational and promotional material from various sources regarding the ever-increasing need to assist their patients with the diagnosis, treatment, and management of Dry Eye Syndrome (DES). Indeed, DES is one of the most common reasons that a typical optometric patient will visit their eye doctor.[1] It is estimated that Dry Eye affects up to 20.7 million people in the United States with nearly 40% of Americans regularly experiencing symptoms of Dry Eye.[2] It is imperative that eye care practitioners aggressively manage DES, as it is a progressive disease, that when left untreated can initiate severe ocular problems including, but not limited to, permanently impaired vision and an increased risk of eye infections.[3]

In years past, the various methods used in the diagnosis of Dry Eye Syndrome have included the observation of fluorescein tear film breakup time (FL-TBUT), determining the height of the tear meniscus, tear secretion tests, and ocular surface staining analysis. Although all yield crucial information, the limitation of these tests has been their subjective methodology. However as modern technology has evolved and made the ability to diagnose, monitor, and treat disorders more precise, little has changed within the typical optometric practice when it comes to the diagnosis and in-office monitoring of patients suffering from Dry Eye symptoms. The reasons for this are numerous as much of the modern instrumentation is entirely impractical for the average practice, is too time-intensive, too costly, or a combination thereof. The authors of this paper questioned whether a corneal topographer, a modern piece of optometric machinery that serves multiple

purposes and is already present in many practices, could be used to analyze the quality and quantity of a patient's tear film as a replacement to the standard FL-TBUT test. Thus a rigorous literature review was conducted that sought to answer this question, notably as to whether an objective method of Tear Film volume and quality via Corneal Topographer is a suitable replacement or supplement to the standard TBUT test done in most eye clinics. The results of this wide-ranging research have the potential to affect each Dry Eye patient that is monitored by eye care professionals. If research indicates the necessity of an objective, non-invasive, testing format for a more comprehensive analysis of a patient's corneal quality then it would behoove current practitioners to modify their practice and exam formats to accommodate such new standards. If, however, the non-invasive techniques add little data that is clinically relevant, then current practices will be recommended.

A clear understanding of the Dry Eye Syndrome (DES) must first be demonstrated in order to properly make a diagnosis and to understand the mechanisms of the ocular system being tested. Dry Eye Syndrome is caused by the ocular system's inability to produce an ideal quality and/or quantity of tears. This type of DES is also known as Keratoconjunctivitis Sicca (KCS) or Xerophthalmia. The International Dry Eye Workshop Study (DEWS) defines Dry Eye as:

> A multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability, with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface. [7]

The causes of DES can vary wildly and have even been attributed to hormonal changes as a result of the normal human aging process or as a byproduct of various medical conditions and pharmaceuticals.[8] This is often worsened by environmental conditions as the main function of the tear film itself is to lubricate the ocular surface and protect it from bacteria and environmental irritants such as dust, pollen, and dander.[9]

The symptoms of Dry Eye vary greatly from one individual to another, which often exhibit daily fluctuations from morning to night. These symptoms may include blurred vision, foreign body sensation, itching, redness, irritation, light sensitivity, a pulling sensation, marked conjunctival injection, or a feeling of dryness.[7] In addition, there may be a stringy discharge and excessive tearing. This is due to an overabundance of reflex tearing compensating for an unusually low amount of baseline tearing. These "reflex" tears are produced in response to injury, strong emotions, or ocular irritation and do not possess the lubricating qualities necessary to prevent DES. As the ocular surface becomes irritated due to a low level of baseline tears, the reflex tearing system begins and subsequently produces an overabundance of tears.

How then, does an eye care professional assess the status of Dry Eye? To this day, many practitioners consider the TBUT the most important assessment tool of the ocular surface. The TBUT is defined as the time an ocular surface maintains a cohesive surface following a blink. We will begin by explaining what is the accepted

process of properly conducting this procedure. The test is performed by first instilling a small amount of fluorescein on the ocular surface via droplet or fluorescein strip. Upon application of the chemical, the patient is instructed to hold their blink until the clinician indicates that the test is complete. If the tear film becomes altered/reduced at 9 seconds or less, as determined by the observer, the patient is deemed to have reduced tear film quality. This standard has been in place since 1973 when a report by Lemp and Hamill (1973) was first released.[4] It is commonplace to designate any test that results in a quality tear film that lasts for 10 seconds or longer as normal. However, in recent years this longstanding belief has been up for debate as Abelson et al (2002) have suggested that the diagnostic cut-off should be at less than 5 seconds when a known volume of fluorescein is instilled.[5] They suggest the use of a micropipette in the placement of Fluress®. onto the cornea in an effort to standardize the acquired results. With the implementation of a micropipette procedure, the amount of Fluress®. applied directly to the ocular surface will be standardized.

Even so, the TBUT test has been widely accepted as a critical clinical tool to quickly and easily assess a patient's tear film through non-invasive methods. In recent years, however, a new clinical test has been the topic of numerous scholastic articles and discussions among eye care professionals.[7,11,13-21] Through the use of video topographers and keratographers, many practicing eye care professionals have begun assessing the tear film noninvasively using these two pieces of modern instrumentation.[6] In fact, many such instruments have scanning software built into

the machinery that provides for both qualitative and quantitative tear film assessments.[6] These tests are both quick to perform and comfortable for the average patient.

For years, the FL-TBUT test, Schirmer's test, and corneal staining have provided for the typical Dry Eye Syndrome evaluation. Understanding the benefits of embracing new technology, we seek to answer the question as to whether performing tear assessment with a video keratographer or topographer would greatly add to the diagnosis and treatment of the Dry Eye patient. There is no argument for this method of tear film assessment to completely replace or eliminate the need for Schirmer's, corneal staining, or any other test; rather we seek to find evidence whether the practice would adequately replace or supplement current Dry Eye evaluations. Through examination of peer-reviewed literature and instrumentation publications, we will provide data relevant to the practicing eye care professional as to whether this new technology is a useful and informative addition to their exam format for the evaluation of Dry Eye patients.

As noted previously, due the complexity of DES, no practical "gold standard" testing procedure yet exists for its diagnosis.[7] In the recent past, it has been claimed that the measurement of a patient's tear osmolarity could be the definitive test for the proper diagnosing of DES, however the practicality of such testing in modern practice leaves much to be desired as few practices have such instrumentation.[10,11] As such, most practitioners have continued to use the FL-TBUT method in their

belief that this is the closest that modern practice offers to a "gold standard", when in fact, TBUT measurements have numerous problems. These include extremely poor reliability due to many influencing factors including the inexact dosage of fluorescein applied to the ocular surface, examiner experience and proficiency, a consistent interval between instillation and TBUT examination, and the instrumentation quality. By incorporating a truly objective test that a noninvasive keratographer/topographer study would bring, many such influencing factors would be reduced or eliminated. By conducting a review of recent published literature it is our hope to offer guidance to the practicing eye care professional as to whether incorporating an objective tear film analysis via keratographer/topographer is a worthwhile endeavor.

Literature Review:

In this literature review, we seek to analyze the validity and practicality of noninvasive, topographer-based tear breakup analysis and its application to the study and management of Dry Eye treatment. An independent approach was taken as to whether modern practice dictates the necessity of an objective non-invasive measurement of the tear film in addition to the standard invasive tear break up test profiled earlier.

This review has been largely divided into two primary categories. The first category consists of literature that supports the theory that the standard invasive Tear Break Up Test methodology is adequate for current practicing eye care

professionals in their diagnosis of Dry Eye Syndrome. The second category contains research that emphasizes studies done on modern methods of objective non-invasive tear analysis. Finally, the authors will offer their opinion based on their extensive research as to whether this technology is a necessity in modern optometric practice.

Savini et al (2008) wrote an extensive review piece analyzing the various methodologies used to diagnose Dry Eye.[21] They believe strongly that despite all of the problems that undoubtedly arise with the invasive TBUT test, the generally accepted guideline that a TBUT shorter than 10 seconds reflects a problem with the tear film is valid and should be continued by current practitioners. They, along with other studies, state that a TBUT shorter than 5 seconds is assuredly Dry Eye.[22] Due to the ease of test performance and convenience, they feel that TBUT will continue to be adequate and valuable for current diagnosis provided if it is performed at the beginning of the Dry Eye diagnostic work up. By pre-empting other invasive diagnostic testing procedures like applanation tonometry or pupil dilation, a more sound result will be achieved due to the tear film being tested in its most natural state. The authors do, however, recommend further study regarding the applicatio of the TBUT test. They question which method of fluorescein delivery will produce the most consistent results, the meaning of the differing TBUT patterns (central spots vs. peripheral break up), and whether it would be possible to define a standardized cut-off value for meibomian gland disorder vs. other causes of Dry Eye.

In addition, it should be noted Savini (2008) repeatedly questions the lack of a standardized testing procedure for applying fluorescein onto the tear film, the amount of fluorescein applied, as well as the simultaneous instillation of preservatives (like benzalkonium chloride) to the corneal surface that could immediately shorten tear break up time. The authors also stated the inherent difficulty and inconsistency when attempting to compare the standard TBUT testing results with those of the non-invasive test time. They declare that the two tests poorly correlate, with the non-invasive method scoring significantly longer than the standard TBUT. Although the article notes the benefits of this modern technology, it acknowledges that these methods have yet to find wide acceptance in current clinical practice due to the problems mentioned previously in this paper, namely access and quantification problems, as many examiners do not fully understand the correlation of these values to dry eye in clinical practice. In addition the authors emphasize an article, Nemeth et al (2002), that focused on the use of a corneal topographer to measure tear film formation and break up time in their patients.[25] It is their opinion that there appears to be a need for a variety of normative values for different aged groups as well as diagnostic criteria in order for the assessment via corneal topographer to be wholly accepted. Further research is strongly recommended.

Despite all of the flaws in the TBUT test mentioned previously, there have been studies conducted which state that even with these deficiencies, the TBUT is a clinically relevant test that should be continued as the standard of care. One such

study states that by simply taking multiple TBUT readings and averaging their results, an examiner is able to achieve suitable information to begin management of Dry Eye Syndrome.[19] The study analyzed the effect of different amounts of fluorescein drops applied to the corneal surface immediately before a TBUT reading was taken. They used 1, 2.7, and 7.4 microL of fluorescein solution instilled via micropipette. They found that the instillation of differing amounts of the solution had a clinically significant effect on the TBUT result. They too recommend the standardization of the amount of fluorescein dye used for a comprehensive TBUT test however they emphasize that accurate, and clinically significant, results can be achieved in the clinical setting by simply performing the test a number of times and averaging the results.

Nichols et al (2002) sought to explore the utility of the Keeler TearScope Plus in comparison to FL-TBUT with the use of real-time digital photographs.[23] The results were evaluated for consistency within and between examiners as well as compared amongst the separate methods. The stated advantage of the TearScope for use in clinical practice is the ability to assess the structure, thickness, and stability of the tear film non-invasively. The advantage of digital photography for TBUT determination being that the practitioner is able to review the images at the examiner's leisure and include them in the patient's chart for later review and/or revision. The study included a sample of 40 patients who had one eye randomly chosen to have either the TearScope or FL-TBUT performed first. For the FL-TBUT procedure, digital images of the fluorescein pattern were captured every second for

60 seconds or until the patient blinked. This was repeated after a rest period if the blink occurred before the tear break-up. For TearScope measurements, the patient was asked to blink normally while lipid-layer interference classifications were assigned. These were classified and scored as (0) none, (1) open meshwork, (2) closed meshwork, (3) wave/flow, (4) amorphous, and (5) colored fringes. These two sets of images were then re-graded by a series of masked examiners. The break-up time in the TearScope image was defined as the point at which the first break, dry spot, or distortion appeared in the tear pattern. The break up time in FL-TBUT was taken as the first appearance of a black spot or disappearance of fluorescein. Statistical analysis of these results showed little to no correlation between overall Non-Invasive tear break-up time (NITBUT) and FL-TBUT, however when the scope was narrowed to only the first 10 seconds after the last blink, the agreement between the two data sets increased remarkably. This is critical because this is the length of time generally considered to define whether patient is likely to be diagnosed with Dry Eye Syndrome. Their analysis also demonstrated that there was greater inter- and intra-observer variability in the NITBUT, with better agreement, especially between practitioners with the FL-TBUT.

The reliability and reproducibility of results obtained via FL-TBUT is also evident in the research studies of Pult and Riede-Pult (2012).[24] Their research sought to produce a solution to one of the biggest downsides of the standard FL-TBUT test; inconsistent dosage from one measurement to the next. This problem has been addressed by other studies in the past using micropipettes to consistently

produce the same volume of fluorescein dye each time. While an effective solution, this is generally considered to be impractical in a clinical setting due to constraints of time, space and portability. The solution posed by this study is a simple modification to the standard fluorescein dye strip coupled with a standard procedure of preparation to increase the consistency of the amount and concentration of dye delivered to the patent's eye. This procedure involves folding over the first millimeter of the fluorescein dye strip so that the folded portion makes a 90-degree angle with the rest of the strip, then adding 1 drop of sterile saline, shaking the strip to remove excess fluorescein, then applying only the folded portion to the conjunctiva. This was performed in 2 experiments, once in vitro onto a filter paper for concentration measurement, and once in vivo to be compared with measurements obtained by VideoKeratoScope (VKS). Ten observers were instructed in this preparation and analysis was performed to measure inter-and intra-observer consistency in the fluorescein delivered by each. The dye in each filter paper was extracted in saline solution then measured by fluorescence analysis to determine concentration as measured by an optical power meter. During the in vivo measurements, FL-TBUT and VKS were analyzed with the observer masked from time in an effort to reduce observer bias. The results showed, in agreement with the consensus found by other studies in this field, that TBUT was significantly shorter than NITBUT on average. This study also found that, as compared to the standard TBUT, the modified TBUT had better inter-observer agreement for in vivo results and practitioners had markedly more consistent concentrations of fluorescein dye. Repeatability of results with the modified TBUT was found to be statistically

comparable to that of VKS, outpacing the standard FL-TBUT, and, based on literature published at the time of the study, also outpacing the reproducibility found via corneal topography.

The popular consensus of the eye care community is that although there are numerous flaws in the TBUT testing system, it should continued to be applied clinically. Plugfelder (2012) summarized this in his study by stating the TBUT is both an easy test to perform and is an inherently valuable diagnostic aid to be used in the assessment of numerous ocular surface disorders.[20] This review emphasizes the importance of performing the test at the beginning of the diagnostic portion of the examination and should always precede all other invasive diagnostic assessments like intraocular pressure measurements or pupil dilation. The clinician should also be reminded that any noninvasive tests such as tear film meniscus measurements should be performed prior as they will be altered by the instillation of fluorescein.

The amount of research currently being done on the various methods of non-invasive tear film measurement is encouraging as it has shown that modern technology can improve our diagnostic capabilities as well as undoubtedly advancing our treatment modalities. Recently, peer reviewed literature has become inundated with various studies and review articles highlighting the potential use of non-invasive methods of TBUT analysis into clinical practice. We have chosen to specifically highlight those studies that address the issue of whether a non-invasive

tear film test should be incorporated into the average clinical practice.

Kojima (2004) proposed that the current gold standard for tear stability evaluation, the fluorescein tear break-up time, has several flaws that make it a less-than-ideal measure of the true state of a patient's tear film.[13] The greatest problem lies in the installation of the drops themselves. Inconsistencies in the volume of the drops placed in each eye as well as variations in concentration of the fluorescein dye will affect the way the drop spreads, dilutes, and how brightly the dye fluoresces during TBUT evaluation. Among the oft-repeated concerns mentioned by this study are the eye's reaction to Benzalkonium chloride, and the effects of reflex tearing. Observer expertise and subjectivity also play an unpredictable role in the evaluation of fluorescein TBUT, leading to inter- and intraobsever variability in TBUT results. These concerns led to the development of the Tear Stability Analysis System, or TSAS. This is a noninvasive method for objectively quantifying the state of tear stability. The TSAS was developed for the TMS-2N corneal topographer, and is a program that performs 10 consecutive corneal topograms at one-second intervals, deriving time-wise changes from the distortion of mire rings. This measurement collects data from 6000-10000 data points on the corneal surface and compiles them into a topographical map of the cornea and tear film surface. During testing, 30 uL of 0.4% oxybuprocaine was applied to assist the patient in keeping their eye open for the 10 seconds required to complete the test and 5 minutes were allowed to elapse before testing began. TSAS was used to gauge the Surface Regularity Index (SRI), which measures the local regularity of the corneal surface within the 4.5 mm

central diameter, comparing each point with the adjacent points to give an overall picture of symmetry or asymmetry. The higher this value, the more asymmetrical the corneal surface. To test the utility of this program, the researchers collected measurements from patients categorized into either healthy or dry-eye subjects. The dry-eye subjects were further categorized into Sjogren's syndrome Dry Eye, or non Sjogren's syndrome Dry Eye. After excluding subjects with conditions known to alter the ocular surface or tear film integrity, TSAS measurements were taken followed by FL TBUT and Rose Bengal staining. To evaluate each patient, they measured FL TBUT three times, noted a fluorescein staining score, and a Rose Bengal staining score. Patients with Dry Eye symptoms, those with FL TBUT less than five seconds, Schirmer 1 results less than 5 mm, or positive staining results were placed into one of the two Dry Eye categories. After statistical analysis, it was found that SRI for normal patients averaged around 0.7 for the ten second duration of the TSAS measurements, and varied very little from second one to second ten. SRI for the Dry Eye group started at approximately 1.50 at one second and finished at 2.0 after ten seconds. For Sjogren's Syndrome patients, the SRI tended to stay fairly stable throughout, ranging between 2.0 and 2.5, likely due to the fact that the tear film was equally unstable from the moment of the blink that it could not "break up" due to its inability to form a cohesive ocular surface, and resulting in immediate dry eye symptomology that lasted throughout the inter-blink interval. These results establish a baseline criterion for differentiating patients who complain of Dry Eye in a way that allows the examiner to objectively measure and evaluate the severity of the tear film instability. This test will show the examiner the magnitude of the tear

film stability as recorded in the SRI, and also the progress of the tear film's cohesion or lack thereof over time.

Goto (2003) also sought to develop a new method to objectively quantify tear film instability via non-invasive procedure.[14] Citing similar concerns as those brought forth by Kojima (2004), the researchers sought to avoid the disadvantages of FL-TBUT, namely problems with reproducibility, objectivity, accuracy, and lack of multiple quantifiable parameters. This study also was performed using the TSAS technology on the corneal topographer, however different criteria were developed to quantify the stability of the tear film. In this study, two new methods for measuring tear film stability were created; the Topographic Modeling System Breakup Time or TMS-BUT and the TMS Breakup Area, or TMS-BUA. In this case, tear breakup was defined as a change in refractive power of the ocular surface by 0.5D or more. By this measure, the TMS-BUT was the time until the ocular surface power changed by 0.5D or more, and the normal/subnormal point was set at 5 seconds, with below 5 seconds indicating an unusually fast breakup. TMS-BUA measured how much of the overall corneal surface experienced a power change of >0.5D within 5 seconds, with any value larger than 0.2 or 20% considered as abnormal. Subjects with a history of ocular disease, surgery, or use of ophthalmic medication within one year were filtered out of the patient pool and then all patients (80 eyes) were examined 3 times with TSAS with 10-minute intervals between measurements. Standard SLE-TBUT was performed on each patient for comparison purposes, with TBUT less than 5 seconds considered abnormal. SLE-

BUT found 57.5% of the patients to have a TBUT below 5 seconds. Sensitivity and specificity based on symptomology reported by patients were 75% and 60% respectively. Out of the 34 eyes that were found to have a normal SLE-BUT, 32.35% had a subnormal TMS-BUT, with 81.8% of these eyes from subjects who reported symptoms of Dry Eye. TMS-BUT reported a 97.5% sensitivity and 62.5% specificity. As a comparison to SLE-TBUT, the specificity was quite similar, however TMS-BUT picked up roughly 23% more of the Dry Eye patients than the standard TBUT. TMS-BUA reported very similar findings, with 35.29% of patients with normal SLE-TBUT testing abnormal on TMS-BUA, resulting in a 95% sensitivity and 65% specificity, again marking it as a better measure to pick up potential Dry Eye cases that SLE-TBUT may miss. This information may be extremely helpful to practitioners who have patients who complain of symptoms but show no clinical signs, giving quantifiable evidence of a tear-film instability issue that may otherwise be missed by standard measures as both low tear-volume and high tear-evaporation Dry Eye resulting in decreased tear film stability.

Montes-Mico (2004) set out to explore how changes in the tear film created aberrations in the refractive surface of the eye and how this is affected by tear film instability created by Dry Eye conditions.[15] Literature has shown that in normal eyes, there is a initially a large amount of surface aberration in the tear film following a blink, after which the tear film rapidly stabilizes, then gradually aberrations increase as the tear film becomes more irregular and begins to break up, with minimal aberrations beginning to occur approximately 6 seconds post-

blink. This phenomenon has been demonstrated by monitoring the aberrations in patients diagnosed with Dry Eye and comparing the eye in its natural state to the measurements taken after artificial tears have been instilled. All patients in this study were diagnosed with Dry Eye on the criteria of SLE-TBUT less than 5 seconds and Schirmer 1 results less than 10 mm. Average TBUT for these patients was 3.3 seconds. VideoKeratoScope measurements were taken at 1-second intervals for 15 seconds after a blink and repeated 3 times per patient. The TMS-2N VideoKeratoScope was used to measure aberrations in the ocular surface throughout the testing procedure. The data was then processed to find the means and standard deviations of the wavefront aberrations for each second after the blink. In each patient it was found that, as in previously acknowledged literature, the aberrations decreased immediately post-blink and then increased with time. For the first 4 seconds after blinking, normal patients and dry-eye patient showed similar data results, however beyond this point, dry-eye patients had significantly greater wavefront aberrations for the remainder of the testing period. This information transfers to patients as decreased retinal image quality as aberrations increase in the inter-blink interval, with increasing time directly correlated to decreasing image quality. As an incidental finding, the researchers noted that the time until minimum aberration could be linked to TBUT by a simple formula:

$$Time_{(minaberration)} = 0.49 \times TBUT_{(sec)} + 1.46$$

This study was able to confirm, through previously unexplored methodology, that the tear film in Dry Eye becomes unstable earlier (at about 3 seconds) than in normal eyes, and that in all eyes the tear film has a large amount of aberrations until

it stabilizes in the 4-6 second range. They also noted that in normal eyes lipid film spread time was 0.3 seconds or less, while in Dry Eyes it ranged from 1.1 to 3.5 seconds. This method was concluded to be a more desirable, however less clinically practical method of evaluating tear film stability in patients with Dry Eyes.

Goto (2004) investigated the link between Laser in Situ Keratomileusis (LASIK) and post-surgical tear film stability.[16] Past research and clinical observation has reported Dry Eye as a common complication of this procedure, and to this point it had been previously unexamined via topographic tear film analysis. Having established TSAS as a preferable alternative to traditional SLE-TBUT due to the complications involved with the invasive nature of placing topical drops into the eye before evaluation and the greater objectivity and sensitivity of the TSAS system, this experiment relied on TSAS as the main means of analysis with SLE-TBUT results included for comparison. Subjects involved in the study were examined by SLE-TBUT with emphasis on evaluation of superficial punctate keratitis (SPK) before LASIK and all patients had a Schirmer 1 test of greater than 10mm with a SLE-TBUT of 5 seconds or more with no history of Dry Eye symptoms. Tear film stability was then evaluated at 1 week, 1 month, 3 months and 6 months post-LASIK. All eyes were treated with 0.1% sodium hyaluronate QID for 1 week as well as ofloxacin 0.3% and fluorometholone acetate 0.1% QID for 2 weeks. These drops had to be taken a minimum of 1 hour before TSAS evaluation to avoid confounding results. TMS-BUT and TMS-BUA were measured on all patients throughout the study at each follow-up visit, with abnormal TMS-BUA defined as 0.2 or larger within 5 seconds

and abnormal TMS-BUT 5 seconds or less. Before LASIK, the average TMS-BUT for the patient group was 6.42 seconds and average TMS-BUA was 0.16, at the 1 week follow-up, the BUT had dropped to 3.48 and the BUA had increased to 0.48. Patients who had normal TSAS values before LASIK showed slightly shortened BUTs after surgery, however those that had abnormal pre-surgical TSAS values showed a markedly decreased TSAS-BUT values at 1 week, 1 month and 3 months. None of the patients in the study had signs or symptoms of Dry Eye via traditional methods (non-TSAS) before LASIK, however 32.8% had abnormal TSAS values before surgery but during the study period 66.7% developed SPK. After the conclusion of the study, 87.5% of eyes that started with normal TSAS values pre-surgery had recovered. This study concluded that while LASIK does cause many patients to develop Dry Eye in the immediate post-operative period, within 6 months the vast majority of patients' symptoms resolve and do not become a lasting problem. They also found that, in agreement with previous studies, TSAS was a more sensitive measure of Dry Eye within the patient population and better prognosticator of patients who were likely to develop greater Dry Eye signs and symptoms after the surgery.

In 2007 the Report of the International Dry Eye Workshop (DEWS) released an "encyclopedic review of Dry Eye disease and, additionally, a guide to resources archived on the internet."[7] This labor-intensive effort took over 3 years to compile and yielded an evidence-based review on the current knowledge of Dry Eye issues, most notably the evaluation and diagnosis of the disorder. The study's Diagnostic Methodology Subcommittee worked to 1) Identify the ideal tests to screen,

diagnose, and monitor Dry Eye Disease 2) Create and research ideal criteria to judge normal and abnormal test performance and 3) Consider whether testing would be valuable in a variety of clinical settings. During their investigation, they stated that there is yet to be an agreed upon "gold standard" in the diagnosis of Dry Eye Syndrome. It was the opinion of the committee that minimally invasive diagnostic methods are the future of Dry Eye diagnosis. These tests are tasked with an assortment of duties including diagnosing DES while differentiating the disorder from other types of external diseases, classifying the DES subtypes, labeling disease severity, as well as tests that have the capability of quantifying changes on the ocular surface and tear film. The DEWS study believes that the practice of tear osmolarity evaluation shows a great deal of promise and is the closest available to a "gold standard." The test provides both quantitative and objective measurements, has no site-to-site variation, is time efficient, and is believed to have the highest correlation to disease severity. The authors are quick to state that this test is unrealistic in many modern optometric offices simply due to the extreme cost of acquiring and maintaining a unit such as TearLab®. One of the tests profiled in the study was the Tear Film Break-Up Test, as such has been discussed extensively in the other studies profiled thus far. The DEWS authors are in agreement with the previously mentioned publications that there are inherent difficulties in the reliability of this test. They emphasize the need for a uniform application of a standard volume of flourescein to be instilled onto the ocular surface and strongly recommend the use of a yellow barrier filter (Wratten) to enhance the visualization of the fluorescent tear break up. The disparity among research as to the normative

values are also brought into discussion as the 1974 Lemp and Hamill study states the accepted value of <10 seconds as being the Dry Eye diagnosis cutoff.[4] This is in contradiction to the 2002 Abelson et al paper that states that the diagnostic cut-off should be <5 seconds when a uniform volume of fluorescein dye is instilled.[5] The DEWS study believes that, in general, the recommended approach to diagnose DES are tests that favor technologies that will monitor tear changes at the ocular surface while causing the least amount of disturbance to the cornea and its tear film dynamics.[7] An ideal noninvasive technique would offer the possibility of testing in a situation most similar to a "steady-state." Many of the DES evaluation tests that are currently run by eye care professionals will, unfortunately, disturb the tear film and can potentially affect the outcome of a subsequently performed test. It is apparent that a noninvasive assessment of the tear film using a video keratographer or topographer satisfies all of these recommendations.

Also, Koury (2011) believes that due to the subjective nature of the tear film breakup test, there are strong limitations to its reliability.[17] She believes that by following the recommendations previously listed in the 2007 Report of the Diagnostic Methodology Subcommittee of the International Dry Eye Workshop, the future of DES diagnosis lies in topographical analysis of the ocular surface's tear film. She advocates for the use of this modern technology in today's eye care professional's exam regimen and believes that it should be used to assess all patients who present to the clinic with Dry Eye symptoms. She also emphasizes the marked success in today's practices that employ this noninvasive method to assess

the effectiveness of their treatment. Perhaps Koury's strongest argument as a proponent for the implementation of this new noninvasive method can be found in its ability to more satisfactorily educate and council Dry Eye patients. In the article, an interviewed doctor adamantly states that after displaying the test results to their patient "They seem to accept treatment regimens more easily and adhere to them with better compliance." Interestingly, the doctor notes that the images from her instrumentation aids in explanation of the condition and has been shown to "...increase patients' compliance with the recommended treatment/management knowing that we will compare the images after treatment." As an early adopter of this technology, the eye care professionals highlighted in this article believe that these new diagnostic imaging modalities greatly increase the accuracy of Dry Eye diagnosis.

Sickenberger et al (2010) developed what they believed to be the first trial of a non-invasive method for tear film assessment using a corneal topographer.[18] Using methods similar to those explained in the study section of this paper, the authors analyzed the TBUT of 34 individuals via corneal topographer. This study led them to the conclusion that the non-invasive method was suitable for the assessment of tear break up time.

Discussion:

As eye care practitioners, optometrists are increasingly recognizing the critical importance of identifying and treating issues that alter the tear film in an

effort to create the best possible visual acuity for our patients. As such, it is the opinion of this paper's authors that the current regimen primarily used to diagnose Dry Eye Syndrome among most within the profession is not adequate. After analyzing an assortment of research regarding the use of various DES testing methods, this opinion seems to be growing within the eye care community. In the 2007 Report of the Diagnostic Methodology Subcommittee of the International Dry Eye Workshop, the authors repeatedly emphasize the necessity of noninvasive techniques to analyze the ocular surface's tear film. They, along with numerous other authors of peer-reviewed literature, continually stress that tests such as the TBUT are not as reliable or repeatable as once thought. This test for example, is believed to possess numerous inherent disadvantages that can cause fluctuation in test results. When one considers the administration of the flourescein dye itself onto the ocular surface, it is difficult to ensure that a consistent volume has been distributed with each attempt. In addition, the most commonly used method to add fluorescein to the ocular surface involves the dropping of Fluress®. This compound contains the harsh preservative Benzalkonium chloride which has been known to cause epithelium destruction, thus causing disruption during subsequent corneal testing. The flourescein dye has also been noted to cause reflex tearing, thus rendering the DES testing inaccurate. Perhaps most significant is the widely accepted inter-observer and intra-observer variability that occurs with this form of testing. Data collected at one office is unreliable when in taken in comparison to data collected at another clinic. Despite all of these difficulties, the FL-TBUT test is

still considered a clinical staple and is widely accepted as one of the most crucial aspects of the testing for Dry Eye.

There are many practitioners within the eye care community that believe the best course of action to diagnose DES lies not in testing, but rather in the development of questionnaires that function to identify Dry Eye via symptoms, discover precipitating and current risk factors, as well as analyze any implications upon quality of life.[7] Many optometric practices claim to have achieved a great deal of success with these questionnaires and adamantly state that they are the most important aspect in their diagnosis of Dry Eye Syndrome. It is the opinion of the authors that these questionnaires, although superb in theory, have many underlying flaws and should be interpreted with a high degree of skepticism. Many studies have been dedicated to the study of symptom-based questionnaires in an attempt to analyze their reliability. The "Hawthorne effect" discovered that whenever individuals are observed within a study or asked to describe their symptoms, their behavior or performance is significantly altered. For this reason the authors believe that these studies should be used solely as supplemental material for a diagnosis of Dry Eye, and should not be heavily relied upon.

What alternative method of quantifying or qualifying Dry Eye should be incorporated into a typical Dry Eye Evaluation at a typical optometric practice to replace or supplement our current testing, most notably the standard FL-TBUT test? It is the opinion of the authors that if a practice prides itself upon its ability to

diagnose, treat, and manage Dry Eye Syndrome, then a video topographer or keratographer is a necessary investment. By incorporating a noninvasive testing unit that functions without the use of BAK or dye, the practice will be providing superior care to their patients, as evidenced in our literature review. This electronic unit will allow for more uniform testing results among offices and staff. As stated in Koury's (2011) article, among the early adopters that have embraced this technology, practitioners have seen a great deal of success with both patient compliance and in testing results. As the adage goes, a picture is worth a thousand words. Using the results of the topographer or keratographer to give patient education will emphasize the truly problematic situation that is caused by DES both optically and from a patient comfort standpoint.

It is the opinion of the authors that nowhere would this technology be more beneficial than in optometric academic institutions. At the Michigan College of Optometry, for example, we recommend that each patient being tested, monitored, or treated for Dry Eye Syndrome have a FL-TBUT and tear film analysis via corneal topography at each of their visits. It is expected that this will greatly reduce the inter-observer inconsistency when examining the patient to assess the quality and stability of their tear film. This will allow for a more thorough analysis of their current treatment modalities as well as allow for consistent monitoring at subsequent visits. At locations such as the academic institution just described, this would help provide superior patient care and allow for continuity of care among an ever-rotating group of practitioners.

References:

1. Pflugfelder SC, Beuerman RW, Stern ME, eds. Chronic Dry Eye. at: http://www.agingeyenet/dryeyesinformation.php. Accessed December 28, 2012. Dry Eye and Ocular Surface Disorders.
2. Lemp MA, Baudoui C, Baum J, et al. The definition and classification of dry eye disease: Report of the Definition and Classification Subcommittee of the International Dry Eye Workshop (2007). Ocular Surface. 2007;5:75-92
3. Asbell, Penny A., and Michael A. Lemp. Dry Eye Disease: The Clinician's Guide to Diagnosis and Treatment. New York: Thieme, 2006. 6-8. Print.
4. Lemp Ma, Hamill Jr. Factors affecting tear film breakup in normal eyes. Arch Ophthalmol 1973; 89:103-5
5. Abelson M, Ousler G 3rd, Nally la, et al. Alternate reference values for tear film break-up time in normal and Dry Eye populations. Adv Exp Med Biol 2002;506(part B):1121-5
6. Sullivan BD, Crews LA, Sönmez B, et al. Clinical utility of objective tests for Dry Eye disease: variability over time and implications for clinical trials and disease management. Cornea. 2012 Sep;31(9):1000-8.
7. Foulks, G et al. 2007 Report of the International Dry Eye Workshop (DEWS) The Ocular Surface / april 2007, VOl. 5, NO. 2 / www.theocularsurface.com
8. Pinho, F, Tavares[1] et al, Dry Eye Disease May 2010, Vol. 25, No. 3, Pages 84-93
9. Mulqueeny SP. Prevent the Onset and Exacerbation of DES. Optometric Management, Issue: November 2011
10. Narayanan, Srihari. Osmolarity: A Diagnostic Test for Dry Eye. Review of Optometry. Web. 28 Dec. 2012.
11. Farris RL. Tear osmolarity—a new gold standard? Adv Exp Med Biol. 1994;350:495-503.
12. Nally L, Ousler GW, Abelson MB. Ocular discomfort and tear film break-up time in Dry Eye patients: a correlation. IOVS 2000 41;4(ARVO Abstract):1436.
13. Kojima T, et al. A new noninvasive tear stability analysis system for the assessment of Dry Eyes. Invest Ophthalmol Vis Sci. 2004; May;45:1369-74
14. Goto T, Zheng X, Klyce SD, et al. A new method for tear film stability analysis using videokeratography. Am J Ophthalmol. 2003;135:607–612.
15. Montés-Mico´ R, C´aliz A, Alio´ JL. Wavefront analysis of higher-order aberrations in Dry Eye patients. J Refract Surg. 2004;20:243–247.
16. Goto T, et al. Evaluation of the Tear Film Stability After Laser in Situ Keratomileusis Using the Tear Film Stability Analysis System. Am J Ophthalmol. 2004; Jan;137:116-20.
17. Koury. New Noninvasive Method of Assessing the Tear Film Uses Corneal Topography, Advanced Ocular Disease. 2011; May/June:36-37

18. Sickenberger W, Michel M, Wiedermann D. Development and first trial of a non-invasive method for tear film assessment using a corneal topographer. 2010. JENVIS Research Institute, University of Applied Sciences Jena, Germany.
19 Johnson ME, Murphy PJ. The Effect of Instilled fluorescein solution volume on the values and repeatability of TBUT measurements. Cornea. 2005. 24(7):811-817
20. Pflugfelder SC, Tseng SC, Sanabria O, et al. Evaluation of subjective assessments and objective diagnostic tests for diagnosing tear-film disorders known to cause ocular irritation. Cornea.1998;17:38–56.
21 Savini G, et al. The challenge of Dry Eye diagnosis. Clin Ophthalmol. 2008; Mar;2(1):31-55
22 Toda I, Shimazaki J, Tsubota K. Dry Eye with only decreased tear break-up time Is sometimes associated with allergic conjunctivitis. Ophthalmology. 1995. 102(2):302-309
23 Nichols J, et al. Evaluation of Tear Film Interference Patterns and Measures of Tear Break-Up Time. Optometry and Vision Science. 2002;79(6):363-369
24 Pult H, Riede-Pult BH. A new modified fluorescein strip:Its repeatability and usefulness in tear film break-up time analysis. Contact Lens & Anterior Eye. 2012;35:35–38
25 Nemeth J, et al. High-speed Videotopographic Measurement of Tear Film Build-Up Time. Invest Ophthalmol Vis Sci. 2002; June;43:1783-1790