

Fluorescence spectroscopy: An emerging excellent diagnostic tool in Medical Sciences

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Abstract

In this article, we will discuss the various diagnostic applications of fluorescence spectroscopy in sub specialties of medical sciences. Fluorescence Spectroscopy (FS) is an emerging excellent diagnostic tool for many diseases especially early stage cancers. Fluorescence Spectroscopy prove to be more sensitive diagnostic tool with high efficacy as compared to routine diagnostic tools currently in use for many disorders. But, still there is great need for arrangement of Clinical trial on large scale to establish the validity of this new diagnostic technique. There is immediate need to highlight this issue.

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INTRODUCTION

Fluorescence Spectroscopy is a type of electromagnetic spectroscopy which analyzes fluorescence from a sample. Sample is excited by using a beam of light which results in emission of light of a lower energy resulting in emission spectrum which is used to interpret results.⁷ There is increased trend to use fluorescence spectroscopy (FS) as a diagnostic tool in various sub specialties of medical sciences. In recent years, due to successful applications in various fields of medical sciences, FS is proved to be more sensitive technique and has potential to become more reliable diagnostic tool with high efficacy. Successful application of FS is achieved because of autofluorescence properties of various tissues of the organs. Also, presence of many chromophores makes it easy to use FP as a diagnostic technique for many disorders. Chromophores which are produce in excess as a result of pathologies in tissues or present in normal state include NADH, collagen, elastin, porphyrins and carotenoids.¹ These chromophores contribute to the emission spectrum which is used for interpretation of diagnostic results along with other parameters.

ONCOLOGY

Cancer is the major killer disease around the world. High mortality rate caused by cancer diseases can be reduced significantly by early diagnosis of cancer. Early diagnosis will enable to start treatment at early stage and chances of cure will increase with early treatment. But, unfortunately,

many types of cancers are diagnosed at late stage which results in the failure of treatment. So, there is great need for diagnostic tools which can diagnose cancer at early stages. FS prove to be very useful in this regard. We will review the application of FS in this regard under various sub specialties headings. Many metabolic compounds like porphyrins are produce in excess amount in cancerous tissues due to rapid metabolism of cancerous tissue. These compounds are responsible for an emission spectrum which can be used for diagnosis of cancerous tissues along with other parameters.

DERMATOLOGY

Fluorescence spectroscopy can be used for in vivo detection of skin pathologies, because skin contains elastin, collagen, keratin, and NADH, which are chromophores and contribute to the fluorescence spectrum. Skin cancers can be diagnosed by Fluorescence from skin e.g., melanoma. By means of FS, Non-dysplastic nevi can be distinguished from melanoma and dysplastic nevi.¹

ENDOCRINOLOGY

Fluorescence spectroscopy especially Fluorescence correlation spectroscopy (FCS) prove to be excellent to understand anatomy and physiology of various hormones. Köhler et al (2005) used Fluorescence correlation spectroscopy (FCS) for study of glucocorticoids (GCs) receptors on the mouse pituitary cell line and found data which is consistent with new cell membrane glucocorticoids (GCs) receptors.² This discovery of new receptor in author's lab will be a key point for future research on HPA axis and

to study the imbalance of HPA axis which is associated with many endocrine disorders and other disorders like depression, anxiety, Cushing disease and sleep disorders.

MICROBIOLOGY

Alexandra Alimova et al (2004) used fluorescence spectroscopy for in situ investigations of bacteriophage as well as their host cells.³ They demonstrated that fluorescence may be a novel tool to detect viruses and monitor viral infection of cells. FCS has been used to study the biophysical characterization of HRV (a major Flu virus) in author's Lab. These studies provide Valuable data for understanding virus-receptor interactions.⁴ FCS can be useful to study infectious processes of various important viruses, like endocytosis and intracellular processing of virus.

GASTROENTEROLOGY

Brigitte Mayinger et al (2001) concluded that Light-induced fluorescence spectroscopy might be a useful tool for endoscopic in vivo detection of dysplasia and for detection of early carcinoma in the upper GI tract.⁵ However, there is need for further trials to test the validity of this new optical detection system. Laser-Induced Fluorescence at 488 nm Excitation can be used for Detecting Benign and Malignant Lesions in Stomach Mucosa.⁶

GYNECOLOGY

Ramanujam et al performed in vivo clinical trial to see efficacy of fluorescence spectroscopy for the diagnosis of pathologies of the cervix. Cervical intraepithelial neoplasia (CIN) was diagnosed with a sensitivity of 87% and a specificity of 73 %.^{7,8} Optical diagnosis of cervical cancer can be made by fluorescence spectroscopy technique.⁹ It is likely that fluorescence spectroscopy (FS) can be used for bio detection of viruses which are associated with cervix cancer like Human Pappiloma Virus (HPV).

OTOLARYNGOLOGY

Dhingra et al (1998) studied the LIF spectroscopic properties of 9, 10-dimethyl-1, 2-benzanthracene (DMBA)-induced precancerous and early cancerous lesions in a hamster buccal pouch mucosa model.¹⁰ The result indicate that LIF spectroscopy may be used as a noninvasive diagnostic technique for early diagnosis of head and neck cancer and a possible biochemical surrogate biomarker in the follow-up of suspected lesions. Noninvasive diagnosis of oral cavity neoplasia can be improved by Fluorescence spectroscopy.¹¹

CARDIOLOGY

FS seems to be very promising diagnostic tool in cardiology field for many disorders. Fluorescent Studies on sheep heart indicate that FS can be applied for diagnosis of cardiomyopathis in human heart.¹² But, there is lack of such studies in human heart tissue up till now. Atherosclerotic lesions can be diagnosed by means of LIFS.¹³ It was first studied by Blankenhorn and Braunstein in 1956. Sartori et al investigated the LIFS as an intraluminal diagnostic technique for arterial tissue.¹⁴ Richards-Kortum et al worked for developing optical-fiber catheters for in vivo use.¹⁵ Papazoglou has tested LIFS for guidance of laser ablation in vitro and in vivo.¹⁶ There are investigations going on for possible use of LIFS in identification of fibrotic myocardium and heart conduction tissue for the treatment of arrhythmia.^{17,18.}

NEUROLOGY

Pitschke et al (1998) detected single amyloid B protein aggregates in CSF of Alzheimer's disease patients by FCS.¹⁹ Pramod V. Butte. et al (2005) investigate the use of time-resolved laser-induced fluorescence spectroscopy (TR-LIFS) as an adjunctive tool for the intraoperative rapid evaluation of brain tumor specimens and delineation of tumor from surrounding normal tissue.²⁰ TR-LIFS can be used as a tool for the identification of meningiomas²⁰.

THYROID DISEASES

Michael Jay Pitman et al (2004) investigated the fluorescent characteristics of different thyroid fresh ex vivo tissues by surfaced scanning with a fluorescence spectrophotometer and found that fluorescent spectrometry may be used as a localization aid for fine needle aspiration, using optical fiber probes.²¹ There is need to do further investigations which may enhance the sensitivity and specificity of fluorescent spectrometry, allowing it to replace or compliment fine needle aspiration.

DIAGNOSIS OF DIABETES MELLITUS

Eppstien and Bursell showed that Fluorescence spectroscopy of the lens can be used for non-invasive diagnosis of diabetes mellitus²².

OPHTHALMOLOGY

Metabolic state of the cornea can be monitored by means of Fluorescence spectroscopy.²³

DENTISTRY

Fluorescence spectroscopy can be used for the detection and

localization of pathological dentin, pulpal remnants, and microorganisms within the root canal.²⁴

CONCLUSIONS

Fluorescence Spectroscopy (FS) is promising diagnostic technique with high efficacy for various diseases of medical importance. Cancer is the second biggest killer in developed world. Cancers are diagnosed usually at late stage by routine diagnostic tools and treatment started at late stage usually fails to cure. There is great need for a diagnostic tool which can detect cancer at initial stages and can help to start treatment at initial stages. Fluorescence Spectroscopy (FS) has been applied successfully for detecting multisystem cancers at initial stages. FCS proves to be very helpful for understanding various stages of viral pathogenesis. But, still there is need for further studies and clinical trial to check efficacy and validity of diagnostic systems based on Fluorescence Spectroscopy use. Also, research should be oriented towards designing flexible systems i.e., endoscopes, probes and portable devices which can be used in routine medical practice. Active collaboration between Physicians, Surgeons, Biochemists and biophysicists is necessary for achieving this goal.

References

1. Lowmann w, and Paul.1989b. Native fluorescence of unstained cryo- section of the skin with melanomas and nevi. *Naturwissenschaften*. 76 (9), 424-426.
2. Köhler et al. 2005. G protein coupled glucocorticoid receptors on the pituitary cell membrane. *J. Cell Science*, 118, 3353-3361.
3. Alimova, A et al. 2004. Virus particles monitored by fluorescence spectroscopy: a potential detection assay for macromolecular assembly. *Photochem Photobiol* 80, 41-46.
4. Köhler et al. 2007. Attachment of VLDL Receptors to an Icosahedral Virus along the 5-fold Symmetry Axis: Multiple Binding Modes Evidenced by Fluorescence Correlation Spectroscopy. *Biochemistry*, 46, 6331-6339.
5. Brigitte et al.2001. Endoscopic fluorescence spectroscopy in the upper GI tract for the detection of GI cancer: initial experience. *The American Journal of Gastroenterology*. 96, 2616-2621.
6. Landulfo Silveira Jr et al.2007.Laser-Induced Fluorescence at 488 nm Excitation for Detecting Benign and Malignant Lesions in Stomach Mucosa. *Journal of Fluorescence*. Volume 18, Number 1. 35-40.
7. Ramanujam N, Mitchell M F, Mahadevan A, Thomsen S, Silva E, and R Richards-Kortum 1994a.Fluorescence spectroscopy:A diagnostic tool for cervical intraepithelial neoplasia *Gynecol. Oncol.* 52 31-8.
8. Ramanujan N, Mitchell M F, Mahadeevan A, Warren S, Thomsen S, Silva E and Richards-Kortum R. 1994b. In vivo diagnosis of cervical intraepithelial neoplasia using 337-nm-excited laser-induced fluorescence *Proc.Natl Acad. Sci. USA* 91 10 193-7.
9. Siddappa M. Chidananda et al. 2006. Optical diagnosis of cervical cancer by fluorescence spectroscopy technique. *International Journal of Cancer*. Volume 119 Issue 1, 139 – 145.
10. Dhingra et al. 1998. Diagnosis of head and neck precancerous lesions in an animal model using fluorescence spectroscopy. *Laryngoscope*. 108(4 Pt 1):471-5.
11. Ann Gillenwater et al.1998. Noninvasive Diagnosis of Oral Neoplasia Based on Fluorescence Spectroscopy and Native Tissue Autofluorescence. *Arch Otolaryngol Head Neck Surg*. 1998; 124:1251-1258.
12. George E. Kochiadakis et al. 2001. The Role of Laser-Induced Fluorescence in Myocardial Tissue Characterization-An Experimental In Vitro Study. *CHEST*. vol. 120 no. 1 233-239.
13. Blankenhorn D H and Braunstein H. 1956. Carotenoids in man III. The microscopic patterns of fluorescence in atheromas, and its relation to their growth *J. Clin. Invest.* 35 160-5.
14. Sartori Met al. 1987. Autofluorescence of atherosclerotic human arteries—a new technique in medical imaging *IEEE J. Quant Elec.* 23 1794-7.
15. Richards-Kortum R, Rava R P, Fitzmaurice M, Tong L L, Ratliff N B, Kramer J R and Feld M S 1989c A one-layer model of laser-induced fluorescence for diagnosis of disease in human tissue: applications to atherosclerosis. *IEEE Trans.Biomed. Eng.* 36 1222-32.
16. Papazoglou T G. 1995. Malignancies and atherosclerotic plaque diagnosis—is laser induced fluorescence spectroscopy the ultimate solution? *J. Photochem. Photobiol. B* 28 3-11.
17. Perk M, Flynn G J, Smith C, Bathgate B, Tulip J, Yue W and Lucas A. 1991. Laser-induced fluorescence emission: 1. The spectroscopic identification of fibrotic endocardium and myocardium *Lasers Surg. Med.* 11 523-34.
18. Perk M et al. 1993. Laser-induced fluorescence identification of sinoatrial and atrioventricular nodal conduction tissue *Paging Clin. Electrophysiol.* 16 1701-12.
19. Pitschke et al. 1998. Detection of single amyloid beta-protein aggregates in the cerebrospinal fluid of Alzheimer's patients by fluorescence correlation spectroscopy. *Nat Med.* 4(7):832-4.
20. Pramod V. Butte. et al. 2005 Diagnosis of meningioma by time-resolved fluorescence spectroscopy. *J. Biomed.* 10(6):064026.
21. Michael Jay Pitman et al .2004. The fluorescence of thyroid tissue. *Otolaryngology—Head and Neck Surgery*. Volume 131, Issue 5, Pages 623-627.
22. Eppstien J and Bursell S-E 1992 Non-invasive detection of diabetes mellitus *Proc. SPIE* 1641 217-26.
23. JoséG. Cunha-Vaz. 1997. Optical sensors for clinical ocular fluorometry. *Progress in Retinal and Eye Research*. Volume 16, Issue 2, 243-270.
24. Ani Sarkissian. 2005. Fiber optic fluorescence microprobe for endodontic diagnosis. *J Dent Educ.* 69 (6):633-8 15947209.

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