Diffuse reflectance spectral analysis in bronchoscopy

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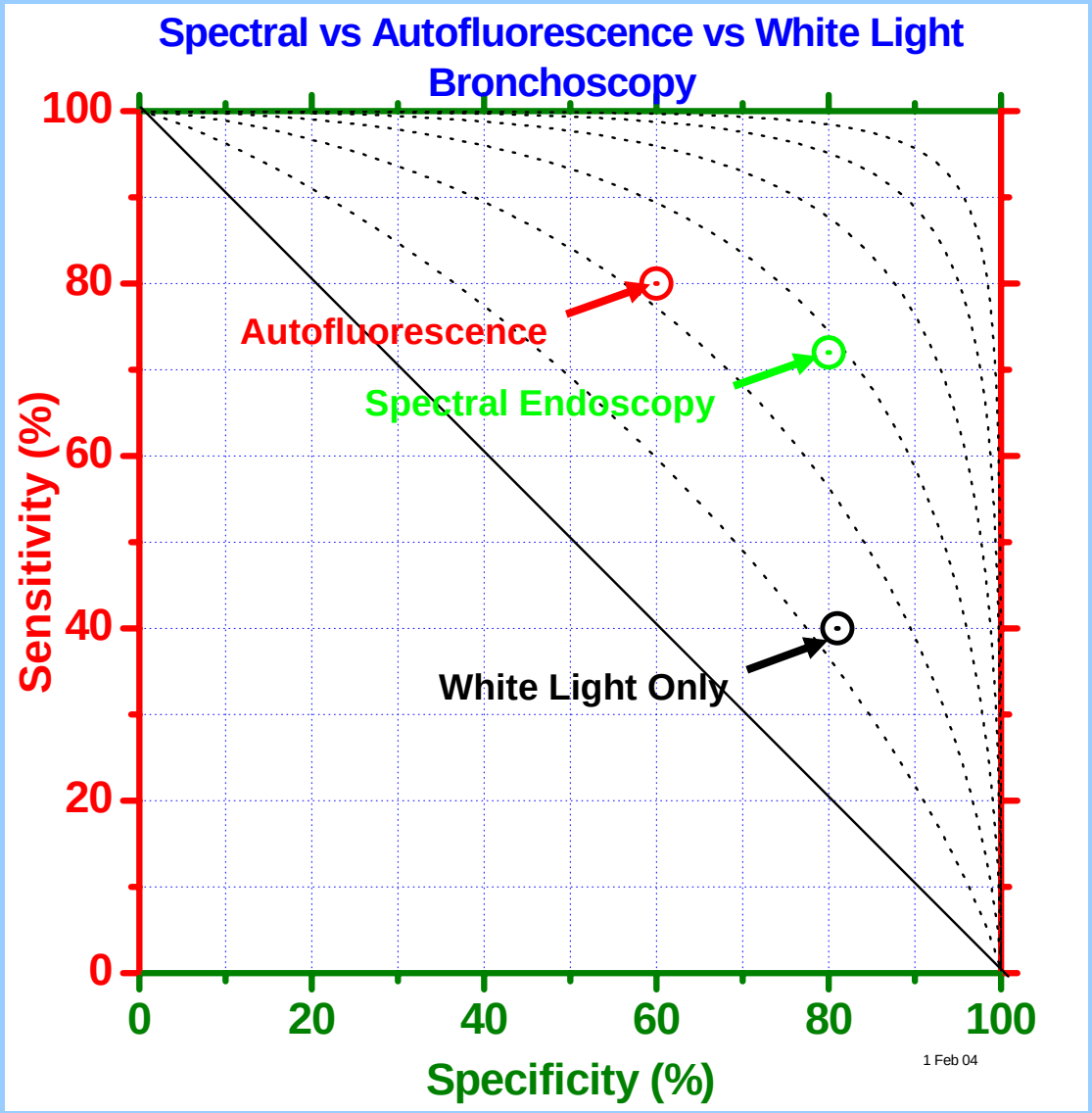
Introduction

- **Fluorescence (FL) imaging significantly improves detection sensitivity for early neoplastic lesions**
- **However, it comes with low specificity – high false positive rate**
  - **unnecessary biopsies**
  - **greater medical costs**
  - **longer procedure times**
  - **increased morbidity to patients**

The aim of the study was

to investigate if the addition of spectroscopy to regular white light (WL) and fluorescent (FL) bronchoscopy would be useful for decreasing the risk of performing unnecessary biopsies.

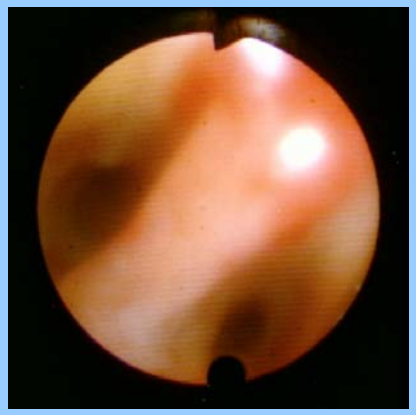
Principle of adding spectral analysis to WL/FL bronchoscopy

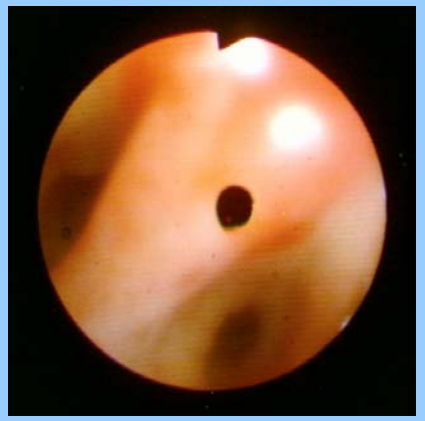


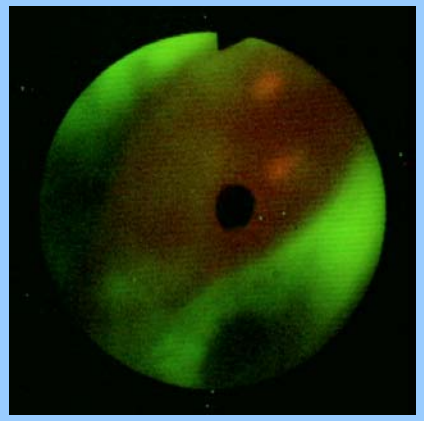
Spectral bronchoscopy requirements:

- acquisition of spectra without touching lung tissue
  - results independent of distance and angle
- rapid switching between the fluorescence and reflectance modes
- continuous visualization and control of spectra acquisition site and biopsy location
- minimal increase of bronchoscopy time

Integrated imaging and spectroscopy system







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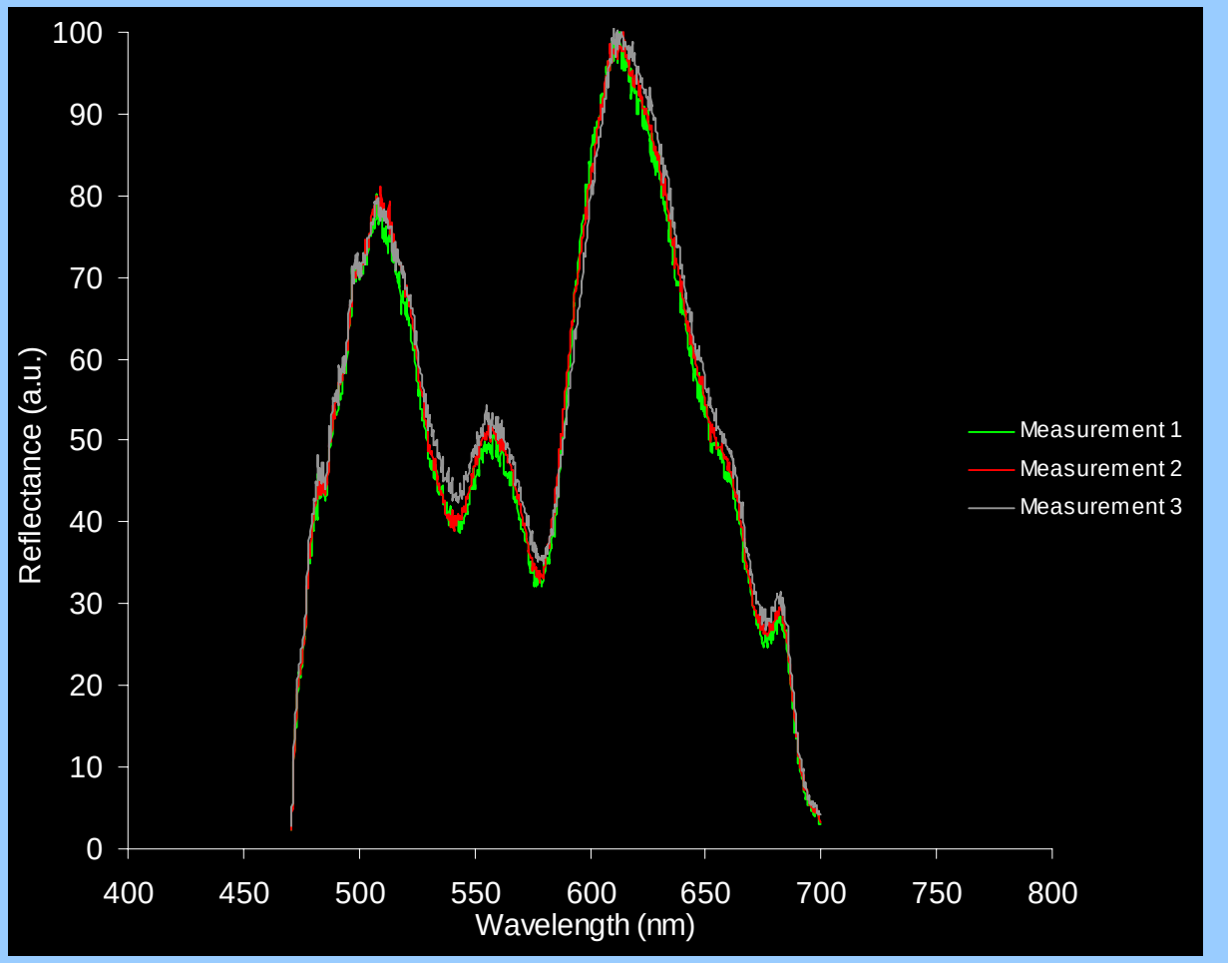
Repeatability of Measurements WL



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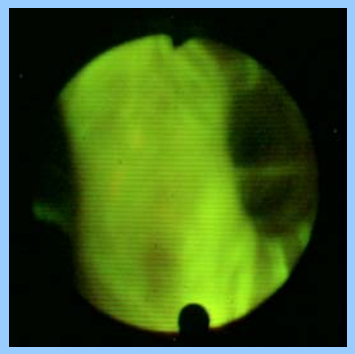
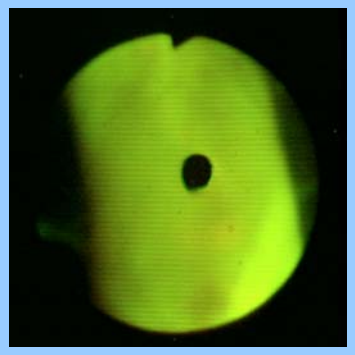
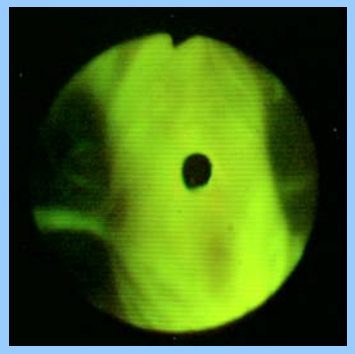
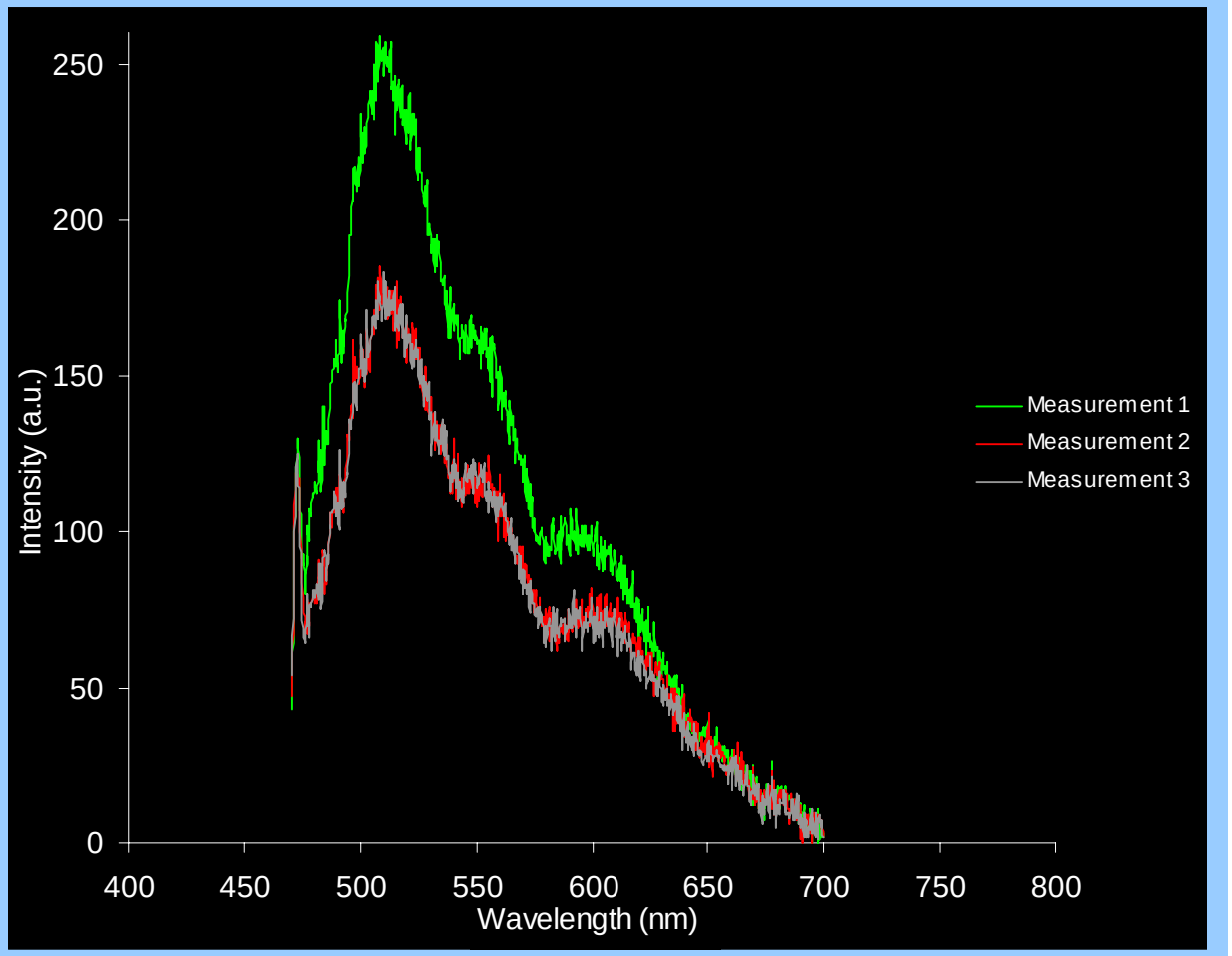
Repeatability of Measurements FL









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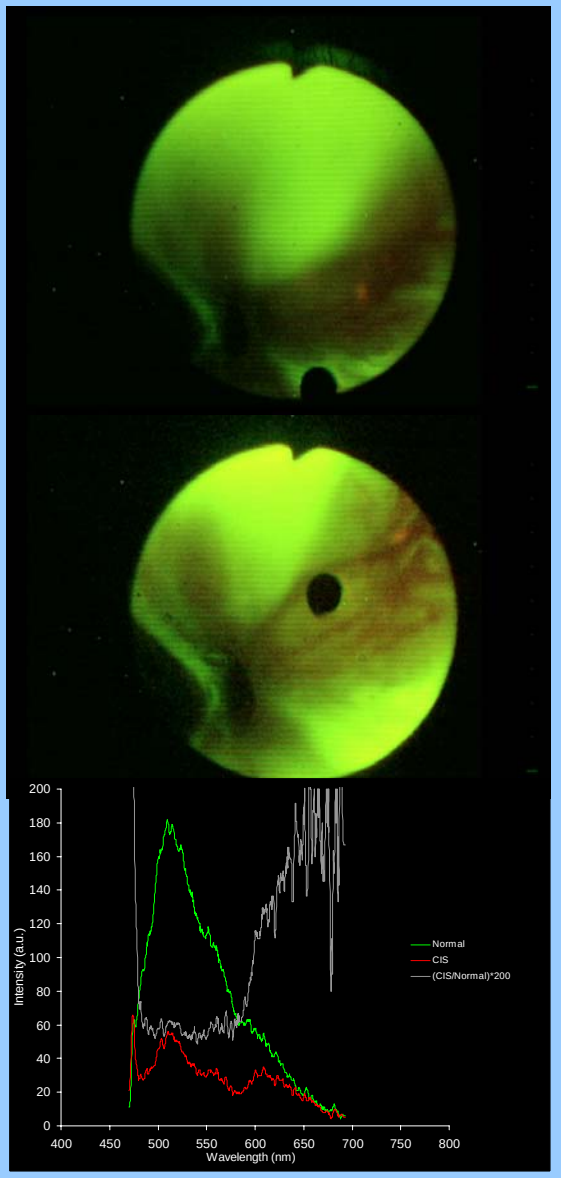
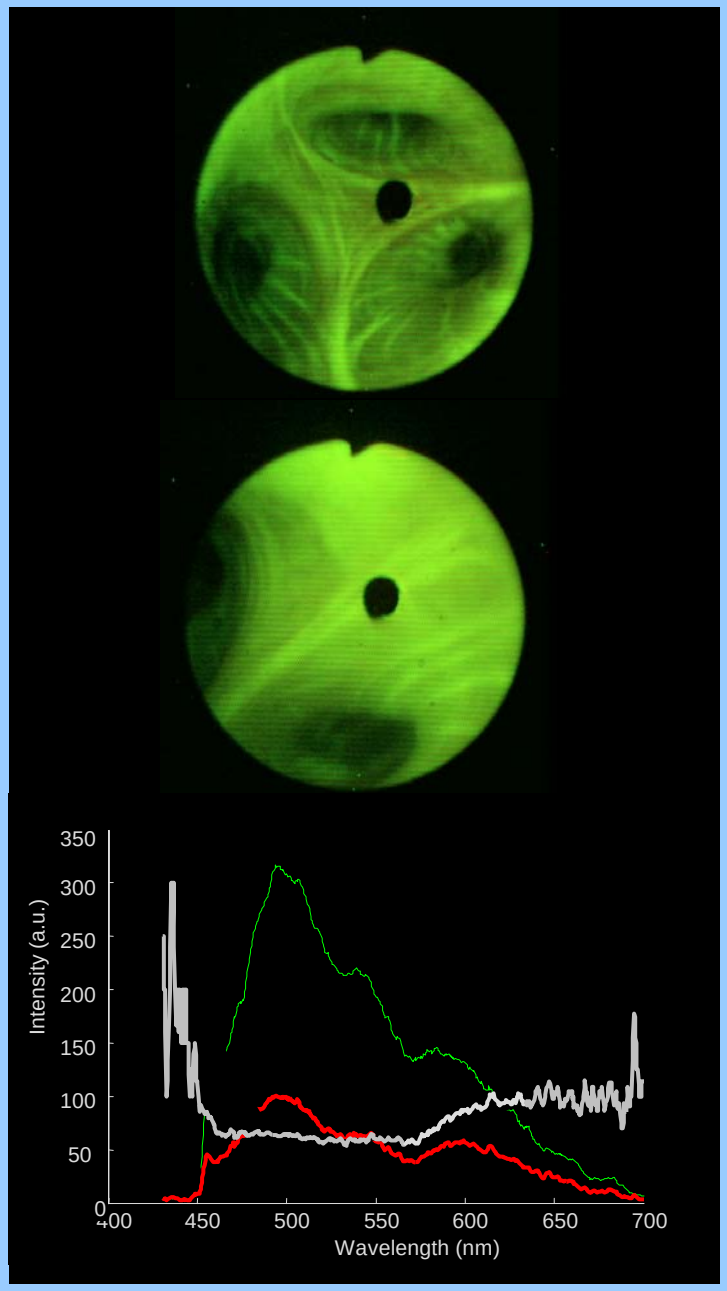
Cancer



Dysplasia


Intensity (a.u.)
350
300
250
200
150
100
50
0
400
450
500
550
600
650
700
Wavelength (nm)

Strategy

- **Macroscopically identify, under WL or FL, sites that are suspicious for cancer/CIS as per standard procedure**
- **Apply spectral analysis to visually suspicious lesions (liberal judgment)**

Study population

Routine diagnostic bronchoscopy was indicated for all subjects in the study

- **radiological or clinical suspicion of carcinoma**
- **follow-up postoperative lung cancer**
- **follow-up postoperative oral cancer**
- **suspicious sputum by classical cytology or automated quantitative sputum cytometry**

Study population *cont.*

May 2003 – June 2004

135 patients:

- **32 Females**
- **103 Males**

Age:

- **Range: 37 – 81**
- **Median: 60.8**

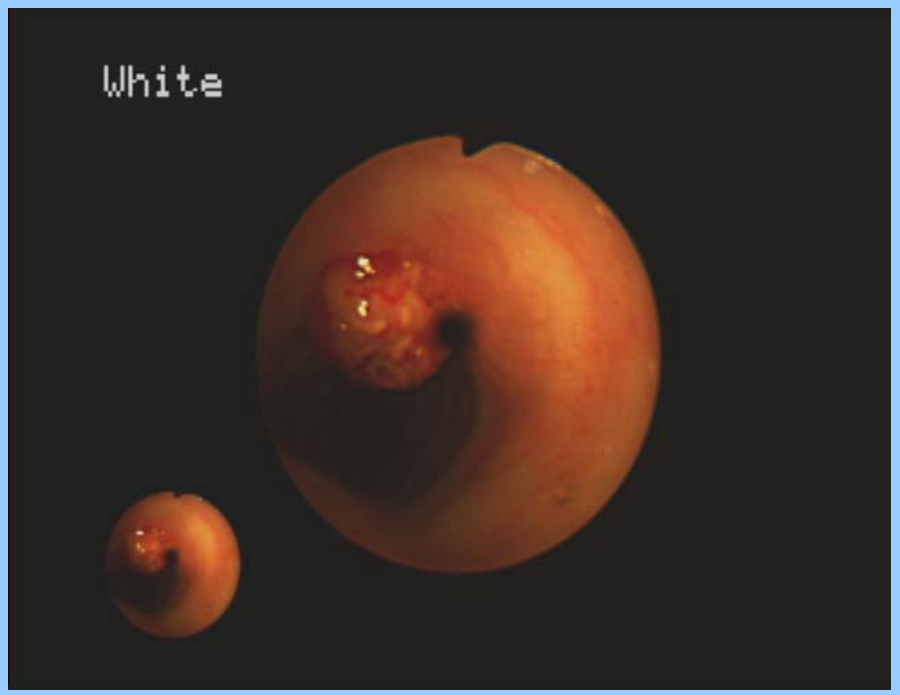
Methods

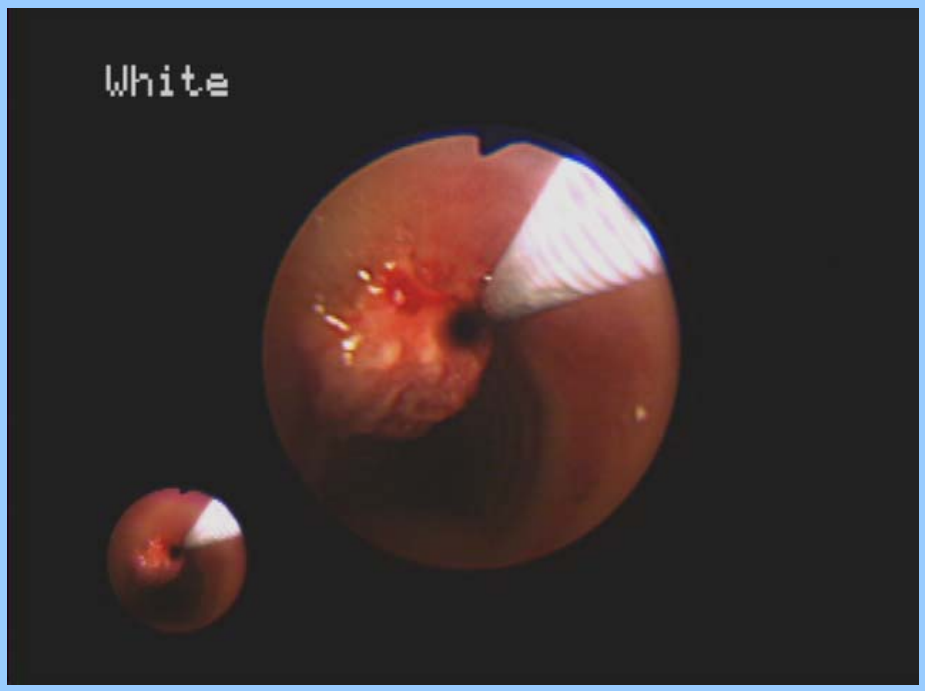
- Perceptronix ClearVu™ Elite spectral system
- Fiberbronchoscope Olympus BF 40
- Standard bronchoscopy with topical anesthesia, Oxygenation > 90%
- Care was taken to inspect the mucosa without causing suction trauma

Procedure

- WL and FL images of suspected abnormal areas were recorded
- respective WL and FL spectra were captured
- bronchial biopsies were taken at these sites

Example Images From Procedure





1) Spectral acquisition

2) Biopsy of suspicious site

Macroscopic evaluation

- **Non-suspicious: normal or nonspecific changes such as general inflammation, scars, granulomas**

- **Suspicious: indicating of “pre” or “early” malignant changes such as irregular mucosa, nodular or polypoid lesions, thickening of carina**

Histological classification

- **negative**
  - **normal, metaplasia, hyperplasia, granuloma, inflammation**
- **dysplasia**
  - **mild and moderate dysplasia**
- **CIS/malignant tumor**

Evaluation of spectroscopy

The spectroscopy spectra were classified using three different scores to define suspect malignancies:

> - 1.0 > 0.0 > + 1.0

Results

Number of dysplasia and normal biopsy sites suspicious by WL/FL and spectroscopy

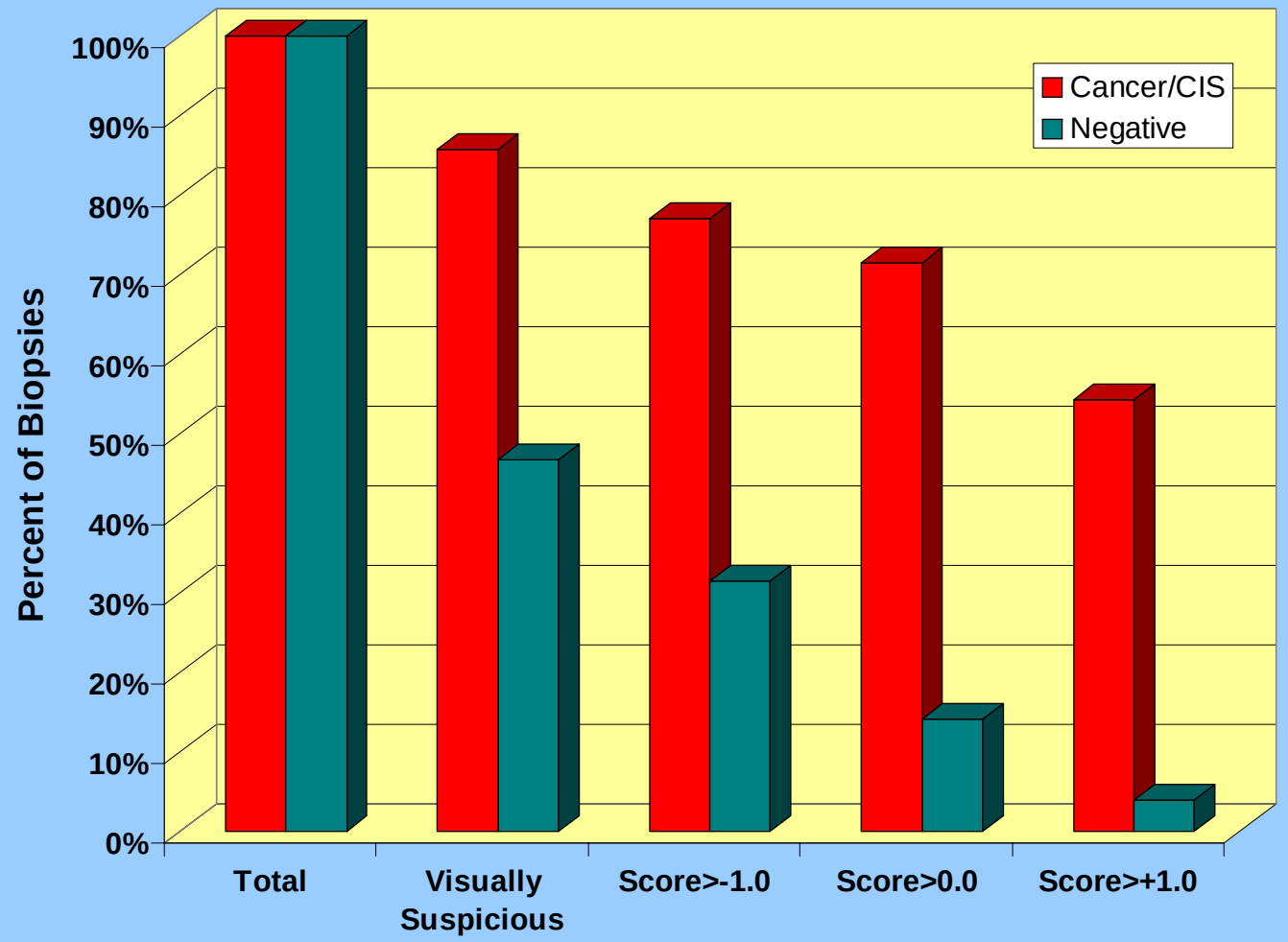
	Total	Dysplasia Mild/Moderate	Normal/ Hyperplasia
Visually Suspicious	**86**	**14**	**72**
Spectroscopy Applied to Visually Suspicious Sites	**n** (%)	**n** (%)	**n** (%)
*** Score> -1.0**	**58** (67)	**11** (79)	**47** (65)
*** Score > 0.0**	**26** (30)	**3** (21)	**23** (32)
*** Score > 1.0**	**7** (8)	**1** (7)	**6** (8)

Results *cont.*

Cancer detected by WL/FL Bronchoscopy and spectroscopy

	Total		Suspicious	
Visually Suspicious	**86**		**30**	
Spectroscopy	n	(%)	n	(%)
* Score> -1.0	58	(67)	27	(90)
* Score > 0.0	26	(30)	25	(83)
* Score > 1.0	7	(8)	19	(63)

Comparative Effect of Macroscopic Evaluation Plus Spectroscopy on Percent-Suspicious For Positive and Negative Biopsies



Results *Cont.*

Effect of spectroscopy on total biopsy positive fraction and number from WL/FL Bronchoscopy

	Positive Predictive Value (SE)	Biopsies with Cancer (n)	Total Biopsies (n)	Biopsies Avoided Due to Spectroscopy (n)
Visually Suspicious	25.8% (4.1%)	30	116	N/A
Suspicious and Score >-1.0	31.7% (5.0%)	27	85	31
Suspicious and Score >0	49.0% (7.0%)	25	51	65
Suspicious and Score >+1.0	73.1% (8.7%)	19	26	90

Results *cont.*

Cancer detected by WL/FL Bronchoscopy and spectroscopy

	Macroscopic Assessment		
	Suspicious		Not suspicious
Biopsies (n)	**30**		**5**
Spectroscopy	**n**	(%)	**n**
*** Score > - 1.0**	**27**	(90)	**4**
*** Score > 0.0**	**25**	(83)	**4**
*** Score > +1.0**	**19**	(63)	**3**

Conclusions

- typically added 5-10 minutes to a standard fiber-optic bronchoscopic procedure
- allowed easy handling and instant ability to switch between WL, FL, and spectroscopy modes
- no adverse effects
- method applicable for routine clinical use

Conclusions *cont.*

If a decision to perform biopsy were based on spectroscopy in addition to WL and FL bronchoscopy, a lower number of unnecessary biopsies would have been performed (33-92% depending on the score).

Conclusions *cont.*

If a decision to perform biopsy were based on spectroscopy in addition to WL and FL bronchoscopy, a number of cancers would not have been detected (10-37% depending on the score).

Hypothesized Spectral Misclassification Causes

Other conditions that are expected to contribute to incorrect spectral classification are:

- **NECROSIS**
- **HYPEREMIA**
- **INFLAMMATION (porphins)**
- **MUCUS**
- **BLOOD**

Observation

In 5 cases WL and FL bronchoscopy were not suspicious but spectroscopy was positive in 4.

The biopsies showed 4 lung cancer and 1 CIS.

Hypothesis

- This suggests that the routine application of spectroscopy might increase the sensitivity in terms of detecting lung cancer.

- This hyposthesis can be tested in further studies.

Acknowledgments

- Many thanks to the patients who participated in this clinical trial.
- This study was sponsored and equipment provided by Perceptronix Medical Inc.
- The assistance of Yasser Fawzy, PhD and Dan Reinders with the preparation of this presentation is gratefully acknowledged.