日本医放会誌：47（4），575—584，1987（昭62）

An Analysis of Lymphographic Signs for Differentiating Cancerous, Lymphomatous, and Normal Lymph Nodes

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Research Code No.: 510.9, 207.1

Key Words: Lymphography, Multivariate analysis, Hayashi's quantification scaling

癌，リンパ腫，正常リンパ節の鑑別におけるリンパ造影所見の解析

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（昭和61年6月23日受付）
（昭和61年9月18日最終原稿受付）

近年，リンパ造影の意義に否定的見解もあるが，リンパ管，リンパ節の直接造影である本法は，撮影方法，解析を精密に行う事で，現時点におけるリンパ系疾患診断の中で重要な役割を果すと考えられる．そこで，リンパ造影の所見の解析を試みた．

癌，悪性リンパ腫，正常例のリンパ造影像中の，204個のリンパ節について，24種類の所見を，最終診断と対比した．そして，解析は，癌—正常，リンパ腫—正常，癌—リンパ腫のそれぞれの鑑別について，相関係数の算出と多変量解析による予測式の作成を行った．

四分点相関係数をとってみると，癌に相関の高い所見は，リンパ節径の増大，被膜の欠損，リンパ管の閉塞，管外漏出，リンパ管相リンパ節相両相での欠損（コンビネーションデフェクト）である．リンパ腫に相関の高い所見は，リンパ節径の増大，リンパ節の厚みの増大，被膜や辺縁洞の欠損，管外漏出であった．

林の数量化理論2類で漸増法を用い，予測式を導くと，癌—正常の鑑別に有効な所見は，コンビネーションデフェクトが陽性か陰性か，各種の特異的パターン，粒状性パターンが微細か粗大か，リンパ節の形，リンパの停滞貯留であった．また，リンパ腫—正常の鑑別には，被膜の欠損，リンパ節の形，各種の特異的パターン，リンパ管の圧排，リンパ節の造影濃度が有効であった．また，癌—リンパ腫の鑑別には，欠損の性質，各種の特異的パターン，リンパ節の変形，軟部陰影，リンパ節の形が有効であった．予測式算出に使用した内部データの，これら予測式による鑑別は良好であった．

リンパ造影による，内部構造の描出，リンパ管の描出といった利点を利用する事によって，診断能はさらに高められると考えられた．

Introduction

Currently, computed tomography (CT) is commonly used for the detection of lymph node metastases or involvements[1)2)]. However, the resolution of CT image is limited, thus CT is not adequate for revealing fine structure. On the contrary, lymphograms give us a direct image, thus enabling us to obtain more precise information about internal structure.

In order to determine what the important factors are and to make differential diagnosis more systematically, we studied lymphographic signs. Two hundred and four lymph node images were chosen from among

lymphograms of cancerous, malignant lymphomatous or normal patients. Each lymph node was studied with respect to 24 factors, i.e. items. In order to differentiate among cancerous, malignant lymphomatous, and normal lymph nodes, the data were analyzed through univariate analysis using correlation coefficient and Hayashi's quantification scaling type 2 multivariate analysis. We derived discriminant functions from the results.

Materials and Methods

Materials

Two hundred and four evaluable lymph nodes were chosen for analysis from the lymphograms. Based on pathological or follow-up examinations, 51 of them were diagnosed ultimately as cancerous, 59 as malignant lymphomatous, and 94 as normal. Lymph nodes of reactive benign changes were excluded from this study.

Examinations

By means of Kinmonth's method[3], 15mm skin incision was made on both pedals, and the lymph vessels were prepared for infusion. After puncturing the lymph vessels gently with a small needle, an oily contrast medium was infused directly into the lymph vessels. Five ml of Lipiodol Ultrafluid® was administered via an infusion pump in a period of 50 minutes. Radiograms were then taken, at two different phases. One was a lymph-vascular phase lymphogram, which primarily revealed the lymph vessels, and the other was a lymph nodal phase lymphogram. Four directional views were taken below the diaphragm level and two views were taken above the diaphragm.

Regions of interest were analyzed by macroradiography. Macroradiography was conducted with a Toshiba Macro-Stereography Unit DRX-431HD. The conditions were as follows: Focus=50 micrometer,

Table 1 Items

Item 1.	Clinical diagnosis
Item 2.	Region
Item 3.	Nodal size
Item 4.	Nodal shape
Item 5.	Deformity
Item 6.	Conglomeration
Item 7.	Granularity
Item 8.	Deficiencies in capsules
Item 9.	Size of defect
Item 10.	Character of defect
Item 11.	Special pattern
Item 12.	Sharpness of defect
Item 13.	Nodal contrast
Item 14.	Ectopic lymph node
Item 15.	Early visualization of lymph node
Item 16.	Block of lymph vessels
Item 17.	Stasis or preservation of lymph vessels
Item 18.	Encasement of lymph vessels
Item 19.	Capillary nets of lymph vessels
Item 20.	Extravasation of lymph vessels
Item 21.	Number of lymph vessels
Item 22.	Dislocation of lymph vessels
Item 23.	Collateral lymph vessels
Item 24.	*Defect in lymph-vascular and nodal phase
Item 25.	Soft tissue shadow
Item 26.	Final diagnosis

*combination or isolation

Table 2 Categories

Item 1. Clinical diagnosis
Category 1. Bladder cancer
2. Prostate cancer
3. Cervical cancer
4. Endometrial cancer
5. Ovarian cancer
6. Testicular tumor
7. Malignant melanoma
8. Paget's disease of pubis
9. Squamous cell cancer of skin
10. Cancer other than above
11. Hodgkin's disease
12. Non-Hodgkin's disease
13. Suspected malignant lymphoma
14. Benign disease other than above

Item 2. Region
Category 1. Lumbar paraaortic lymph node
2. Common iliac lymph node
3. External iliac lymph node
4. Internal iliac lymph node
5. Rosenmüller's lymph node
6. Deep inguinal lymph node
7. Superficial inguinal lymph node
8. Axillary lymph node
9. Others

Item 3. Nodal size*
Category 1. Enlargement
2. Minimal enlargement
3. Normal
4. Small
**5. Indeterminable
* in comparison with the normal range of each region
** for example, a lymph node in which the defect is too large to determine the size.

Item 4. Nodal shape
Category 1. Circular shape from both frontal and lateral (oblique) views … (spheroid type)
*2. Circular shape from frontal view, flat shape from lateral (oblique) view … (saucer type)
3. Elliptic shape from both frontal and lateral views
4. Elliptic shape from frontal view, flat shape from lateral (oblique) view
5. Others
* Category 2 includes lymph nodes that are round from the frontal view and flat from the lateral view.

Item 5. Deformity
Category 1. Deformity is detected
2. Deformity is not detected
*3. Equivocal
**4. Indeterminable
* Category 3 includes lymph nodes for which it is not possible to determine whether the deformity is in the lymph node itself or is a marginal defect.
** Category 4 includes lymph nodes that are too small to discriminate.

Item 6. Conglomeration
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 7. Granularity
Category 1. Fine granular
2. Coarse granular
*3. Others
* Category 3 inclues lymph nodes which have defects large enough to make its inner structure unrecognizable.

Item 8. Deficiencies in capsules
Category 1. Irregularities or deficiencies in capsules or marginal sinuses are detected.
2. Undetected
3. Equivocal
4. Indeterminable

Item 9. Size of defect
Category 1. Minimal
2. Half of the node
3. Most part of the node
4. Almost all of the node

Item 10. Character of defect
Category 1. Predominantly marginal
2. Predominantly central
3. Both marginal and central
4. Complete defect

Item 11. Special pattern
Category 1. Single central defect
2. Microlacunary pattern
3. Coarse granular pattern
4. Lacy pattern
5. Foamy pattern
6. Category 4 mixed with 5
7. Crescent type or rim sign
8. Complete defect
9. Halo sign
10. Necrosis droplets
11. Macrolacunary defect
12. Greasy pattern
13. No such pattern
14. Indeterminable

Item 12. Sharpness of defect
Category *1. Sharp margin
2. Invasive margin
3. Indeterminable
* including microlacunary pattern

Item 13. Nodal contrast(compared with the other lymph node in same region)
Category 1. Thick
2. Normal
3. Thin

Item 14. Ectopic lymph node
Category 1. Detected

2. Undetected

Item 15. Early visualization of the lymph node
Category 1. Early visualization
2. Normal
3. Late visualization
4. Equivocal
5. Indeterminable

Item 16. Block of lymph vessels
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 17. Stasis or preservation of lymph vessels
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 18. Encasement of lymph vessels
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 19. Capillary nets of lymph vessels
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 20. Extravasation of lymph vessels
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 21. Number of lymph vessels
Category 1. Increase
2. Normal
3. Decrease
4. Indeterminable

Item 22. Dislocation of lymph vessels
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 23. Collateral lymph vessels
Category 1. Detected
2. Undetected
3. Equivocal
4. Indeterminable

Item 24. Defect in lymph-vascular and nodal phase
Category 1. Combination
2. Isolation
3. Equivocal
4. Indeterminable

Item 25. Soft tissue shadow
Category 1. The defect is visualized as a positive soft tissue shadow and there are lymph vessels around the node.
2. The defect is visualized as a positive soft tissue shadow and there are no lymph vessels around the node.
3. The defect is visualized as a positive soft tissue shadow but lymph vessels are indeterminable.
4. A soft tissue shadow is not detected.
5. Indeterminable, due to bone shadow or smallness of lymph node.

Item 26. Final diagnosis
Category 1. Metastasis of cancer
2. Involvement of malignant lymphoma
3. Normal or benign change

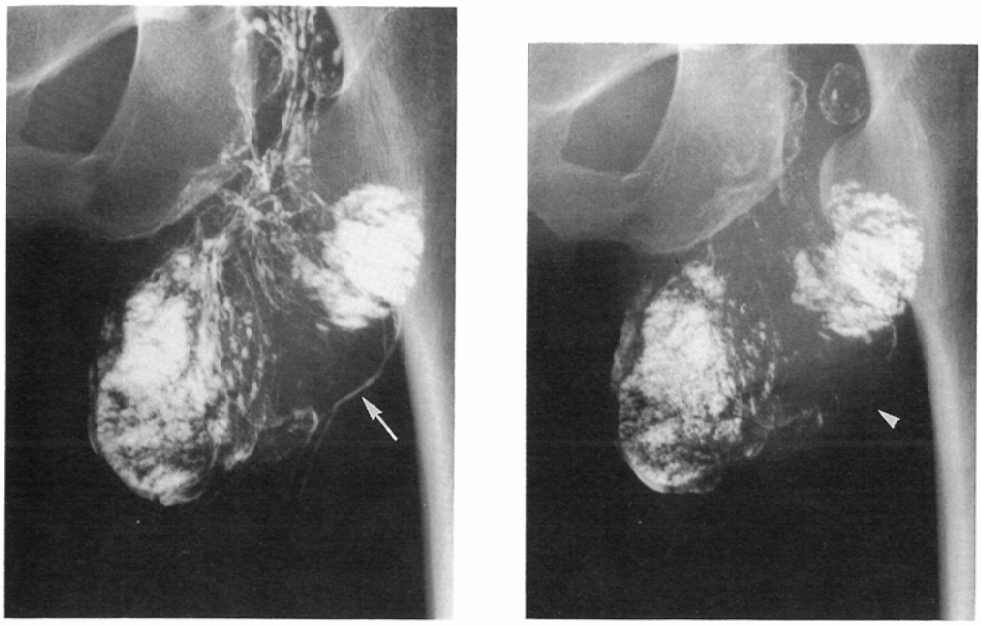
magnifying power=2.5, FFD=105cm, voltage=90kVp (routinely), current=10mA, exposure time=1.6 second. Three directional views were taken for each lesion.

Analysis

Each lymph node was examined by two radiologists (T.N. and M.A.) with respect to 24 items listed in Table 1 (Item 3—26). Each item has categories as showed in Table 2 and one category was chosen for each lymph node. Some of the signs in Table 2 are showed in the figures. 'Item 4. Nodal shape'—'Category 1. Circular shape from two projections' and 'Category 3. Elliptic shape from two projections' are showed on Fig. 3. 'Item 8. Deficiencies in capsules'—'Category 1. Irregularities or deficiencies in capsules or marginal sinuses' are showed on Fig. 3. 'Item 11. Special pattern'—'Category 4 and 5. Lacy pattern and foamy pattern' are showed in Fig. 1. 'Item 11. Special pattern'—'Category 10. Necrosis droplets' means a round deposit of contrast material in defect[4]. 'Item 13. Nodal contrast' is showed in Fig. 4. 'Item 15. Early visualization of the lymph node' is showed in Fig. 1. 'Item 17. Stasis or preservation of lymph vessels' is showed in Fig. 2b. 'Item 24. Defect in lymph-vascular and nodal phase'—'Category 1. Combination' is showed in Fig. 2. 'Item 25. Soft tissue shadow'[4] is showed in Figs. 1 and 5.

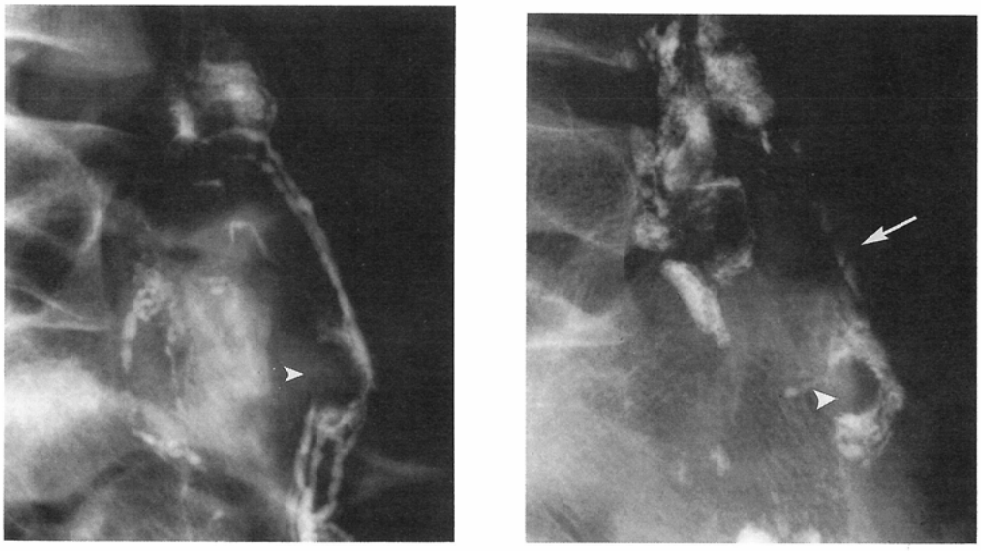
The data were analyzed by univariate analysis and multivariate analysis[5]. A four-fold point correlation coefficient between each category and 'Final diagnosis' was calculated in order to reveal typical signs for diagnosis. (See Appendix)

For deriving discriminant functions, Hayashi's quantification scaling (type 2) multivariate analysis was used[6][7]. An SPSS (Statistical Package for the Social Sciences) program was employed for the analysis on



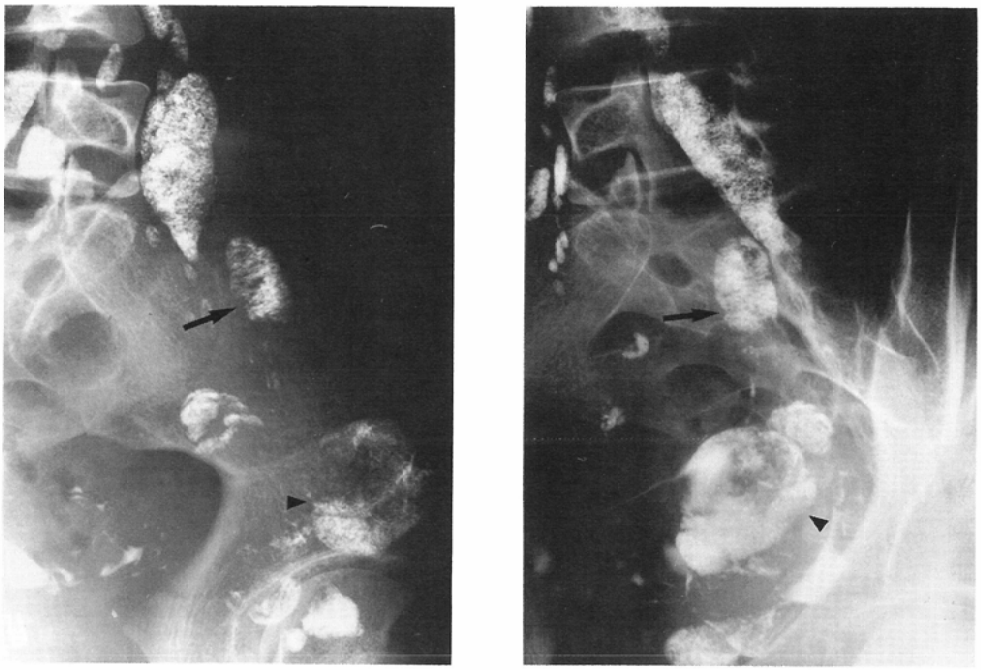
1a 1b

Fig. 1 Lymph node involved with malignant lymphoma. a: lymph-vascular phase, b: Nodal phase. Enlarged nodal size, lacy and foamy pattern, early visualization of the lymph node. Dislocation of lymph vessels (arrow), soft tissue shadow (arrowhead) are observed.



2a 2b

Fig. 2 Lymph node metastasis from ureteral cancer. a: lymph-vascular phase, b: Nodal phase. Stasis or preservation of lymph vessels (arrow) and combination defects (arrowheads) are observed.



3a 3b

Fig. 3 Lymph node metastasis from malignant melanoma. a: RAO, b: LAO. Irregularities or deficiencies in capsules or marginal sinuses (arrow), elliptic shape from two projections (arrow), circular shape from two projections (arrowhead) are observed. Contrast material after hysterography remained in the pelvic space.

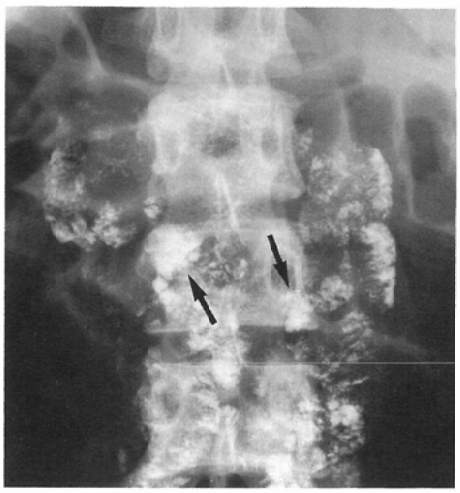
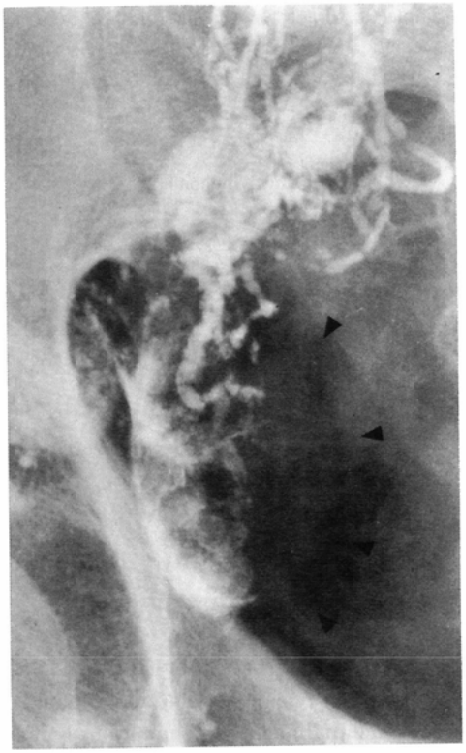
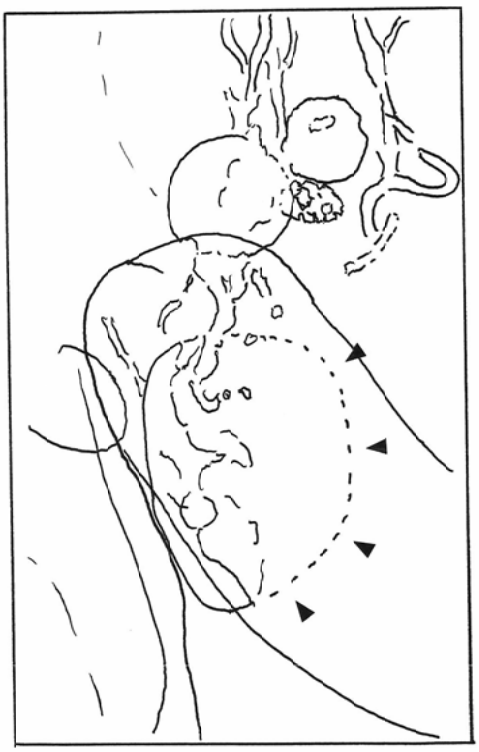


Fig. 4 Lymph node involved with malignant lymphoma: Nodal phase. Thick contrasted lymph nodes are observed (arrow).



5a



5b

Fig. 5 Lymph node metastasis from prostatic cancer. a: lymph-vascular phase, b: diagram of fig. a. Soft tissue shadow are observed (arrowhead).

main frame computer Fujitsu M-380 at University of Tsukuba. The 'Final diagnosis' was established as an outside criterion, and analysis was made between two groups at a time: Cancer-normal, malignant lymphoma-normal, cancer-malignant lymphoma. Variables were selected from the 23 items in a stepwise fashion. The item making the greatest contribution to the separation of the groups was chosen to be the first variable. After it was entered into the discriminant function, the variable with the next largest correlation ratio was selected, and so on, until 5 variables were ranked according to their relative discriminatory importance. Based on the 5 variables, we derived the optimal discriminant function.

Results

Univariate analysis

With regard to the discrimination between cancerous and normal lymph nodes, categories with a four-fold point correlation coefficient greater than 0.6 are showed in Table 3a. As for the discrimination between malignant lymphomatous and normal ones, such categories are showed in Table 3b. As for the discrimination between cancerous and malignant lymphomatous ones, the category which has a correlation coefficient of over 0.4, is only 'marginal defect'. The correlation coefficient of this category is +0.54 and the category is typical for cancer.

Multivariate analysis

The five most important discriminant items were found to be as follows (in order of discriminatory importance). For the differentiation between cancerous and normal lymph nodes, 'Defect in lymph-vascular and nodal phase', 'Special pattern', 'Granularity', 'Nodal shape', and 'Stasis or preservation of lymph vessels' were found to be important. For distinguishing between malignant lymphomatous and normal lymph nodes,

Table 3a Factor with four-fold point correlation coefficient greater than 0.6 at discrimination-between cancer and normal

Factor	Corr. coefficient
related to cancer	
Enlarged nodal size	+0.60
Irregularities or deficiencies in capsules or marginal sinuses	+0.68
Block of lymph vessels	+0.62
Extravasation	+0.72
Combination defect in both phase	+0.77
related to normal	
Normal nodal size	−0.62
Fine granularity	−0.61
No deficiencies in capsules	−0.64
Minimal size defect	−0.65
No block of lymph vessels	−0.60
No stasis nor preservation of lymph vessels	−0.66
No dislocation	−0.64

Table 3b Factor with four-fold point correlation coefficient greater than 0.6 at discrimination between malignant lymphoma and normal

Factor	Corr. coefficient
related to malignant lymphoma	
Enlarged nodal size	+0.71
Elliptic shape from 2 projections	+0.76
Irregularities or deficiencies in capsules or marginal sinuses	+0.79
Extravasation	+0.71
related to normal	
Normal nodal size	−0.68
Fine granularity	−0.68
No deficiencies in capsules	−0.61
No block of lymph vessels	−0.67
No extravasation	−0.76
No dislocation	−0.71
No collateral lymph vessels	−0.61
No soft tissue shadow	−0.61

'Deficiences of capsules', 'Nodal shape', 'Special pattern', 'Dislocation of lymph vessels', and 'Nodal contrast' were found to be valuable. In differentiating between cancerous and malignant lymphomatous lymph nodes, 'Character of defect', 'Special pattern', 'Deformity', 'Soft tissue shadow', and 'Nodal shape' were important.

The discriminant functions are expressed by the following formula:

$Y = X1 + X2 + X3 + X4 + X5$ (Positive Y indicates the former diaynosis)

The numeric values of each X are presented in Table 4a, Table 4b, and Table 4c.

Discussion

Lymphography provides more information concerning lymph nodes than CT[8]. This information deals mainly with internal structure of lymph nodes or lymph vessels, and is useful for determining whether a lymph node is cancerous, malignant lymphomatous or normal[9]. Furthermore, we can use this information for the detection of minimal nodal involvement with malignant lymphoma[10]. Therefore, analyses of lymphographic findings and the derivation of a discriminant function were thought to be useful for making more accurate diagnosis possible.

Four-fold point correlation coefficient has almost the same meaning as Peason's correlation coefficient. Thus, the factors chosen by univariate analysis indicate the typical character of lymph nodes afflicted by each disease. The categories chosen for discrimination between cancerous and malignant lymphomatous lymph nodes are in accordance with results of previous studies[4]. In those factors, 'extravasation' and 'combination defect' have very high correlation coefficients. These two factors are highly specific for cancer. In the discrimination between malignant lymphomatous and normal, 'elliptic shape from two projections' showed a high correlation coefficient with lymphoma, in contrast to cancer. This reveals that lymph nodes of malignant lymphoma tend to become spherical. Wiljasalo has reported that cancerous lymph nodes tend to become spherical[11]. In the results of this study, the correlation coefficient between cancer and 'elliptic shape from two projections' was slightly high, +0.48. But this sign was more closely related to malignant lymphoma (correlation coefficient = +0.76). In the discrimination between cancerous and malignant lymphomatous lymph nodes, there was no category which showed a strong correlation. It follows that lymph nodes of these two diseases have similar character.

The multivariate analysis identified the items with the greatest value for discrimination. They were

Table 4a Numeric values for differentiation of cancer from normal

			numeric value
X1 : Item 24 Defect in lymph-vascular and nodal phase	Category	1	0.586
		2	−0.307
		3	0.070
		4	−0.208
X2 : Item 11 Special pattern	Category	1	−0.055
		2	0.201
		3	0.000
		4	−0.283
		5	0.000
		6	0.000
		7	0.377
		8	−0.302
		9	0.367
		10	0.485
		11	−0.283
		12	−0.256
		13	−0.285
		14	0.000
X3 : Item 7 Granularity	Category	1	−0.198
		2	0.452
		3	0.985
X4 : Item 4 Nodal shape	Category	1	0.375
		2	−0.311
		3	0.544
		4	−0.284
		5	−0.159
X5 : Item 17 Stasis or preservation of lymph vessels	Category	1	0.154
		2	−0.145
		3	0.254
		4	0.809

Table 4b Numeric values for differentiation of malignant lymphoma from normal

			numeric value
X1 : Item 8 Deficiencies in capsules	Category	1	0.489
		2	−0.277
		3	−0.323
		4	−0.138
X2 : Item 4 Nodal shape	Category	1	0.160
		2	−0.430
		3	0.441
		4	−0.295
		5	−0.158
X3 : Item 11 Special pattern	Category	1	−0.762
		2	0.242
		3	0.000
		4	0.232
		5	0.133
		6	0.145
		7	0.000
		8	0.688
		9	−0.117
		10	0.274
		11	0.546
		12	−0.399
		13	−0.142
		14	−0.077
X4 : Item 22 Dislocation of lymph vessels	Category	1	0.357
		2	−0.144
		3	0.297
		4	0.229
X5 : Item 13 Nodal contrast	Category	1	0.152
		2	−0.147
		3	0.175

Table 4c Numeric values for differentiation of cancer from malignant lymphoma

			numeric value
X1 : Item 10 Character of defect	Category	1	1.228
		2	−0.171
		3	−0.295
		4	−2.252
X2 : Item 11 Special pattern	Category	1	0.000
		2	−0.555
		3	0.000
		4	−0.317
		5	−0.714
		6	−0.493
		7	0.029
		8	1.643
		9	−0.600
		10	0.878
		11	−0.071
		12	−1.508
		13	0.748
		14	−0.232
X3 : Item 5 Deformity	Category	1	−0.223
		2	−0.099
		3	−0.198
		4	2.748
X4 : Item 25 Soft tissue shadow	Category	1	0.595
		2	−0.090
		3	−0.883
		4	0.308
		5	−0.393
X5 : Item 4 Nodal shape	Category	1	0.621
		2	0.000
		3	−0.067
		4	−0.254
		5	−0.495

'Defect in lymph-vascular and nodal phase' for cancer-normal differentiation, 'Deficiencies in capsules' for lymphomanormal differentiation, and 'Character of defect' for cancer-lymphoma differentiation. These factors have been said to be important. 'Deficiencies in capsules' is implicated in destruction of internal structure. Therefore, it is important to make a minute examination of the lymph node[12]. The items chosen are different from that of the univariate analysis. The reason is that intercorrelations between categories influenced the results of multivariate analysis. Therefore, unnoticed items such as 'nodal contrast' were involved in the discriminant functions. However, these factors give the most effective discriminant functions. By these functions, our examined lymph nodes were diagnosed with an accuracy of 98.6%, 98.7%, and 91.8% for cancer-normal, lymphoma-normal, and cancer-lymphoma differentiation, respectively. The efficacy of these functions should be confirmed further with other data not included in this study.

Appendix

The four-fold point correlation coefficient (r) was calculated with the below formula as showed in Table 5.

$$r=\frac{f_{11}\cdot f_{22}-f_{12}\cdot f_{21}}{\sqrt{n_1\cdot n_2\cdot n_3\cdot n_4}}$$

Table 5 Example of point correlation coefficient

	Positive	Negative	Total
Cancer	f_{11}	f_{12}	n_1
Normal	f_{21}	f_{22}	n_2
Total	n_3	n_4	N

References

1) Breiman, R.S., Castellino, R.A., Harell, G.S., Marshall, W.H., Glatstein, E. and Kaplan, H.S.: CT-pathologic correlations in Hodgkin's disease and non-Hodgkin's lymphoma. Radiology, 126: 159—166, 1978
2) Peters, P.E.: Lymphography: Overview. (In) Donner, M.W. and Heuck, F.H.W.: Radiology Today 1. pp. 315—326, 1981, Springer-Verlag, Berlin, Heidelberg
3) Dumont, A.E.: In memorium John B. Kinmonth. Lymphology, 15(4): 13, 1982
4) Lüning, M. and Wiljasalo, M.: Lymphographische Metastasenkriterien. (In) Lüning, M., Wiljasalo, M., Weissleder, H. ed.: Lymphographie bei malignen Tumoren. 2. überarbeitete Auflage. pp. 124—151, 1983, Georg Thieme Verlag, Stuttgart, New York
5) Taylor, T.V., Torrance, B., Rimmer, S., Hillier, V. and Lucas, S.B.: Operative cholangiography: Is there a statistical alternative? Am. J. Surgery, 145: 640—643, 1983
6) Hayashi, C.: On the prediction of phenomena from qualitative data and the quantification of qualitative data from the mathematico-statistical point of view. Annals of the Institute of Statistical Mathematics, 3(2): 69—98, 1952.
7) Hayashi, C.: Multidimensional quantification with the applications to analysis of social phenomena. ibid, 5(2): 121—143, 1954
8) Castellino, R.A., Hoppe, R.T., Bland, N., Young, S.W., Neumann, C., Rosenberg, S.A. and Kaplan, H.S.: Computed tomography, lymphography, and staging laparotomy: Correlations in initial staging of Hodgkin's Disease. Am. J. Roentgenol., 143: 37—41, 1984
9) Dunnick, N.R. and Javadpour, N.: Value of CT and lymphography: Distinguishing retroperitoneal metastases from nonseminomatous testicular tumors. Am. J. Roentgenol., 136: 1093—1099, 1981
10) Asakura, K.: Early abnormal lymphographic pattern of malignant lymphoma. (in Japanese) Nippin Acta Radiologica, 37(2): 125—139, 1977
11) Wiljasalo, M.: Lymphographic differential diagnosis of neoplastic disease. Acta Rdiol. Suppl., 247: 33—42, 1965
12) Nakajima, T.: Basic and clinical study of lymphography. (in Japanese) Ph.D. Thesis, University of Tsukuba, 1984