

# Prospective Study to establish the Standard Value of Tear Film Osmolarity of eye-healthy, asymptomatic Subjects



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## Introduction:

The prevalence of the dry eye syndrome has increased in recent years. It is estimated that approx. 3.2 million women and 1.68 million men (aged 50 years and older) are affected by dry eye syndrome.[1] Every third patient consulting an eye care provider complains about problems related to dry eye. The symptoms are manifold and range from burning eyes to inflammation, visual blurring and reduced visual acuity.[2] However, the diagnosis of these eye problems is not trivial due to the fact that dry eye is commonly assessed subjectively until today. Recent studies have demonstrated that tear film osmolarity (TFO) seems to play a major role in diagnosis of dry eye.[2; 3]



Fig. 1: Hand-held osmometer/ overview display of location for tear collection / magnified display of tear collection at lower tear meniscus (Source: bon Optic Vertriebsges. mbH)

## Purpose:

Aim of this study was to define the standard value of TFO among eye-healthy (without ocular diseases), asymptomatic participants using an osmometer based on electrical conductivity (TearLab Corporation) and to compare this value with past studies to establish the standard value of TFO.

## Methods:

In this prospective, randomized (eye order, with measure pen) clinical trial, 304 participants from eight different regions in Germany were included. Data were collected at the first visit. After a baseline examination, 134 participants (56 male/78 female; average age 40.9±15.9 years) met the inclusion criteria. Participants using medication for regulation of water/electrolyte balance and medication which influenced tear production or tear film were excluded. The *McMonnies* DEQ was used to detect dry eye disease. A meta-analysis was conducted on the basis of 21 studies which examined asymptomatic participants fulfilling pre-defined criteria such as medication use or defined age of participants.

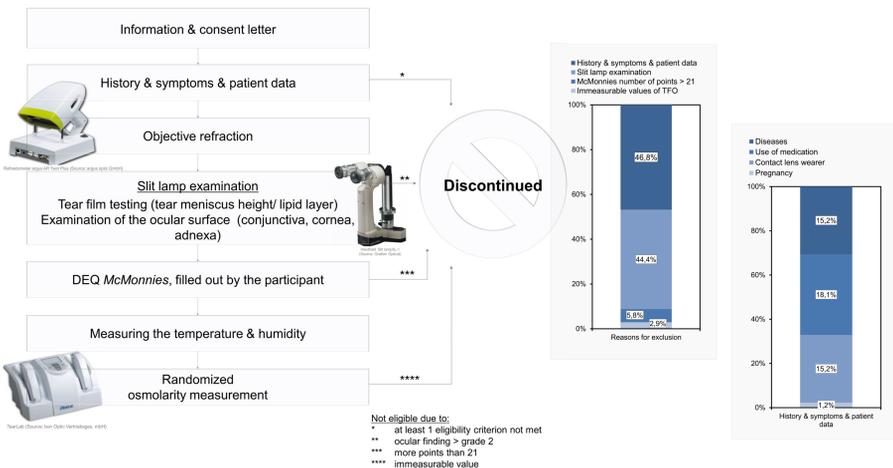


Fig. 2: Study plan and distribution of excluded participants; 304 participants were included and 170 were not eligible

## Results 1: Standard Value of TFO

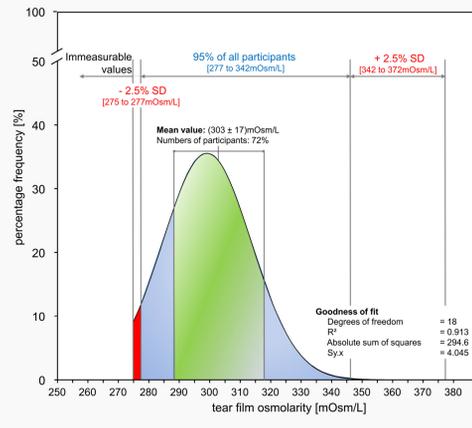


Fig. 3: Frequency distribution of the tear film osmolarity (n=134 both eyes included). The Gaussian curves were adjusted using ordinary least-square fit. This sample was a non-Gaussian distribution (p<0.0001; kurtosis 1.324; skewness 0.966) tested by means of D'Agostino & Pearson omnibus normality test.[4]

The measured values were transformed with  $y=1/x$  (Gaussian distribution p=0.1040; kurtosis 0.399; skewness -0.606; tested by means of D'Agostino & Pearson omnibus normality test [4]) in order to determine the margin areas of  $\pm 2.5\%$  standard deviation (SD). Eight participants were not in the 95% area and were excluded from the following analysis.

The measured TFO was between 275 and 372mOsm/L. The median was 300mOsm/L and the mean TFO in asymptomatic participants, mostly without intermittent factors, (303.3 ± 17.3)mOsm/L.

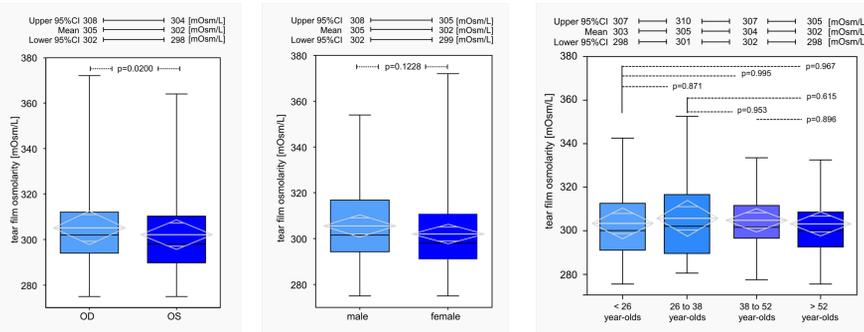


Fig. 4: Distribution of TFO grouped by eye order (n=134); gender (male n=56; female n=78; both eyes included); age group (<26-year-olds n=34; 26 to 32-year-olds n=33; 32 to 52-year-olds n=34; >52-year-olds n=33; both eyes included). The gray boxes show the mean value and the 95%CI of the standard error. There was a statistically significant but not clinically relevant difference between right and left eye (t-test, paired samples, two-tailed). There was neither a significant difference between males and females (t-test, paired samples, two-tailed) nor between age groups (Post HOC Turkey HSD).

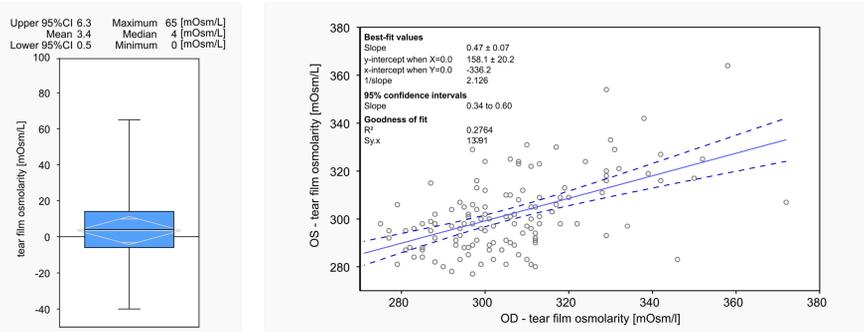


Fig. 5: Distribution of inter-eye TFO (subtracting TFO OD minus OS) (n=134). The gray boxes show the mean value and the 95%CI of the standard error. The mean value of inter-eye differences with absolute values ( $|x| = \sqrt{(x^2)}$ ) was (13.3±10.9)mOsm/L. The maximum with 65mOsm/L was found at a TFO of OD 372 and OS 307mOsm/L. The correlation of TFO between the right and the left eye was significant (effective of pairing: r(Pearson)=0.526 with p<0.0001). In total, 65 points were located above the regression line and 69 below the line (number of runs = 72). When the osmolarity of only one eye was measured and the recommended Cut-Off-Value of 316mOsm/L was used to diagnose dry eye, the sensitivity of the test decreased from approx. 95% to 61.6%.[2]

## Results 2: Meta-Analysis

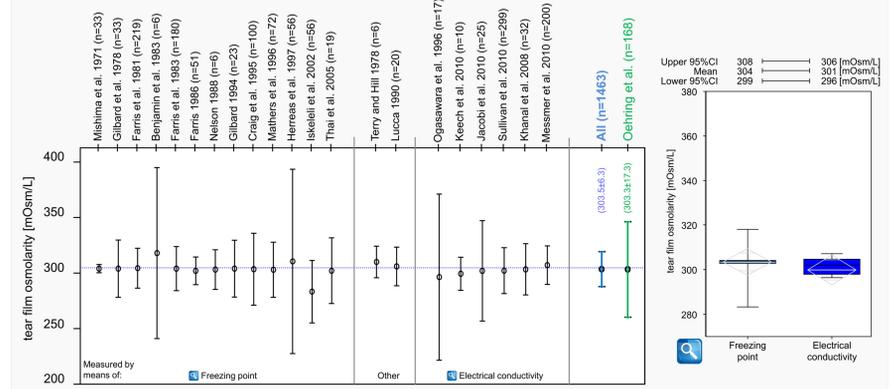


Fig. 6: The meta analysis was carried out on the basis of 21 literature references (each study displayed with lead author's name). In doing so, a mean osmolarity of (303.5±6.3)mOsm/L (n=1,463) was calculated. The TFO measured in this study (303.3±17.3)mOsm/L corresponds to the osmolarity determined in the meta analysis (t-test: p=0.901).

## Conclusion:

In this study, very stringent criteria (e.g. exclusion of participants using medication) were used in order to select asymptomatic, normal participants. Because of this, the TFO value of (303.3±17.3)mOsm/L, as determined in this study, may be used as reference value to describe the tear film osmolarity that may be expected in asymptomatic normals. The most important fact is that the "normals" were not the control group but the experimental group, which is different from previous studies conducted. It is true that the standard area determined in this study in „normal“ participants – without dry eye sensation, ocular or systemic diseases – is higher (95% of participants were between 277 and 342mOsm/L) than in previous studies but correlates, on average, very well with their results.

The results of this examination indicate a statistically, significantly higher value in the right eye compared to the left eye but the clinical relevance is to discuss in further studies. Lemp et al. [5] have also found an inter-eye difference. When using the Cut-Off-Value of 316mOsm/L, the measurement of only one eye is not sufficient to make an exact diagnosis. Consequently, it is highly recommended that both eyes be measured in order to diagnose dry eye disease.

The results of this study indicate that several substantial factors have an impact on tear film osmolarity. However, the correlation between these factors and osmolarity still raise further questions. For this reason, further confirmatory studies are required.

## References:

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