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OUTLINE

- Primary and Secondary Hypotheses
- Results of MRMC-ROC Analysis

  (areas under ROC curves)
- Sensitivity and Specificity based 50% confidence rate
  - Averaged
  - Individual for each radiologist
- Sensitivity and Specificity based on location
  - Averaged
  - Individual for each radiologist
- Summary

Hypotheses

The Primary Hypothesis:
Radiologists using RapidScreen would increase their detection of *lung cancers 9-30 mm in size*

The Secondary Hypotheses:

I. Radiologists using RapidScreen would increase their detection of *lung cancers that had previously been missed by two screening radiologists.*

II. Radiologists using RapidScreen would increase their detection of *lung cancers 9-14 mm in size.*

Reading conditions:

- Independent without CAD
- Sequential without CAD
- Sequential with CAD

The MultiReader MultiCase (MRMC) method was used for statistical analysis of these 3 reading conditions. The *area under ROC curve* (Az) was considered as a measure of diagnostic accuracy.

In this analysis, *only information about confidence rate* for each film was used. The information about locations of marks and recommended actions was not used in this type of analysis.

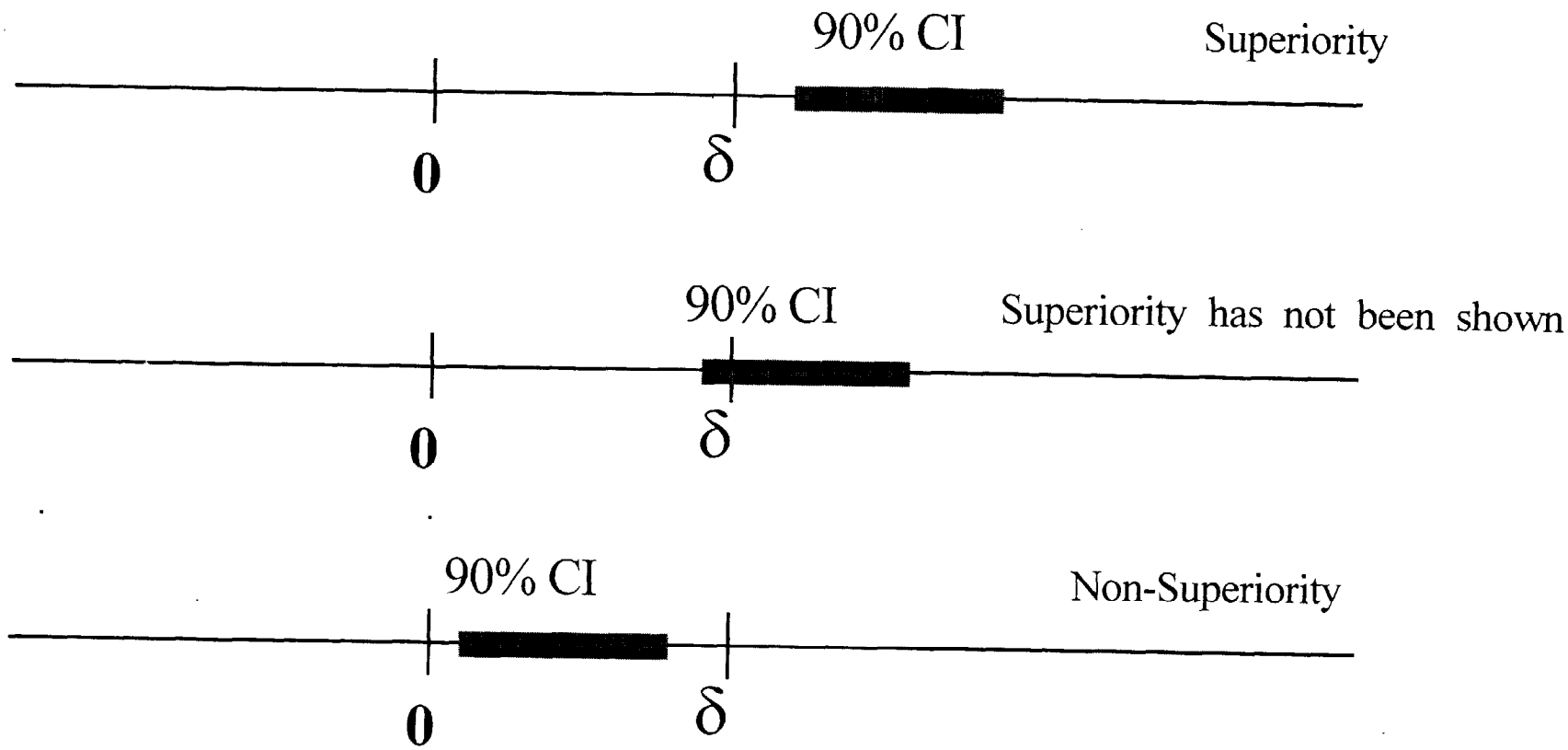
Statistical Hypotheses

Efficacy of the RapidScreen = Superiority (in terms of Az)

For superiority, the following statistical hypotheses with clinical important difference δ should be considered:

If, on the basis of the results from the study, the H_0 is rejected, then H_a is true, i.e. we may conclude that the reading with CAD is superior to the reading without CAD.

The hypothesis H_0 is rejected if the lower limit of the one-sided 95% CI (or the lower limit of the two-sided 90% CI) of the difference $Az_{with\ \ CAD} - Az_{without\ \ CAD}$ is larger than δ .



Which reading condition is the baseline reading:

Independent without CAD or

Sequential without CAD?

Independent without CAD :

- Corresponds to current practice;
- Gives less biased point estimate of difference.

Sequential without CAD:

- Gives more biased point estimate of difference;
- Provides more sensitive probe of difference because this reading condition is more correlated with Sequential with CAD reading.

Conclusion: Both reading conditions should be used in comparison with the reading with CAD.

For example, Primary Hypothesis (all cancers):

Az for Sequential with CAD = 0.865

Az for Independent w/o CAD = 0.829
Az for Sequential w/o CAD = 0.835

Difference between
Sequential with CAD and Independent w/o CAD is
0.036 with 90% CI: (0.016; 0.058)

Difference between
Sequential with CAD and Sequential w/o CAD is
0.030 with 90% CI: (0.019; 0.043)

It was demonstrated that

$$Az_{with\ \ CAD} - Az_{without\ \ CAD} > 1.9\%$$

Results of the MRMC-ROC Study (areas under ROC curves)

	w/o CAD est. of Az	with CAD est. of Az	It was demonstrated $AZ_{with\ CAD}$-$AZ_{w/o\ CAD}$ > Ω
All cancers (80 films)	0.829	0.865	$AZ_{with\ CAD}$-$AZ_{w/o\ CAD}$ > **3.6%**
Priors (18 films)	0.723	0.744	$AZ_{with\ CAD}$-$AZ_{w/o\ CAD}$ > **1.0%**
Currents	0.861	0.901	$AZ_{with\ CAD}$-$AZ_{w/o\ CAD}$ > **1.5%**
Small 9-14 mm (38 films)	0.798	0.848	$AZ_{with\ CAD}$-$AZ_{w/o\ CAD}$ > **2.6%**
Medium 15-19 mm	0.840	0.870	$AZ_{with\ CAD}$-$AZ_{w/o\ CAD}$ > **0.5%**
Large 20-27 mm	0.889	0.889	No improvement

Question: whether these improvements in the areas under ROC curves ($\triangleq$) are of clinical value.

The area under ROC curve (Az) is sensitivity averaged over all specificities.
The meaning of $\triangleq$ is a such increase in averaged sensitivities which is clinically important.

Sensitivity and Specificity Based on 50% Confidence Rate

Primary Hypothesis: All cancer cases

	Sensitivity	Specificity
Independent without CAD	0.703	0.800
Sequential with CAD	0.777	0.778
	+0.074	-0.022

Comparing the two reading conditions

Without CAD $Se_{without\ CAD}$, $Sp_{without\ CAD}$

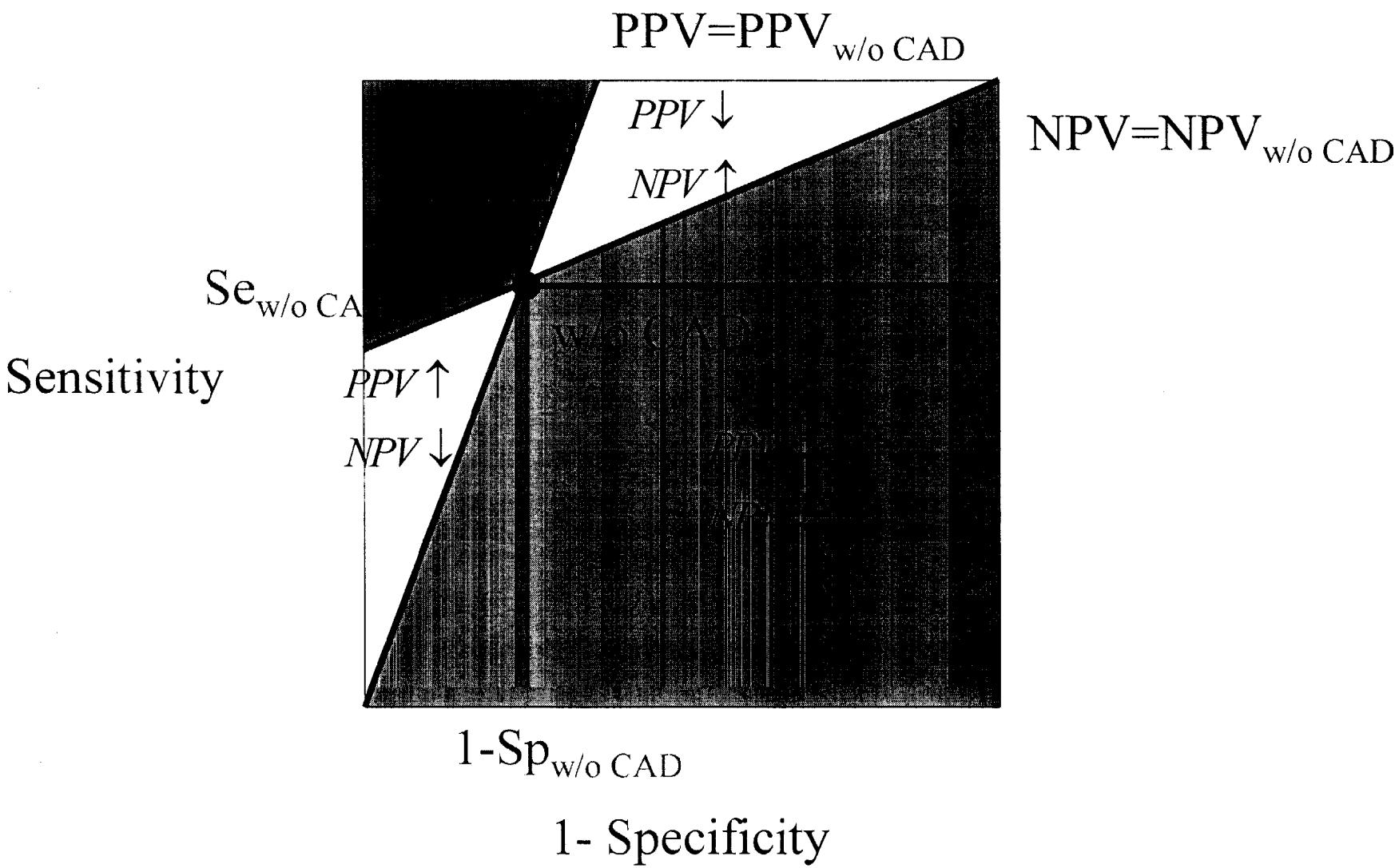
With CAD $Se_{with\ CAD}$, $Sp_{with\ CAD}$

If $Se_{with\ CAD} > Se_{without\ CAD}$
$Sp_{with\ CAD} > Sp_{without\ CAD}$

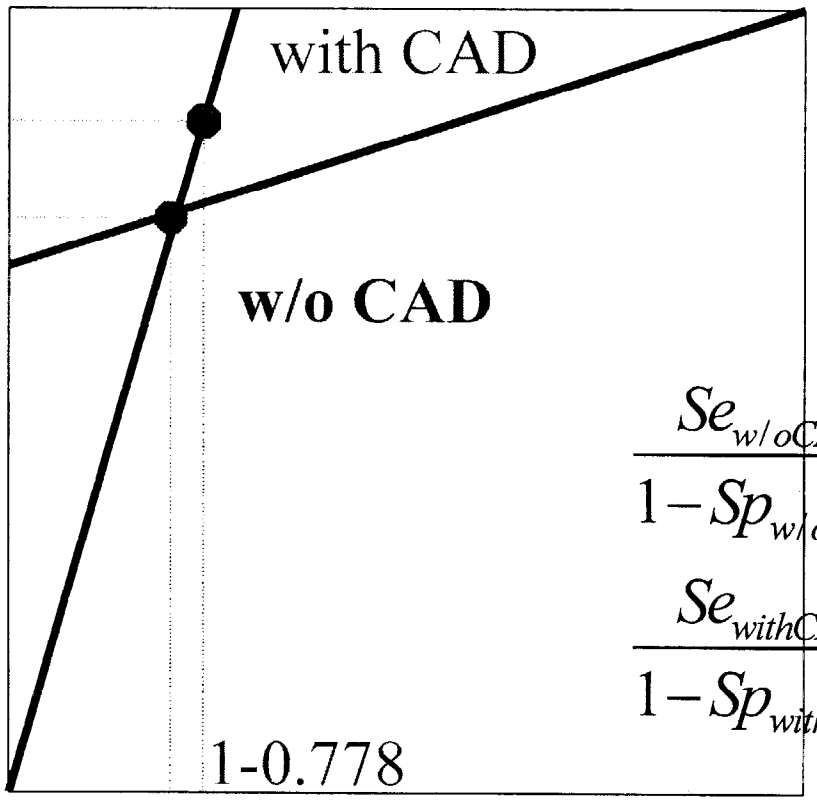
then with CAD is clearly preferred.

If $Se_{with\ CAD} > Se_{without\ CAD}$
$Sp_{with\ CAD} < Sp_{without\ CAD}$

?


PPV=PPV w/o CAD
PPV ↓
NPV ↑
NPV=NPV w/o CAD
Se w/o CA
Sensitivity
PPV ↑
NPV ↓
1-Sp w/o CAD
1- Specificity

Comparing the Reading w/o CAD and Reading with CAD



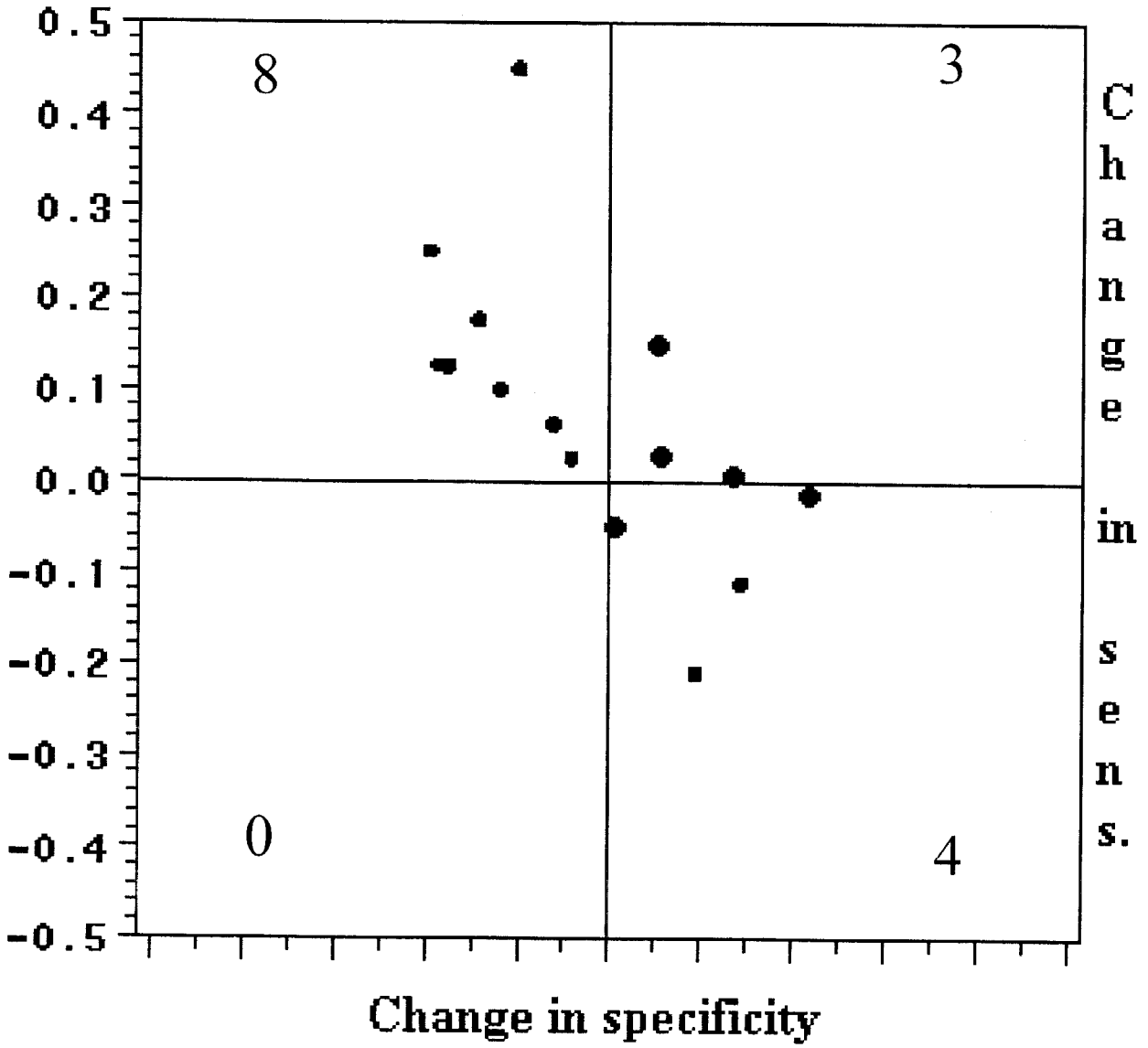
$$\frac{Se_{w/oCAD}}{1-Sp_{w/oCAD}} = \frac{0.703}{1-0.800} = 3.5$$

$$\frac{Se_{withCAD}}{1-Sp_{withCAD}} = \frac{0.777}{1-0.778} = 3.5$$

Conclusion: $NPV_{\text{with CAD}} > NPV_{\text{w/o CAD}}$

$PPV_{\text{with CAD}} = PPV_{\text{w/o CAD}}$

Sensitivity and Specificity Based on 50% Confidence Rate



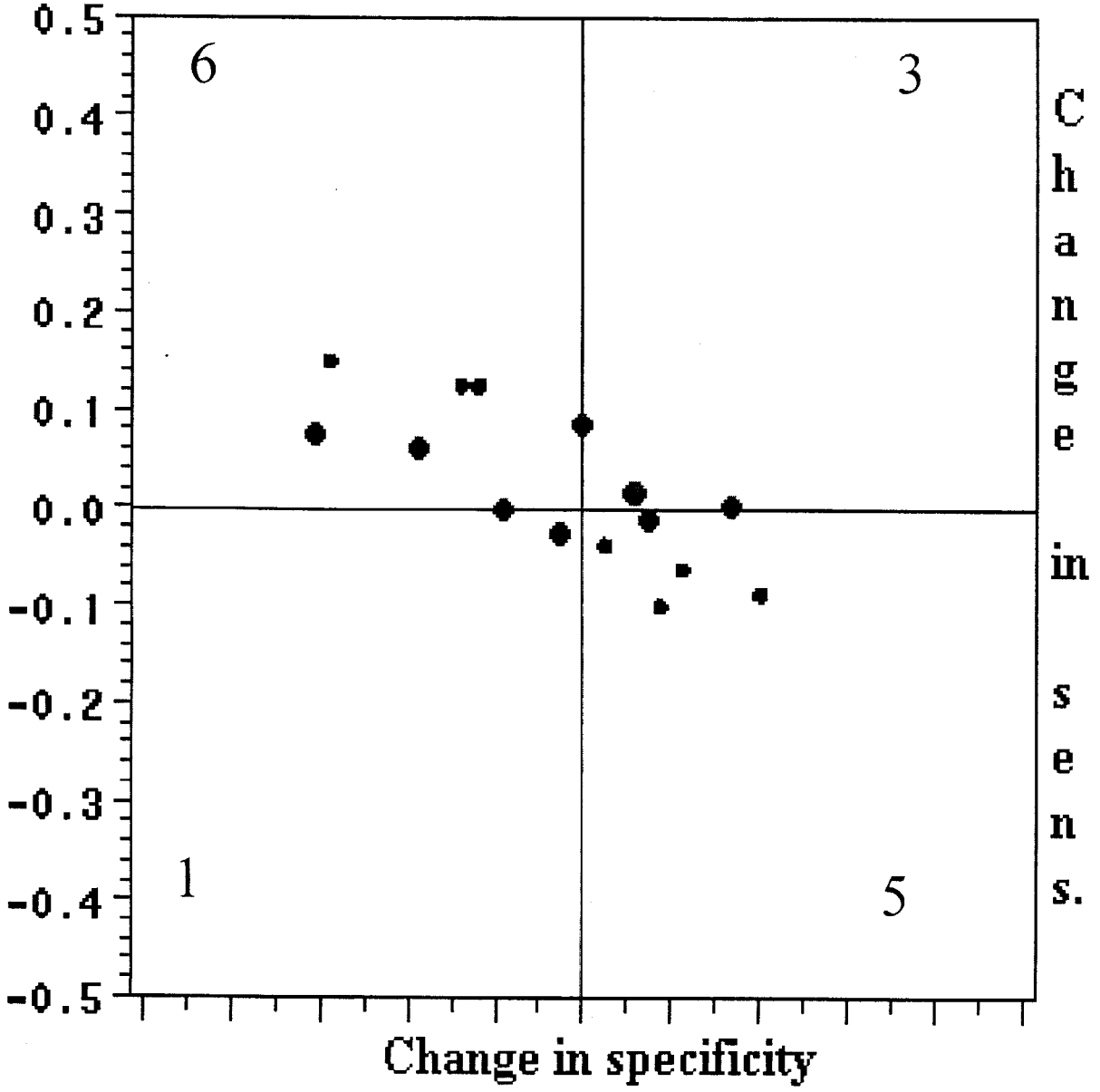
	PPV↑	*PPV*↓
NPV↑	4	8
NPV↓	2	1

Sensitivity and Specificity based on location

Primary Hypothesis: All cancer cases

	Sensitivity	**Specificity**
Independent without CAD	0.662	0.759
Sequential with CAD	0.683	0.730
	+0.021	-0.029

Sensitivity and Specificity Based on Location



	$PPV\uparrow$	$PPV\downarrow$
$NPV\uparrow$	4	3
$NPV\downarrow$	4	4