Optical Diagnosis of Predysplastic Stage of Colon Carcinogenesis

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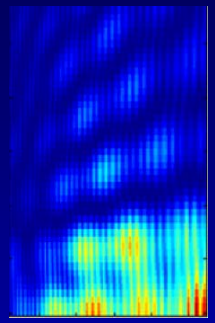
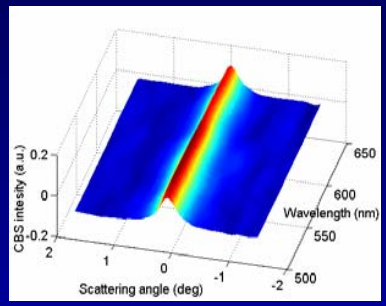
National Science Foundation (BES-0238903)

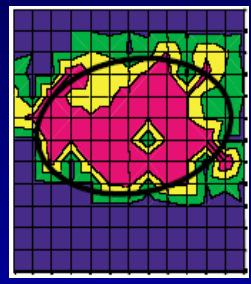
Northwestern University Biophotonics Laboratory: optics for early cancer diagnosis



Elastic Light Scattering Fingerprinting

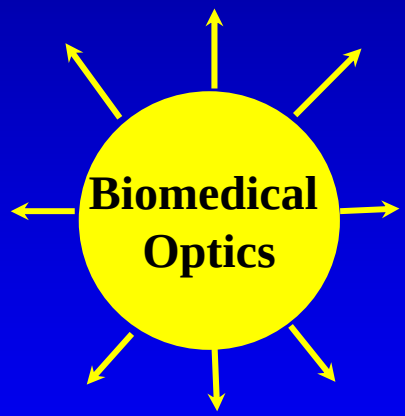


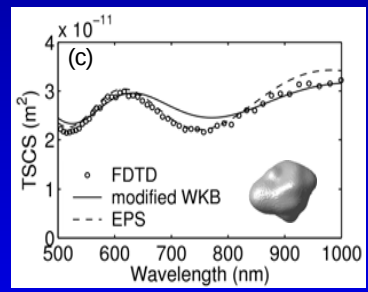
Coherent Backscattering Spectroscopy



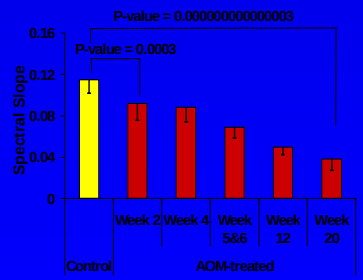
Molecular Imaging

Microfabrication of Clinical Fiber-Optic Instrumentation





Analytical and Numerical Methods of Analysis of Light Scattering in Tissue



Early Detection and Screening of Colon and Pancreatic Cancers

Early Increase of Blood Supply in Carcinogenesis

Why study predysplastic stages of colon carcinogenesis?

Screening

- Entire colon visualization is the "gold-standard" but presently impractical for widespread screening.
- Development of an accurate relatively non-invasive risk-stratification technique is of paramount importance in reducing colon cancer mortality.

Biological understanding

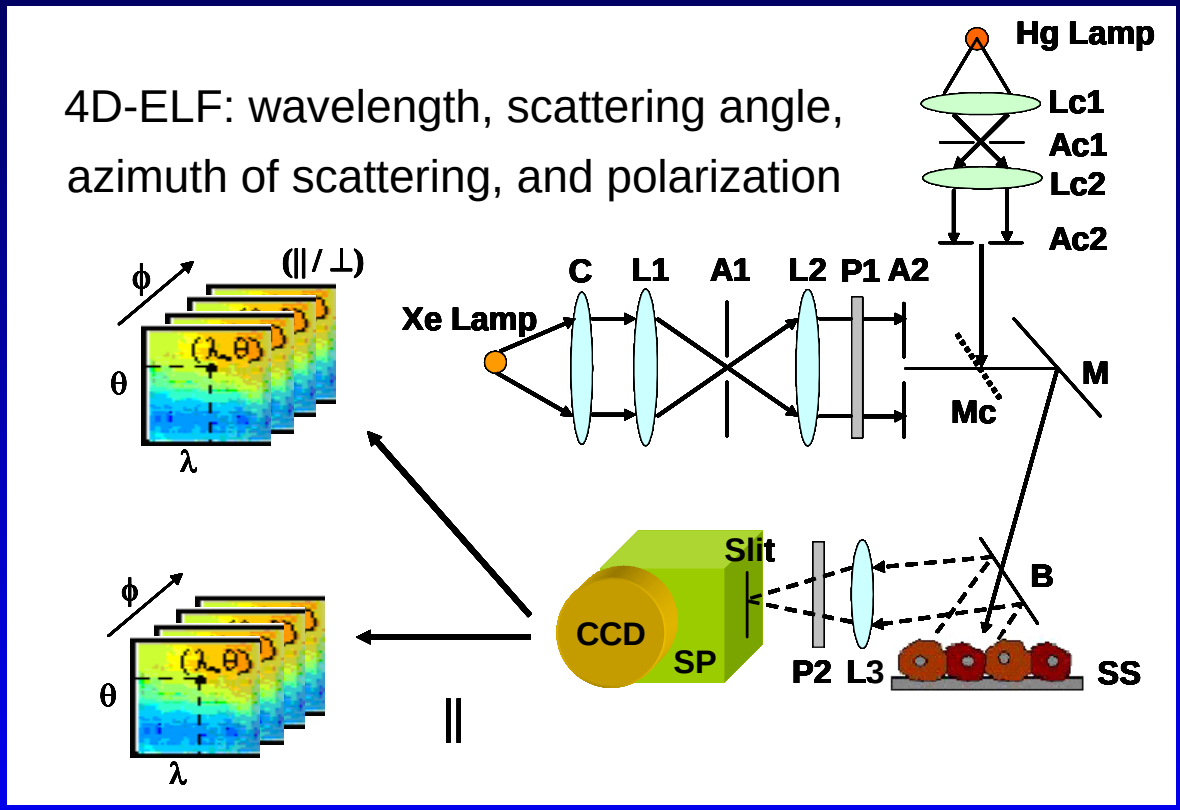
Potential treatment

Extension to other cancers, e.g. pancreatic cancer

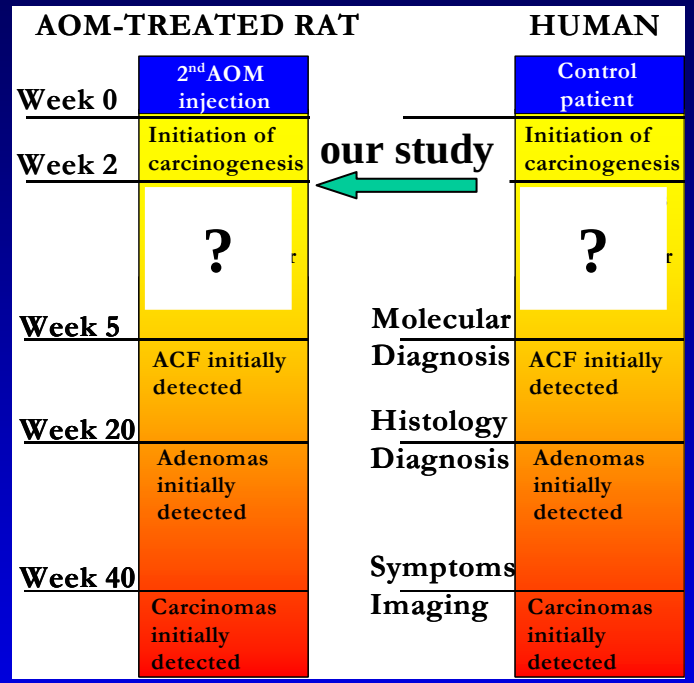
Screening can be based on the "*field effect*":

- Environmental/genetic milieu that leads to a neoplastic lesion in one area of the colon should be detectable throughout the entire colonic mucosa
- "Field Effect" Based Screening techniques:
  - Morphological: polyps detected on flexible sigmoidoscopy, aberrant crypt foci (ACF)
  - Cellular: apoptosis, proliferation
  - Biochemical: protein kinase C, mucus disaccharide (Gal-GalNAc)

Four-dimensional elastic light scattering fingerprinting (4D-ELF)



IEEE J Sel. Top. Quant. Elect., **9**(2), 2003.



- **AOM** (azoxymethane) – **distal colon specific** carcinogen.
- AOM-treated rat model is one of the most robust and widely used animal models of CRC.

4D-ELF diagnosis of predysplastic stage of colon carcinogenesis

control AOM-treated (week 2)

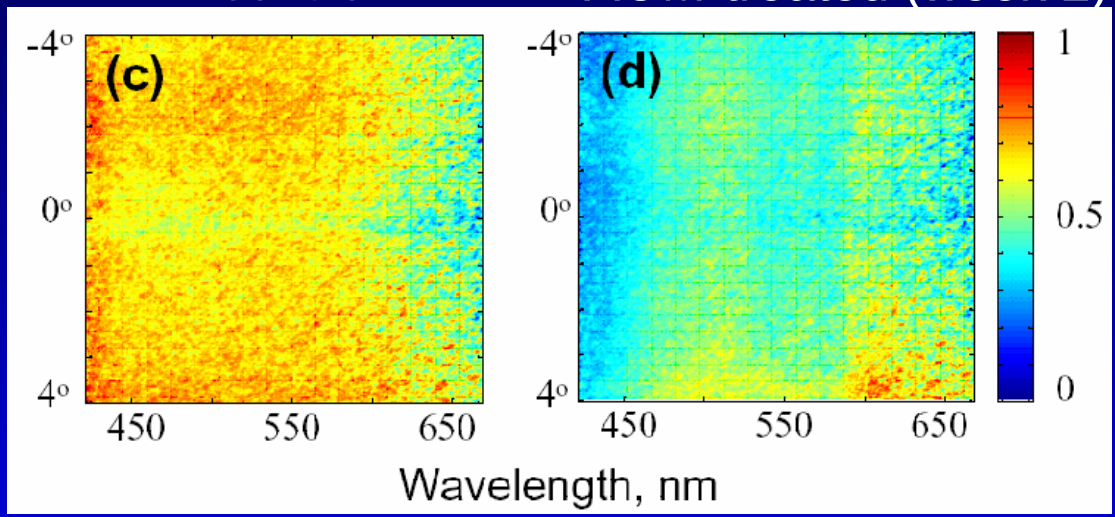
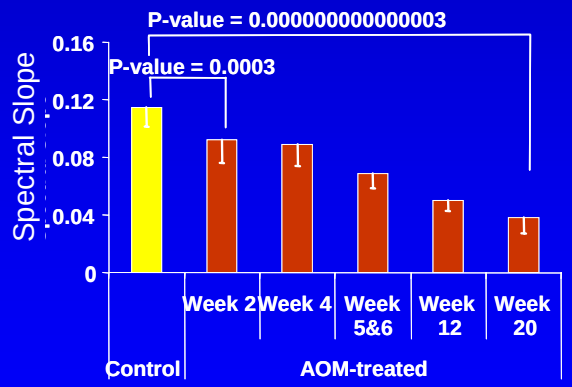


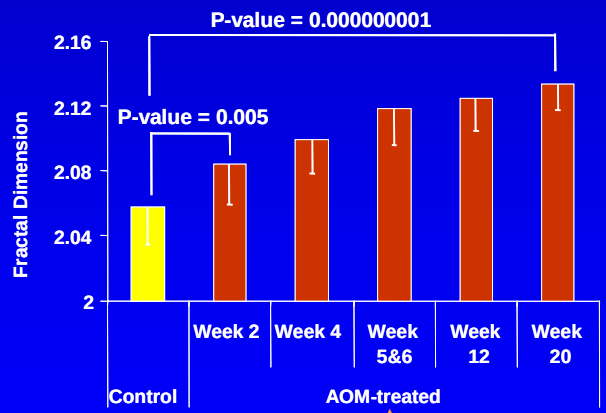
Table 1

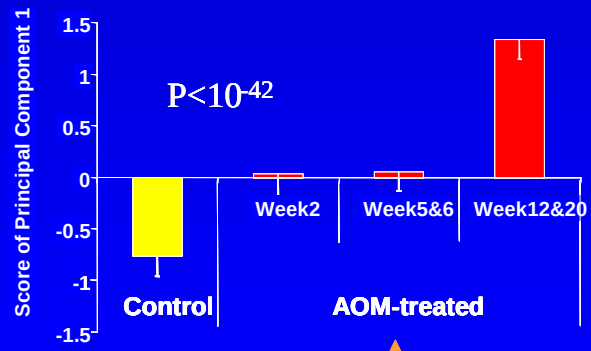
Light Scattering Marker	P-value (2-20 weeks post AOM-treatment)
Spectral slope	$<10^{-14}$
PC 1	$<10^{-42}$
D_f	$<10^{-9}$

Table 2

	2 weeks post AOM-treatment	12 weeks post AOM-treatment
Sensitivity	92%	100%
Specificity	100%	100%
Positive Predictive Value	94%	100%
Negative Predictive Value	100%	100%







Inject AOM → ACF Develop → Adenomas Develop

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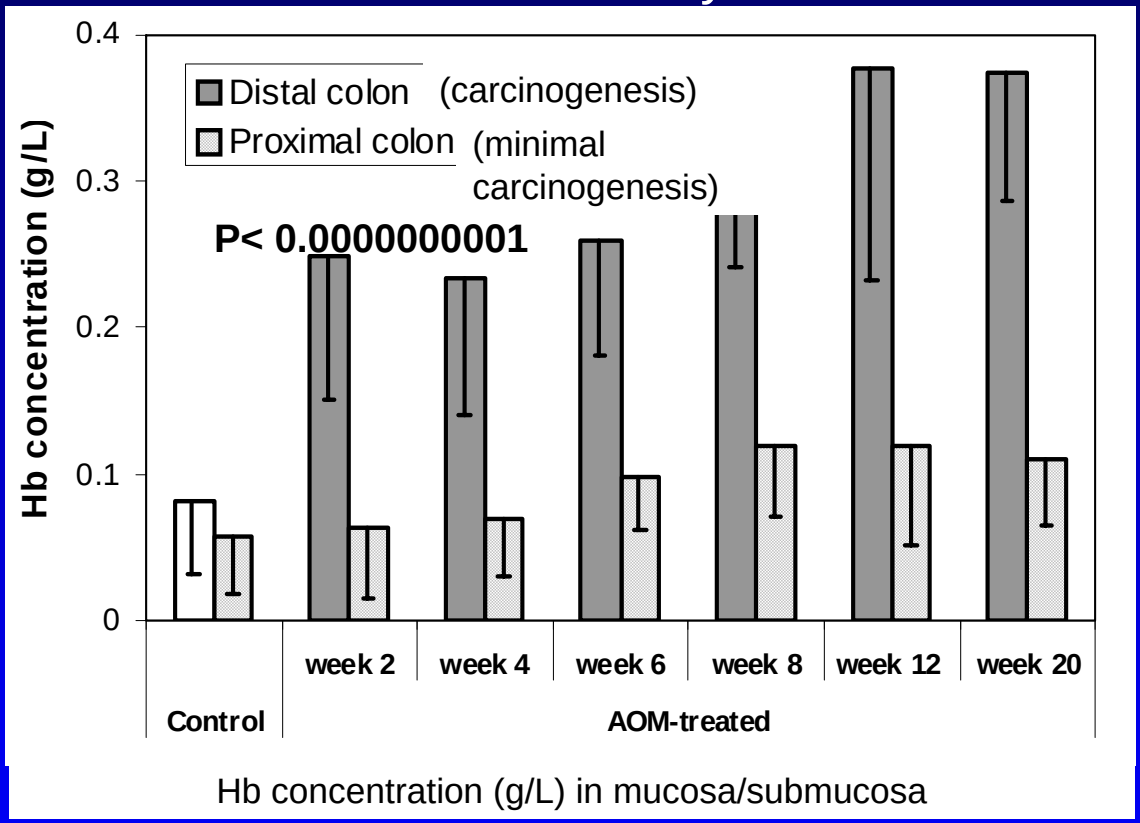
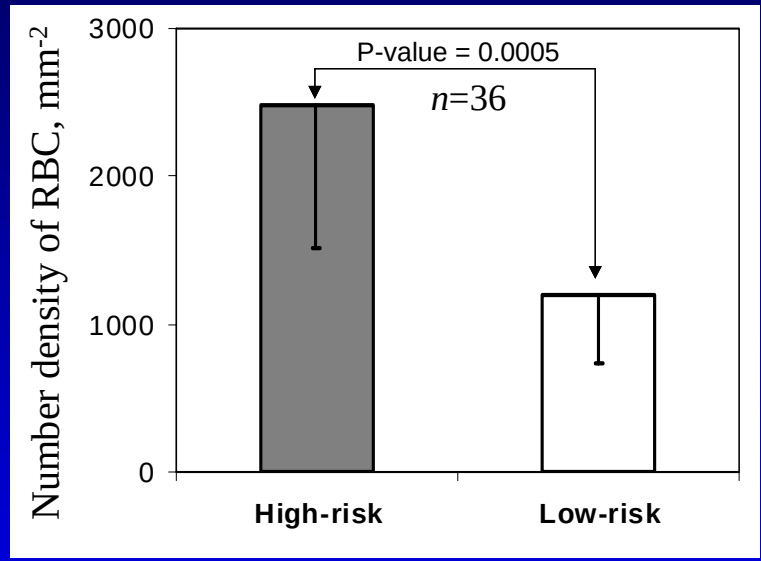
Gastroenterology, **126,** 1071-1081 (2004).

Early increase of subepithelial blood supply (EIBS) in preinvasive neoplasia

Animal Study



Pilot Human Study



	Pre-ACF, pre-adenoma stage	ACF, pre-adenoma stage
Sensitivity	94%	100%
Specificity	96%	100%
PPV	97%	100%
NPV	92%	100%

control → **ACF** → adenoma

angiogenesis