Detecting Early Choroidal Thickness Changes using Piecewise Rigid Image Registration and Eye-Shape Adherent Regularization

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Universitätsspital Basel

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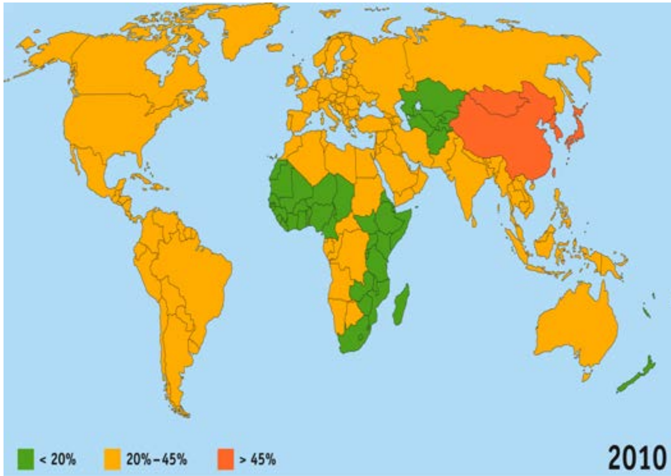
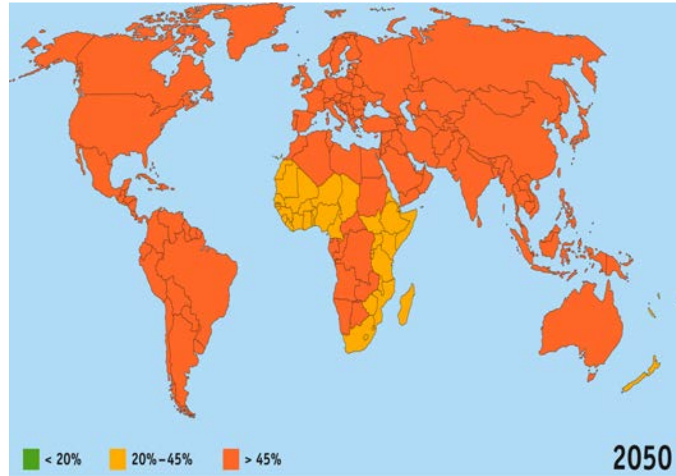
Myopia - prevalence worldwide



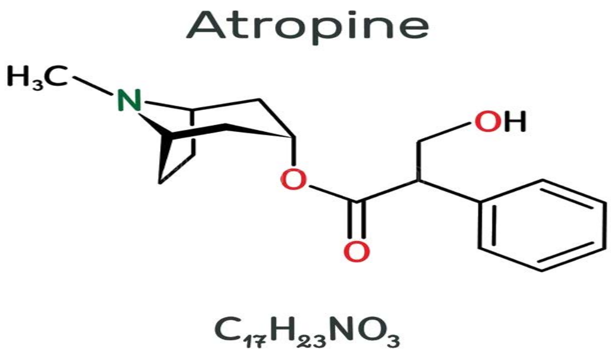


Myopia prevalence worldwide in 2010 and projected for 2050

(data source: Holden BA, Fricke TR, Wilson DA et al., Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology, 123(5), pp.1036-1042)

Myopic vision

Myopia control

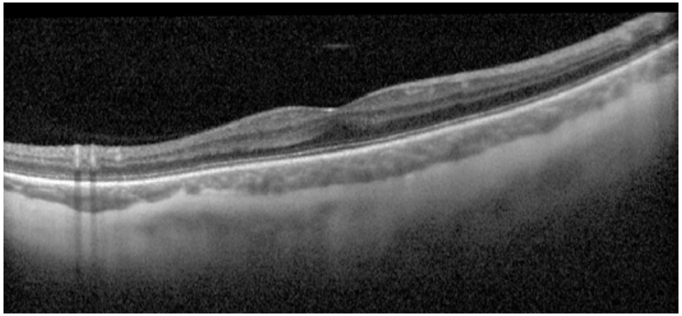


(a) Low-dose atropine eye drops

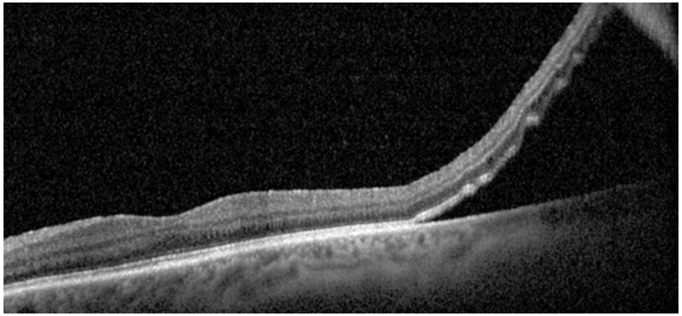
(b) Corneal reshaping lenses

(c) Defocus incorporated lenses

High myopia and its risks



(a) High myopic eye



(b) Retinal detachments

(The image (a) was kindly provided by the Eye Clinic at the University Hospital in Basel, (b) by the Eye Clinic at the Lindenhofspital in Bern, Switzerland.)

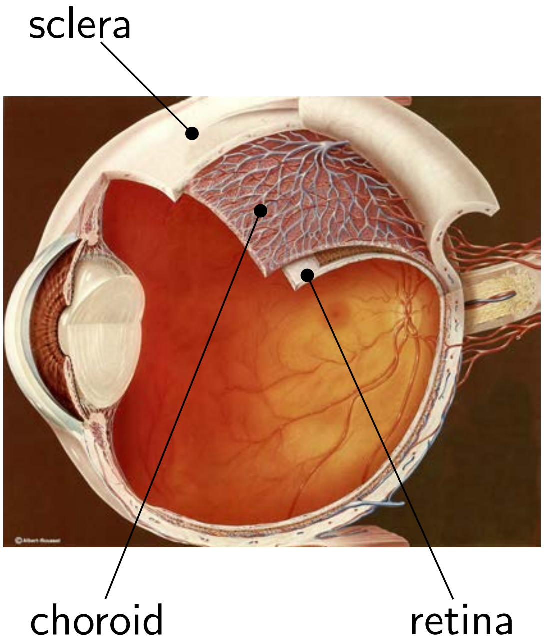
Choroidal thickness (ChT)

ChT as biomarker in predicting and monitoring myopia

- Read, et al. "Choroidal changes in human myopia: insights from OCT imaging." Wiley Online Library, Vol. 102, Issue 3, 2019.
- Pichi, et al. "Choroidal biomarkers." Indian J. of Ophthal., 2018.
- Nickla, et al. "The multifunctional choroid." Progress in retinal and eye research, 2010.
- Mutti, et al. "Myopia - yesterday, today, and tomorrow." Optometry and vision science: official publication of the American Academy of Optometry, 2013.
- Chhablani, et al. "Choroidal imaging: A review." Saudi J. of Ophthal., 2014.

Choroidal thickness (ChT)

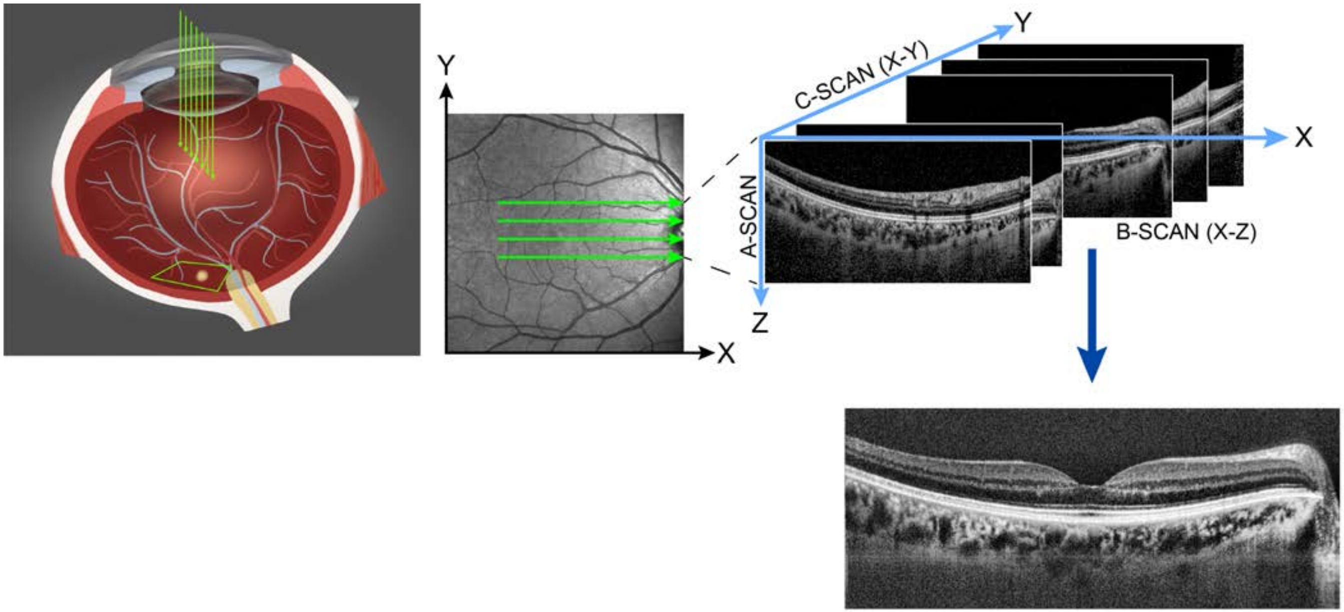
ChT as biomarker in predicting and monitoring myopia



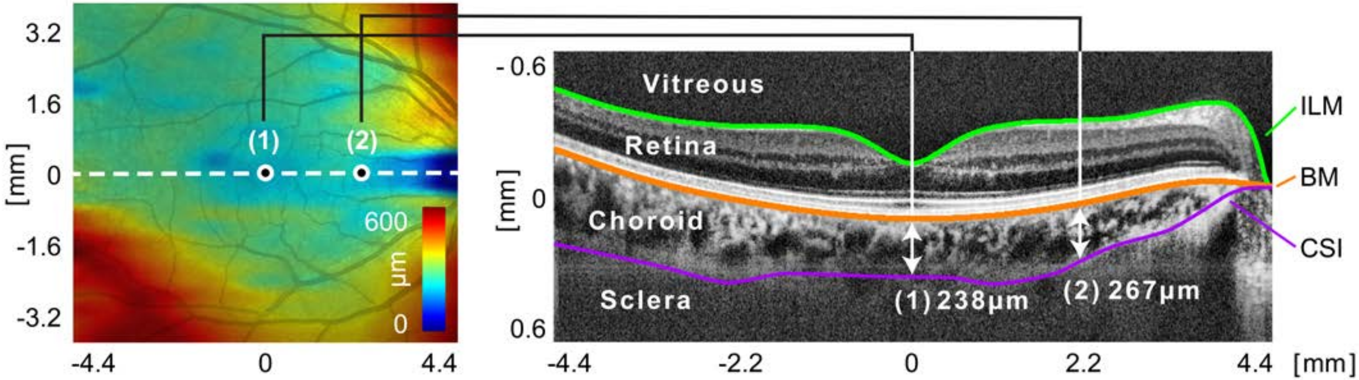
The choroid

- vascular tissue located between the sclera and the retina,
- blood-filled, 0.1 to 0.22 mm thick,
- provides the outer retina with oxygen and metabolites, and
- regulates the temperature and position of the retina.

Image acquisition with OCT



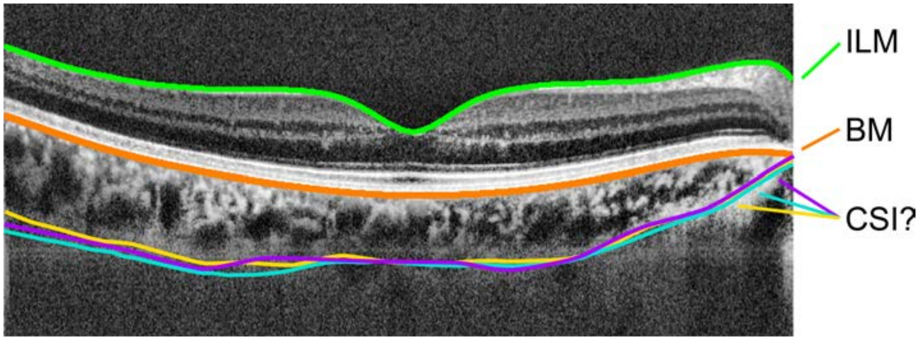
Choroidal thickness map



Thickness of the choroid = distance BM–CSI

Challenge 1

Finding the exact position of the CSI is a major challenge



- poor contrast
- weak signal
- OCT artifacts
- $(\cdots)$

$\Longrightarrow$ *image segmentation not suitable for this task*

Challenge 1

Finding the exact position of the CSI is a major challenge

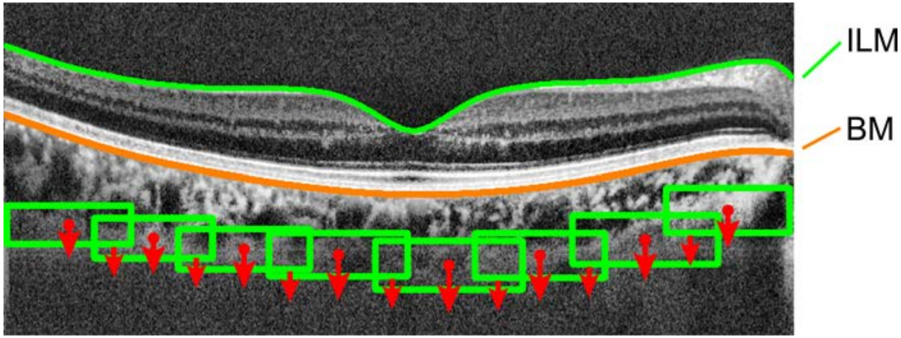
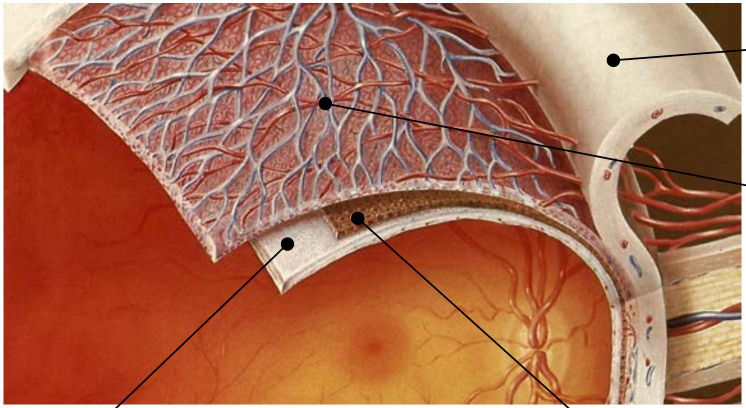


image registration (instead of segmentation)

Challenge 2

Interleaved nature of the human eye

The interleaved nature of the eye must be taken into account

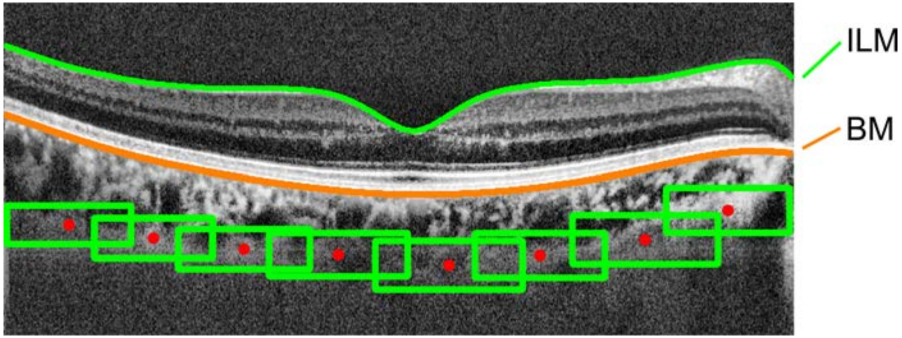


$\Longrightarrow$ *piecewise rigid registration strategy*

Challenge 2

Interleaved nature of the human eye

$\Longrightarrow$ *piecewise rigid registration strategy*



The new approach

- Interleaved nature of the human eye

piecewise rigid image registration eye shape adherent regularization

- Independent on any definition of the CSI

- Uniform smoothness of the results

$\Longrightarrow$ **ICR** $=$ **I**ntensity-based **C**horoidal **R**egistration using regularized block-matching (prototype)

The new approach CRAR

- Interleaved nature of the human eye

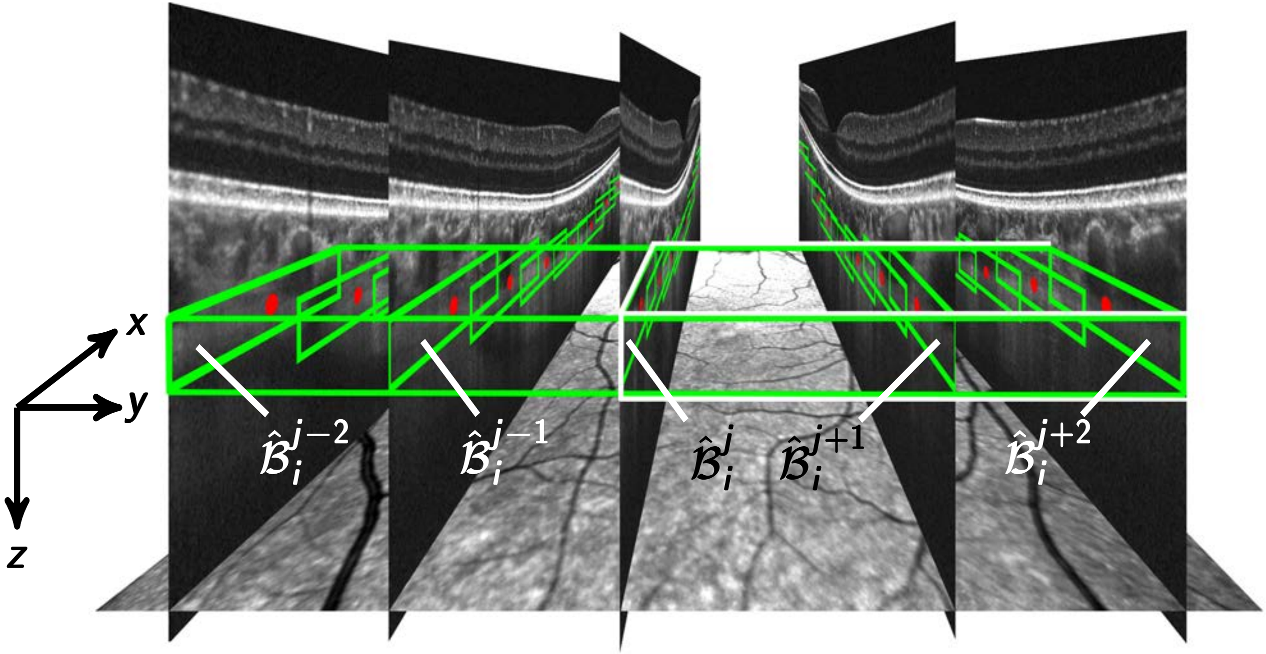
piecewise rigid | image registration | eye shape adherent regularization

- Independent on any definition of the CSI

- Uniform smoothness of the results

$\Longrightarrow$ **CRAR** = **C**horoidal thickness changes detection using piecewise rigid **R**egistration and eye-shape **A**dherent **R**egularization

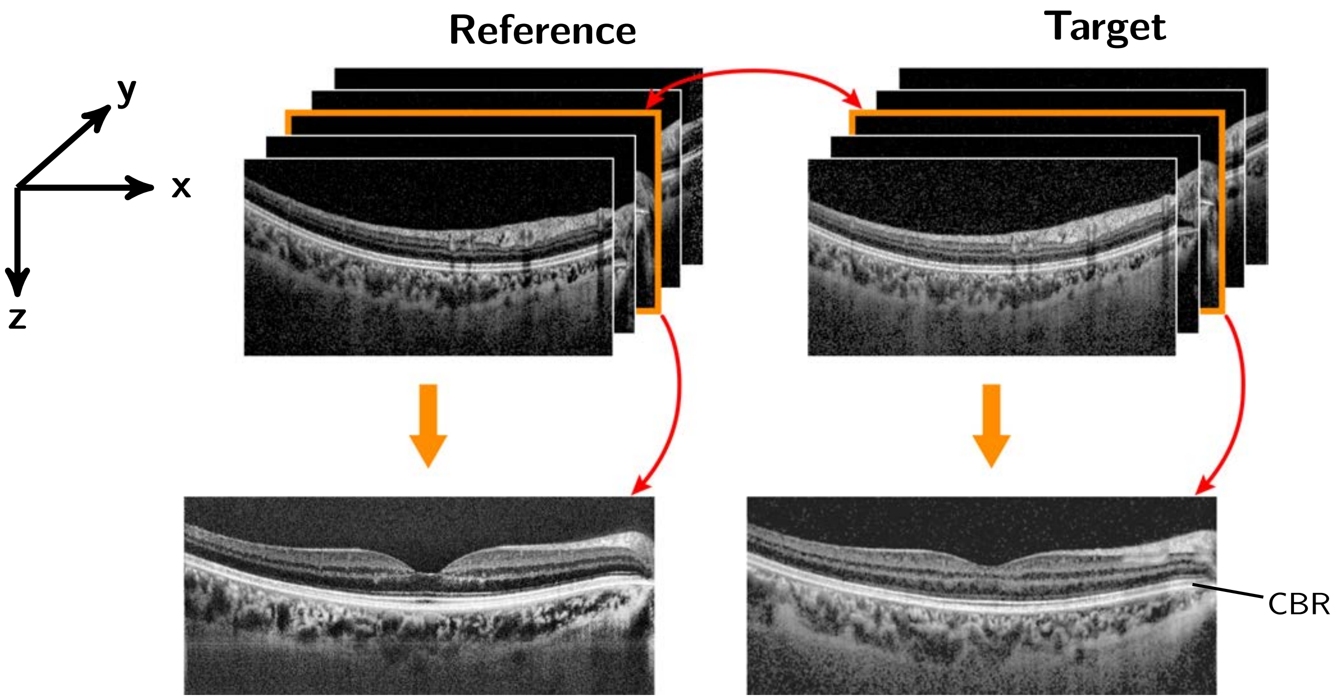
CRAR - 3D overlapping cuboidal blocks



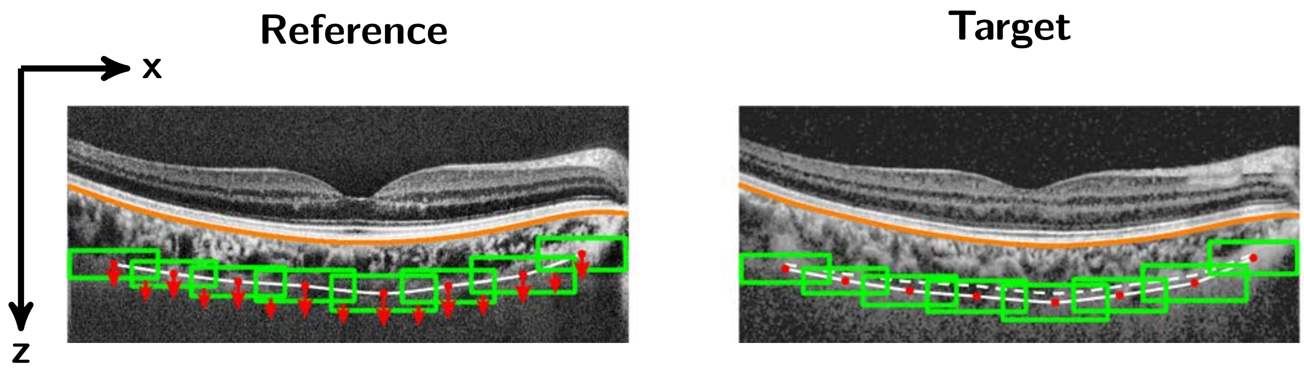
$$\mathcal{C}_i^{s+1} = \hat{\mathcal{B}}_i^{j} \cup \hat{\mathcal{B}}_i^{j+1} \cup \hat{\mathcal{B}}_i^{j+2} \cup \hat{\mathcal{B}}_i^{j+3} \cup \hat{\mathcal{B}}_i^{j+4}$$

(If not noted otherwise, the OCT scans were acquired using the "Hydra-Spectralis," which was developed by the HuCE-optoLab of the Bern University of Applied Sciences, Biel, Switzerland.)

CRAR - 3D piecewise rigid registration

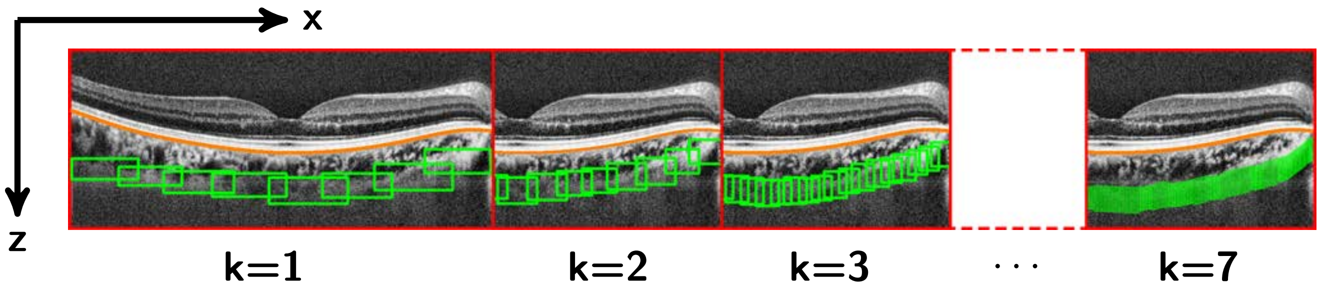


CRAR - 3D piecewise rigid registration



CRAR - 3D piecewise rigid registration

Refinement of the blocks



k: resolution depth level

k=1 $\iff$ 8 blocks (in the x-direction)

k=2 $\iff$ 16 blocks (in the x-direction)

... ...

k=7 $\iff$ 128 blocks (in the x-direction)

Mathematical principle

Image registration as regularized minimization problem

GOAL: find the **displacement field** $\mathcal{U} = \{\psi_{u_i^s}\}$ such that

$$\underset{\psi_{u_i^s} \in \mathcal{U}}{\arg\min} \; \underbrace{\underbrace{\mathcal{D}[I_R, I_T, \psi_{u_i^s}]}_{\textit{dissimilarity}} + \lambda \underbrace{\mathcal{R}[\psi_{u_i^s}]}_{\textit{regularizer}}}_{\textit{energy functional}}$$

where $I_R, I_T : \Omega \to \mathbb{R}^+$, and

$$\mathcal{D}[I_R, I_T, \psi_{u_i^s}] := \underbrace{-\sum_{s=1}^{\bar{S}} \sum_{i=1}^{N} \int_{\hat{\mathcal{C}}_i^s} \frac{\sum_{p \in \hat{\mathcal{C}}_i^s} \left[I_T \circ \psi_{u_i^s}(p) - \mu_T\right]\left[I_R(p) - \mu_R\right]}{\sqrt{\sum_{p \in \hat{\mathcal{C}}_i^s} \left[I_T \circ \psi_{u_i^s}(p) - \mu_T\right]^2} \sqrt{\sum_{p \in \hat{\mathcal{C}}_i^s} \left[I_R(p) - \mu_R\right]^2}}}_{\textit{inverse normalized cross correlation}}$$

Mathematical principle

Image registration as regularized minimization problem

GOAL: find the **displacement field** $\mathcal{U} = \{\psi_{u_i^s}\}$ such that

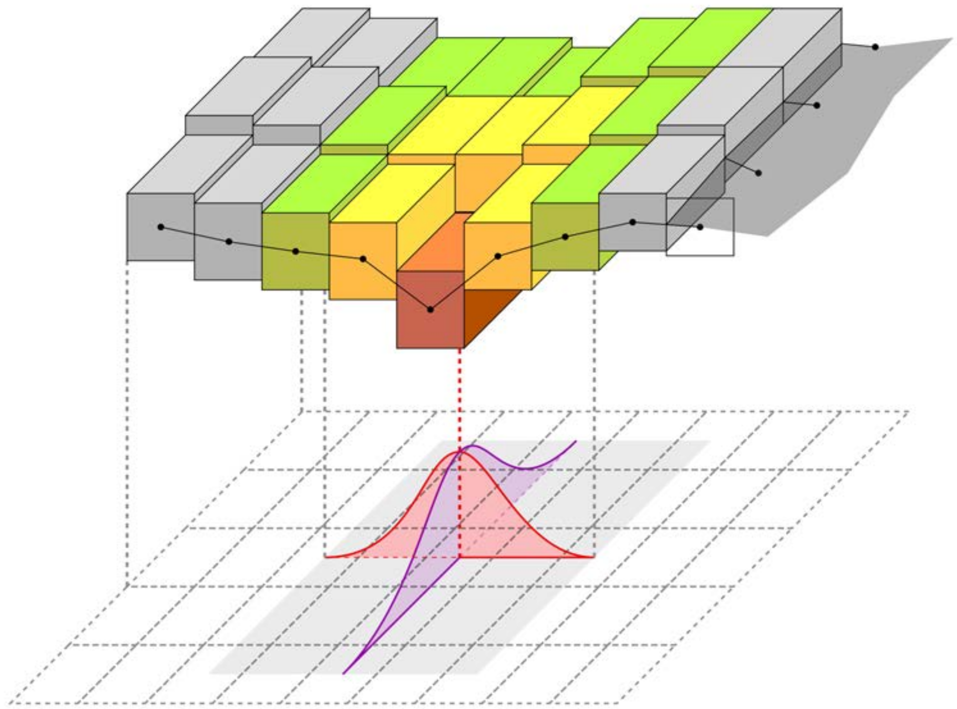
$$\underset{\psi_{u_i^s} \in \mathcal{U}}{\arg\min} \quad \underbrace{\underbrace{\mathcal{D}[I_R, I_T, \psi_{u_i^s}]}_{dissimilarity} + \lambda \underbrace{\mathcal{R}[\psi_{u_i^s}]}_{regularizer}}_{energy\ functional}$$

where $I_R, I_T : \Omega \to \mathbb{R}^+$, and

$$\mathcal{R}[\psi_{u_i^s}] = \frac{1}{\mathcal{N}} \sum_{s,t=1}^{\bar{S}} \sum_{i,j=1}^{N} \left|\left| u_i^s(p_i^s) - u_j^t(p_j^t) \right|\right|^2 \cdot K_b(p_i^s, p_j^t)$$

where $u_i^s(p_i^s)$ and $u_j^t(p_j^t)$ are the displacement vectors of p_i^s and p_j^t, the centers of the blocks $\hat{\mathcal{C}}_i^s$ and $\hat{\mathcal{C}}_j^t$.

CRAR - Eye-shape adherent regularization



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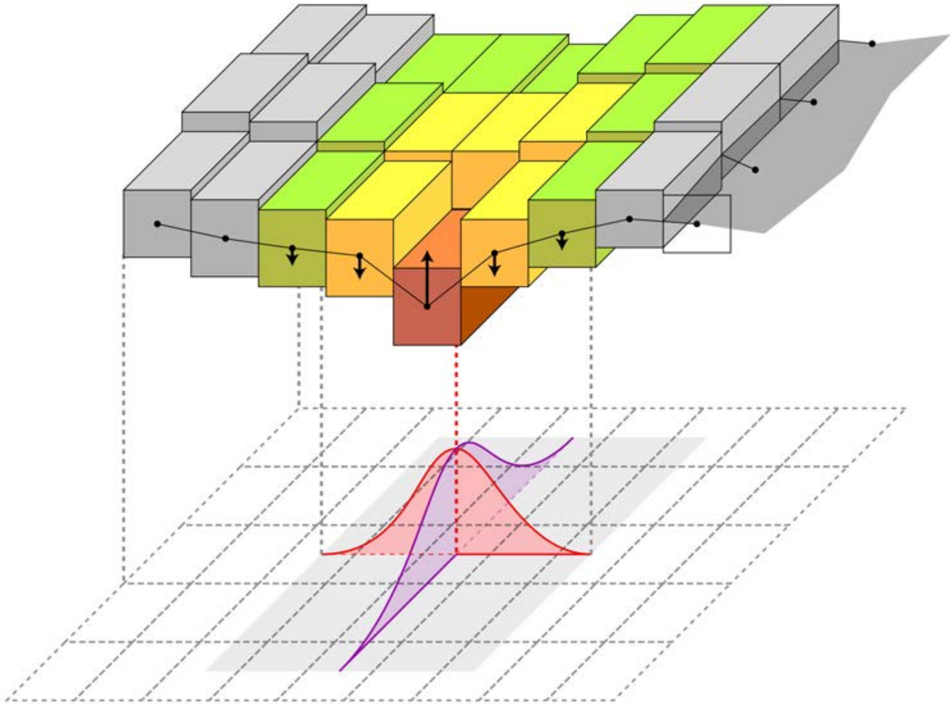
CRAR - Eye-shape adherent regularization



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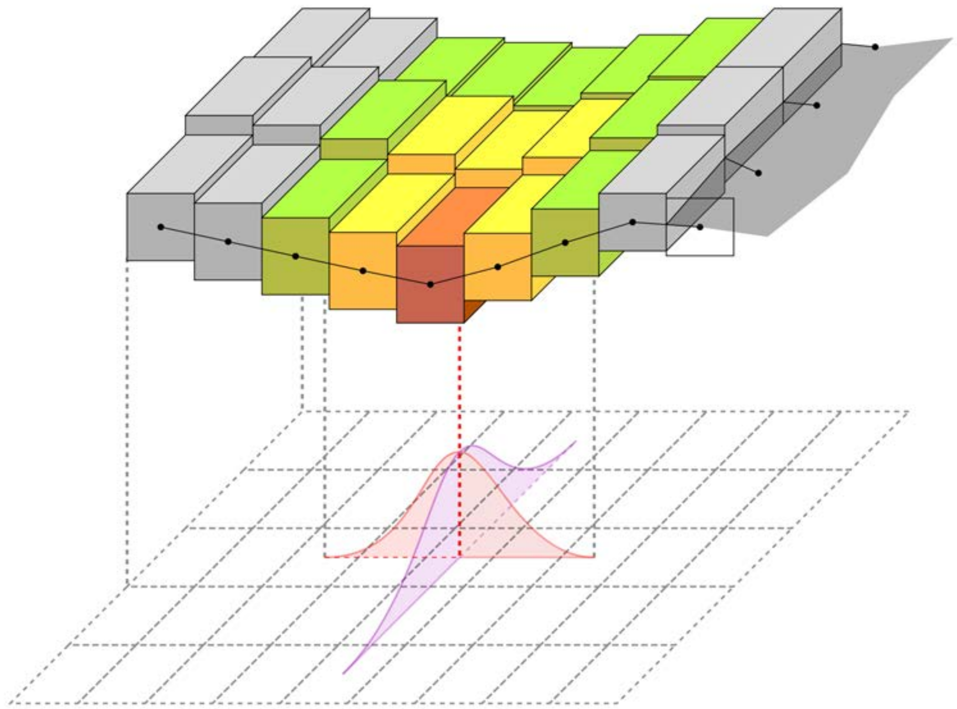
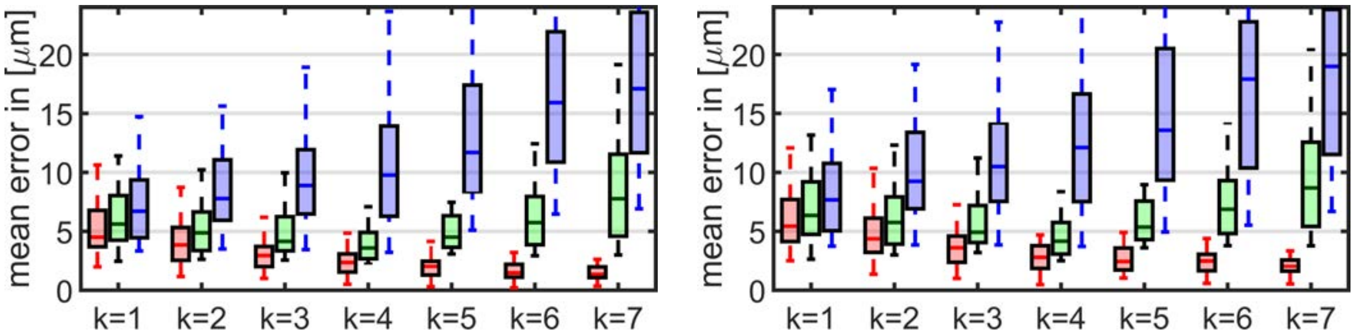
CRAR - Eye-shape adherent regularization



$$\mathcal{R}[\psi_{u_i^s}] = \frac{1}{\mathcal{N}} \sum_{s,t=1}^{\bar{S}} \sum_{i,j=1}^{N} \left|\left|u_i^s(p_i^s) - u_j^t(p_j^t)\right|\right|^2 \cdot K_b(p_i^s, p_j^t)$$

Evaluation of CRAR/1

Displacements by scan-rescan and simulated changes



(a) Scan vs rescan

(b) Artificially modified rescans

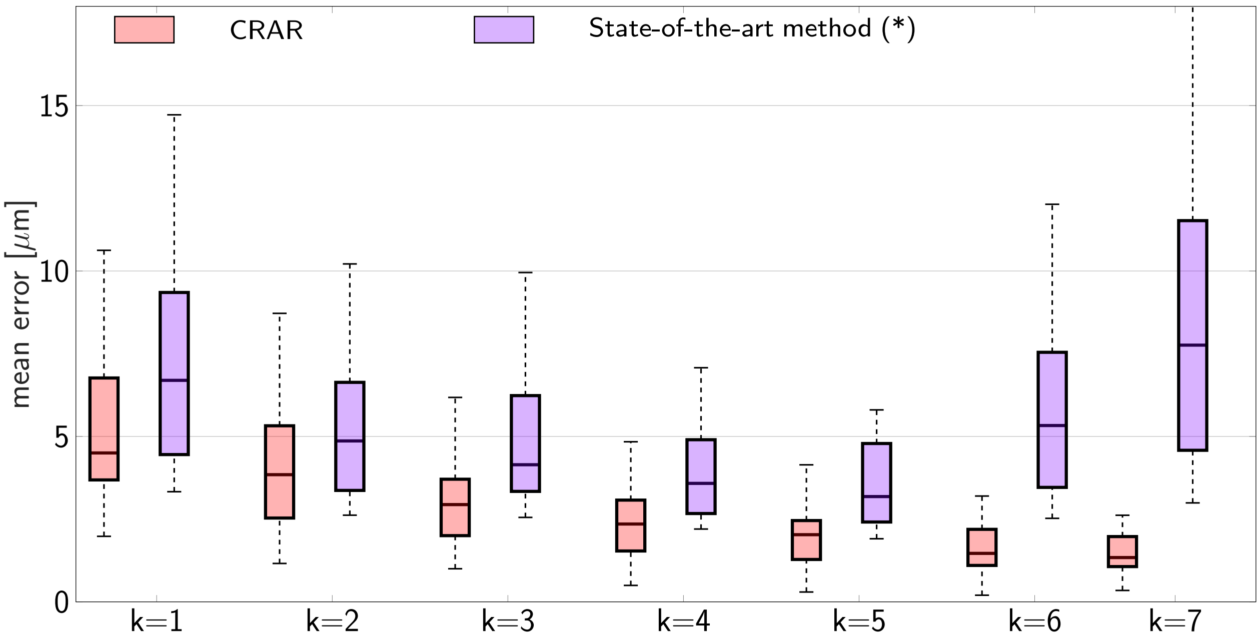
Detection performance:

CRAR (red):	$\lvert\Delta z\rvert < 2\,\mu\text{m}$	(k=7)
ICR (green):	$\lvert\Delta z\rvert > 4\,\mu\text{m}$	(k=4)
Expert (blue):	$\lvert\Delta z\rvert > 7\,\mu\text{m}$	(k=1)

$\Longrightarrow$ **subvoxel accuracy!**

Evaluation of CRAR/2

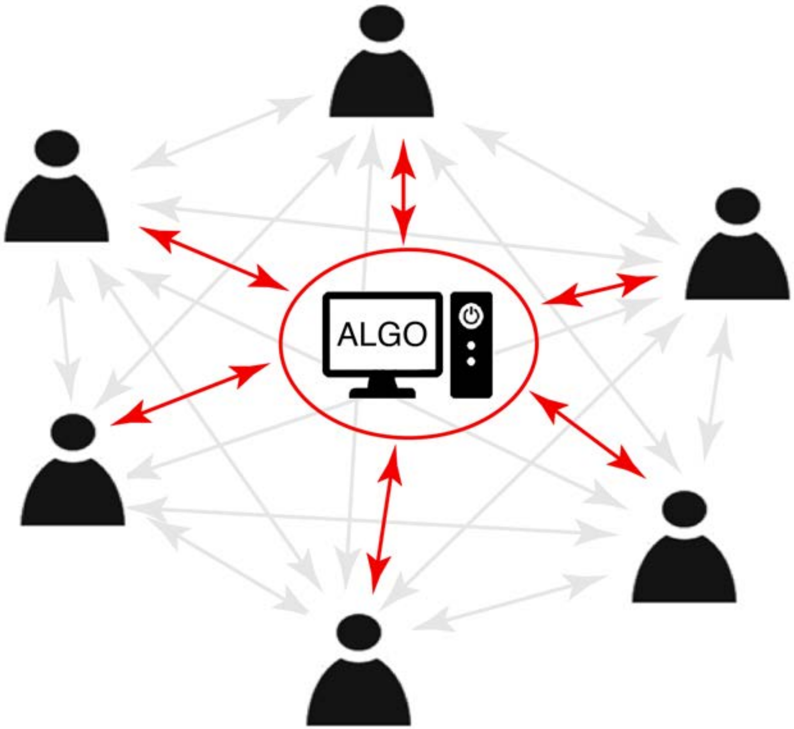
CRAR vs. state-of-the-art method



(* a courtesy of: Mazzaferri, et al. "Open-source algorithm for automatic choroid segmentation of OCT volume reconstructions", Scientific Reports, Vol. 7, p. 42112, 2017.)

Statistical validation framework

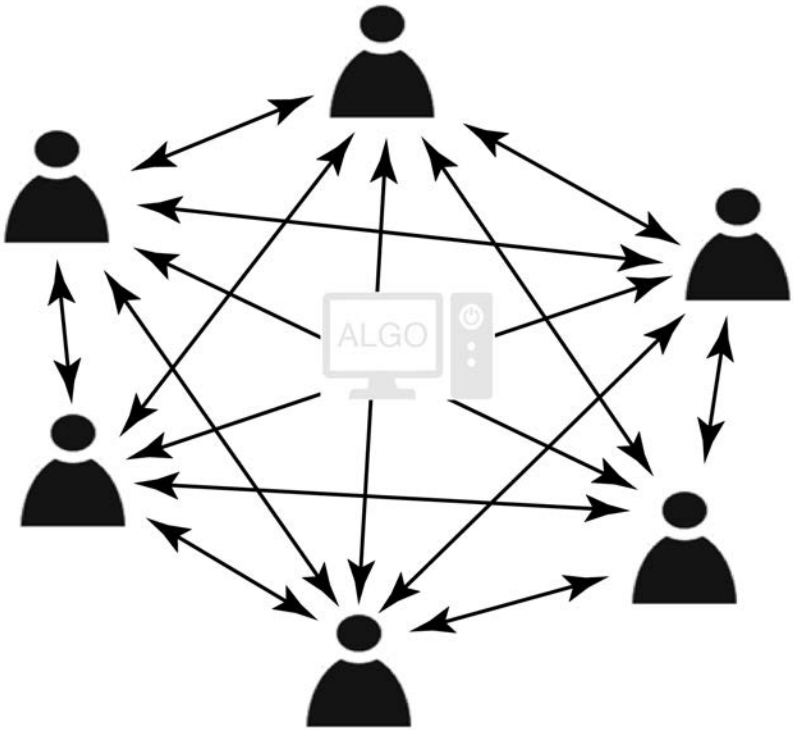
Phase 1: Evaluation based on common agreement using WI_j



$$WI_j = \frac{(r-2)\sum_{j' \neq j}^{r} s(\mathcal{E}_j, \mathcal{E}_{j'})}{2\sum_{j' \neq j}^{r} \sum_{j'' \neq j}^{j'-1} s(\mathcal{E}_{j'}, \mathcal{E}_{j''})}$$

Statistical validation framework

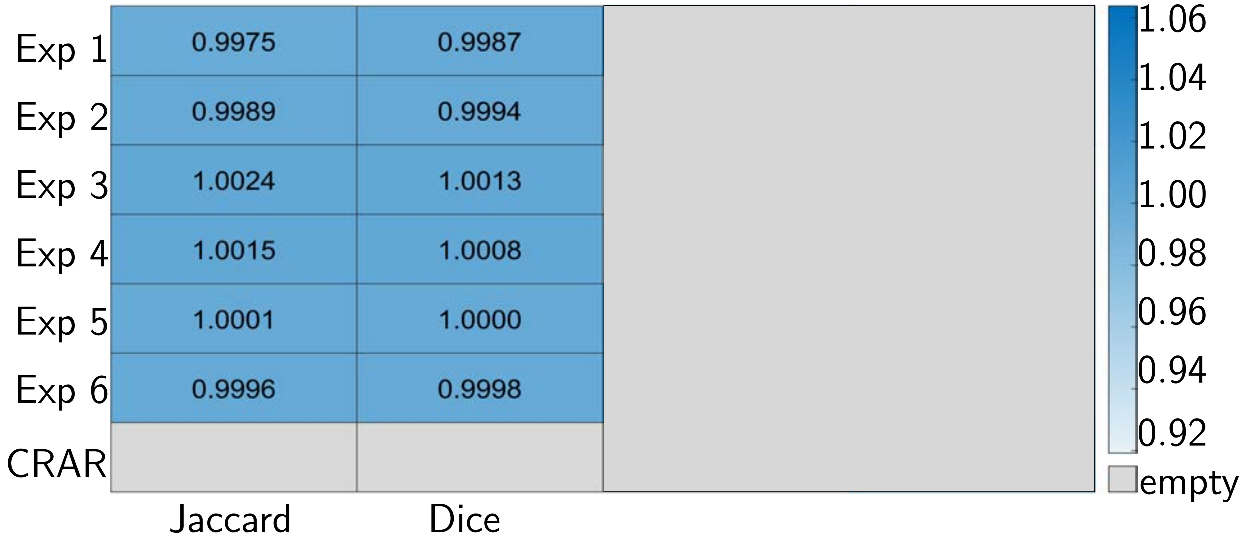
Phase 1: Evaluation based on common agreement using WI_j



$$WI_j = \frac{(r-2)\sum_{j' \neq j}^{r} s(\mathcal{E}_j, \mathcal{E}_{j'})}{2\sum_{j' \neq j}^{r}\sum_{j'' \neq j}^{j'-1} s(\mathcal{E}_{j'}, \mathcal{E}_{j''})}$$

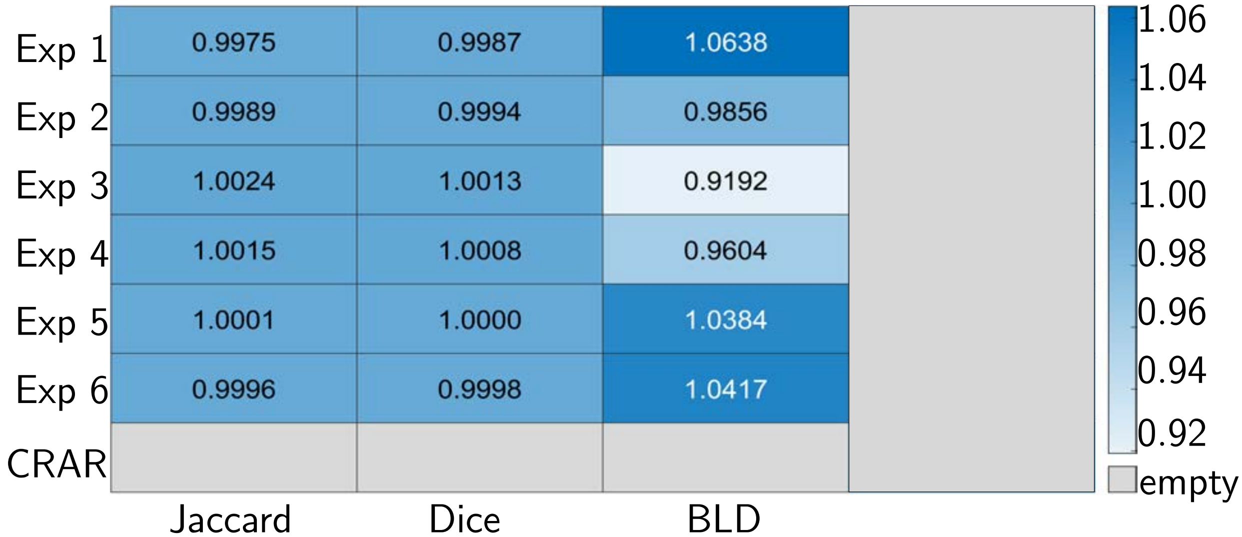
Statistical validation framework

Phase 1: William's index using Jaccard & Dice

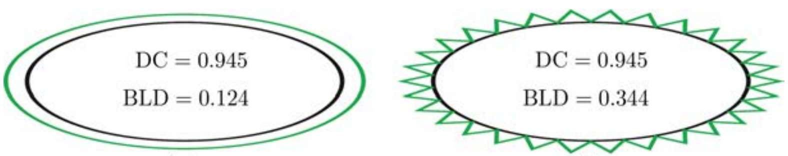


Statistical validation framework

Phase 1: William's index using BLD



$$\mathrm{BLD}(\mathcal{E}_j, \mathcal{E}_{j'}) = \sum_{s=1}^{S} \sum_{p \in \mathcal{E}_j^s} \frac{\mathrm{BLD}(p, \mathcal{E}_{j'}^s)}{n \max_{p \in \mathcal{E}_j^s} \{\mathrm{BLD}(p, \mathcal{E}_{j'}^s)\}}$$



(a) (b)

Statistical validation framework

Phase 1: William's index using diffZ

	Jaccard	Dice	BLD	diffZ
Exp 1	0.9975	0.9987	1.0638	1.0254
Exp 2	0.9989	0.9994	0.9856	1.0257
Exp 3	1.0024	1.0013	0.9192	0.9535
Exp 4	1.0015	1.0008	0.9604	0.9895
Exp 5	1.0001	1.0000	1.0384	0.9810
Exp 6	0.9996	0.9998	1.0417	0.9974
CRAR				

$$\mathrm{diffZ}(\Delta\mathcal{E}_j, \Delta\mathcal{E}_{j'}) = 1 + \frac{\sum_{s=1}^{S}\sum_{i=1}^{n}\left|\Delta\mathcal{E}_j^s(i) - \Delta\mathcal{E}_{j'}^s(i)\right|}{mnS}$$

Statistical validation framework

Phase 1: William's index using diffZ

	Jaccard	Dice	BLD	diffZ
Exp 1	0.9975	0.9987	1.0638	1.0254
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Exp 5	1.0001	1.0000	1.0384	0.9810
Exp 6	0.9996	0.9998	1.0417	0.9974
CRAR				

$\Longrightarrow$ average $WI_j = 0.9992 \pm 0.0221$

Statistical validation framework

Phase 1: William's index using diffZ

$\Longrightarrow$ *WI_j is independent of the choice of the similarity measure*

Statistical validation framework

Phase 1: William's index using diffZ

$\Longrightarrow$ *CRAR performs at the level of an expert*

Statistical validation framework

Phase 2: Adapted power analysis with leave-one-out cross validation

Artificial ground truth $\overline{\mathcal{G}}_j$ (after leaving out the results of expert j)

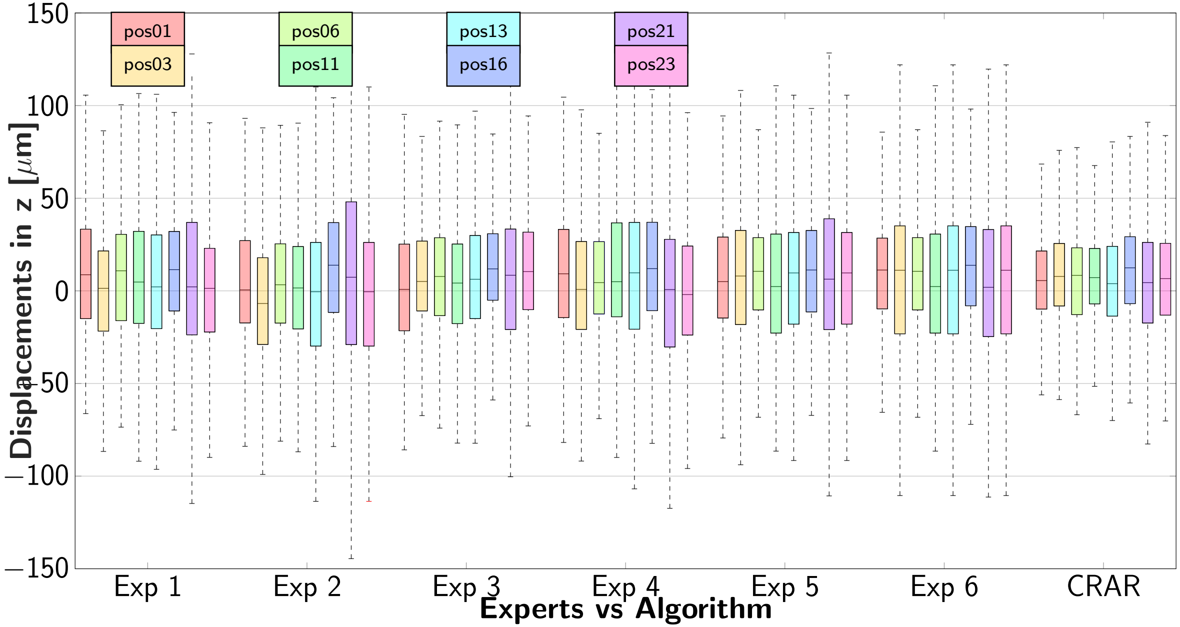
$$\overline{\mathcal{G}}_j = \frac{1}{r-1} \sum_{j' \neq j}^{r} \Delta\mathcal{E}_{j'}, \quad \text{for all} \;\; \Delta\mathcal{E}_{j'} \in \Delta\mathcal{E} \setminus \{\Delta\mathcal{E}_j\},$$

Paired t-test is performed to compare the errors of algo and expert,
i.e. $X_j = X - \overline{\mathcal{G}}_j$ and $Y_j = \Delta\mathcal{E}_j - \overline{\mathcal{G}}_j$

$\Longrightarrow$ p-value < 0.01, $\text{Cohen's } d \in [0.41; 0.49]$ (medium-large effect)
where $\text{Cohen's } d_j = \dfrac{\mu(X_j) - \mu(Y_j)}{\sqrt{\mathcal{S}}}$

$\Longrightarrow$ CRAR shows a superior detection-performance than the experts

Clinical applicability of CRAR

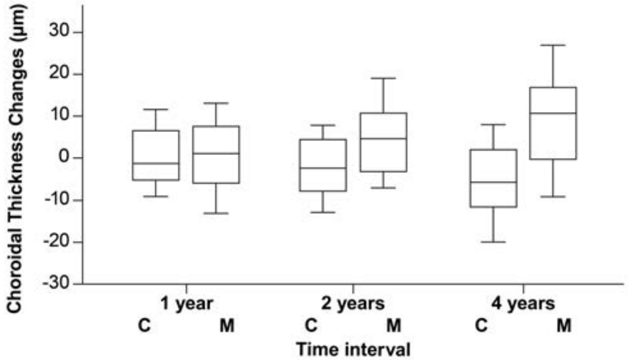


Detected ChT changes grouped by expert and CRAR per scan position

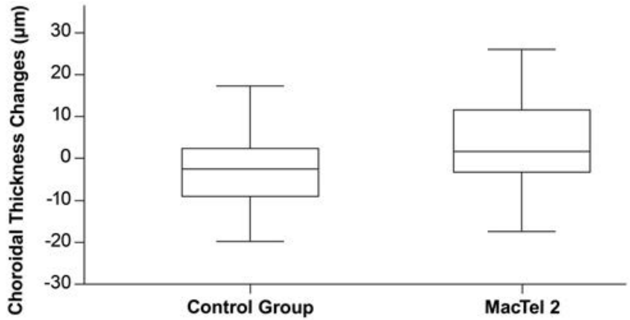
Macular Telangiectasia Type 2 (MacTel2)

Feasibility study - Our main findings

Goal: *To evaluate the impact of ChT over time on MacTel2*



Subfoveal ChT per time interval
(M=MacTel 2, C=Control group)



Total subfoveal ChT

Macular Telangiectasia Type 2 (MacTel2)

Feasibility study - Our main findings

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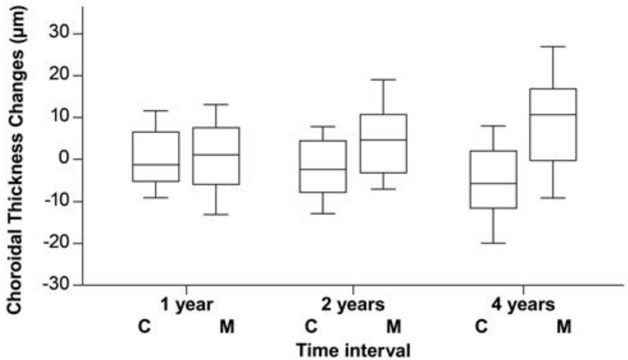

Subfoveal ChT per time interval

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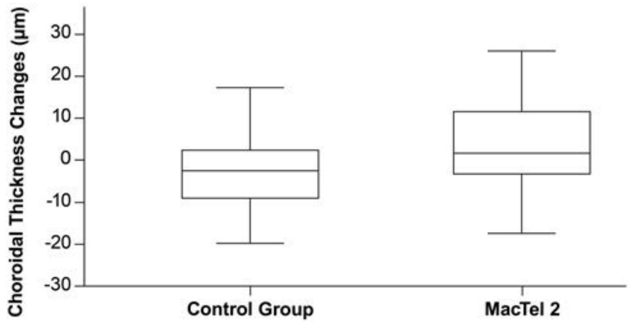

Total subfoveal ChT

$\Longrightarrow$ *A thickened choroid may be a valuable diagnostic and monitoring clue in identifying MacTel2*

Achievements - 1^{st} publication

- Low SNR tackled

Achievements - 1^{st} publication

- Low SNR tackled
- Interleaved nature taken into account

Achievements - 2^{nd} publication

- Low SNR tackled
- Interleaved nature taken into account
- 3D-volumetric analysis performed

Achievements - 2^{nd} publication

- Low SNR tackled
- Interleaved nature taken into account
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- Adherence to the natural eye shape

Achievements - 2^{nd} publication

- Low SNR tackled
- Interleaved nature taken into account
- 3D-volumetric analysis performed
- Adherence to the natural eye shape
- Subvoxel accuracy achieved

Achievements - 3^{rd} publication

- Low SNR tackled
- Interleaved nature taken into account
- 3D-volumetric analysis performed
- Adherence to the natural eye shape
- Subvoxel accuracy achieved
- Lack of a real ground truth solved

Achievements - 3^{rd} publication

- Low SNR tackled
- Interleaved nature taken into account
- 3D-volumetric analysis performed
- Adherence to the natural eye shape
- Subvoxel accuracy achieved
- Lack of a real ground truth solved
- Sensitive progress indicator for myopia

Achievements - 4^{th} publication

- Low SNR tackled
- Interleaved nature taken into account
- 3D-volumetric analysis performed
- Adherence to the natural eye shape
- Subvoxel accuracy achieved
- Lack of a real ground truth solved
- Sensitive progress indicator for myopia
- Extended applicability

Publications

Iowa Research Online
University of Iowa
Iowa Research Online

Proceedings of the Ophthalmic Medical Image Analysis International Workshop
2016 Proceedings

Intensity-based Choroidal Registration Using Regularized Block Matching

Tiziano Ronchetti[1,2], Peter Maloca[3], Christoph Meier[2], Selim Orgül[3], Christoph Jud[1], Pascal Hasler[3], Boris Považay[2], and Philippe C. Cattin[1]

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X. Chen, M. K. Garvin, J. Liu, E. Trucco, Y. Xu (Eds.): OMIA 2016, Held in Conjunction with MICCAI 2016, Athens, Greece, Iowa Research Online, pp. 33–40, 2016. Available from: http://ir.uiowa.edu/omia/2016_Proceedings/2016/

Lecture Notes in Computer Science

Detecting Early Choroidal Changes Using Piecewise Rigid Image Registration and Eye-Shape Adherent Regularization

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M.J. Cardoso et al. (Eds.): FIFI/OMIA 2017, LNCS 10554, pp. 92–100, 2017.
DOI: 10.1007/978-3-319-67561-9_10

PLOS | ONE

RESEARCH ARTICLE

Statistical framework for validation without ground truth of choroidal thickness changes detection

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Feasibility Study of Subfoveal Choroidal Thickness Changes in Spectral-Domain Optical Coherence Tomography Measurements of Macular Telangiectasia Type 2

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Future Work

- Computational time
- Longitudinal study on changes in the ChT and the onset of myopia
- Impact of the subfoveal ChT on MacTel2
- Thickness changes in intraretinal layers (e.g. to monitor glaucoma)
- CRAR in other fields of medicine (e.g. dermatology)
- Development of a synthetic ground

Conclusions

A new method CRAR was developed, a sensitive progression indicator for unsupervised automated detection of choroidal changes to reliably predict and monitor eye disorders and diseases with subvoxel accuracy.

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