

# VU Research Portal

## Quantitative retinal imaging with optical coherence tomography

Gräfe, M.G.O.

2020

### **document version**

Publisher's PDF, also known as Version of record

[Link to publication in VU Research Portal](#)

### **citation for published version (APA)**

Gräfe, M. G. O. (2020). *Quantitative retinal imaging with optical coherence tomography: From early diagnosis to follow-up monitoring*.

### **General rights**

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal ?

### **Take down policy**

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

### **E-mail address:**

[vuresearchportal.ub@vu.nl](mailto:vuresearchportal.ub@vu.nl)

# Contents

<b>CHAPTER 1</b>  .....	<b>1</b>
<b>INTRODUCTION</b> .....	<b>1</b>
1.1 General Introduction.....	2
1.2 The Eye.....	2
1.3 The retina.....	3
1.4 Vascular network of the eye .....	4
1.5 Other Biomarkers.....	6
1.6 Outline of the thesis .....	6
<b>CHAPTER 2</b>  .....	<b>11</b>
<b>TECHNIQUES FOR FLOW QUANTIFICATION</b> .....	<b>11</b>
2.1 Techniques for flow quantification .....	12
2.1.1 Fluorescence angiography .....	12
2.1.2 Fluorescence particle tracking .....	12
2.1.3 Intrinsic contrast .....	12
2.1.4 Laser Doppler and laser speckle flowmetry .....	13
2.2 Approaches for OCT flow quantification .....	14
2.2.1 Principle of OCT .....	14
2.2.2 Doppler OCT .....	18
2.2.3 Resolving the angular ambiguity of DOCT .....	21
2.2.4 Flow quantification through decorrelation .....	24
<b>CHAPTER 3</b>  .....	<b>33</b>
<b>POLARIZATION SENSITIVE OCT</b> .....	<b>33</b>
3.1 Birefringence.....	34
3.2 Mathematical formalisms.....	34
3.2.1 Jones-calculus .....	35
3.2.2 Mueller-Stokes-calculus .....	35
3.3 Implementation of polarization-sensitivity in OCT .....	36
3.3.1 Early PS-OCT .....	36
3.3.2 Fiber-based PS-OCT.....	37
<b>CHAPTER 4</b>  .....	<b>43</b>

<b>PRECISION ANALYSIS AND OPTIMIZATION IN PHASE DECORRELATION OCT VELOCIMETRY.....</b>	<b>43</b>
4.1 Introduction.....	44
4.2 Theory & Simulations.....	45
4.2.1 Theory.....	45
4.2.2 Simulations.....	52
4.3 Experimental setup.....	55
4.3.1 OCT-system.....	55
4.3.2 Phantoms.....	56
4.3.3 Data processing.....	56
4.4 Results.....	57
4.5 Discussion.....	59
4.6 Conclusion.....	61
<b>CHAPTER 5  .....</b>	<b>65</b>
<b>OPTICAL COHERENCE TOMOGRAPHY VELOCIMETRY BASED ON DECORRELATION ESTIMATION OF PHASOR PAIR RATIOS (DESPPAIR).....</b>	<b>65</b>
5.1 Introduction.....	66
5.2 Theory.....	67
5.3 Experiments.....	74
5.3.1 Setup.....	74
5.3.2 Processing.....	74
5.4 Results.....	76
5.5 Discussion.....	79
5.6 Conclusion.....	82
5.7 Appendix: conversion of PDFs.....	82
<b>CHAPTER 6  .....</b>	<b>87</b>
<b>SUBRETINAL FIBROSIS DETECTION USING POLARIZATION SENSITIVE OPTICAL COHERENCE TOMOGRAPHY.....</b>	<b>87</b>
6.1 Introduction.....	88
6.2 Methods.....	89
6.2.1 Participants.....	89
6.2.2 Examinations.....	89
6.2.3 Defining fibrosis.....	90
6.2.4 Polarization sensitive optical coherence tomography.....	90
6.2.5 Processing & evaluation.....	90

---

6.3	Results.....	91
6.4	Discussion.....	96
6.5	Supplementary Material.....	98
6.5.1	Overlay of the depth multiplexed polarization state images.....	98
6.5.2	PS-OCT post-processing improvements.....	98
6.5.3	Visualization of local birefringence.....	99
<b>CHAPTER 7  .....</b>		<b>105</b>
<b>GENERAL DISCUSSION &amp; OUTLOOK.....</b>		<b>105</b>
7.1	Flow quantification.....	106
7.2	Polarization sensitive imaging.....	109
<b>CHAPTER 8  SUMMARY.....</b>		<b>117</b>
<b>CHAPTER 9  LIST OF PUBLICATIONS.....</b>		<b>121</b>
<b>CHAPTER 10  .....</b>		<b>123</b>
<b>ACKNOWLEDGEMENTS.....</b>		<b>123</b>

# List of figures

Fig. 1.1. Anatomy of the eye. ....	3
Fig. 1.2. A cross-sectional image from the posterior pole acquired with OCT .....	4
Fig. 1.3. The retinal vascular network. ....	5
Fig. 2.1. Simplified schematic drawing of a Michelson interferometer .....	14
Fig. 2.2. Fiber based setup principles of FD-OCT .....	16
Fig. 2.3. Illustration of the origin of the phase shift in Doppler OCT.....	19
Fig. 2.4. Schematic illustration of DOCT phase distributions. ....	20
Fig. 2.5. Illustrations for <i>en face</i> DOCT and vessel segmentations. ....	21
Fig. 2.6. DOCT with multiple illumination directions. ....	22
Fig. 2.7 Illustration of the decomposition of a light field in Fourier optics. ....	23
Fig. 2.8. Principle of frequency spectrum analysis in jSTdOCT. ....	24
Fig. 3.1. Effect of birefringence on two orthogonal polarizations. ....	34
Fig. 3.2. Bulk-optics PS-OCT system based on TD-OCT. ....	37
Fig. 3.3. Example for a polarization-delay-unit (PDU). ....	37
Fig. 4.1 Schematic illustration of the incident and backpropagating field focused by a lens or objective onto a sample. ....	46
Fig. 4.2 Comparison of PDF for phase decorrelation and Gaussian fit.....	53
Fig. 4.3. Simulation of the estimated velocity and the velocity precision as a function of actual velocity determined by three estimation methods. ....	54
Fig. 4.4 Interferometer for phase sensitive measurements as well as polarization sensitive acquisition.....	56
Fig. 4.5. Phantom and ophthalmic interface. ....	57
Fig. 4.6 Analysis of the velocity estimation uncertainties .....	58
Fig. 4.7 Double logarithmic plot of the velocity estimation uncertainty over varying samples per velocity estimation .....	59
Fig. 5.1 Simulation of the complex E-field when a collection of point scatterers move (laterally) through the detection volume. ....	68
Fig. 5.2 Plots of PDFs for different normalized motion $\beta$ . ....	72
Fig. 5.3 CRLBs and variance ratios .....	73
Fig. 5.4. Setup and cross section of retina phantom.....	74
Fig. 5.5. Illustration of the derivative of the joint likelihood .....	76
Fig. 5.6. Verification of linear estimation behavior and dynamic range of motion estimation with phasor-based MLE .....	77
Fig. 5.7 Uncertainty estimations for three analysis bases .....	78
Fig. 5.8. Illustration of the combination of multiple dynamic ranges and their relative error.....	81
Fig. 6.1. The left eye of a patient suffering from neovascular AMD and suspected fibrosis.....	93
Fig. 6.2. The right eye of a patient suffering from neovascular AMD. ....	93
Fig. 6.3. The left eye of a patient suffering from neovascular AMD with no suspected subretinal fibrosis.....	94

---

<b>Fig. 6.4. The left eye of a patient suffering from multifocal choroiditis with doubt among the three retinal specialists (two positive, one negative) as to the presence of subretinal fibrosis.....</b>	<b>94</b>
<b>Fig. 6.5. The right eye of a patient suffering from neovascular AMD with doubt among the three retinal specialists as to the presence of subretinal fibrosis.....</b>	<b>95</b>
<b>Fig. 6.6 En face views of the left eye of a patient suffering from neovascular AMD and suspected fibrosis. ....</b>	<b>96</b>

