# INPLASY PROTOCOL

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**Conflicts of interest:**
**None declared.**

# Diagnostic test accuracy of spectral-domain optical coherence tomography used to Differentiate PCV from nvAMD and other diseases that tend to cause serous or serosanguinous retinal pigment epithelial detachment: a systematic review protocol

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**Review question / Objective:** **This systematic review aims to evaluate the diagnostic value of spectral-domain optical coherence tomography (SD-OCT) in terms of sensitivity and specificity in differentiating PCV from other lesions causing serous or serosanguinous retinal pigment epithelial detachment (PED), especially neovascular age-related macular degeneration (nvAMD). To this end, the proposed systematic review will include the following aspects: 1. Types of participants: Our study will include a broader treatment-naive group of serous or serosanguinous macular retinal pigment epithelium detachment (PED), including PCV and nvAMD other diseases. 2. Types of interventions: In this study, PCV is identified by SD-OCT. 3. Types of Comparisons: Patients with diagnosed serious or serosanguinous maculopathy, including nvAMD, central serous chorioretinopathy(CSC), occult choroidal neovascularization (occult CNV), or retinal angiomatous proliferation (RAP), will be eligible for comparisons. 4. Types of outcome measures: The following outcomes will be eligible for inclusion. Pooled sensitivity and specificity; pooled positive and negative likelihood ratio; pooled diagnostic odds ratio (DOR); the area under the src curve (AUC); clinical application value; literature quality; the primary source of heterogeneity; publication bias.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 December 2021 and was last updated on 09 December 2021 (registration number INPLASY2021120048).

## INTRODUCTION

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causing serous or serosanguinous retinal pigment epithelial detachment (PED), especially neovascular age-related macular degeneration (nvAMD). To this end, the proposed systematic review will include the following aspects: 1. Types of participants: Our study will include a broader treatment-naive group of serous or serosanguinous macular retinal pigment epithelium detachment (PED), including PCV and nvAMD other diseases. 2. Types of interventions: In this study, PCV is identified by SD-OCT. 3. Types of Comparisons: Patients with diagnosed serious or serosanguinous maculopathy, including nvAMD, central serous chorioretinopathy(CSC) , occult choroidal neovascularization (occult CNV), or retinal angiomatous proliferation (RAP), will be eligible for comparisons. 4. Types of outcome measures: The following outcomes will be eligible for inclusion. Pooled sensitivity and specificity; pooled positive and negative likelihood ratio; pooled diagnostic odds ratio (DOR); the area under the src curve (AUC); clinical application value; literature quality; the primary source of heterogeneity; publication bias.

**Rationale:** The indocyanine green angiography(ICGA)has been proved to be the gold standard for diagnosing PCV. However, ICGA is an invasive and expensive test, and some patients are forbidden to use ICGA due to impaired liver and kidney function, contrast agent allergy, and pregnancy. In addition, equipment limitations in developing countries also result in limited clinical application.SD-OCT can display the structure of the macular area at the cross-section. In addition, it has the advantages of being non-invasive, convenient, economical, so it is gradually applied in clinical PCV. Different studies use their respective SD-OCT diagnostic strategies to diagnose PCV. sensitivity and specificity are different, and no study has summarized and analyzed these data to reach a unified conclusion. Therefore, we conducted a systematic review and meta-analysis to explore the diagnostic value of SD-OCT in PCV lesions.

**Condition being studied:** Polypoidal choroidal vasculopathy (PCV) usually occurs in Asia, and the fundus presents orange-red retinal lesions. Recurrent serous or serosanguinous retinal pigment epithelial detachment (PED) is often associated with retinal hemorrhage or exudation in the macular region that severely impair visual function. Over the past, many scholars believed that PCV is a subtype of neovascular age-related macular degeneration (nvAMD). Still, a series of significant differences exist in pathogenesis, clinical features, the natural course of the disease, and prognosis, especially in terms of treatment response. So it is essential to identify PCV at the early stage.

## METHODS

**Search strategy:** We will select the pieces of literature from Pubmed, Embase, Cochrane, Web of Science, CNKI, Wanfang, VIP, CBM, and other databases during 2010-2021, and we will retrieve relevant Chinese and English literature. This operation will be carried out by combining MeSH and keywords. The search MeSH is "Polypoidal choroidal vasculopathy," The search keyword is "PCV."The search MeSH is "tomography, optical coherence," The search keyword is "coherence tomography, optical" " OCT tomography," " tomography, OCT," "optical coherence tomography," "spectral-domain optical coherence tomography," " spectral-domain optical coherence tomography," " SD-OCT." The search keyword is "Sensitivity and Specificity," "Predictive value of Tests," "Accuracy." One author (JY) implements the policy, the other author (QSX) reviews the policy independently, and the decision is made through open consultation when the two authors disagree.

**Participant or population:** Cases of PCV confirmed by ICGA and or included in the diagnostic criteria by fundus fluorescein angiography (FFA) will be mainly included. Each patient who has undergone SD-OCT or any angiography suggests serous or serosanguinous retinal pigment epithelial

detachment in the macular area, including nvAMD, CSC, RAP, and occult CNV also be included. Patients with no exclusions based on ethnicity or age will be eligible for this review.The exclusion criteria are that subjects suffered from other common ocular diseases, such as pathological myopia, diabetic retinopathy, and retinal artery or vein occlusion. The subjects who had low visual acuity, poor fixation, severe refractive interstitial opacity, and severe subretinal hemorrhage, which resulted in poor quality of SD-OCT images, will also be excluded. At least the suffered eye has received any treatment be excluded.

**Intervention:** Interventions will include all participants receiving ICGA and SD-OCT independently to confirm PCV.If possible, patients can take FFA or fundus photography and other examinations simultaneously to confirm or differentiate the diagnosis.

**Comparator:** The diseases identified with PCV in this study include other conditions that cause macular serous or serosanguinous retinal pigment epithelium detachment, such as nvAMD, CSC, RAP, and occultCNV.

**Study designs to be included:** This study is a prospective observational study. Some patients suspected of PCV will be randomly selected to undergo OCT and gold standard test successively and be divided into the test group and control group according to the gold standard test results.

**Eligibility criteria:** We will search all the Chinese and English literature published in the above databases from 2010 to 2021 or obtained through other means (trial registers or grey literature). We will select the kinds of literature according to the inclusion and exclusion criteria. We performed a sensitivity analysis to ensure no significant bias risk.

**Information sources:** We will search published literature from Pubmed, Embase, Cochrane, Web of Science, CNKI, Wanfang, VIP, China Biomedical Literature Database (CBM), and other databases. Simultaneously, we will search unpublished literature in the Chinese Clinical Trial Registry database and Clinical trials gov (National Institutes of Health, NIH) database. We should also perform additional sources, including manual search, conference summary, contact with the author.

**Main outcome(s):** Sensitivity and specificity of the diagnostic test; The clinical application value of the diagnostic test; Evaluate the bias risk of the included literature according to the "QUADAS-2 Scale." Whether there is heterogeneity in this study ,If there is significant heterogeneity, the source of heterogeneity will be analyzed by meta-regression and subgroup analysis. Sensitivity analysis and publication bias tests.

**Quality assessment / Risk of bias analysis:** We will evaluate the bias risk of the literature according to the "QUADAS-2 Scale".The QUADAS-2 tool mainly consists of four parts: Case selection, trials to be evaluated, gold criteria, and case flow and progress, all components will be assessed for risk of bias, and the first three components will be reviewed for clinical applicability. We can determine the risk level of discrimination as "low," "high," or "uncertain" according to the answers of "yes," "no," or "uncertain" to the relevant landmark questions included in each part. If the answer to all landmark questions within a range is "yes," it can be rated as low bias risk; If any one of the answers to all informatization questions is "no," it is considered as high risk; "uncertain" grading means that there is no explicit content in the literature which makes it difficult for the evaluator to make a judgment; if one answer is "uncertain," the risk assessment is not clear.

**Strategy of data synthesis:** We will use the Review ManagerV5.3 software (Cochrane Collaboration, London, United Kingdom) to evaluate the bias risk of the included literature. Meta Disc 1.4 software (Clinical Biostatistics Team of the Ramon Y Cajal Hospital, Madrid, Spain) will be used for Meta-analysis. First, the Spearman

correlation coefficient between the logarithm of sensitivity and the logarithm of (1-specificity) will be calculated, drawing the sROC curve. If the sROC curve is a typical "shoulder arm" distribution or the Spearman correlation coefficient is strongly positive, it suggests the existence of threshold effect heterogeneity. Cochran-Q test and I 2 will be further used to analyze non-threshold effect heterogeneity among studies. If the included studies have no statistical heterogeneity (P > 0.05, I2 < 50%), A fixed-effect model (Mantel - Haenszel Method) will be used to pool and analyze the effect sizes. Instead, a random-effect model (DerSimonian - Laird method) is used. Then the sensitivity (Se), specificity (Sp), positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnosis odds ratios (DOR) will be calculated. At the same time, we will draw the sROC curve and calculate the area under the curve (AUC). If the heterogeneity is substantial, we will conduct meta-regression analysis to analyze the source of heterogeneity and further subgroup analysis. We will draw Fagan diagrams using Stata V15.0 software (StataCorp LLC, Texas, America), and sensitivity analysis and Deeks publication bias test will be performed.

**Subgroup analysis:** If the heterogeneity is substantial, the source of heterogeneity will be analyzed by meta-regression, and subgroup analysis will be conducted step by step according to the influence factors shown by meta-regression.

**Sensitivity analysis:** We use Stata V15.0 software for sensitivity analysis. If the sensitivity analysis results show that removing individual original studies one by one does not significantly affect the calculation results, the results can be considered morerobust.

**Language:** Only clinical trials published in English and Chinese will be considered for inclusion.

**Country(ies) involved:** The systematic review is being carried out in China.

**Keywords:** Spectral-domain optical coherence tomography; Polypoid choroidal vasculopathy; Sensitivity; Specificity; Diagnostic value; Meta-analysis.

**Contributions of each author:**

Author 1 - Jiang Yang - The contributions of the first author to the review include conceiving the review, designing the review, data collection, data management, analysis of data, interpreting data, and drafting the manuscript.
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Author 2 - Qi Shixin - The contributions of the second author to the review include data collection, data management, quality assessment, manuscript editing.
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