Summary of Optical Biopsy Technology at the IUSL

Optical Biopsy is a novel approach based on optical spectroscopy to diagnose the state of a tissue (*in vivo* or *ex vivo*) without removing the tissue from the body. Dr. Robert Alfano and coworkers at the City College of New York (CCNY) pioneered the field of Optical Biopsy after its discovery in 1984 by the CCNY group. Over the years, the CCNY group has laid the foundations for Optical Biopsy by developing technology based on UV-visible fluorescence, excitation, Raman, time-resolved, diffuse reflectance, and most recently, Stokes shift spectroscopies. A full list of publications by the CCNY group is attached. Using the appropriate wavelengths, at this time, Optical Biopsy can determine whether a tissue is malignant, dysplastic (pre-cancer) or benign, in addition to whether it being invasive cancer. Seminal patents have been issued over the years for various approaches to Optical Biopsy (a list of relevant patents by the CCNY group is attached).

The Optical Biopsy program at the IUSL has characterized the fluorescence signatures from normal and malignant tissue from multiple organ sites and developed algorithms to distinguish malignant tissue from normal. The onset of carcinogenesis causes molecular and structural changes in tissues. These molecular and structural changes can be observed in the differences in the fluorescence spectra between benign, precancerous and cancerous tissues. The important diagnostic fluorophores found in human tissue include several amino acids, proteins and other biomolecules (i.e. tryptophan, collagen, nicotinamide adenine dinucleotide [NADH], elastin, flavins and porphyrins). Optical Biopsy offers some significant improvements over classical methods. It does not require removal of tissue, results are available in real time, and it is highly sensitive to changes occurring on a sub millimeter size scale. Our instrumentation is lamp-based. It does not require the use of lasers. The use of broadband UV-visible lamps as an excitation source extends the capability of the technology by allowing the instrumentation to probe multiple fluorophores. Our instrumentation permits acquisition of emission, excitation, diffuse reflection, and, the recently developed, Stokes shift spectra for enhanced diagnostic accuracy.

Ex vivo studies have been performed on breast, cervical, oral cavity, esophageal, colon and lung tissue. These studies have been performed in collaboration with Memorial Sloan Kettering Cancer Center (MSKCC) - oral cavity, breast; New York Eye and Ear Infirmary - oral cavity; Weill Medicine College of Cornell University, New York Hospital and Columbia Presbyterian Hospital (now New York Presbyterian) - esophageal and digestive tract; St. Vincent's hospital of Staten Island; and Hackensack University Medical Center. An *in vivo* study was performed, in collaboration with MSKCC, on oral cancer patients. In the *ex vivo* studies, the accuracy (sensitivity) of our fluorescence methods varied from 87% to 97% and the specificity varied from 87% to 100%. The results of our research are tabulated (Table 1) on the following page, and have been confirmed by researchers at other universities, who have employed our type of technology.

In an *ex vivo* study of the esophagus, fluorescence measurements were able to differentiate between normal, Barrett's, dysplastic and adenocarcinoma tissue specimens. In similar research, an animal study performed by CCNY and MSKCC, using a rat esophageal model demonstrated that fluorescence could detect precancerous changes in the rat esophagus prior to any visual indication of malignancy.

The *in vivo* oral cancer study at MSKCC was able to discern differences between normal healthy controls and “normal” appearing contra lateral sites in oral cancer patients.

A preliminary study performed at the IUSL, which focused on *ex vivo* breast cancer specimens, demonstrated that fluorescence spectroscopy could identify different types of cancer. In this study, spectral differences were observed between invasive carcinoma, mixed invasive and *in situ* carcinoma, fibroadenoma and normal breast tissues. In this study is was shown that diffuse reflectance spectra reflected differences in proteins and DNA from tissues with different disease states. A larger study, involving a greater number of specimens with a more detailed histopathological analysis should be implemented to confirm these results.

Currently, three generations of instrumentation have been developed at the IUSL. We currently have instrumentation, which may probe the following organ sites: oral cavity, cervix, aerodigestive tract and colon. Use in the aerodigestive tract and colon requires that our instrumentation be coupled to an endoscope. We have already coupled our instrumentation to a GI tract endoscope.

Table 1. Optical Biopsy Accuracy Statistics

Tissue Type	Number of	Pathology	Sensitivity	Specificity	Year
Breast	16	Cancer	87.5%		1988
	15	Normal		87%	
Breast	40	Cancer	92.5%		1988
	47	Benign and Normal		98%	
GYN	22	Malignant	95%		1992
	10	Non-Malignant		100%	
GYN	65	Cancer	97%		1994
	24	Normal		87.5%	
Colon	35	Cancer	94%		1995
	39	Normal		92%	
Breast	99	Cancer	90%		1995
	67	Normal		90%	
Breast	97	Cancer	95%		1996
	127	Normal		93%	
Esophagus	31	Cancer	93%		1998
	33	Normal		93%	
Breast	103	Cancer	90%		1998
	63	Normal		90%	
Colon	11	Cancer	95%		1999
	11	Normal		95%	

List of Refereed Publications on Optical Biopsy

1. Alfano, R. R., Tata, D., Cordero, J., Tomashefsky, P., Longo, F. W., and Alfano, M. A. *Laser induced fluorescence spectroscopy from native cancerous and normal tissues*, IEEE J Quantum Electron. **20***:* 1507, 1984.

2. Tata, D. B., Foresti, M., Cordero, J., Tomashefsky, P., Alfano, M. A., and Alfano, R. R. *Fluorescence polarization spectroscopy and time-resolved fluorescence kinetics of native cancerous and normal rat kidney tissues*, Biophys J. **50***:* 463, 1986.

3. Alfano, R. R., Tang, G., Pradham, A., Lam, W., Choy, D. S. J., and Opher, E. *Fluorescence spectra from cancerous and normal human breast and lung tissues*, IEEE Journal of Quantum Electronics. **QE-23***:* 1806, 1987.

4. Alfano, R. R., Pradhan, A., Tang, G. C., and Wahl, S. J. *Optical spectroscopic diagnosis of cancer and normal breast tissues*, Journal of the Optical Society of America B (Optical Physics). **6,***:* 1015, 1989.

5. Tang, G. C., Pradhan, A., and Alfano, R. R. *Spectroscopic differences between human cancer and normal lung and breast tissues*, Lasers Surg Med. **9***:* 290, 1989.

6. Liu, C. H., Tang, G. C., Pradhan, A., Sha, W. L., and Alfano, R. R. *Effects of self-absorption by hemoglobins on the fluorescence spectra from normal and cancerous tissues*, Lasers in the Life Sciences. **3,***:* 167, 1990.

7. Alfano, R. R., Das, B. B., Cleary, J., Prudente, R., and Celmer, E. J. *Light sheds light on cancer--distinguishing malignant tumors from benign tissues and tumors*, Bull N Y Acad Med. **67***:* 143, 1991.

8. Alfano, R. R., Das, B. B., Cleary, J., Prudente, R., and Celmer, E. J. *Light sheds light on cancer - distinguishing malignant tumors from benign tissues and tumors*, Bulletin of the New York Academy of Medicine. **67***:* 143, 1991.

9. Alfano, R. R., Liu, C. H., Sha, W. L., Zher, H. R., Akins, D. L., Cleary, J., Prudente, R., and Cellmer, E. *Human breast tissues studied by IR Fourier transform Raman spectroscopy*, Lasers in the Life Sciences. **4***:* 23, 1991.

10. Glassman, W. S., Liu, C. H., Tang, G. C., Lubicz, S., and Alfano, R. R. *Ultraviolet excited fluorescence spectra from non-malignant and malignant tissues of the gynecological tract*, Lasers in the Life Sciences. **5,***:* 49, 1992.

11. Liu, C.-H., Das, B. B., Sha-Glassman, W. L., Tang, G. C., Yoo, K. M., Zhu, H. R., Akins, D. L., Lubicz, S. S., Cleary, J., Prudente, R., Celmer, E., Caron, A., and Alfano, R. R. *Raman, fluorescence, and time resolved light scattering as optical diagnostic techniques to separate diseased and normal biomedical media*, Journal of Photochemistry and Photobiology. **16***:* 187, 1992.

12. Pradhan, A., Das, B. B., Yoo, K. M., Cleary, J., Prudente, R., Celmer, E., and Alfano, R. R. *Time-resolved photoexcited fluorescence kinetics from malignant and non-malignant human breast tissues.*, Lasers in the Life Sciences. **4***:* 225, 1992.

13. Pradhan, A., Das, B. B., Yoo, K. M., Cleary, J., Prudente, R., Celmer, E., and Alfano, R. R. *Time-resolved UV photoexcited fluorescence kinetics from malignant and non-malignant human breast tissues*, Lasers in the Life Sciences. **4,***:* 225, 1992.

14. Schantz, S. P. and Alfano, R. R. *Tissue autofluorescence as an intermediate endpoint in cancer chemoprevention trials*, J Cell Biochem Suppl 199, 1993.

15. Glasgold, R., Glasgold, M., Savage, H., Pinto, J., Alfano, R., and Schantz, S. *Tissue autofluorescence as an intermediate endpoint in NMBA-induced esophageal carcinogenesis*, Cancer Letters. **82***:* 33, 1994.

16. Glassman, W. S., Steinberg, M., and Alfano, R. R. *Time resolved and steady state fluorescence spectroscopy from normal and malignant cultured human breast cell lines*, Lasers in the Life Sciences. **6***:* 91, 1994.

17. Glassman, W., Liu, C.-H., Lubicz, S., and Alfano, R. R. *Excitation spectroscopy of malignant and non-malignant gynecological tissues*, Lasers in the Life Sciences. **6,***:* 99, 1994.

18. Silberberg, M. B., Savage, H. E., Tang, G. C., Sacks, P. G., Alfano, R. R., and Schantz, S. P. *Detecting retinoic acid-induced biochemical alterations in squamous cell carcinoma using intrinsic fluorescence spectroscopy*, Laryngoscope. **104***:* 278, 1994.

19. Cordeiro, P. G., Kirschner, R. E., Hu, Q. Y., Chiao, J. J., Savage, H., Alfano, R. R., Hoffman, L. A., and Hidalgo, D. A. *Ultraviolet excitation fluorescence spectroscopy: a noninvasive method for the measurement of redox changes in ischemic myocutaneous flaps*, Plast Reconstr Surg. **96***:* 673, 1995.

20. Yang, Y., Tang, G. C., Bessler, M., and Alfano, R. R. *Fluorescence spectroscopy as a photonic pathology method for detecting colon cancer*, Lasers in the Life Sciences. **6,***:* 259, 1995.

21. Sacks, P. G., Savage, H. E., Levine, J., Kolli, V. R., Alfano, R. R., and Schantz, S. P. *Native cellular fluorescence identifies terminal squamous differentiation of normal oral epithelial cells in culture: a potential chemoprevention biomarker*, Cancer Lett. **104***:* 171, 1996.

22. Yang, Y., Katz, A., Celmer, E. J., Zurawska-Szczepaniak, M., and Alfano, R. R. *Optical spectroscopy of benign and malignant breast tissues*, Lasers in the Life Sciences. **7,***:* 115, 1996.

23. Schantz, S. P., Savage, H. E., Sacks, P., and Alfano, R. R. *Native cellular fluorescence and its application to cancer prevention*, Environ Health Perspect. **105 Suppl 4***:* 941, 1997.

24. Yang, Y., Celmer, E. J., Zurawska-Szczepaniak, M., and Alfano, R. R. *Excitation spectrum of malignant and benign breast tissues: a potential optical biopsy approach*, Lasers in the Life Sciences. **7,***:* 249, 1997.

25. Yang, Y., Katz, A., Celmer, E. J., Zurawska-Szczepaniak, M., and Alfano, R. R. *Fundamental differences of excitation spectrum between malignant and benign breast tissues*, Photochem Photobiol. **66***:* 518, 1997.

26. Zhang, J. C., Savage, H. E., Sacks, P. G., Delohery, T., Alfano, R. R., Katz, A., and Schantz, S. P. *Innate cellular fluorescence reflects alterations in cellular proliferation*, Lasers Surg Med. **20***:* 319, 1997.

27. Ganesan, S., Sacks, P. G., Yang, Y., Katz, A., Al-Rawi, M., Savage, H. E., Schantz, S. P., and Alfano, R. R. *Native fluorescence spectroscopy of normal and malignant epithelial cells*, Cancer Biochem Biophys. **16***:* 365, 1998.

28. Schantz, S. P., Kolli, V., Savage, H. E., Yu, G., Shah, J. P., Harris, D. E., Katz, A., Alfano, R. R., and Huvos, A. G. *In vivo native cellular fluorescence and histological characteristics of head and neck cancer*, Clin Cancer Res. **4***:* 1177, 1998.

29. Schantz, S. P., Kolli, V., Savage, H. E., Yu, G., Shah, J. P., Harris, D., Katz, A., Alfano, R. R., and G., H. A. *In Vivo Native Cellular Fluorescence and Histological Characteristics of Head and Neck Cancer*, Clinical Cancer Research. **4***:* 1177, 1998.

30. Guo, Y., Savage, H. E., Liu, F., Schantz, S. P., Ho, P. P., and Alfano, R. R. *Subsurface tumor progression investigated by noninvasive optical second harmonic tomography*, Proc Natl Acad Sci U S A. **96***:* 10854, 1999.

31. Papadopoulos, A. J., Zhadin, N. N., Steinberg, M. L., and Alfano, R. R. *Fluorescence spectroscopy of normal, SV40-transformed human keratinocytes, and carcinoma cells*, Cancer Biochem Biophys. **17***:* 13, 1999.

32. Yang, Y., Celmer, E. J., Koutcher, J. A., and Alfano, R. R. *UV reflectance spectroscopy probes DNA and protein changes in human breast tissues*, J Clin Laser Med Surg. **19***:* 35, 2001.

33. Katz, A., Savage, H. E., Schantz, S. P., McCormick, S. A., and Alfano, R. R. *Noninvasive Native Fluorescence Imaging of Head and Neck Tumors*, Technology in Cancer Research and Treatment. **1***:* 9, 2002.

34. Yang, Y., Celmer, E. J., Koutcher, J. A., and Alfano, R. R. *DNA and protein changes caused by disease in human breast tissues probed by the Kubelka-Munk spectral function*, Photochem Photobiol. **75***:* 627, 2002.

35. Alfano, R. R. and Yang, Y. *Stokes Shift Emission Spectroscopy of Human Tissue and Key Biomolecules*, IEEE Journal of Selected Topics in Quantum Electronics. **9***:* 148, 2003.

List of Conference Proceedings and Book Chapters on Optical Biopsy

1. Alfano, R. R. and Yang, Y. *Stokes shift emission spectroscopy of human tissue and key biomolecules*. In: **Optical Biopsy V**, Vol. **5326**, SPIE Proceedings, San Jose, CA, Jan 27-28, 2004, To be published.
2. Katz, A. and Alfano, R. R. *Fluorescence-based instrumentation for cancer detection*. In: **In-Vitro Diagnostic Instrumentation**, Vol. **3913**, SPIE Proceedings, San Jose, CA, January 26-27, 2000.
3. Yang, Y., Celmer, E. J., Koutcher, J. A., and Alfano, R. R. *Excitation Spectroscopy Reveals Changes of Proteins and the Degree of Invasion in Malignant Tissues*. In: **Optical Tomography and Spectroscopy of Tissue III**, Vol. **3597**, SPIE Proceedings, San Jose, CA., 1999, 511.
4. Katz, A., Savage, H. E., Zeng, F.-A., Rome, J., Tang, G. C., D.Harris, Koutcher, J., Schantz, S. P., and Alfano, R. R. *Fluorescence ratio mapping system for tissue diagnosis*. In: **Optical Biopsy II**, Vol. **3250**, SPIE Proceedings, San Jose, CA, 1998, 64.
5. Zhadin, N. N., Yang, Y.-L., Ockman, N., and Alfano, R. R. *Biochemical distinctions between normal and cancerous human breast tissues obtained from fluorescence spectroscopy*. In: **Optical Tomography and Spectroscopy of Tissue: Theory, Instrumentation, Model, and Human Studies II**, Vol. **2979**, SPIE Proceedings, San Jose, CA, 1997, 585.
6. Zhadin, N., Yang, Y.-L., S.Ganesan, Ockman, N., and Alfano, R. R. *Enhancement of the fluorescence cancer diagnostic method of tissues using diffuse reflectance and the analysis of oxygenation state*. In: **Advances in Laser and Light Spectroscopy to Diagnose Cancer and Other Diseases III: Optical Biopsy**, Vol. **2679**, SPIE Proceedings, San Jose, CA, 1996, 142.
7. Yang, Y.-L., Katz, A., Celmer, E. J., Zurawska-Szczepaniak, M., and Alfano, R. R. *Optical spectroscopy of benign and malignant breast tissues*. In: **Advances in Laser and Light Spectroscopy to Diagnose Cancer and Other Diseases III: Optical Biopsy**, Vol. **2679**, SPIE Proceedings, San Jose, CA, 1996, 51.
8. Tang, G. C., Celmer, E. J., and Alfano, R. R. *Phosphorescence and fluorescence spectra from breast tissue*. In: **Advances in Laser and Light Spectroscopy to Diagnose Cancer and Other Diseases III: Optical Biopsy**, Vol. **2679**, SPIE Proceedings, San Jose, CA, 1996, 102.
9. Katz, A., S.Ganesan, Yang, Y.-L., Tang, G. C., Y.Budansky, Celmer, E. J., Savage, H. E., Schantz, S. P., and Alfano, R. R. *Optical biopsy fiber-based fluorescence spectroscopy instrumentation*. In: **Advances in Laser and Light Spectroscopy to Diagnose Cancer and Other Diseases III: Optical Biopsy**, Vol. **2679**, SPIE Proceedings, San Jose, CA, 1996, 118.
10. Katz, A. and Alfano, R. R. *Photonic Pathology - Fluorescence and Raman Spectroscopy for Tissue Diagnosis and Charcterization*. In: Kohen and Hirschberg (eds.), Analytical Use of Fluorescent Probes in Oncology. New York: Plenum Press, 1996.
11. Tang, G. C., Yang, Y. L., Huang, Z. Z., Zhou, F., Cosloy, S., and Alfano, R. R. *Spectroscopic Properties of Tryptophan and Bacteria*. In: **Advances in Laser and Light Spectroscopy to Diagnose Cancer and Other Diseases II**, Vol. **2387**, SPIE Proceedings, San Jose, CA, 1995, 169.
12. Savage, H. E., Kolli, V., Saha, S., Zhang, J.-C., Glasgold, M., Sacks, P. G., Alfano, R. R., and Schantz, S. P. *Development of in vitro models to elucidate mechanisms of intrinsic cellular and tissue fluorescence*. In: **Advances in laser and light spectroscopy to diagnose cancer and other diseases II**, Vol. **2387**, SPIE, San Jose, CA, 1995 1995, 44.
13. Savage, H. E., Kolli, V., Ansley, J., Chandawarkar, R. Y., Alfano, R. R., and Schantz, S. P. *Innate tissue fluorescence of the oral mucosa of controls and head and neck cancer patients.* In: **Advances in laser and light spectroscopy to diagnose cancer and other diseases II**, Vol. **2387**, SPIE, San Jose, CA, 1995, 2.
14. Yang, Y., Tang, G. C., Bessler, M., and Alfano, R. R. *Optical Spectroscopy Methods to Detect Colon Cancer*. Vol. **2135**, SPIE Proceedings 1994.
15. Savage, H. E., Kolli, V., Zhang, J., Alfano, R. R., Sacks, P. G., and Schantz, S. P. *Tissue autofluorescence spectroscopy: in vivo alterations may reflect cellular proliferation*. In: **Advances in**

laser and light spectroscopy to diagnose cancer and other diseases, Vol. **2135**, SPIE, Los Angles, CA, 1994, 16.

16. Huang, Z. Z., Glassman, W. S., Tang, G. C., Lubicz, S., and Alfano, R. R. *Fluorescence diagnosis of gynecological cancerous and normal tissues*. Vol. **2135**, SPIE Proceedings 1994, 42.

17. Tang, G., Oz, M. C., V.Reid, K.Steinglass, M.Ginsberg, Jacobowitz, L., and Alfano, R. R. *Native fluorescence spectroscopy of thymus and fat tissues*. In*:* **Physiological Imaging, Spectroscopy, and Early Detection**, Vol. **1887**, SPIE Proceedings, Los Angeles, CA, 1993, 165.

18. Schantz, S. P., Savage, H. E., Sacks, P. G., Silverberg, M., Lipkin, M., Yang, K., Tang, G., and Alfano, R. R. *Tissue autofluorescence spectroscopy: an intermediate endpoint for chemopreventive agents*. In*:* **Physiological Imaging, Spectroscopy, and Early Detection**, Vol. **1887**, SPIE Proceedings, Los Angeles, CA, 1993, 195.

19. Liu, C. H., Das, B. B., Glassman, W. L. S., Tang, G., Zhu, H. R., Akins, D. L., Lubicz, S., Cleary, J., R. Prudente, E. Celmer, E. Caron, and Alfano, R. R. *NIR Raman and fluorescence spectroscopies diagnose cancer!* In: **Physiological Imaging, Spectroscopy, and Early Detection**, Vol. **1887**, SPIE Proceedings, Los Angeles, CA, 1993, 188.

20. Das, B. B., Glassman, W. L., Alfano, R. R., Cleary, J., R. Prudente, E. Celmer, and Lubicz, S. *UV-fluorescence spectroscopic technique in the diagnosis of breast, ovarian, uterus, and cervix cancer*. In*:* **Laser-Tissue Interaction II**, Vol. **1427**, SPIE Proceedings, Los Angeles, CA, 1991, 368.

List of Optical Biopsy Related Patents

1. Method for Detecting Cancerous Tissue using Visible Native Luminescence, R. R. Alfano and M. A. Alfano, #4,930,516 June 5, 1990.

2. Method and Apparatus for Detecting Cancerous Tissue using Luminescence Excitation Spectra, R. R. Alfano, #5,042,494, August 27, 1991.

3. Optical Method and Apparatus for Diagnosing Human Spermatozoa, R. R. Alfano, George R. Nagamatsu, Nobutoshi Oka, #5,061,075, October 29, 1991.

4. Method and Apparatus for Distinguishing Cancerous Tissue from Benign Tumor Tissue, Benign Tissue or Normal Tissue using Native Fluorescence, R. R. Alfano, B. Das, G. Tang, #5,131,398, July 21, 1992.

5. Method for determining if a Tissue is a Malignant Tumor Tissue, a Benign Tumor Tissue, or a Normal Benign Tissue using Raman Spectroscopy, R. R. Alfano, C.-H. Liu, W. S. Glassman, #5,261,410, November 16, 1993.

6. Method for Distinguishing between Calcified Atherosclerotic Tissue and Fibrous Atherosclerotic Tissue or Normal Cardiovascular Tissue Using Raman Spectroscopy, R. R. Alfano, C. H. Liu #5,293,872, March 15, 1994.

7. Method for determining if Tissue is Malignant as opposed to Non-Malignant using Time-Resolved Fluorescence Spectroscopy, R. R. Alfano, A. Pradhan, G. C. Tang, L. Wang, Y. Budansky, B. B. Das, #5,348,018, September 20, 1994.

8. Method and Apparatus for Mapping a Tissue Sample for and Distinguishing Different Regions thereof based on Luminescence Measurements of Cancer-indicative Native Fluorophor, R. R. Alfano, #5,413,108, May 9, 1995.

9. Method for Determining if Tissue is Malignant as opposed to Non-Malignant using Time-resolved Fluorescence Spectroscopy, R. R. Alfano, Asima Pradhan, G. C. Tang, L. Wang, Y. Budansky, B. B. Das, #5,467,767, November 21, 1995.

10. Technique for Determining whether a Cell is Malignant as opposed to Non-malignant using Extrinsic Fluorescence Spectroscopy, R. R. Alfano, Cheng H. Liu, Wei L. Sha, Yury Budansky, #5,635,402, June 3, 1997.

11. Method for Detecting Cancerous Tissue using Optical Spectroscopy and Fourier Analysis, R. R. Alfano, A. Katz, Y. Yang, #5,769,081, June 23, 1998.

12. Method for Detecting Cancerous Tissue using Visible Native Luminescence, R. R. Alfano, M. A. Alfano, #B1 4,930,516, August 4, 1998.
13. Optical Imaging of Breast Tissues to enable the Detection therein of Calcification Regions Suggestive of Cancer, R. R. Alfano, P. P. Ho, L. Wang, X. Liang, P. Galland, #5,799,656, September 1, 1998.
14. Method for Monitoring the Effects of Chemotherapeutic Agents on Neoplasmic Media, R. R. Alfano, G. C. Tang, S. P. Schantz, #5,849,595, December 15, 1998.
15. Method and apparatus for in vivo examination of subcutaneous tissues inside an organ of a body using optical spectroscopy, R. R. Alfano, Y. Budansky, #5,983,125, November 9, 1999.
16. Method and apparatus for detecting the presence of cancerous and precancerous cells in a smear using native fluorescence spectroscopy, Robert R. Alfano, Singaravelu Ganesan, and Yury Budansky, #6,080,584, June 27, 2000.
17. Detection of cancer and precancerous conditions in tissues and/or cells using native fluorescence excitation spectroscopy, Robert R. Alfano, Singaravelu Ganesan, Alvin Katz, Yang Yuanlong, #6,091,985, July 18, 2000.
18. Remote-Controllable, Micro-Scale Device for use in In Vivo Medical Diagnosis and/or Treatment, Robert R. Alfano, Scott Alfano, Quan-Zhen Wang, Ping Pei Ho, #6,240,312, May 29, 2001.
19. Technique for Examining Biological Materials Using Diffuse Reflectance Spectroscopy and the Kubelka-Munk Function, R. R. Alfano, Y. Yang, #6,615,068 B1, September 2, 2003.
20. System and Method of Fluorescence Spectroscopic Imaging for Characterization and Monitoring of Tissue Damage, R. R. Alfano, J. Tang, P. P. Ho, #6,631,289 B2, October 7, 2003.
21. Method and Apparatus for Examining a Tissue Using the Spectral Wing Emission Therefrom Induced by Visible to Infrared Photoexcitation, R. R. Alfano, S. G. Demos, G. Zhang, #6,665,556 B1, December 16, 2003.

Biological and Chemical Patents

1. Noninvasive Method and Apparatus for Characterizing Biological Materials, R. R. Alfano, K. M. Yoo, G. C. Tang, #5,369,496, November 29, 1994.
2. Method and Device for Detecting Biological Molecules and/or Microorganisms within a Desired Area or Space, R. R. Alfano, #5,474,910, December 12, 1995.
3. Method and Apparatus for Evaluating the Composition of an Oil Sample, R. R. Alfano, C. H. Liu, #5,656,810, August 12, 1997.
4. Photon-Mediated Introduction of Biological Materials into Cells and/or Cellular Components, Robert R. Alfano, Cheng-Hui Liu, #6,346,101 B1, February 12, 2002.
5. Method and System for Examining Biological Materials Using Low Power CW Excitation Raman Spectroscopy, R. R. Alfano, Wubao Wang, #6,560,478 B1, May 6, 2003.

Contact Information

Principal Investigator

R. R. Alfano, Distinguished Professor of Science and Engineering

212-650-5531, alfano@sci.ccny.cuny.edu

Biomedical Research Program Leader

Al Katz, Ph.D.

212-650-5591, akatz@ccny.cuny.edu

Business Development

Alan Doctor

212-650-8265, doctor@ee.ccny.cuny.edu