Analysis and Classification of Confocal Laser Endomicroscopic Images to Distinguish Pathological from Healthy Tissue

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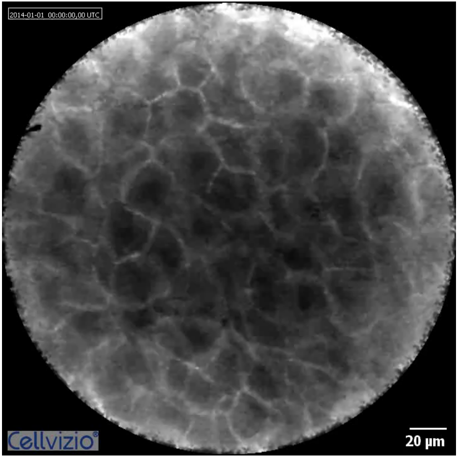
Structure

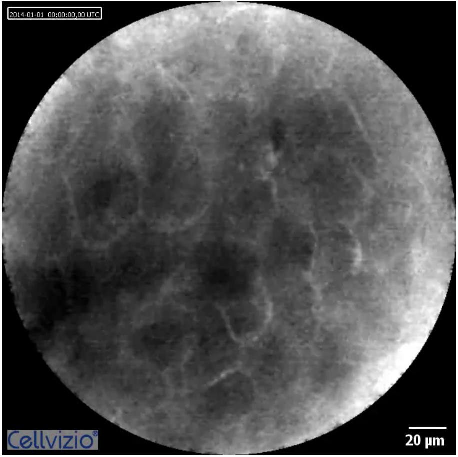
- Motivation
- Background
- Data & Methods
- Experiments and Results
- Summary & Conclusion

Motivation

Motivation – Initial Problem



Motivation – Initial Problem



Motivation – Cancer of the Oral Cavity

Sixth most common kind of cancer

Problems of diagnosis

- subjectivity of physician
- histological analysis
- surgical resection

Early diagnosis $\Rightarrow$ difficult!

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Early diagnosis $\Rightarrow$ difficult!

$\Rightarrow$other solutions?

Motivation – Objectives of this Thesis

Overall: separate patholgical from healthy images

Benefits:

- objective method to support the physician
- supports diagnosis & finding of the resection site
- time-saving and less harmful for the patient

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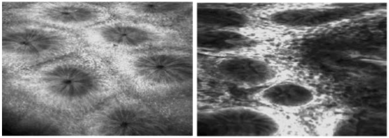
Three problems:

1. creation of image database ⇒ pre-processing ✓
2. annotation of images ⇒ needs to be solved
3. classification of images ⇒ depending on annotation problem

Motivation – State of the Art

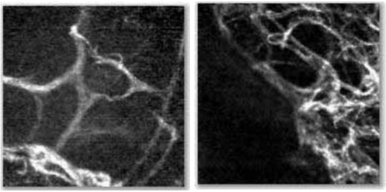
Couceiro et al. [Couceiro, 2012]

- gastrointestinal tract
- arrangement of glands
- Scale Invariant Feature Transform (SIFT)



Désir et al. [Désir, 2012]

- distal lung
- texture description
- Local Binary Patterns (LBP), SIFT

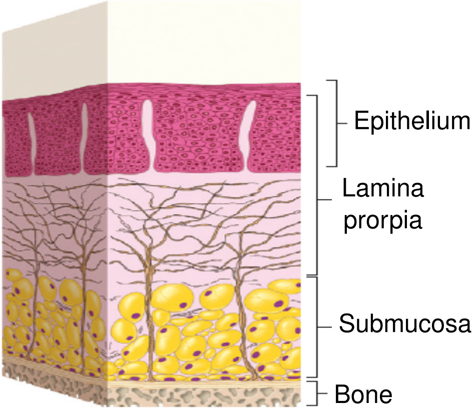


Background

Background – Mucous Membrane

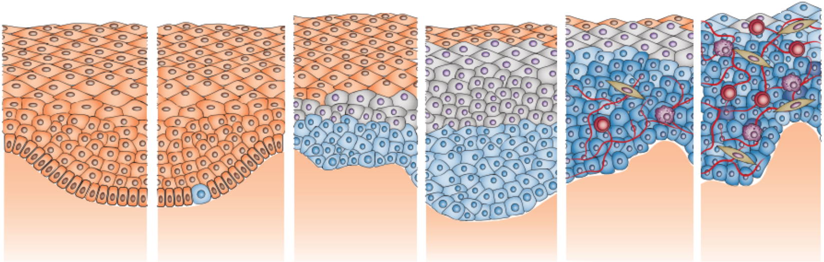
Epithelial layer described by:

- cytology
- architecture



Background – Carcinogenesis

Development stages of oral cancer

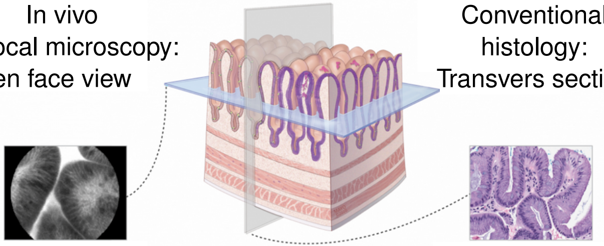


Normal	Squamous hyperplasia	Mild dysplasia	Moderate dysplasia	Severe dysplasia	Carcinoma in situ

Background – Optical Biopsy

In vivo
confocal microscopy:
en face view

Conventional
histology:
Transvers section

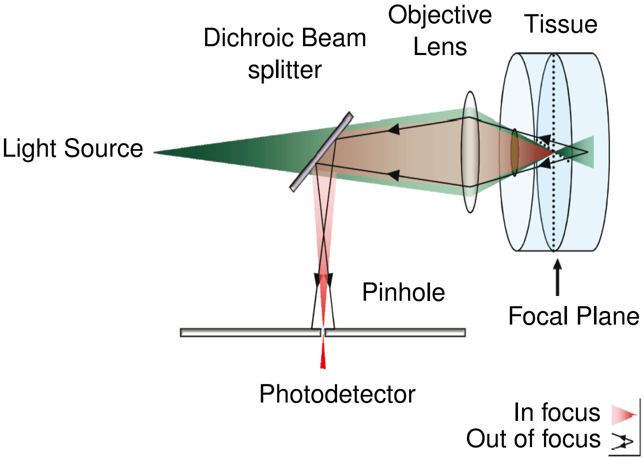


Example of
Optical Biopsy

Example of Physical
Biopsy Image

Confocal LaserEndomicroscopy (CLE) allows real time visualization of epithelial layer **in vivo**!

Background – Principle of CLE



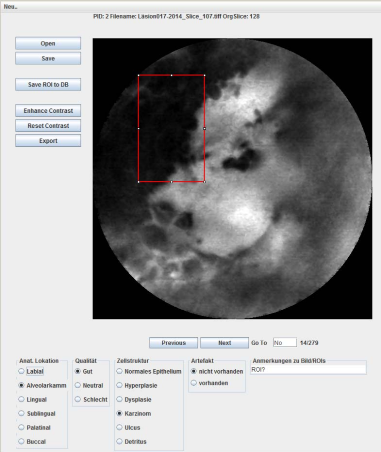
Data & Methods

Data – Hardware

Cellvizio Gastro-flex UHD

Imaging rate (frames/s)	12.8
Probe diameter (mm)	2.7
Depth of imaging (μm)	55-65
Lateral resolution (μm)	1
Field of view (μm)	$\varnothing$ 240
Image resolution (px)	576 $\times$ 576

Data – Software

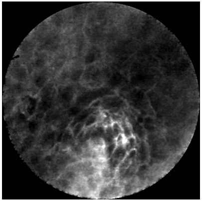


Data – Patient Data

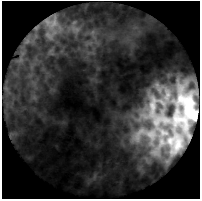
	Control Group	Patient Group
Gender (m/f)	1/-	1/1
Age (years)	30	63.5 ± 2.1

Data – Image Database – Classification Method

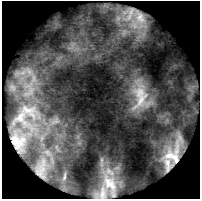
Location	Control	Patient 1	Patient 2
Alveolar Ridge (h/c)	71/-	94/45	41/-
Buccal mucosa (h/c)	-/-	32/15	-/-
Lingual mucosa (h/c)	-/-	-/-	29/27



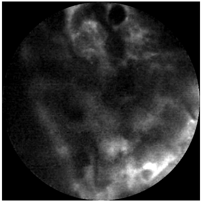
(a) Healthy



(b) Carcinoma



(c) Carcinoma

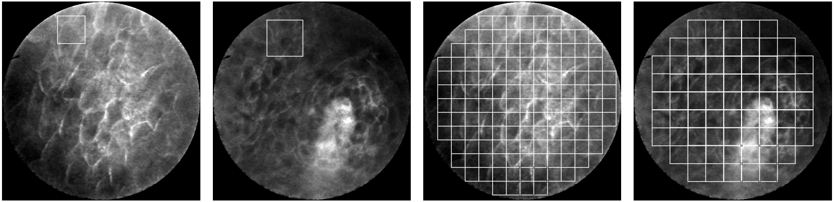


(d) Carcinoma

Methods – Classification Algorithm

Subdivide images

- 110/51 rectangular patches $\Rightarrow$ precalculated coordinates
- sidelength 80/105 px
- step length 0.5 $\times$ side length $\Rightarrow$ 50 % overlap in x-direction



(a) 1 $\times$ 80 (b) 1 $\times$ 105 (c) 110 $\times$ 80 (d) 51 $\times$ 105

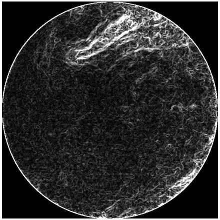
Methods – Extracted Features

Histogram features

- frequency of gray level occurrences of an image
- no information concerning structure or arrangement
- computation of statistics
- 256/512/768 bins

Homogeneity features

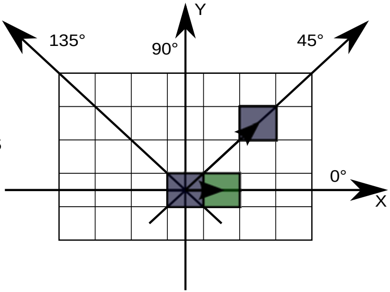
- evaluates gray values
- evaluates edge images
- simple features



Methods – Extracted Features

Grey Level Co-Occurrence Matrices [Haralick, 1973]

- frequency of gray values
- geometrical arrangement of gray values
- different orientation and distances
- lower amount of gray values
- features by Haralick, GLCM (8/16/32 lmglvl)



Methods – Extracted Features

Local Binary Pattern classical (LBPc) [Ojala, 1996]

- pixel by binary pattern
- binary pattern describe structures
  $\Rightarrow$ histogram
- statistical information
- LBPc(R1, N8)

113	176	9
85	100	110
60	30	105

a) 3x3 Image region

1	1	0
0		1
0	0	1

b) Thresholding results

1	2	4
128		8
64	32	16

c) Weighting of Pixels

1	2	0
0	27	8
0	0	16

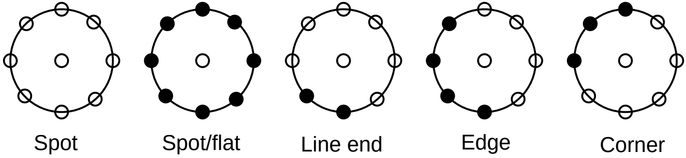
d) Contribution to pixel

Methods – Extracted Features

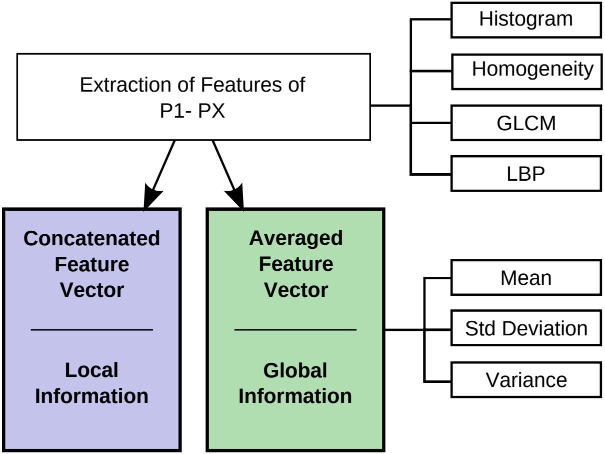
Extensions of Local Binary Patterns (LBPr) [Ojala,2002]

- uniform & rotation invariant
- variable radius & neighborhood
- variable histogram size
- LBPr(R1/2, N8/16)

uniform: $\leq$ two transitions from 1 to 0 or 0 to 1
rotation invariant: $\mathrm{LBP}^{ri}_{R,N} = \min(\mathrm{ROR}(\mathrm{LBP}_{R,N}\, i))$



Methods – Feature Vectors



Methods – Classifier & Evaluation

Classification algorithms

- Support Vector Machine (SVM)
- Random Forest (RF)
- Bagging (Bag)
- AdaBoostM1 (Ada)

Evaluation methods

- 10-fold crossvalidation
- classification rate (Acc)
- average recall (Rec)

Software

- CONRAD $\rightarrow$ image analysis & feature extraction
- Weka $\rightarrow$ classification tasks

Experiments and Results

Experiments – Classification Method

Pathological vs. non-pathological

One patient – same location

- P1 vs. P1 – alveolar ridge
- P1 vs. P1 – buccal
- P2 vs. P2 – lingual

Between subjects – same location

- P1 vs. P2 – alveolar ridge
- P1 vs. P2 & Ctrl – alveolar ridge

All subjects – all locations

Experiments – Classification Method

Pathological vs. non-pathological

One patient – same location

- P1 vs. P1 – alveolar ridge $\Rightarrow$ Acc / Rec: 100.0 % / 100.0 %
- P1 vs. P1 – buccal $\Rightarrow$ Acc / Rec: 100.0 % / 100.0 %
- P2 vs. P2 – lingual $\Rightarrow$ Acc / Rec: 100.0 % / 100.0 %

Between subjects – same location

- P1 vs. P2 – alveolar ridge $\Rightarrow$ Acc / Rec: 100.0 % / 100.0 %
- P1 vs. P2 & Ctrl – alveolar ridge $\Rightarrow$ Acc / Rec: 99.2 % / 98.6 %

All subjects – all locations $\Rightarrow$ Acc / Rec: 95.8 % / 93.3 %

Results – All Subjects all Locations

Concatenated feature vector

Features	Property	Patchsize **51** × **105** concatenated Acc / Rec (SVM) in (%)	Acc / Rec (Ada) in (%)	Acc / Rec (Bag) in (%)	Acc / Rec (RF) in (%)
Histogram	256 bins	81.6 / 65.4	74.6 / 50.2	82.8 / 69.6	83.9 / 71.9
Histogram	512 bins	80.5 / 63.8	74.6 / 50.2	81.6 / 68.1	83.6 / 69.4
Histogram	768 bins	80.5 / 63.4	74.6 / 50.2	82.2 / 68.4	85.3 / 72.4
Homogeneity	—	87.0 / 74.3	84.2 / 72.1	86.7 / 75.3	90.7 / 82.2
GLCM	8 Imglvl	94.4 / 92.0	88.1 / 82.8	88.1 / 77.4	87.6 / 75.1
GLCM	16 Imglvl	94.6 / 92.2	88.4 / 81.9	87.6 / 76.6	89.0 / 78.4
GLCM	32 Imglvl	**94.9 / 92.8**	89.3 / 82.0	88.4 / 77.6	89.0 / 78.4
LBPc	R1 N8	78.8 / 68.1	78.0 / 58.3	79.9 / 63.5	81.6 / 66.5
LBPr	R1 N8	78.8 / 67.0	81.6 / 70.0	83.6 / 71.7	89.0 / 79.9
LBPr	R2 N16	81.4 / 68.3	78.0 / 61.8	83.1 / 71.7	85.0 / 74.2

Results – All Subjects all Locations

Concatenated feature vector

Features	Property	Patchsize **110** × **80** concatenated Acc / Rec (SVM) in (%)	Acc / Rec (Ada) in (%)	Acc / Rec (Bag) in (%)	Acc / Rec (RF) in (%)
Histogram	256 bins	83.9 / 73.8	75.7 / 57.5	82.2 / 68.8	84.5 / 70.7
Histogram	512 bins	84.5 / 74.6	75.4 / 53.1	83.3 / 70.7	84.2 / 71.3
Histogram	768 bins	84.2 / 74.0	76.3 / 57.9	81.6 / 68.1	85.3 / 72.1
Homogeneity	—	90.4 / 82.4	84.7 / 71.7	89.0 / 79.9	89.0 / 78.0
GLCM	8 Imglvl	95.2 / 92.6	87.9 / 79.5	88.4 / 79.1	87.9 / 76.4
GLCM	16 Imglvl	94.9 / 92.4	89.3 / 83.6	88.7 / 78.6	86.4 / 74.0
GLCM	32 Imglvl	**95.5 / 93.1**	89.0 / 81.8	89.3 / 80.5	87.3 / 75.7
LBPc	R1 N8	84.7 / 78.7	81.9 / 70.6	81.4 / 65.6	81.4 / 65.9
LBPr	R1 N8	79.7 / 70.2	80.8 / 68.7	85.0 / 74.2	86.4 / 75.9
LBPr	R2 N16	81.1 / 70.8	81.9 / 65.5	85.9 / 75.1	86.4 / 74.7

Results – All Subjects all Locations

Averaged feature vector

Features	Property	Patchsize **51** × **105** averaged Acc / Rec (SVM) in (%)	Acc / Rec (Ada) in (%)	Acc / Rec (Bag) in (%)	Acc / Rec (RF) in (%)
Histogram	256 bins	75.4 / 50.0	76.3 / 54.0	84.5 / 73.8	83.6 / 72.9
Histogram	512 bins	75.4 / 50.0	75.4 / 53.1	85.6 / 75.0	85.9 / 75.5
Histogram	768 bins	75.4 / 50.0	75.7 / 56.0	84.2 / 72.5	84.5 / 73.8
Homogeneity	—	79.9 / 59.2	77.1 / 56.5	89.3 / 81.6	90.4 / 84.3
GLCM	8 Imglvl	94.9 / 91.2	93.2 / 90.9	92.9 / 89.9	93.5 / 88.7
GLCM	16 Imglvl	94.9 / 91.2	93.5 / 89.5	94.4 / 91.2	**95.8 / 93.3**
GLCM	32 Imglvl	94.4 / 90.1	93.2 / 89.3	93.8 / 90.8	94.4 / 90.1
LBPc	R1 N8	75.4 / 50.0	76.6 / 53.1	81.6 / 67.3	79.1 / 63.7
LBPr	R1 N8	75.7 / 51.7	76.6 / 58.5	83.9 / 73.1	82.8 / 71.1
LBPr	R2 N16	76.0 / 51.1	75.4 / 51.5	84.7 / 73.2	84.7 / 73.2

Results – All Subjects all Locations

Averaged feature vector

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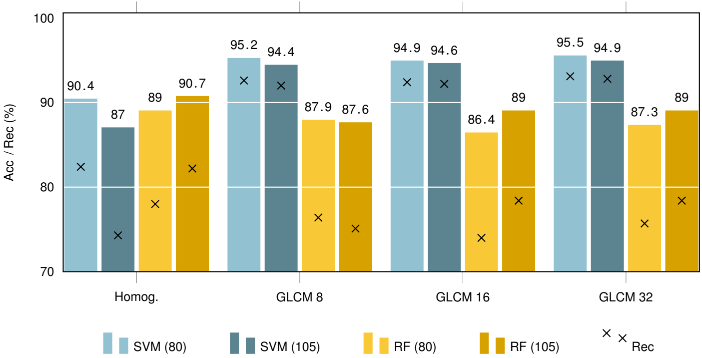
Histogram	768 bins	75.4 / 50.0	76.3 / 54.4	85.0 / 74.2	84.5 / 74.6
Homogeneity	—	79.4 / 58.0	82.2 / 67.7	88.1 / 81.3	92.1 / 85.1
GLCM	8 Imglvl	94.9 / 91.2	92.7 / 87.4	92.4 / 87.6	94.9 / 91.2
GLCM	16 Imglvl	94.6 / 91.0	92.7 / 87.4	93.2 / 88.9	94.1 / 89.5
GLCM	32 Imglvl	94.1 / 90.3	91.2 / 85.7	92.4 / 87.2	94.9 / 90.4
LBPc	R1 N8	75.4 / 50.0	76.6 / 55.8	85.3 / 74.0	81.4 / 69.4
LBPr	R1 N8	76.6 / 53.5	78.8 / 58.8	83.9 / 73.4	82.2 / 71.2
LBPr	R2 N16	77.1 / 53.8	76.6 / 53.1	85.6 / 73.8	84.7 / 74.4

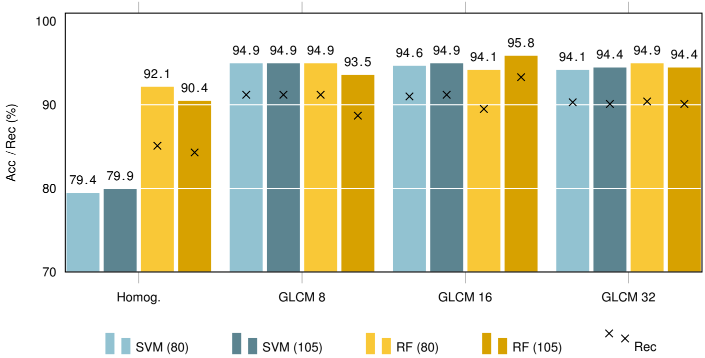
Results – All Subjects all Locations

Comparison of feature vector – concatenated feature vector results



Results – All Subjects all Locations

Comparison of feature vector – average feature vector results



Results – All Subjects all Locations

Confusion Matrix

	H	C
Healthy	262	5
Carcinoma	10	77

Best classification result: 95.8 % / 93.3 % (avg. RF)

True positive rate

- *Healthy* 98.1 %
- *Carcinoma* 88.5 %

Summary & Conclusion

Summary

- decomposition into individual images
- annotation of images
- classification of pathological from healthy images

Drawbacks

- patient data set
- image database
- correlation of images

Possible improvements

- edge evaluating features
- disease staging
- segmentation of cancer

Conclusion

Objective of this thesis: separate patholgical from healthy images

Three problems:

1. creation of image database ✓
2. annotation of images ✓
3. classification of images ✓ **95.8 % / 93.3 %**

Benefits:

- objective method to support the physician
- supports finding of the resection site
- time-saving and less harmful for the patient

$\Rightarrow$ monitor progress of cancer?

The End