

Neural network approach for histopathological diagnosis of breast diseases with images

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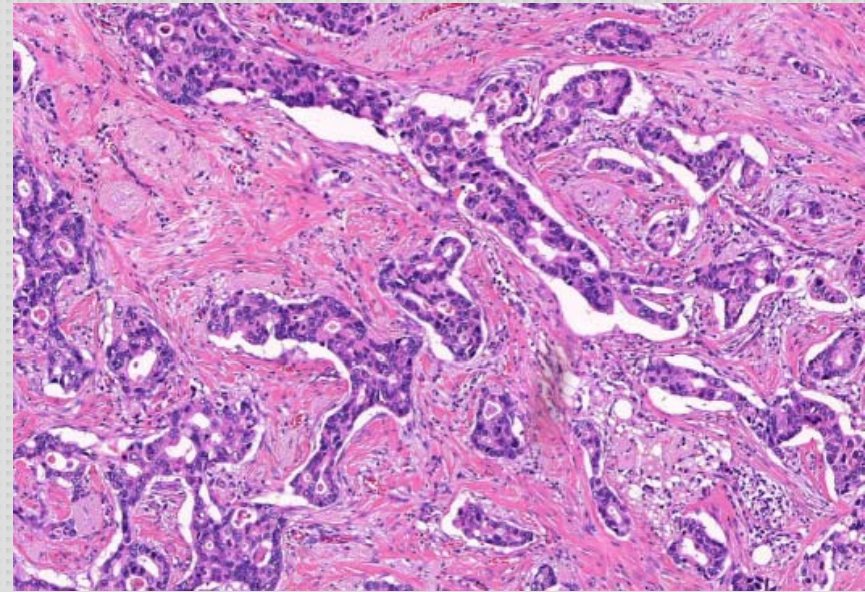
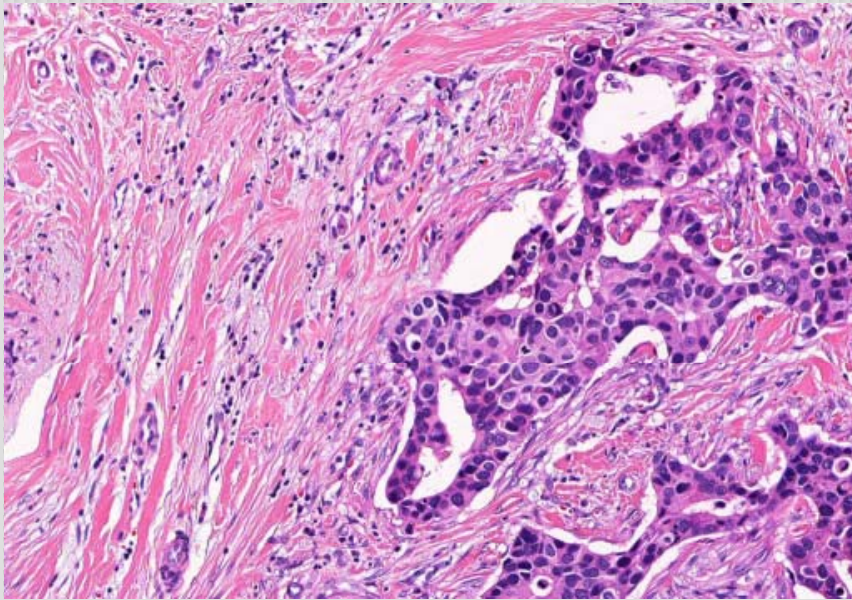
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Abstract

- Diagnosis of breast diseases relies on recognizing diseased tissue in histopathological images. The tissues studied will contain both diseased and normal areas.



Examples of breast cancer: Invasive ductal carcinoma (scirrhus type)

Abstract

The method to insure a correct diagnosis

1. to subdivide the histopathological image into sections.
 2. These subdivisions will then all be digitized by Wavelet transformation.
 3. To evaluate by neural network analysis.
- The collective evaluation of subdivisions will increase the accuracy of diagnosis and help to avoid missing cancerous or inflamed tissue.

Histopathological diagnosis

Determines whether the lesion is

{ tumor or not tumor { benign or malignant

If it is a tumor then it is important to decide what kind of treatment would be required



Diagnosing the kind of tumor is important.

Classification of breast cancer

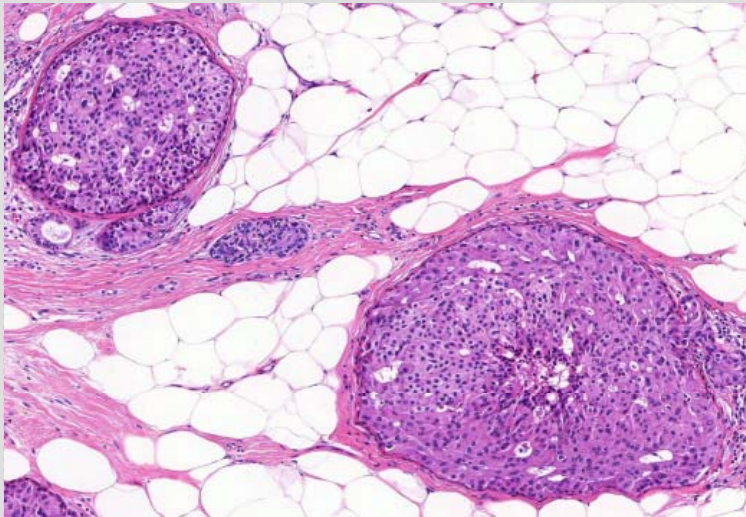
Classification				Disease		
EPITHELIAL TUMORS	Benign			IA1	1. Intraductal papilloma	
				IA2	2. Ductal adenoma	
				IA3	3. Adenoma of the nipple	
				IA4	4. Adenoma	
				IA5	5. Adenomyoepithelioma	
	Malignant	Noninvasive			IB1a	a. Noninvasive ductal carcinoma
					IB1b	b. Lobular carcinoma in situ
		Invasive	Invasive ductal carcinoma		IB2a1	a1. Papillotubular carcinoma
					IB2a2	a2. Solid-tubular carcinoma
					IB2a3	a3. Scirrhous carcinoma
			Special types		IB2b1	b1. Mucinous carcinoma
					IB2b2	b2. Medullary carcinoma
					IB2b3	b3. Invasive lobular carcinoma
					IB2b4	b4. Adenoid cystic carcinoma
					IB2b5	b5. Squamous cell carcinoma
					IB2b6	b6. Spindle cell carcinoma
					IB2b7	b7. Apocrine carcinoma
					IB2b8	b8. Carcinoma with cartilaginous and/or osseous metaplasia
					IB2b9	b9. Tubular carcinoma
					IB2b10	b10. Secretory carcinoma (Juvenile carcinoma)
	IB2b11	b11. Invasive micropapillary carcinoma				
	IB2b12	b12. Matrix-producing carcinoma				
	IB2b13	b13. Others				
	Paget's disease	IB3	3. Paget's disease			

Classification of breast cancer

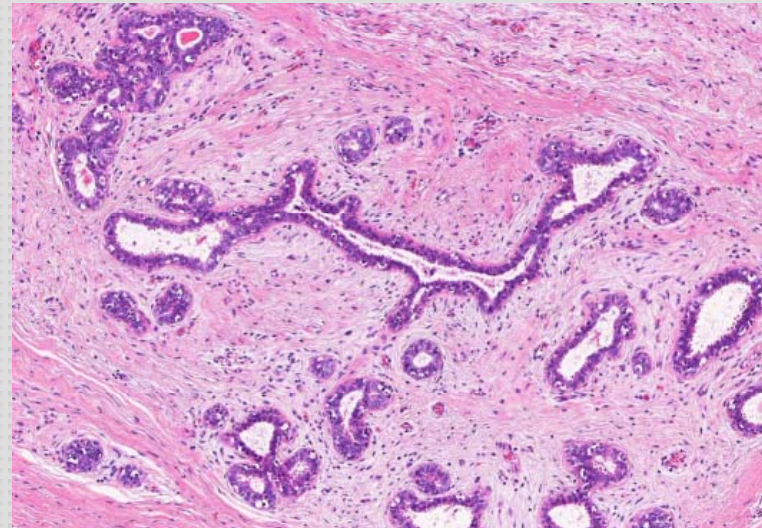
Classification				Disease	
MIXED CONNECTIVE TISSUE AND EPITHELIAL TUMORS				IIA	A.Fibroadenoma
				IIB	B.Phyllodes tumor
				IIC	C.Carcinosarcoma
NONEPITHEILIAL TUMORS				IIIA	A.Stromal sarcoma
				IIIB	B.Soft tissue tumors
				IIIC	C.Lymphomas and hematopoietic tumors
				IIID	D.Others
UNCLASSIFIED TUMORS				IV	IV.UNCLASSIFIED TUMORS
MASTOPATHY				V	V.MASTOPATHY (FIBROCYTSTIC DISEASE, MAMMARY DYPLASIA)
TUMOR-LIKE LESIONS				VIA	A.Duct ectasia
				VIB	B.Inflammatory pseudotumor
				VIC	C.Hamartoma
				VID	D.Gynecomastia
				VIE	EAccessory mammary gland
				VIF	F.Others
BORDERLINE LESION				VIIA	A.Atypical ductal hyperplasia
				VIIIB	B.Atypical lobular hyperplasia
				VIIIC	C.others

Diagnosis by images

- This study attempts to differentiate not only tumors but also inflammations and borderline lesions.



DCIS(cribriform-type)
Non invasive ductal carcinoma



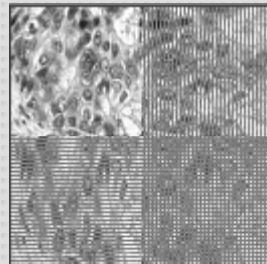
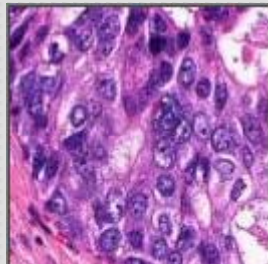
Fibrocystic disease(fibroadenomatosis)

Texture analysis

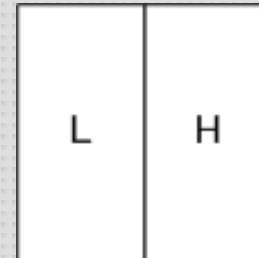
- To numerically characterize the specific variation pattern of image element values in the picture image region
- We digitized the texture information of histopathological images in order to examine the structural patterns of specimens.
- Wavelet transformation was applied

Wavelet transformation

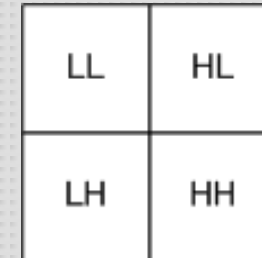
1. In the horizontal direction one-dimensional Wavelet transform for each row divides the image into high and low frequency components.
2. Then, for each column this converted signal is performed by one-dimensional transformation in the vertical direction. One two-dimensional wavelet transform in horizontal and vertical directions divides the original signal into four components, such as LL, LH, HL and HH sub-bands.
3. Two-dimensional Wavelet transformation is adapted to LL component recursively.



Original image

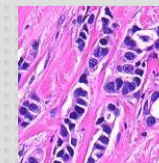
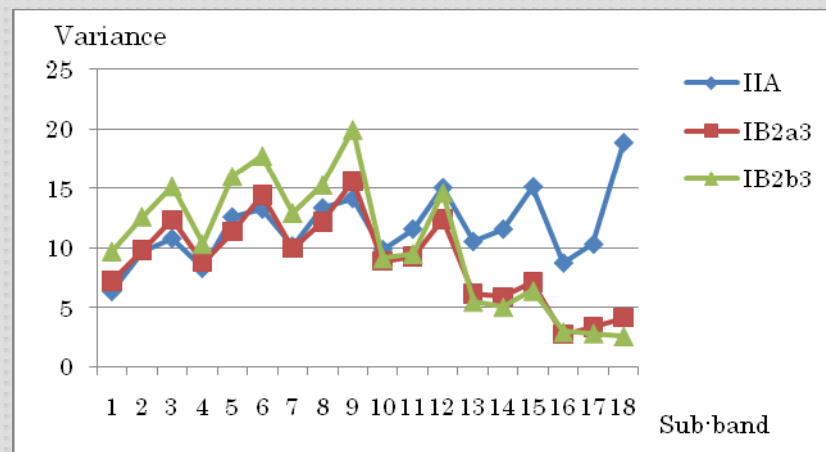


Dual-partitioning
for each row

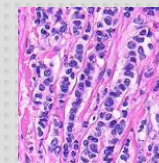


Dual-partitioning
for each column

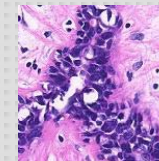
The variances in each sub-band



IB2a3



IB2b3

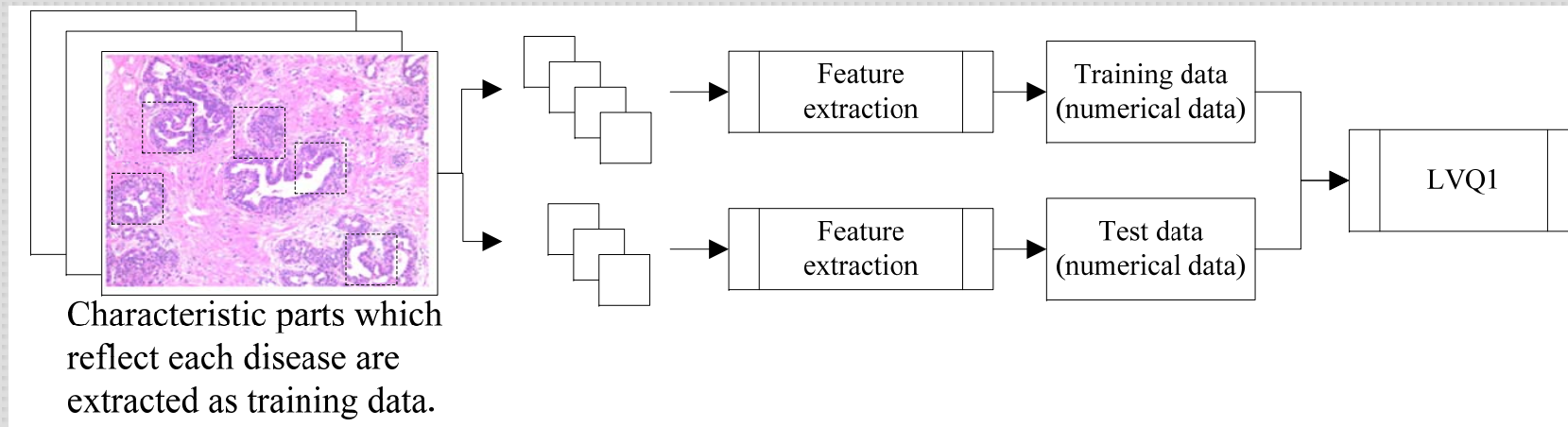


IIA

128X128 pixel images on the right side are extracted as characteristic parts.

Restibrachium is found in IB2a3(Scirrhus carcinoma)and IB2b3(Invasive lobular carcinoma) and the forms of changes in the graph are similar. But IIA(Fibroadenoma) is different from the others in the graph and image. As described above Wavelet feature reflects texture information, therefore classification and recognition using Wavelet feature is appropriate.

Feature extraction and recognition by Neural Network (LVQ1)



Pattern recognition using neural network

The algorithm of LVQ1

Input data: $\mathbf{x} \in R^p$ Label: $y \in \{1,2,\dots,G\}$

Training data: $\{(\mathbf{x}_1, y_1), \dots, (\mathbf{x}_n, y_n)\}$

Assuming that k sets of codebook vector and label: $\{(\mathbf{m}_i, l_i), i = 1, \dots, k\}$

LVQ divides an input space using a finite number of labeled codebook vectors and differentiates. In sequential type one data is selected at time t and the codebook vector is updated. In LVQ1 the codebook vector and the label are updated by the following expression.

$$\mathbf{m}_c(t+1) = \begin{cases} \mathbf{m}_c(t) + \alpha(t)(\mathbf{x}(t) - \mathbf{m}_c(t)), & y(t) = l_c(t) \\ \mathbf{m}_c(t) - \alpha(t)(\mathbf{x}(t) - \mathbf{m}_c(t)), & y(t) \neq l_c(t) \end{cases}$$

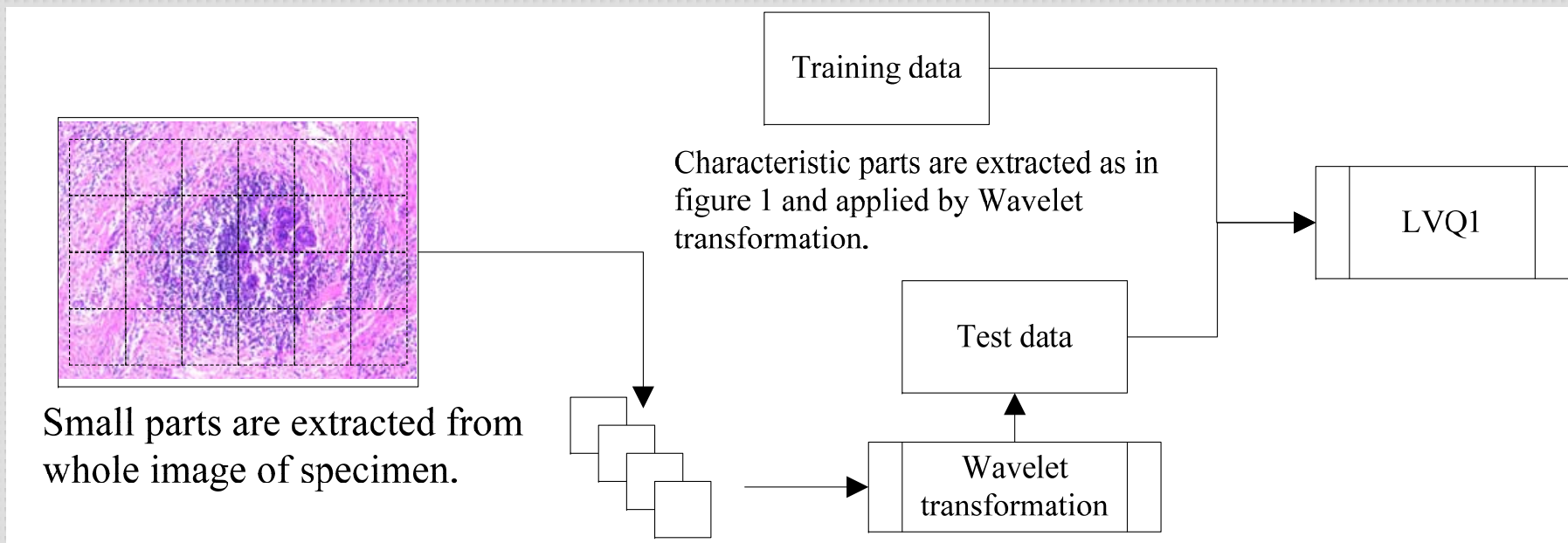
Recognition results by LVQ1

There were 211 small images extracted from 9 kinds of diseases. Each disease contains 3 to 5 different cases. 211 images were divided into 141 training data and 70 test data.

Classification		IB1a	IB1b	IB2a1	IB2a2	IB2a3	IB2b3	IIA	IX	VIIA	Error Rates
IB1a	Noninvasive ductal carcinoma	8	0	1	0	0	0	0	0	1	0.200
IB1b	Lobular carcinoma in situ	0	10	0	0	0	0	0	0	0	0.000
IB2a1	Papillotubular carcinoma	0	1	3	0	1	0	0	1	1	0.571
IB2a2	Solid-tubular carcinoma	0	0	0	5	0	0	0	0	0	0.000
IB2a3	Scirrhou carcinoma	0	1	0	1	9	0	0	0	0	0.182
IB2b3	Invasive lobular carcinoma	0	0	0	0	0	5	0	0	0	0.000
IIA	Fibroadenoma	0	0	0	0	0	0	3	1	0	0.250
IX	Normal	0	1	0	0	0	0	1	5	0	0.286
VIIA	Atypical ductal hyperplasia	0	0	0	0	0	0	0	2	9	0.182
Total											0.186

Wavelet transformation for a whole case image and the method of recognition by LVQ1

Test data are transformed values by Wavelet transformation from the 128X128 pixel areas which are all over the image of a new case.

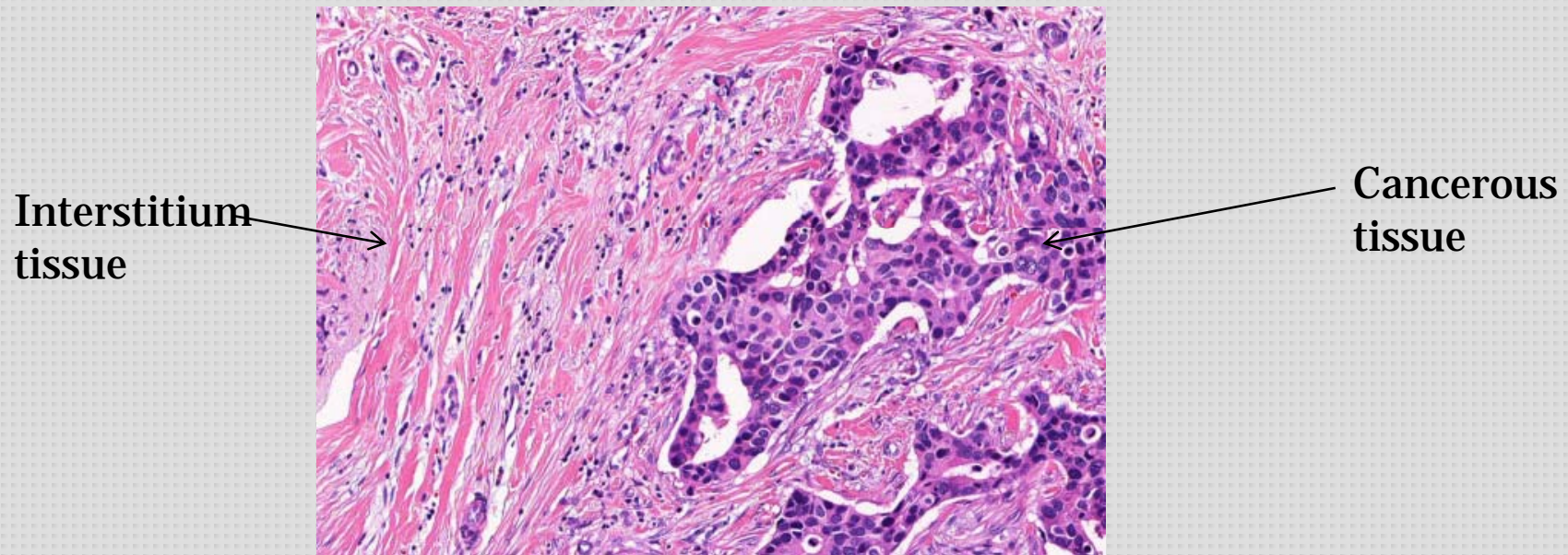


Recognition results by LVQ1 for a whole case image

Classification		IB1a	IB1b	IB2a1	IB2a2	IB2a3	IB2b3	IIA	IX	VIIA	Error Rates
IB2a1	Papillotubular carcinoma	0	0	138	0	0	0	2	0	0	0.014
IB2a2	Solid-tubular carcinoma	5	4	4	69	39	4	0	1	0	0.452
IB2a3	Scirrhous carcinoma	0	61	0	0	61	0	0	1	2	0.512
IB1a	Noninvasive ductal carcinoma	55	0	0	0	15	0	0	28	29	0.567
IB1b	Lobular carcinoma in situ	0	122	0	0	3	0	0	0	2	0.039
IB2b3	Invasive lobular carcinoma	6	4	0	3	10	102	0	0	1	0.190
VIIA	Atypical ductal hyperplasia	0	0	0	0	0	0	0	0	127	0.000
IIA	Fibroadenoma	2	1	0	0	50	0	14	30	30	0.890
IX	Normal	1	44	0	3	5	0	0	36	37	0.714

Including non-characteristic parts for training data

Training data are extracted from characteristic parts of each disease, but a specimen contains not only characteristic parts but also non characteristic parts, such as interstitium tissue etc. Neural network tries to recognize non-characteristic parts as some sort of disease.



Invasive ductal carcinoma (scirrhous type)

Recognition results of improved method by LVQ1 for a whole case image

Classification	IB1 _a	IB1 _b	IB2 _{a1}	IB2 _{a2}	IB2 _{a3}	IB2 _{b3}	II _A	IIA _N	I _X	IX _N	VII _A	Error*
IX Normal	1	3	0	17	2	0	0	4	32	52	15	0.333
II _A Fibroadenoma	5	0	0	1	5	0	18	51	30	0	17	0.457

Classification	Error rate	
	Only characteristic parts	Including non-characteristic parts
IX Normal	0.714	0.333
IIA Fibroadenoma	0.890	0.457

Conclusion

- LVQ with Wavelet transformation of different diseases as training data enables the diagnosis of breast disease.
- There are more than 50 types of breast disease and some types contain different patterns of lesion, such as atypical ductal hyperplasia.
- Many more kinds of image data should be accumulated in order to diagnose these diseases.

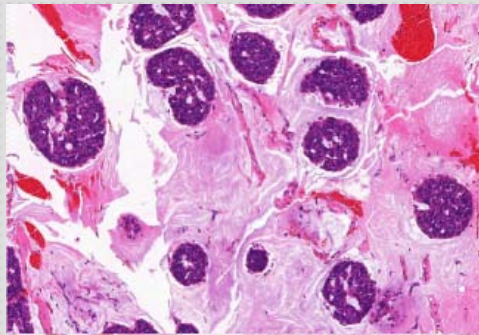
Histopathological information data base

The interface displays two histological sections (H&E stained) of glandular tissue. The top image shows a low-magnification view of several glandular units. The bottom image shows a high-magnification view of the same tissue, highlighting a large, solid, eosinophilic (red) area of necrosis.

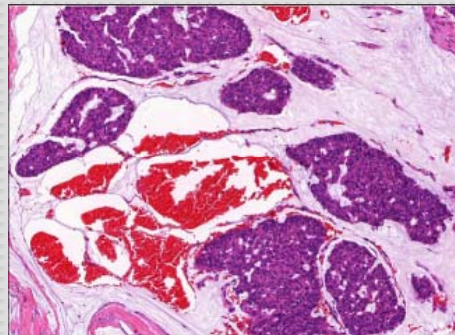
The right side of the interface contains a search and data entry panel. At the top, there are fields for '検索キーワード' (Search Keyword) and '検索条件' (Search Conditions), with buttons for '検索' (Search) and '閉じる' (Close). Below this is a grid of thumbnail images. The bottom right section, titled '検索条件' (Search Conditions), includes fields for '検索番号' (Search Number), '診断' (Diagnosis), and '病名' (Disease Name). The '病名' field contains 'Adenocarcinoma'. Below these fields is a large text area containing detailed pathology information, including a description of the specimen: 'Specimen: 3cm x 2.5cm x 1.5cm, grossly yellowish-tan, firm, cut surface shows multiple lobules of varying sizes, some lobules are surrounded by fibrous tissue, and some lobules are surrounded by necrotic debris. Microscopic: (H&E) Moderate to high grade adenocarcinoma, tubular and glandular growth pattern, moderate nuclear atypia, mitotic activity, and some areas of necrosis. Immunohistochemistry: (IHC) CK7(+), CK20(+), CK5(-), CK14(-), CK19(+), CK34(+), CK56(-), CK8(+), CK9(+), CK13(+), CK17(+), CK26(+), CK31(-), CK34(+), CK35(+), CK36(+), CK39(+), CK40(+), CK41(+), CK42(+), CK43(+), CK44(+), CK45(+), CK54(+), CK56(+), CK57(+), CK58(+), CK59(+), CK60(+), CK61(+), CK62(+), CK63(+), CK64(+), CK65(+), CK66(+), CK67(+), CK68(+), CK69(+), CK70(+), CK71(+), CK72(+), CK73(+), CK74(+), CK75(+), CK76(+), CK77(+), CK78(+), CK79(+), CK80(+), CK81(+), CK82(+), CK83(+), CK84(+), CK85(+), CK86(+), CK87(+), CK88(+), CK89(+), CK90(+), CK91(+), CK92(+), CK93(+), CK94(+), CK95(+), CK96(+), CK97(+), CK98(+), CK99(+), CK100(+).'

Similar image retrieval in database

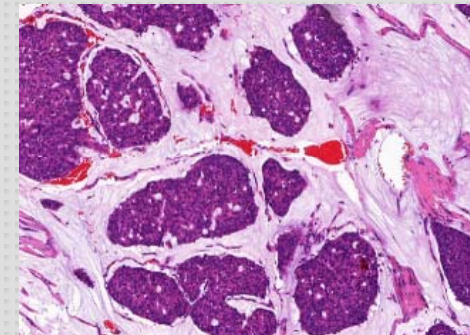
Test data



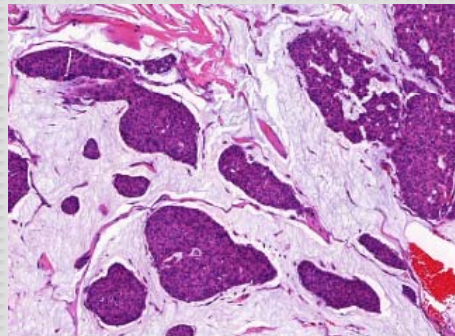
Retrieved images



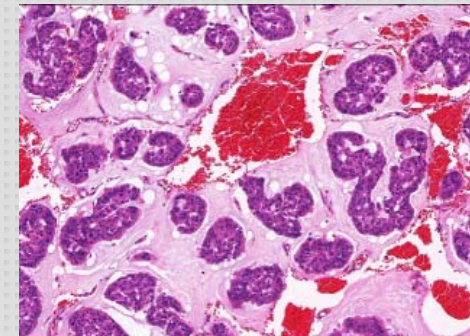
IB2b1(Mucinous carcinoma)



IB2b1(Mucinous carcinoma)



IB2b1(Mucinous carcinoma)



IB2b1(Mucinous carcinoma)