Diagnostic Studies
SDOCT Retinal Nerve Fiber Layer

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Diagnosing Preperimetric Glaucoma with Spectral Domain Optical Coherence Tomography

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- **134 glaucoma suspects followed for average of 14 ± 3.6 years**
  - **42 progressive GON (photos)**
  - **86 control eyes (no progression followed untreated)**

Ophthalmology 2012 (E-pub ahead of publication)

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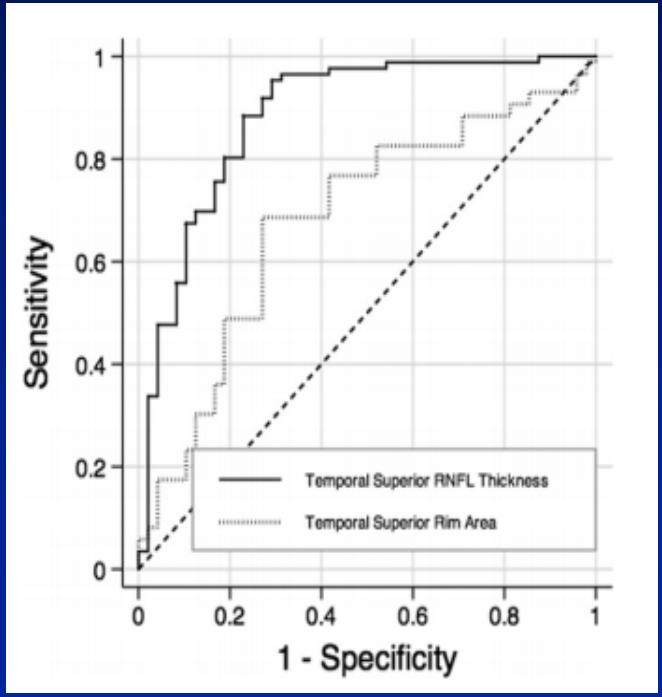
RNFL parameters performed significantly better than topographic disc parameters for diagnosing damage in suspects

ROC area SDOCT average thickness = 0 .86

ROC area HRT rim area = 0.72

Sector	SD-OCT	CSLO	*P* Value
Temporal superior	0.88±0.03	0.68±0.05	0.001
Temporal inferior	0.81±0.04	0.64±0.05	0.01
Nasal superior	0.73±0.05	0.67±0.05	0.40
Nasal	0.70±0.05	0.66±0.05	0.52
Nasal inferior	0.68±0.04	0.61±0.05	0.27
Temporal	0.62±0.05	0.60±0.05	0.75

CSLO = confocal scanning laser ophthalmoscopy; SD-OCT = spectral domain optical coherence tomography.



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RNFL versus optic disc topography

- In clinical practice, patients are usually referred as suspected of having glaucoma because of suspicious rim thinning or large cups

- In this situation, RNFL parameters seem to offer more benefit as a complementary test to clinical examination

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Comparison of the Diagnostic Accuracies of the Spectralis, Cirrus, and RTVue Optical Coherence Tomography Devices in Glaucoma

Mauro T. Leite, MD,[1,2] Harsha L. Rao, MD,[1,3] Linda M. Zangwill, PhD,[1] Robert N. Weinreb, MD,[1] Felipe A. Medeiros, MD, PhD[1,2]

- **138 eyes with glaucomatous visual field defects**
- **106 healthy eyes**
- **Diagnostic accuracies of the 3 SDOCT instruments**

Ophthalmology 2011;118:1334–1339

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Comparison of Cirrus HDOCT, RTVue and Spectralis

Areas under ROC curves

	Spectralis	Cirrus	RTVue
Global RNFL thickness	0.862	0.864	0.844
Inferior thickness	0.837	0.849	0.846
Superior thickness	0.865	0.863	0.841

Ophthalmology 2011;118:1334–1339

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Diagnostic Studies of RNFL parameters

- Diagnostic accuracy estimates obtained from "conventional studies" (healthy versus glaucomatous field loss) are similar to those estimates obtained from cohort studies of suspects

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Disease severity still affects accuracy of RNFL parameters…

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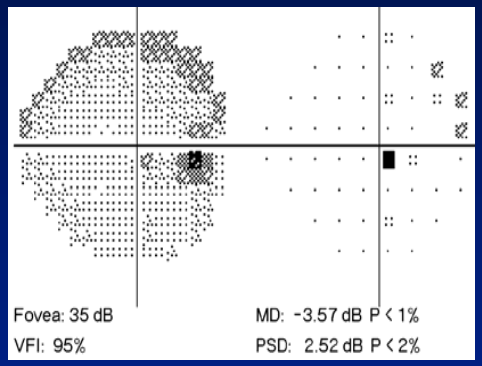
Glaucoma

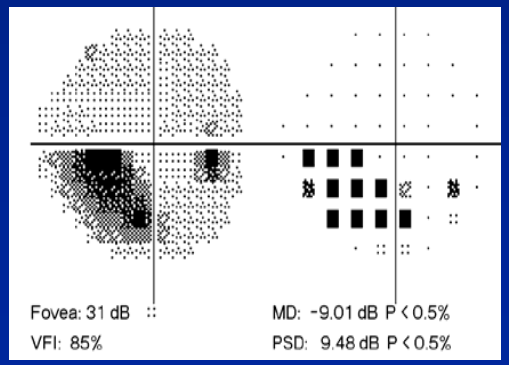
Effect of Disease Severity on the Performance of Cirrus Spectral-Domain OCT for Glaucoma Diagnosis

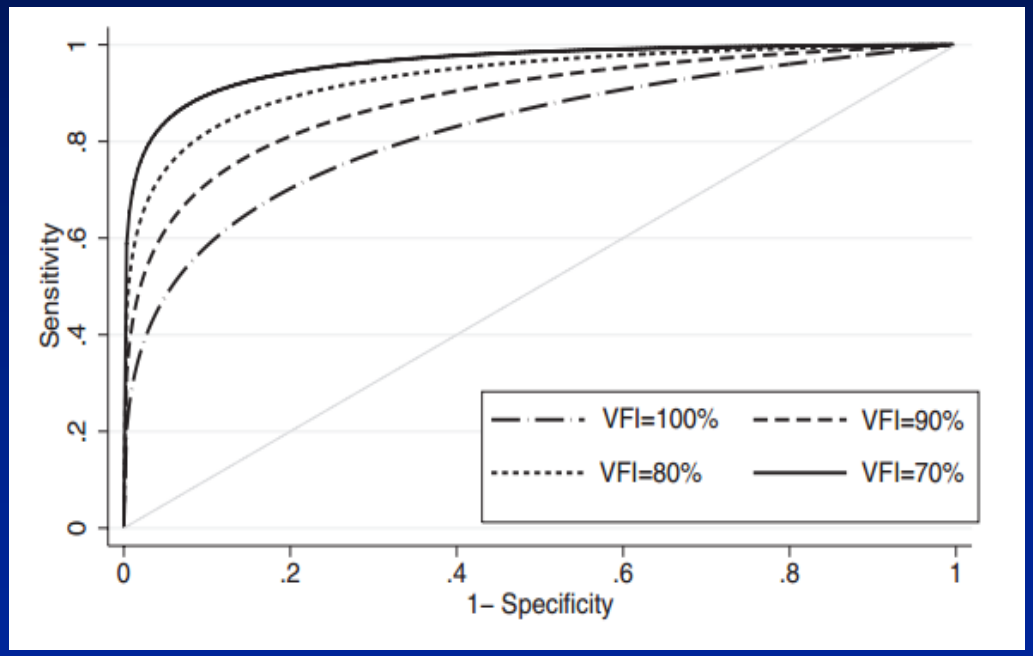
Mauro T. Leite,[1,2] Linda M. Zangwill,[1] Robert N. Weinreb,[1] Harsha L. Rao,[1,3] Luciana M. Alencar,[1,4] Pamela A. Sample,[1] and Felipe A. Medeiros[1,2]

VFI = 95%



VFI = 85%





IOVS 2010;51:4104–4109

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Areas under ROCs for different levels of disease severity (SDOCT)

	RNFL thickness		
VFI	**Global**	**Inferior**	**Superior**
100%	0.822	0.851	0.812
90%	0.886	0.871	0.874
80%	0.932	0.920	0.921
70%	0.962	0.954	0.952

IOVS 2010;51:4104–410

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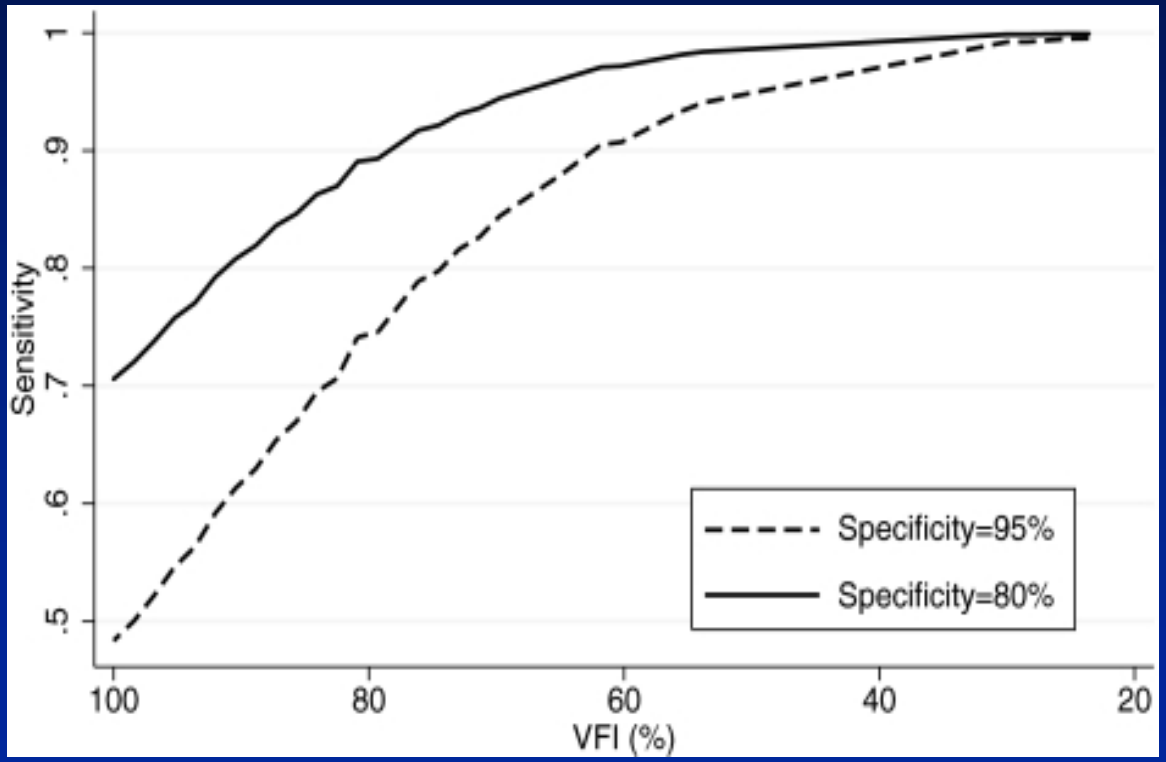

IOVS 2010;51:4104–4109

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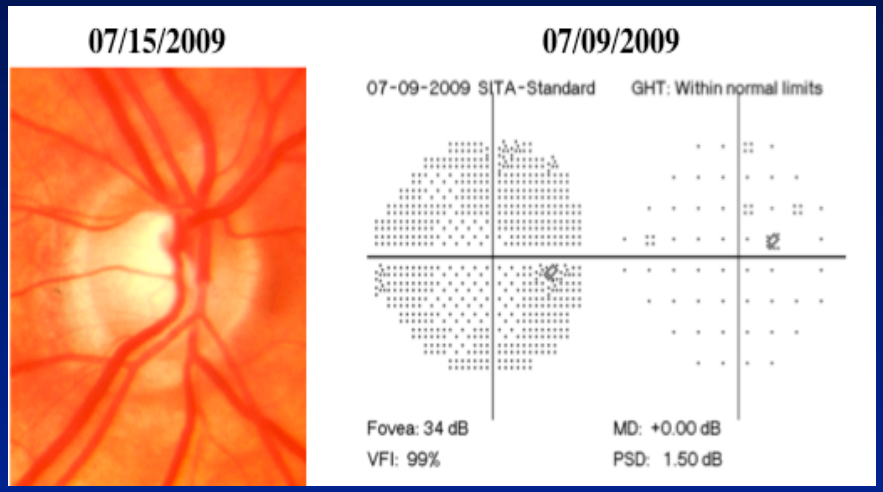
Does SDOCT RNFL assessment assist in glaucoma diagnosis?

"Diagnosis is not about finding the truth but limiting uncertainty"

(Straus SE et al. Evidence-Based Medicine: How to Practice and Teach it)

Evaluating a Glaucoma Suspect



Pre-test probability of disease = 30%

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How can SDOCT help us with this patient ?

Pre-test probability of glaucoma (30%)

IMAGING TEST

SDOCT result

Post-test probability of glaucoma ?

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How do we calculate the post-test probability?

Post-test odds of disease = LR x Pre-test odds of disease

Odds = probability / 1- probability

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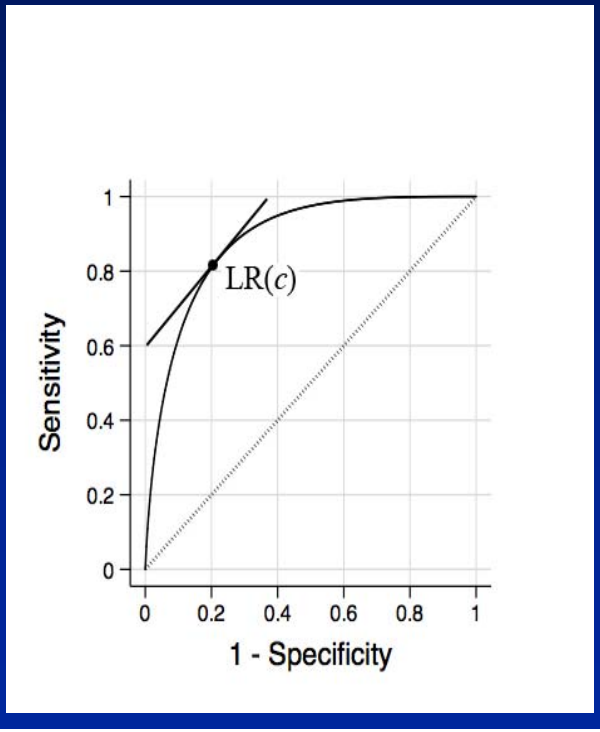
Continuous Likelihood Ratios for Glaucoma Diagnosis with Spectral Domain OCT

The likelihood ratio for a specific test value is the

is the tangent to the ROC curve at the corresponding value



Lisboa R, Mansouri K, Zangwill L, Weinreb RN and Medeiros FA. ARVO 2011

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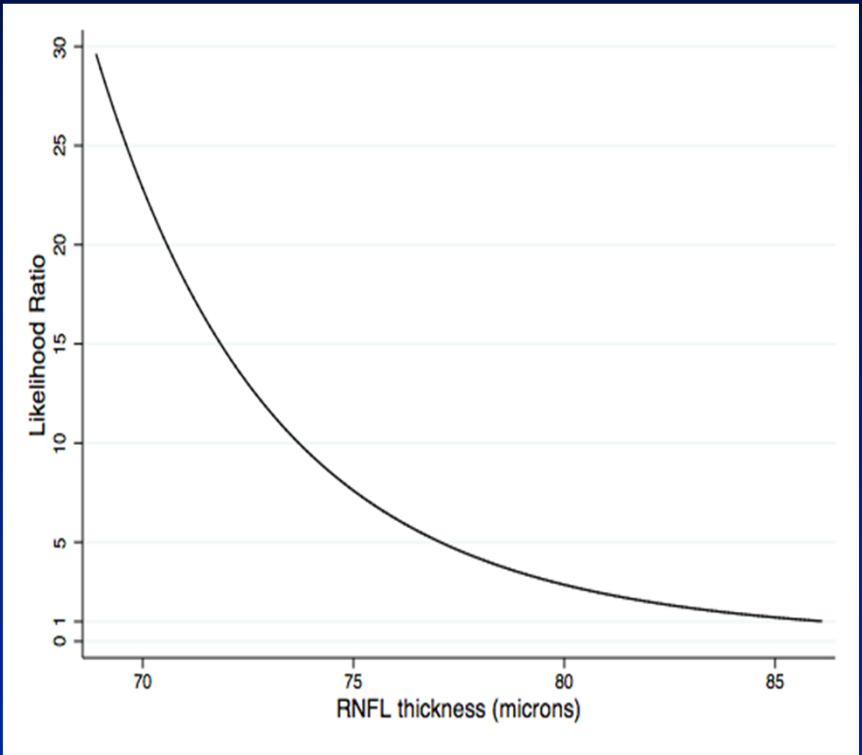
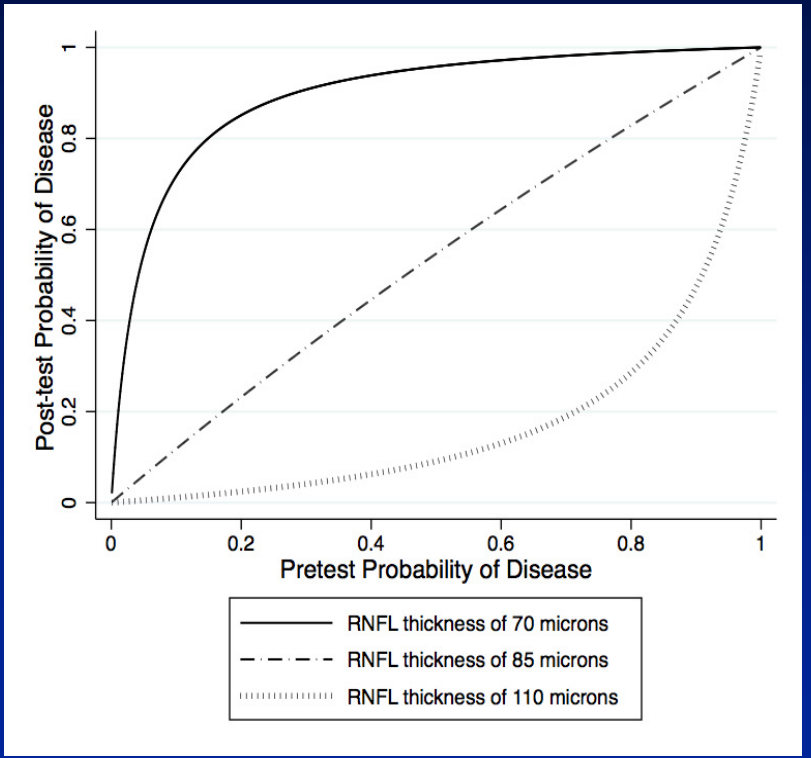
Continuous Likelihood Ratios for Glaucoma Diagnosis with Spectral Domain OCT





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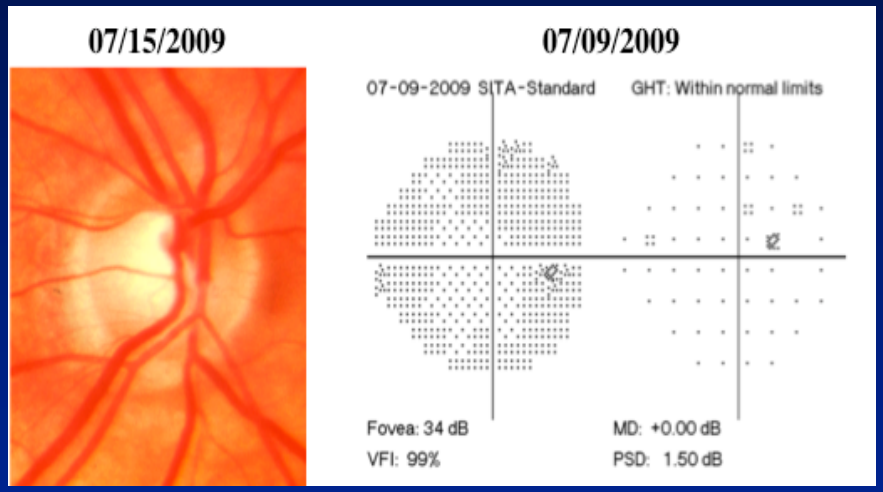
Evaluating a Glaucoma Suspect



Pre-test probability of disease = 30%

Post-test probability of disease = 93%

SDOCT result

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Diagnostic Accuracy of SDOCT RNFL

- Diagnostic accuracy studies involving the clinically relevant population show a clear benefit of RNFL assessment with SDOCT in decreasing uncertainty in glaucoma diagnosis

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Addressing the Questions Asked…

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For a cross-sectional study describing the distribution of measurements in known normal and known diseased subjects (excluding suspects):

a) How should the diseased subject population be defined? What clinical work-up should be done to establish these populations?

A: Cross-sectional studies including only clearly disease subjects versus healthy normals may lead to biased estimates of accuracy. This seems to be worse for certain instruments/parameters versus others.

Studies involving healthy versus glaucomatous field loss should be conducted for initial evaluation, but should be followed by studies evaluating the clinically relevant population (suspects)

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Can the diseased population be further divided by severity of disease using a clinical reference method (e.g., perimetry)? If so, should the clinical performance of the imaging device be characterized separately for each severity group?

A: YES. Important to include a broad spectrum of disease severity and use methods to evaluate diagnostic performance according to disease severity (e.g., ROC regression methods).

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For a longitudinal diagnostic performance study where the structural measurement is taken at baseline and the clinical reference standard consists of a baseline assessment with follow-up:

a) What subjects should be included in the study population (including glaucoma suspects)?

This is a prognostic study. What are you trying to predict?

If we are trying to predict development of glaucoma, the population should be of suspects (without clear signs of damage)

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For a longitudinal diagnostic performance study where the structural measurement is taken at baseline and the clinical reference standard consists of a baseline assessment with follow-up:

b) What is an appropriate clinical reference standard?

Again, depends on what you are trying to predict. If development of glaucoma, then appropriate standards could be development of visual field loss and/or progressive optic nerve damage

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For a longitudinal diagnostic performance study where the structural measurement is taken at baseline and the clinical reference standard consists of a baseline assessment with follow-up:

c) What minimum follow-up period would provide assurance that the subject has been appropriately classified?

Not necessarily we need to establish a minimum period, as long as we take into account censoring. It is very important to adequately evaluate prognostic ability (c-index, modified R2, reclassification tables, predictiveness measure)

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