

# CONTENTS

<b>List of Tables</b> .....	<b>xi</b>
<b>List of Figures</b> .....	<b>xii</b>
<b>Abbreviation and Acronyms</b> .....	<b>xiv</b>

## **Chapter 1**

### **Background, purpose and definition of the problem**

1.1	Introduction.....	1
1.2	Oral cancer: A global health concern .....	2
1.1.1	Etiology of oral cancer .....	3
1.1.2	Oral cancer incidence in India .....	5
1.3	Aim and Objectives .....	7
1.3.1	Aim.....	7
1.3.2	Objectives .....	8
1.4	Current clinical practices for oral cancer detection.....	8
1.4.1	Biopsy procedure for the diagnosis of oral cancer.....	10
1.4.2	Premalignant lesions/conditions of epithelial origin.....	12
1.4.2.1	Dysplasia .....	13
1.4.2.2	Leukoplakia.....	13
1.4.2.3	Erythroplakia .....	14
1.4.2.4	Oral Sub-mucous Fibrosis.....	14
1.4.3	Importance of early detection and criteria for screening and screening test.....	14
1.4.4	Conventional non-invasive screening and diagnostic methods of oral cancer and its limitations.....	17
1.4.4.1	Brush biopsy.....	18

1.4.4.2	Toluidine blue staining.....	20
1.4.4.3	Chemiluminescence.....	20
1.5	Optical spectroscopy for cancer diagnostics.....	21
1.6	Conclusions.....	24

## Chapter 2

### Interaction of light with biological tissues

2.1	Introduction.....	26
2.2	Optical spectroscopy in medical diagnostics.....	27
2.2.1	Light.....	27
2.2.2	Epithelial tissue.....	28
2.3	Structure of oral mucosa and oral anatomy.....	29
2.4	Fundamentals of light-tissue interaction.....	30
2.4.1	Absorption and scattering – the basics.....	32
2.4.2	Absorption in biological tissues.....	33
2.5	Autofluorescence Spectroscopy.....	35
2.5.1	Heme synthesis.....	38
2.5.2	Fluorescence spectroscopic techniques in cancer detection.....	39
2.6	Diffuse reflectance in cancer diagnostics.....	43
2.6.1	DR Imaging.....	44
2.7	Cancer diagnosis- National scenario .....	46
2.8	Conclusions.....	46

## Chapter 3

### Instrumentation and Analytical Techniques

3.1	Introduction.....	48
3.2	Point Monitoring & Imaging Systems.....	49
3.3	LIFRS System for Oral Cancer diagnosis.....	49
3.3.1	Choice of Light Source and Wavelength.....	51

3.3.2	Data Acquisition using point monitoring system.....	51
3.4	DR Imaging system.....	53
3.4.1	Operation of DRIS.....	55
3.5	Protocol and Ethical issues.....	57
3.6	Clinical trials.....	58
3.6.1	Point monitoring.....	58
3.6.2	Diffuse Reflectance Imaging.....	59
3.7	Analytical methods.....	60
3.7.1	Principal component analysis (PCA).....	60
3.7.2	Linear discriminant analysis (LDA).....	61
3.8	Diagnostic Accuracies.....	62
3.8.1	Sensitivity and Specificity.....	62
3.8.2	Positive and Negative Predictive Values.....	63
3.8.3	ROC curve and AUC.....	64
3.9	Conclusions.....	65

## **Chapter 4**

### **Clinical trial for non-invasive detection of oral lesions by point monitoring of laser-induced autofluorescence**

4.1	Introduction.....	67
4.2	Materials and Methods.....	67
4.2.1	Study Population and Protocol.....	67
4.2.2	Data processing & Statistical Analysis.....	68
4.3	Results.....	70
4.3.1	Spectral features.....	70
4.3.2	Lesion classification.....	71
4.4	Discussion.....	73
4.5	Conclusions.....	76

## Chapter 5

### Clinical trial for detection and classification of oral lesions using diffuse reflectance spectroscopy

5.1	Introduction.....	78
5.2	Materials and methods.....	78
5.2.1	Study population and study settings.....	78
5.2.2	Spectral data processing.....	79
5.2.3	Statistical procedure.....	80
5.3	Results.....	81
5.3.1	Demographic details.....	81
5.3.2	Spectral features.....	82
5.3.3	Lesion classification.....	82
5.4	Discussion.....	84
5.5	Conclusions.....	87

## Chapter 6

### In vivo discrimination of benign lesions of the oral cavity from pre-malignant with autofluorescence and diffuse reflectance spectroscopy

6.1	Introduction.....	89
6.2	Materials and methods.....	90
6.3	Results.....	91
6.3.1	AF spectral features.....	91
6.3.2	DR spectral features.....	92
6.3.3	DR imaging.....	93
6.4	Discussion.....	93
6.5	Conclusions.....	97

## **Chapter 7**

### **Diagnostic performance of autofluorescence and diffuse reflectance in clinical studies: A comparative evaluation**

7.1	Introduction.....	99
7.2	Materials and methods.....	99
7.2.1	Volunteer patient population.....	99
7.2.2	Data Acquisition/ Protocol.....	100
7.3	Results.....	100
7.3.1	Spectral features.....	101
7.3.2	Lesion classification.....	102
7.3.2.1	Fluorescence spectral data.....	103
7.3.2.2	DR spectral data.....	104
7.4	Discussion.....	105
7.5	Conclusions.....	108

## **Chapter 8**

### **Diffuse reflectance spectral imaging: a novel non-invasive technique for early diagnosis and screening of oral malignancies**

8.1	Introduction.....	110
8.2	Materials and Methods.....	111
8.3	Results.....	113
8.4	Discussion.....	116
8.5	Conclusions.....	121

## **Chapter 9**

**Conclusions and future perspectives..... 123**

**List of publications..... 131**

**Bibliography ..... 133**