

# **Comparability of subjective and objective measurements of nuclear density in cataract patients**

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# Comparability of subjective and objective measurements of nuclear density in cataract patients

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#### ABSTRACT.

Purpose: To evaluate the relationship between subjective and objective measurements of lens density and the energy of phacoemulsification.

Setting: University Eye Clinic, Maastricht University Medical Centre, Maastricht, the Netherlands.

Design: Cross-sectional study.

Methods: The study population included 69 patients. Nuclear opalescence (NO) was graded with the Lens Opacities Classification System III (LOCS III). Thereafter, lens density was measured objectively with Scheimpflug imaging, anterior segment optical coherent tomography and spectral fundus reflectometry (SFR). Cumulative dissipative energy (CDE) and total ultrasound time (US t.t.) of the phacoemulsification were noted. The relationship between the different measurement techniques and energy of phacoemulsification was assessed using Spearman's correlation coefficients.

Results: We found moderate to strong correlations between LOCS III and objective measurements of the lens density (rho's from 0.53 to 0.78,  $p < 0.05$ ) and a moderate correlation between three objective measurement techniques (rho's between 0.29 and 0.57,  $p < 0.05$ ). There was a moderate correlation between CDE, US t.t. and lens density measurements (rho's from 0.29 to 0.55, p < 0.05), and the highest correlation was found between CDE and NO scores. Exclusion of patients with advanced cortical and posterior subcapsular opacities improved the correlation between SFR and lens density measurements but not the correlation with the energy of phacoemulsification.

Conclusion: Lens Opacities Classification System III has shown the highest correlation with phacoemulsification energy and may be a preferred technique for prediction of use of phacoemulsification energy. Advanced cortical and posterior opacities may interfere with the quality of objective measurements but do not affect the correlation between lens density measurements and phacoemulsification energy.

Key words: anterior segment OCT – cataract surgery – lens density – reflectometry Scheimpflug photography

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# Introduction

Assessment of opacities of the crystalline lens is essential for evaluation of type, severity and progression of cataract as well as for prediction of dynamics of phacoemulsification. There are various subjective and objective methods for evaluation and classification of lens opacities. The most common clinical classification is the Lens Opacities Classification System III (LOCS III), where opacities of the lens are graded at the slit lamp using a standard set of colour photographs (Chylack et al. 1993; Kirwan et al. 2003). However, experience of the observer and accuracy of settings of the slit lamp may affect the reliability of the evaluation (Chylack et al. 1993; Karbassi et al. 1993; Kirwan et al. 2003).

Objective assessment of lens opacities in terms of nuclear lens density can be performed using Scheimpflug imaging and anterior segment optical coherence tomography (AS-OCT). Previous studies have shown validity and reliability of both methods and a strong correlation with nuclear opalescence (NO) grades evaluated with LOCS III. (Grewal et al. 2009; Wong et al. 2009; Gupta et al. 2013) In addition, Scheimpflug imaging and NO grades were also positively correlated with phacoemulsification energy (Davison & Chylack 2003; Bencic et al. 2005; Kim et al. 2009; Gupta et al. 2013; Lim et al. 2014).

Another potential objective measurement of lens density is spectral fundus reflectometry (SFR) (van de Kraats et al. 1996, 2006; Berendschot et al. 2003). Analysis of the light reflected out of the eye across the visible wavelength region allows the determination of the optical density of the lens. However, validity and reliability of fundus reflectometry in assessment of the optical lens density in eyes with cataract have not yet been studied before.

In this study, we compared lens density measurements, which were obtained by LOCS III, Scheimpflug imaging, SFR and AS-OCT, and correlations between measured lens densities and phacoemulsification energy.

# Patients and Methods

This prospective study evaluated 69 patients who underwent phacoemulsification between August 2014 and July 2015 at the University Eye Clinic in Maastricht. Adult patients with any types of lens opacities were included. Exclusion criteria were central corneal scarring, mydriasis of <6 mm, history of intraocular pressure rise after pharmacological pupil dilatation, inability to fixate the target of the measuring device and physical or mental impairment that might hinder participation in the study. The study was conducted according to the principles of the Declaration of Helsinki and was approved by the local ethical committee. All patients provided written informed consent. Preoperative examination included corrected distance visual acuity (CDVA), manifest refraction, Goldman applanation tonometry and slit-lamp examination. Assessment of the lens opacities was performed by the same trained clinician in the darkroom after pharmacologically dilatation of the pupil using one drop of 2.5% phenylephrine and one drop of 0.5% tropicamide.

## Lens Opacities Classification System

Opacities of the lens were graded using a LOCS III set of standard transparency images. All patients were examined under standard settings at a Haag-Streit BQ 900 slit lamp (Haag-Streit, Koeniz, Switzerland) (Chylack et al. 1993; Kirwan et al. 2003). Decimal grades from 0.0 to 6.9 were assigned to NO and nuclear colour (NC). Subsequently, scores ranging from 0.0 to 5.9 were assigned to cortical (C) and posterior subcapsular opacities (PSC).

### Scheimpflug imaging

The Pentacam HR (Oculus Optikgeräte GmbH, Wetzlar, Germany) is a noncontact device based on the Scheimpflug principle. A rotating Scheimpflug camera obtains 25 single slit images in 2 seconds using a blue UV-free lightemitting diode with a wavelength of 475 nm as a light source. Software, after correction for artefacts, creates a three-dimensional (3D) image of the anterior segment of the eye and the crystalline lens. Lens density was measured on the horizontally oriented images with a linear density and a Pentacam Nucleus Staging (PNS) tools (Fig. 1A,B). To measure the linear density, a vertical line was drawn through the centre of the nucleus and average and maximal linear densities were expressed in pixel intensity units ranging from 0 (clear lens) to 100 (completely opaque lens). With the PNS tool (Nixon 2010), we obtained a PNS grade from 0 to 5 and Pentacam Densitometry of Zones (PDZ) values which were calculated automatically by the software. Pentacam Densitometry of Zones (PDZ) values represent an average density of the 3D-zones in the lens, which are centred around the corneal apex and have fixed size with the diameter of 2 mm (PDZ1), 4 mm (PDZ2) and 6 mm (PDZ3). Finally, average and maximal densities of a 3D region of interest (ROI) with the diameter of 2500  $\mu$ m, height 1500  $\mu$ m and back and front curvatures of four dimensions were calculated, as it was described previously by Mayer et al. (2014).

#### Anterior segment optical coherence tomography

The AS-OCT (Casia, SS-1000; Tomey Corporation, Nagoya, Japan) is a noncontact device, which achieves a highresolution, two-dimensional (2D) or 3D imaging of the anterior segment of the eye, based on the principle of sweptsource OCT. The AS-OCT utilizes the swept-source laser with the wavelength of 1310 nm. The system obtains 30 000 A-scans per second with an axial resolution of 10  $\mu$ m and a transverse resolution of 30  $\mu$ m. Although biometric measurements of the anterior segment have shown high reliability and repeatability, (Szalai et al. 2012; Aptel et al. 2014) this system was not used yet for evaluation of lens density. In this study, we obtained a 2D scan of the eye using 'angle analysis mode' with the depth of 6 mm, which allowed us to capture the whole lens. Thereafter, we exported raw data representing log intensities of pixels in a 16-bit grey colour scale and analysed it using MAT-LAB software (version R2013b; The MathWorks, Inc., Natick, MA, USA). Lens density was measured on the images oriented horizontally. A ROI with height and width of 50 pixels was manually selected and located in the centre of the posterior half of the nucleus (Fig. 1C), and average and maximal densities were calculated. The posterior half of the nucleus was chosen, because it appears brighter than the anterior half of the nucleus, as in the angle analysis mode, the point of the highest sensitivity is located in the bottom of the scan and the sensitivity gradually decreases through the depth of the scan.

Each swept laser has different sensitivity decay, and the data are not routinely available. To assess the sensitivity decay of our AS-OCT scanner, we measured reflectivity from the front surface of a thick glass, positioned at the different distances from the OCT scanner, that is in the different depth areas of the scan. Thereafter, we calculated the sensitivity decay as a linear function of the depth of the scan. Finally, we corrected the measured average and maximal density of the ROI using this function.

## Spectral fundus reflectometry

The macular pigment reflectometer (MPR) was used to measure the reflected light that was projected onto the retina (van de Kraats et al. 2006). The MPR was designed to measure the macular pigment optical density. However, spectral analysis of the reflected light also provides the lens optical density. The MPR is a fast and objective technique that does not require pupil dilatation and was previously described in details by van de Kraats et al. (2006). The MPR system was calibrated, and spherical equivalent



Fig. 1. (A) Scheimpflug image with linear density measurement (red line); (B) Scheimpflug image with PNS grade, PDZ values and density of a ROI (red area); (C) AS-OCT image with a ROI (green area).

refraction was installed with a dioptre scale of the instrument. Thereafter, a visible illumination beam from a 30-W halogen lamp was projected onto the subjects' pupil just above the centre and the patient was asked to fixate an 1-deg spot.

The spectral absorption of the natural lens changes significantly with age. At birth, the lens is perfectly transparent and nearly colourless, whereas in old age, a (healthy) lens is yellowish

brown. This is caused by different chromophores, the concentration of which changes with age. This can be approximated with a quadratic age dependence for the main ones as described by van Norren & van de Kraats (2007). The 'virtual lens age' that described our data best was determined by a full spectral analysis of the reflected light between 400 and 800 nm (van de Kraats et al. 1996; Berendschot et al. 2003; van de Kraats & van Norren 2008). The model describes the spectral aspects of light reflected from the fundus using a limited number of absorbing and reflecting layers. In short, the incoming light is thought to be reflected from three layers: the inner limiting membrane, the pigment epithelium and the choroid. In the model, the light travelling through the eye is absorbed by four layers in the eye with known spectral characteristics: media, macular pigment, melanin and a blood layer. The light conditions were such that all photopigments were bleached. In the optical model, the densities of these absorbers, including the virtual lens age, and the reflectances at the interfaces are optimized to fit the measured spectral reflectance. As all absorbers have different spectral fingerprints, they can be determined independently.

#### Surgical technique

Surgeries were performed by 18 different surgeons in the Academic Hospital setting under local or subtenonal anaesthesia. A superior self-sealing corneal incision of 2.2 mm was created, and 1% sodium hyaluronate (Provisc; Alcon Laboratories, Inc, Fort Worth, TX, USA) was injected in the anterior chamber followed by continuous curvilinear capsulorhexis. Standard phacoemulsification was performed with a divide-and-conquer technique using the Infinity phacoemulsification system (Alcon Laboratories, Inc). A foldable acrylic intraocular lens was implanted in the posterior chamber, and the viscoelastic was removed. Cumulative dissipated energy (CDE) and total ultrasound time (US t.t.) were recorded.

#### Statistical analysis

One eye of each patient was selected randomly for statistical analysis. Snellen visual acuities were converted into LogMAR values. Means and standard deviations (SD) were calculated for continuous variables. The relationships between lens density measurements, which were obtained by LOCS III, Scheimpflug imaging, SFR and AS-OCT, and phacoemulsification energy were analysed using the Spearman rho' because the data deviated from normal distribution. p-values <0.05 were considered significant. To evaluate

the influence of advanced  $(\geq$ grade 4) cortical and PSC opacities on the relationship between lens density measurements and phacoemulsification energy, the correlations were re-evaluated after exclusion of these patients.

# **Results**

The study population comprised 69 patients (31 females, 38 males) with a mean age of 70  $\pm$  8 years. The mean preoperative corrected visual acuity (VA) was  $0.3 \pm 0.3$  LogMAR. Distribution and the mean values of the LOCS III scores are shown in Table 1. The mean values and SD of objective measurements of the lens density and phacoemulsification energy are shown in Table 2. There was no significant correlation between the age of the patients and either subjective or objective measurements of the lens density (Table 3). Because there was almost no difference between the correlations with NO and NC, only correlations with NO will be discussed.

The relationships between the different measurements of the lens density and phacoemulsification energy are shown in Table 3 and in Fig. 2. There were strong positive linear relationships between NO and the lens density measurements obtained with Scheimpflug imaging (rho's from 0.65 to 0.78, p < 0.001). The highest correlation was found between NO and PDZ1 and PDZ2 values (rho's  $= 0.77$  and rho' respectively). There were also moderate to strong correlations between NO and lens density measured with AS-OCT and MPR (rho's from 0.53 to 0.58, p < 0.001). Objective measurements of the lens density, Scheimpflug imaging, AS-OCT and SFR were moderately correlated (rho's from 0.29 to 0.57, p from  $\leq 0.001$  to 0.024).

The mean CDE was 12 seconds  $\pm$  7 (SD), and the mean US t.t. was 76 seconds  $\pm$  38 (SD). There were moderate correlations between CDE, US t.t. and lens density measurements (rho's from 0.29 to 0.55, p from  $\leq 0.001$  to 0.023), and the highest correlation was found between CDE and NO scores, rho = 0.55, p < 0.001 (Table 3 and Fig. 3).

Exclusion of patients with advanced cortical and PSC opacities led to

Table 1. Distribution and the mean values of Lens Opacities Classification System III scores.

Score	Eyes, $n = 69$			
	Nuclear opalescence	Nuclear colour	Cortical opacities	Posterior subcapsular opacities
$0.0 - 1.9$	$0(0\%)$	$0(0\%)$	22(32%)	46 $(67\%)$
$2.0 - 2.9$	22(32%)	17(25%)	20(29%)	10(15%)
$3.0 - 3.9$	22(32%)	$24(35\%)$	$15(22\%)$	5(7%)
$4.0 - 4.9$	24(35%)	$24(35\%)$	$8(12\%)$	$6(9\%)$
$5.0 - 5.9$	$1(1\%)$	$3(4\%)$	$4(6\%)$	2(3%)
$6.0 - 6.9$	$0(0\%)$	$1(1\%)$	-	
Mean score	$3.4 \pm 0.8$	$3.6 \pm 0.9$	$2.2 + 1.7$	$1.1 + 1.5$

Table 2. The mean values and SD of objective measurements of the lens density and phacoemulsification energy.



AS-OCT = anterior segment optical coherence tomography, SD = standard deviation.

increase in the correlation between SFR and both objective and subjective measurements of the lens density but not with the CDE or US t.t. (Table S1). There was no improvement in the correlations between other measurements and phacoemulsification energy.

# **Discussion**

In this study, we compared evaluation of lens opacities by the LOCS III with lens density measured by Scheimpflug imaging, AS-OCT and SFR, and we assessed correlations between these measurements and phacoemulsification energy. Only nuclear opacities were included in the correlational analysis, as the degree of nuclear sclerosis but not cortical and PSC opacities are related to the hardness of the lens (Heyworth et al. 1993). In addition, an exponential relationship was reported previously between phacoemulsification energy and NO and NC, but not with the amount of cortical and PSC opacities (Davison & Chylack 2003; Bencic et al. 2005).

We have found positive correlations between NO and Scheimpflug imaging which were comparable to the correlations found in the previous studies (Grewal & Grewal 2012; Lim et al. 2014, 2015; Pan et al. 2015). The PNS grades and average and maximal densities of the ROI have shown the lowest correlation with NO (rho's from 0.65 to 0.67), and the linear densities and PDZs have shown the highest correlation (rho's from 0.72 to 0.78). NO grades provide the assessment of the lens opacification on the continuous scale, whereas PNS system reduces evaluation to five ordinal categories. The differences in the scales might lead to the low correlation between NO and PNS grades, compared to the correlation between NO and other Scheimpflug measurements. With a 3-D ROI mode, a smaller volume  $(6.4 \text{ mm}^3)$  of the nucleus was analysed than with PDZ values. Interestingly, the highest correlation was found between NO and the 3-D PDZ2 zone with a diameter of 4 mm, whereas the smaller PDZ1 (2 mm diameter) and the larger PDZ3 zone (6 mm diameter) showed a lower correlation. The mean density of the smaller 3D zones might be affected by the light reflex artefacts within the lens which increase the measured density (Table 2), whereas the largest PDZ3



density of the region of interest, ROImax = maximal density of the region of interest, US t.t. = ultrasound total time.  $t \cdot t = u$  details total time density of the region of interest, ROImax = maximal density of the region of interest, US  $*_{\text{D}} < 0.05$ ,  $*_{\text{D}} < 0.01$ .  $*< 0.05$ ;  $*< 0.01$ . zone might be affected by the overlapping of the reference block and the anterior chamber as well as the inclusion of the zones in the lens shadowed by the cortical opacities which can decrease the measured mean density (Weiner et al. 2014). The high correlation of the linear density with the NO grades might be explained by the manual positioning of line in the centre of nucleus in the zone free of the cortical opacities and the light artefacts.

There were moderate correlations between NO and maximal and average density measured by Casia AS-OCT (rho's = 0.53 and 0.55, respectively) which were lower than the correlations between NO and average lens density measured by Visante AS-OCT as reported by Wong et al. (2009)  $(r = 0.77)$ . Image acquisition and analysis differed between these two studies. In our study, the whole lens was captured in one scan, as the scan depth was 6 mm being larger than the thickness of the lens. Because of the decay in sensitivity, the image was corrected before the lens density was measured. A small ROI was selected in the centre of the posterior half of the nucleus, which was less affected by the sensitivity decay and required a smaller correction than the anterior half of the nucleus. The scan depth of AS-OCT, used by Wong et al. (2009), was 3 mm, which is smaller than the thickness of the lens. Therefore, in their study, the anterior and posterior halves of the lens were captured separately (Wong et al. 2009). Pixel intensities in the both parts of the nucleus were calculated afterwards, and after adjustment for background noise, they determined the average density of the whole nucleus (Wong et al. 2009).

We also found positive correlations between NO and SFR (rho's  $= 0.58$ ). Although, optical density of the lens was related to age in the population with clear lenses, (van de Kraats & van Norren 2007) this relationship was not found in our cases with cataract. We suppose that light absorption by the lens may increase because of the cataract, and therefore, SFR measurement can be used for estimation of lens density in eyes with cataract. However, advanced cortical and posterior opacities, causing light scattering, might decrease the quality of the measurements as correlation between NO and SFR increased from  $rho = 0.58$  to 0.68





Fig. 2. (A) Correlation between NO and Scheimpflug maximal linear density; (B) correlation between NO and maximal density of ROI measured with AS-OCT; (C) correlation between NO and SFR; (D) correlation between Scheimpflug maximal linear density and maximal density of ROI measured with AS-OCT; (E) correlation between Scheimpflug maximal linear density and SFR; (F) correlation between maximal density of ROI measured with AS-OCT and SFR. AS- $OCT$  = anterior segment optical coherence tomography, LDmax = maximal linear density,  $MPR$  = spectral fundus reflectometry,  $NO$  = nuclear opalescence,  $ROI$  = region of interest.

after exclusion of patients with advanced cortical and PSC opacities (Table S1). Interestingly, the correlation between NC and SFR was slightly higher than the correlation between NO and SFR both before (0.58 versus 0.64) and after (0.68 versus 0.73) exclusion of patients with advanced cortical and posterior opacities. Because SFR was determined by a full spectral analysis of the reflected light, lens colour appears to be a more appropriate measurement for assessment of the correlation between LOCS III and SFR.

In this study, moderate correlations were found between Scheimpflug imaging, AS-OCT and SFR. Different regions of the lens were analysed during these measurements that might reduce the comparability of the measurement techniques. In SFR, the optical density of the whole lens was measured at the visual axis, whereas a ROI was located posteriorly in the nucleus in AS-OCT. The Scheimpflug densitometry was performed at the optical axis (linear density), in the centre of the nucleus (ROI) and in the whole lens (PDZ values). Interestingly, the highest correlations were found between SFR measurements and PDZ2 and PDZ3 values (rho's 0.53 and 0.51, respectively) which included the largest analysed area of the Scheimpflug images. In addition, correlations between SFR and Scheimpflug imaging increased after exclusion of patients with advanced cortical and PSC cataract (Table S1).

We have found moderate correlations between the lens density measurements and CDE and US total time of the phacoemulsification procedure (rho's from 0.29 to 0.55) with the highest correlation found between the NO and CDE (rho  $= 0.55$ ). This correlation between NO and CDE was slightly lower compared to rho  $= 0.61$ which was reported previously (Kim et al. 2009; Gupta et al. 2013). Although previous studies reported a high correlation between objective Scheimpflug nuclear density and CDE in patients with isolated nuclear opacities,  $rho = 0.85$  (Gupta et al. 2013) and rho 0.8 (Kim et al. 2009), current study does not support the advantage of objective measurements over subjective assessment. Advanced cortical and PSC opacities had almost no effect on the correlations between lens density measurements and phacoemulsification energy. This supports the previous statements that only the degree of nuclear sclerosis but not cortical and PSC opacities is expected to affect the hardness of the lens (Heyworth et al. 1993) and therefore the phacoemulsification energy (Davison & Chylack 2003; Bencic et al. 2005). However, it is worth to mention that this conclusion is based only on subjective LOCS III evaluation, as we did not perform objective measurement of cortical and PSC opacities in the current study. A limitation of our study is that patients were operated by experienced surgeons as well as by surgeons in training. Because of the limited group size, we could not make a comparison between these two different surgeon groups.

We did not include cortical and posterior subscapular opacities in the correlational analysis. Although these types of opacities can be evaluated accurately with LOCS III, the objective evaluation is problematic. In SFR,



Fig. 3. (A) Correlation between CDE and NO; (B) correlation between CDE and Scheimpflug maximal linear density; (C) correlation between CDE and maximal density of ROI measured with AS-OCT; (D) correlation between CDE and SFR. AS-OCT = anterior segment optical coherence tomography,  $CDE =$  cumulative dissipative energy,  $LDmax =$  maximal linear density,  $SFR$  = spectral fundus reflectometry,  $NO$  = nuclear opalescence,  $ROI$  = region of interest.

analysis of the total reflection of light does not allow to distinguish between different types of cataract. Posterior cortical and subcapsular opacities are usually not visible on the Scheimpflug images, because of shadows cast by the anterior cortex and the nucleus. Therefore, measurement of posterior subscapular cataract is impossible, and measurement of cortical cataract might be incomplete as only anterior cortical opacities could be measured. However, despite this shortcoming, a sigmoidshape relationship was found by Ullrich & Pesudovs (2012) between the number of Scheimpflug images with significant cortical cataract and cortical opacities measured by LOCS III  $(r = 0.72, p < 0.01)$  with a near linear correlation between grades 2 and 4 of cortical cataract and a ceiling effect above the grade 4. This ceiling effect was present because all Scheimpflug images included some cataract when half of the lens was covered by cortical opacities (Ullrich & Pesudovs 2012). In

AS-OCT, both anterior and posterior cortical opacities are visible, but the shadowing by the anterior cortical opacities reduces the visibility of the posterior cortex. Moreover, the visibility of the anterior cortex is decreased due to the sensitivity decay that may lead to the underestimation of the cortical opacities. To overcome this problem, the scan of the posterior and anterior part of the lens should be taken and analysed separately as it was done by Wong et al. (2009) It would be interesting to look at the correlation between cortical opacities measured by Scheimpflug images and AS-OCT in the future. With regard to PSC cataract, it is difficult to distinguish between the fine opacities and the light reflex from the posterior capsule that may lead to overestimation of a beginning subcapsular cataract.

In conclusion, NO measured by LOCS III has shown a higher correlation with the energy of phacoemulsification compared to the objective measurements. Therefore, subjective evaluation of the lens density may be a preferred technique for prediction of dynamics of phacoemulsification. Advanced cortical and PSC opacities may interfere with the quality of the objective measurements. In addition, the differences in the size and position of the ROI might reduce the comparability of objective measurements and might lead to a lower correlation between objective densitometry techniques and phacoemulsification energy.

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# Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Spearman correlations coefficients between age, lens density measurements and energy of phacoemulsification after exclusion of eyes with advanced (≥grade 4) cortical and posterior subcapsular cataract.