

# Reproducibility of choroidal thickness measurements in hemodialysis patients: A spectral domain optical coherence tomography study

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## Abstract

Aside from general body fluid fluctuation, hemodialysis (HD) may cause changes in ocular fluid balance, resulting in changes in subfoveal choroidal thickness (SFCT) and other ocular parameters. As a result, the purpose of this study was to investigate the effects of hemodialysis on the reproducibility of SFCT measured by spectral domain-optical coherence tomography (SD-OCT). Twenty-six HD (26 eyes) patients had their pre- and post-HD SFCT measured, and the results were compared for reproducibility. Following a thorough ophthalmic examination, SD-OCT was performed three times in a row during a single session. The same physician measured SFCT after automatically identifying choroid with a software caliper. Reproducibility parameters, including intra-class correlation coefficients (ICCs), coefficients of variation (COV), and test-retest variability (TRTV) were then calculated. Males made up 53.85% of the 26 HD patients. There was a significant IOP difference between pre-HD (16.42±3.14 mmHg) and post-HD (14.21±2.78 mmHg) (P<0.001). SFCT decreased significantly from pre-HD 243.50±10.23 µm to post-HD 234.29±9.41 µm (P<0.001). ICC value increased significantly after HD, rising from 0.948 to 0.989 (P<0.001, for all). Pre- and post-HD COV values were 1.6% and 0.65%, respectively. Also, pre- and post-HD TRTV values were 7.864±1.996 µm and 3.074±1.536 µm, respectively. In this study, the reproducibility of SFCT as measured by OCT was lower during pre-HD compared to post-HD. Post-HD SD-OCT assessment appears to improve the reliability of clinical outcomes in the diagnosis and monitoring of HD patients.

**Keywords:** Hemodialysis, spectral domain-optical coherence tomography, subfoveal choroidal thickness, reproducibility

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## Introduction

Hemodialysis (HD) is a life-saving treatment for patients with end-stage renal disease. Uremia, volume load, and serum osmolality in the body all decrease secondary to HD [1]. Changes in ocular fluid balance may also result from this procedure. Intraocular pressure (IOP), corneal thickness, retinal nerve fiber layer, as well as subfoveal choroidal thickness (SFCT) have been reported to change following HD [2-4].

Our understanding of ocular structures is growing in tandem with a rapid advancement of optical coherence tomography (OCT) technology. More precise choroidal measurements have been made possible thanks to enhanced depth imaging-OCT. Choroidal thickness has been shown to be affected by some diseases and to be an important predictor of treatment response in recent studies [5-9]. As a consequence, accurate SFCT measurements are critical in assessing and monitoring certain retinal diseases.

Reproducibility of SFCT has been a subject of several studies, which were performed in homogeneous groups of patients [10-14]. Furthermore, reproducibility of SFCT measurements in patients with various types of retinal fluid was found to be lower in patients with subretinal fluid [11].

We therefore hypothesized that changes in body fluids would also influence SFCT measurements before and/or after HD for similar reasons. As a result, we intended to look into the effects of HD on SFCT reproducibility using spectral domain-OCT (SD-OCT).

## Material and Methods

### *Study design and participants*

Twenty-six eyes from 26 patients who received HD therapy secondary to diabetic nephropathy at Afyonkarahisar Health Sciences University Ethics Committee (Approval Code: 2011-KAEK-2; 07 September, 2018). Hospital were included in this comparative study. The study protocol complied with the ethical principles of the Declaration of Helsinki and received full approval from the institutional review boards

of Afyonkarahisar Health Sciences University Ethics Committee (Approval Code: 2011-KAEK-2; 07 September, 2018). Prior to the study, all patients provided written consent. Our study included patients who underwent HD three days a week due to an end-stage renal failure, had an axial length (AL) of 22-26 mm, no retinal pathology, as well as no prior intra and/or extraocular surgery.

### *Ophthalmic examination and optical coherence tomography imaging*

A comprehensive ophthalmic examination was performed before HD, including measurement intraocular pressure by Goldmann applanation tonometer (Goldmann; Haag-Streit AG, Köniz, Switzerland), axial length by AL-Scan (Nidek CO., Gamagori, Japan) as well as anterior and posterior segment slit-lamp biomicroscopy before and after full pupil dilation.

Spectral domain-OCT (Spectralis, Heidelberg Engineering, Inc., Heidelberg, Germany) scanning was performed 30 minutes before and after HD using the Macula Line Raster scanning protocol. The measurements were taken three times, with two-minute rest periods in between. Subfoveal CT was measured by a physician who was blinded to the patients as a vertical distance between the outer boundary of the retinal pigment epithelium-Bruch membrane layer and the manually drawn sclera-choroidal interface automatically determined by SD-OCT from the subfoveal region.

### *Statistical analysis*

Statistical analysis was performed using SPSS v. 21.0 for Windows (SPSS, Inc., Chicago, IL, USA). The Shapiro-Wilk test was used to determine the normality of the data distribution. Since variables were normally distributed, the paired-t test was used to compare them before and after HD. Reproducibility was analyzed using the intra-class correlation coefficient (ICC), coefficient of variation (COV), as well as test-retest variability (TRTV). For choroidal measurement comparison, the mean of the three scans was used. Data significance level was set at  $P < 0.05$ .

**Table 1.** Demographic characteristics and other findings of HD patients

Parameter	$(\bar{x}\pm s)$		
HD duration (months)	56.54 $\pm$ 7.76		
AL (mm)	23.76 $\pm$ 1.45		
	Pre-HD $(\bar{x}\pm s)$	Post-HD $(\bar{x}\pm s)$	P-value
IOP (mmHg)	16.42 $\pm$ 3.14	14.21 $\pm$ 2.78	<b>0.001</b>
SCT ( $\mu\text{m}$ )	243.50 $\pm$ 10.23	234.29 $\pm$ 9.41	<b>0.001</b>

$\bar{x}$ : Mean; s; Standard deviation; HD: Hemodialysis; AL: Axial length; IOP: Intraocular pressure; SCT: Subfoveal choroidal thickness; P<0.05 was accepted as statistically significant.

**Table 2.** Intra-session reproducibility of consecutive SFCT measurements based on changes in pre- and post-HD ICC, COV, and TRTV values.

Parameter	Pre-HD	Post-HD	P value
ICC (95% CI)	0.948 (0.895-0.976)	0.989 (0.977-0.995)	0.001
COV $(\bar{x}\pm s)$ (%)	0.016 $\pm$ 0.004	0.006 $\pm$ 0.003	
TRTV $(\bar{x}\pm s)$ ( $\mu\text{m}$ )	7.864 $\pm$ 1.996	3.074 $\pm$ 1.536	

$\bar{x}$ : Mean; s; Standard deviation; HD: Hemodialysis; SFCT: Subfoveal choroidal thickness; ICC: Intra-class correlation coefficient; COV: Coefficient of variation; TRTV: Test re-test variability. P<0.05 was accepted as statistically significant.

## Results

Twenty-six HD patients (female-to-male: 14:12) who met the predetermined inclusion criteria were investigated. These patients were 46.23 $\pm$ 9.54 years old on average. Table 1 displays demographic characteristics of the study patients. There was a statistically significantly decreased IOP following HD (P<0.001). When compared to pre-HD measurements, there was also a statistically significantly decreased post-HD SFCT measurements (P<0.001).

Post-HD ICC increased statistically significantly when compared to pre-HD ICC (P<0.001, for all). Pre- and post-HD COVs were 1.6% and 0.6%, respectively. The pre-HD TRTV measured 7.864 $\pm$ 1.996  $\mu\text{m}$ , while the post-HD TRTV measured 3.074 $\pm$ 1.536  $\mu\text{m}$  (Table 2).

## Discussion

Pre- and post-HD reproducibility of SFCT measurements in diabetic nephropathy patients were investigated in this study. Overall, pre-HD SFCT measurements were associated with significantly lower intra-session reproducibility values, including ICC, COV, and TRTV, compared to post-HD SFCT measurements.

The relationship between SFCT and various

retinal diseases is becoming more understandable as OCT technology advances. Several studies have focused on the role of SFCT in especially diabetic retinopathy and its treatment. One study reported choroidal thinning prior to diabetic retinopathy, as well as the association of thin choroid with microalbuminuria [15]. Another study described the short-term anatomic and functional responses to anti-VEGF therapy in patients with thicker SFCT, emphasizing the significance of SFCT as a prognostic marker in the treatment of diabetic macular edema [16]. Moreover, several factors, including AL, age, body mass index, diurnal variation, and systolic blood pressure, have been reported to affect choroidal thickness in healthy individuals [17-20].

Subfoveal CT has also been measured before and after HD in previous studies, with the majority of them reporting lower post-HD SFCT values [21-25]. This could be ascribed to a decreased osmotic gradient in serum and choroidal interstitium as a result of post-HD decreased serum osmolality. Lower SFCT has previously been correlated with lower serum osmolality, body weight, and a low systolic blood pressure [23]. In addition to a significantly lower post-HD IOP (P<0.001), our study's findings of a significantly lower post-HD SFCT compared to pre-HD SFCT (P<0.001)

in diabetic nephropathy patients who had HD for nearly five years were in line with previous reports. An increase in post-HD SFCT, on the other hand, has been observed in another study [26]. This finding, which is inconsistent with our study, could have resulted from misleading measurements caused by the low reproducibility of pre-HD SFCT.

Various studies have addressed SFCT reproducibility, and it has been noted that SFCT reproducibility ranges between 0.89 and 0.99, especially in healthy individuals [27,28]. In a study of patients with neovascular age-related macular degeneration, swept-source OCT was found to be capable of detecting SFCT changes of  $\geq 57.2 \mu\text{m}$  [14]. The same study also noted that SFCT changes  $> 35 \mu\text{m}$  in SD-OCT could be detected in the same group of patients. Swept-source OCT may also be used to measure SFCT with high reproducibility in diabetic macular edema patients [13]. Furthermore, SFCT measurements taken from the edge of choroidal stroma have been reported to be more reproducible [29]. Contrastingly, another study found no difference in SFCT reproducibility between healthy subjects and patients with diabetic retinopathy [10]. And, the presence of subretinal fluid has been shown to decrease CT reproducibility, which has been attributed to fluid signal attenuation and shadowing caused by the subretinal fluid [11]. Besides, several studies have found that as choroid thickness increases, reproducibility decreases [11,12]. Pre-HD SFCT measurements had lower reproducibility in our study. Several hypotheses have been advanced to explain the lower pre-HD SFCT measurements. As previously stated, it is possible that increasing SFCT has a negative impact on reproducibility. Another possibility is that chronic renal failure may cause an increase in extracellular fluid volume, resulting in hemodynamic instability.

We acknowledge the limitations of this study. Importantly, the size of the study population was just not high enough to improve the efficacy of our study. The measurements were carried out only horizontally. Moreover, we evaluated only the reproducibility of SFCT, which was the goal

of our study. Again, residual influencing factors might have led to an unexplained analytical preference. Thus, long-term prospective studies with a larger sample size may yield clinically useful results in determining relatively accurate reproducibility of SFCT and other ocular microstructures not only before but also after HD in diabetic patients with and/or without diabetic nephropathy

## Conclusions

Besides changes in systemic hemodynamics, HD may result in ocular fluid imbalance, which may be accompanied by changes in SFCT and other ocular parameters. Reproducibility of SFCT has been studied using enhanced depth imaging-OCT technology, but mostly in homogeneous groups of patients, with choroidal thickness in patients with different types of retinal fluid associated with lower reproducibility. Changes in body fluids are expected to influence SFCT measurements before and/or after HD for similar reasons. Significant changes in post-HD SFCT as well as reproducibility were observed in HD patients with diabetic nephropathy. Post-HD OCT assessment during diagnosis and follow-up of HD patients may be associated with more consistent outcomes. Regardless, determining the consistent and accurate consequences of HD on SFCT measurements, as well as its reproducibility, necessitates large-scale randomized OCT studies.

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## Conflict of interest

The authors claim no conflict of interest.

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