Quantitative Diagnosis of Breast Thermograms by a Computer

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Research Code No.: *205*

Key Words: *Thermography, Breast cancer, Computer image processing, ROC curve*

乳房サーモグラムのコンピュータによる定量診断

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（昭和53年9月1日受付）

（昭和53年10月31日受付）

乳房サーモグラムの診断を改善するために，サーモグラムをコンピュータで解析するシステムを開発した．本処理システムは Thermoviewer MA（日本電子製）と TOSBAC-40A（東芝製）をオンラインで結び，Thermoviewer で検出した前胸部の温度情報を対話形式で収集，画像表示，処理，およびファイリングを行うシステムである．本システムの有用性を検討するため，99名の被検者（癌54，良性疾患34，正常11）の前胸部正面像について処理を行つた．本処理システムで使用される乳房サーモグラムの各種診断規準に対して得られるデータは，両側乳房間の温度差やその温度差に基づかれた数値であるが，各種診断規準について得られたその平均値は悪性，良性，正常グループの順に増加または減少した．そして悪性および良性グループの平均値の差は5％危険率で統計的に有意であつた．次に各診断規準の診断能を定量的に評価するため ROC 曲線による解析と情報容量による解析方法がとられた．その結果本研究で導入された vein pattern に対する診断規準 Vp（index）のみが悪性と良性グループを鑑別するよりよい診断規準であることが判明した．Vp（index）と他の診断規準の組合せにより得られた最良の結果は true-positive rate が87.1％，false positive rate が26.7％，情報容量の最大値は0.290ビット，またこれの入力情報量に対する割合は29.1％であつた．

Introduction

Since Lawson[1] published the results of his studies on the increase of skin temperature above malignant tumor of the breast, many papers appeared dealing with the possibilities for detection of breast cancer through thermography. However, there is a wide variation in the reported diagnostic accuracy of breast thermography.[2)-6)] The absence of specific diagnostic criteria used to differentiate between normal and abnormal thermograms may be considered as the main reason for it. Several authors,[7)-10)] therefore, have claimed that thermography is of little value for breast cancer detection. On the contrary, in order to improve thermographic diagnosis, application of a computer to the quantitative analysis of breast thermograms has been studied by several investigators,[11)-15)] but the improvement of diagnostic accuracy has not yet been obtained. For the same purpose as above, we have developed an on-line image processing system for breast thermogram analysis, with reference to Barash's diagnostic criteria.[16)] The purpose of the present study is to evaluate the effectiveness of the breast thermogram processing system developed, using a receiver operating characteristic (ROC) curve and information capacity.

Materials and Methods

1. Materials and performance of thermographic examination

The total material consisted of thermograms of 99 women examined at the Cancer Institute Hospital, Tokyo. Of these 99 women, 54 were cancer patients, 34 were patients with benign lesion, and 11 were normal. Carcinomas and benign lesions were histologically verified and normals as control were volunteers who had no symptom and were diagnosed as normal by clinical examination. Thermographic examination was carried out at a room temperature of $23\pm3°C$ and the patient, who was seated facing the thermograph with her hands on her head, was examined in frontal and both oblique projections after reasonable temperature equilibration. The thermograph used in the present study was a Thermoviewer MA (JEOL Ltd., Tokyo) and the frame-time for each projection was 30 sec.

2. Breast thermogram processing system

The block diagram of the breast thermogram processing system is given in Fig. 1. In this

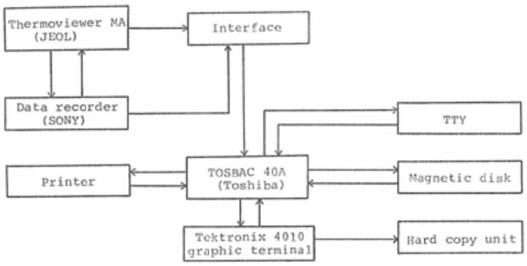

Fig. 1. Block diagram of breast thermogram processing system.

system, the Thermoviewer MA has been interfaced to a Tosbac-40A computer (Toshiba Electric Co., Tokyo) and the temperature informations of the breasts from a thermograph are digitized in 0.1°C steps by means of an analog-to-digital converter incorporated in an interface and each temperature of sampling elements is stored in one byte. All the aquisition data are stored on a data recording analog tape and are transferred into a magnetic disk through the core memory of the computer at the same time or at need. Namely, in the case of off-line processing, data are transferred into a magnetic disk through the interface from the data recording tape. Therefore, the present system can select the on-line or off-line processing of breast thermograms.

Thermogram is displayed on a Tektronix 4010 graphic terminal.

3. Software system for breast thermogram processing

The software system for breast thermogram processing consists of data aquisition, data filing, data display, and data processing, and each system program progresses by communication with TTY. The image-processing program for each diagnostic criterion is executed by a code sent from a key-board of the Tektronix 4010 graphic terminal to the computer. All the temperature informations obtained for each diagnostic criterion are printed out using a printer and are stored on a magnetic disk at the same time.

These system programs were written in the Assembler language.

A. Data aquisition, filing, and data display

A 150-line picture, each line containing 100 or 200 picture elements, called pixels, is the aquisition data per thermogram. The aquisition data are stored together with the patient's name, age, date of examination, center temperature, and a thermogram identification number on a magnetic disk for analysis and output.

The processed image is displayed in a dot pattern of 16 levels based on Bayer's theory[16] on the Tektronix 4010 graphic terminal and the size of temperature per level in each case is freely changeable.

B. Data processing

Data processing procedures are made for the following six diagnostic criteria.

(1) Areolar temperature (At):

At (max) and At (mean) are defined as the difference in maximum temperature and mean temperature, respectively, between the bilateral areolar regions.

(2) Hot spot temperature (Ht):

Ht (max) and Ht (mean) are defined as the difference in maximum temperature and mean temperature, respectively, between a hot spot and the corresponding area of the opposite breast.

(3) Vein temperature (Vt):

Vt (max) is defined as the difference in maximum temperature between the hottest vein and normal vein of the opposite breast.

(4) Vein pattern (Vp):

Vp is the difference in vein patterns between the bilateral breasts. In the present study, Vp (ratio) and Vp (index) are expressed, respectively as follows:

$$\mathrm{Vp(ratio)} = \frac{\sum_{i=l\mathrm{th}}^{l\max} \mathrm{N}_{\mathrm{R},i}}{\sum_{i=l\mathrm{th}}^{l\max} \mathrm{N}_{\mathrm{L},i}} \quad \text{or} \quad \frac{\sum \mathrm{N}_{\mathrm{L},i}}{\sum \mathrm{N}_{\mathrm{R},i}} \leq 1 \qquad (1)$$

$$\mathrm{Vp(index)} = \sum_{i=l\mathrm{th}}^{l\max} (\mathrm{N}_{\mathrm{R},i} - \mathrm{N}_{\mathrm{L},i})^2 \qquad (2)$$

where $N_{R,i}$ and $N_{L,i}$ are the number of pixels of the temperature level, i, in the right and left breasts, and are normalized by the total number of pixels in each processed area of the right and left breasts, respectively. l_{max} and l_{th} are the maximum and threshold-levels in the processed area, respectively.

(5) Breast temperature (Brt):

Brt (max) and Brt (mean) are defined as the difference in maximum temperature and mean temperature, respectively, between the bilateral whole breast.

Table 1. Contents obtained for each criterion by computer analysis

Criterion	Processed contents
At	Maximum temperature and co-ordinates, mean temperature, number of pixels, and number of pixels per temperature level
Ht	Same as At
Vt	Maximum temperature and co-ordinates
Vp	Number of pixels and sum of square of the differences in number of pixels per temperature level of the bilateral breasts*
Brt	Maximum temperature and co-ordinates, mean temperature, number of pixels, and number of pixels per temperature level**
E	Temperature distribution along contour of the breast

*These are data over the temperature level assigned and are normalized by the total number of pixels in the processed area.
**Exclusive of the processed areas of At and Ht or At, Ht, and Vp.

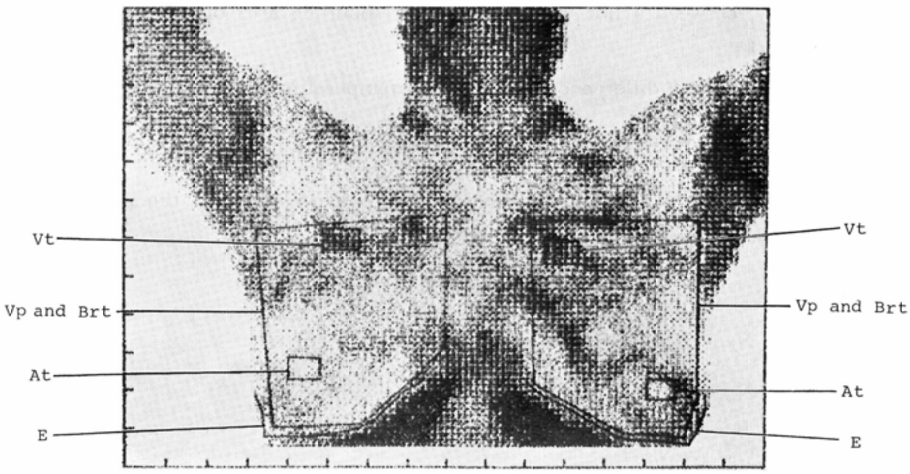

Fig. 2. Breast thermogram displayed in dot pattern of 16 levels based on Bayer's theory on Tektronix 4000 graphic terminal. Solid lines in the thermogram represent the processed areas for various diagnostic criteria.

(6) Edge sign (E):

E is defined as the loss of uninterrupted smooth convex margin of the normal breast contour.[18]

The processed content for each diagnostic criterion described above is given in Table 1. The size of temperature per level is 0.3°C and the processings for Vp and Brt are performed on the same area. The areas to be processed on a CRT display for each criterion are determined by moving cross-hair cursor using two thumbwheels of the keyboard of the Tektronix 4010 graphic terminal and can be selected in arbitrary shape. Each processing program for six criteria is executed by sending codes to the computer after determination of the processed areas.

A processed image of breast thermogram is shown in Fig. 2.

Results

1. Statistical analysis

Table 2. Summary of data obtained for each criterion by computer analysis

Criterion	Group	Mean	Standard deviation	Standard error of mean	Result of statistical test***
	M	1.01	1.04	0.14	
At(max)	B	0.60°C	0.61°C	0.10°C	P<0.05
	N	0.57	0.51	0.15	
	M	1.02	0.88	0.12	
At(mean)	B	0.61°C	0.53°C	0.09°C	P<0.02
	N	0.54	0.39	0.12	
	M	0.93	1.05	0.15	
Vt(max)	B	0.47°C	0.46°C	0.08°C	P<0.01
	N	0.26	0.29	0.09	
	M	0.47	0.27	0.04	
Vp(ratio)	B	0.64	0.23	0.04	P<0.01
	N	0.69	0.25	0.08	
	M	318.7	490.1	66.7	
Vp(index)	B	102.5	224.9	38.0	P<0.01
	N	98.2	160.4	48.4	
	M	0.58	0.57	0.08	
Brt(max)	B	0.35°C	0.41°C	0.07°C	P<0.05
	N	0.27	0.47	0.14	
	M	0.64	0.62	0.08	
Brt(mean)*	B	0.39°C	0.31°C	0.05°C	P<0.02
	N	0.31	0.17	0.05	
	M	0.30	0.33	0.04	
B′rt(mean)**	B	0.28°C	0.23°C	0.04°C	P>0.05
	N	0.20	0.15	0.04	

M, malignant; B, benign; N, normal

*Exclusive of the processed areas of At

**Exclusive of the processed areas of At and Vp

***Statistical test of the difference in mean values between the malignant and benign groups

The processed results of breast thermograms of 99 women using the computer processing system are summarized in Table 2. The mean values obtained for each of diagnostic criteria, At (max), At (mean), Vt (max), Vp (ratio), Vp (index), Brt (max), and Brt (mean), increased or decreased in the order of malignant, benign, and normal groups. The difference between the mean values of the malignant and benign groups for each of the criteria was statistically tested and the results are also given in Table 2. It was found from this table that, with the exception of Brt (mean), there was a significant difference between the two groups ($p<0.05$). These results are also valid for the difference in mean values between the malignant and normal groups. Criteria Ht and E were excluded from Table 2 because the number of cases found for Ht and E was only 2 and 1, respectively.

2. Analysis by methods of ROC curve and information capacity

The accuracy of diagnostic medical tests is frequently expressed in terms of true-positive, false-positive, and overall accuracy rates, but these values will change if the diagnostic criterion level is altered. In recent years, ROC curves have been used to evaluate medical imaging systems.[19] ROC curves can avoid ambiguous results by comparing true-positive and false-positive rates over a wide and continuous range of criterion levels, and ROC curves can also be used to determine optimum criterion levels that maximize overall accuracy.

Metz et al.[20] have proposed the method of information content as a meaningful measure of imaging system performance based on ROC curve data. Namely, by considering diagnostic system as a communication system, it is possible to quantify the information lost in the process of diagnosis in terms of information theory. When information capacity, R, and information content of input side, H(x), mean exactly transmitted information content and input information content, respectively, they will be given by the following equations.[21][22]

$$H(x) = -\sum_{i=1}^{2} p(x_i)\log_2 P(x_i) \quad (3)$$

$$R = H(x) + \sum_{i=1}^{2}\sum_{j=1}^{2}\left\{P(y_j|x_i)\cdot P(x_i)\cdot \log_2\left[\frac{P(y_j|x_i)\cdot P(x_i)}{P(y_j)}\right]\right\} \quad (4)$$

$$P(y_i) = \sum_{i=1}^{2} P(y_j|x_i)\cdot P(x_i) \quad (5)$$

$$P(x_i) = \frac{x_i}{x_1 + x_2} \quad (6)$$

Where, in the present study,

$P(y_1|x_1)$ = true-positive rate,

$P(y_1|x_2)$ = false-positive rate,

$P(y_2|x_1)$ = false-negative rate,

$P(y_2|x_2)$ = true-negative rate,

x = variable representating input information,

x_1 = cancer,

x_2 = benign or normal,

y = variable representating output information,

y_1 = positive, and

y_2 = negative.

Both methods were employed to analyze the ability of each diagnostic criterion used in the present processing system. The ROC curves for various criteria are shown in Figs. 3 and 4. It is evident from these graphs that Vp (index) is the best of criteria used to differentiate between the malignant group and both benign and normal groups. R and R/H(x) were calculated using the above equations at the single operating point giving maximum information capacity on each ROC curve. H(x) was 0.994 bit. These results are summarized in Table 3. From the above results, its was found that Vp(index) was the best criterion, and the single operating point giving maximum information capacity on the ROC curve for Vp (index) showed a true-positive rate of 83.3% and a

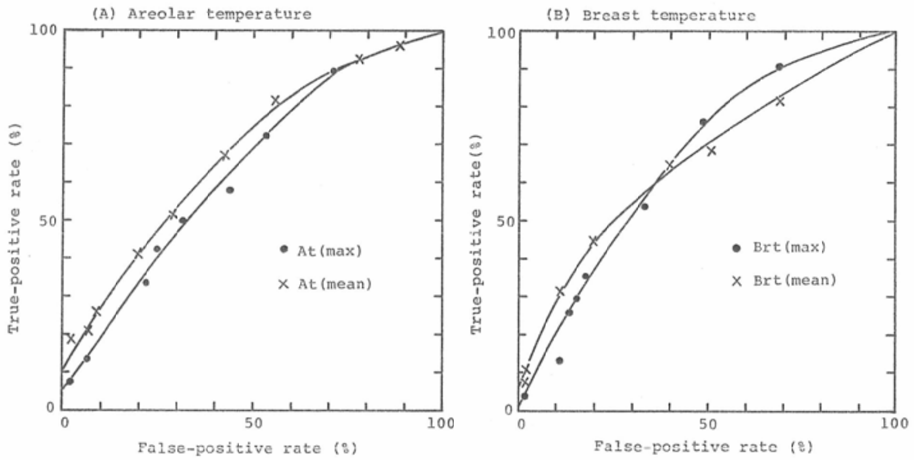

Fig. 3. Receiver operating characteristic (ROC) curves for areolar temperature, At (max), and At (mean), and breast temperature, Brt(max) and Brt (mean)

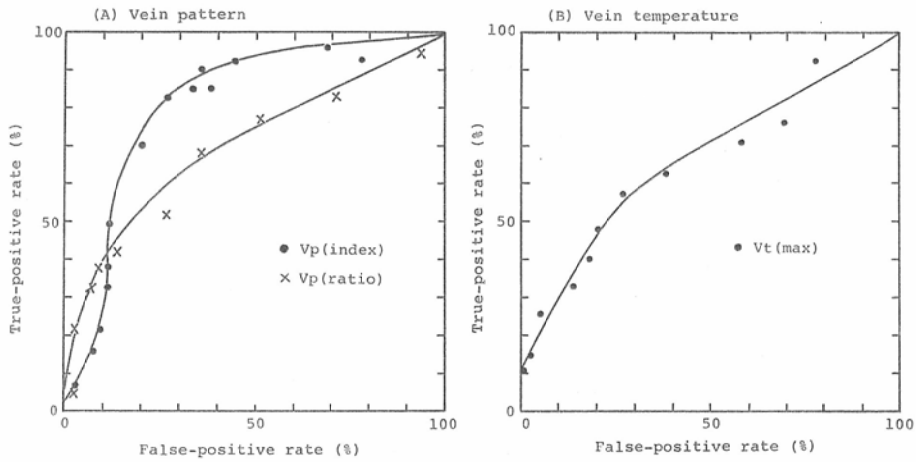

Fig. 4. Receiver operating characteristic (ROC) curves for vein temperature, Vt(max), and vein pat tern, Vp(ratio) and Vp(index).

Table 3. Comparison of diagnostic abilities of various criteria

Criterion	True-positive (%)	False-positive (%)	R (bit)	R/H (x) (%)
At(max)	27/54=50.0	14/45=31.1	0.027	2.7
At(mean)	36/54=66.7	19/45=42.2	0.044	4.4
Vt(max)	31/54=63.0	12/45=26.7	0.071	7.1
Vp(ratio)	37/54=68.5	16/45=35.6	0.079	8.0
Vp(index)	45/54=83.3	12/45=26.7	0.249	25.0
Brt(max)	41/54=75.9	22/45=48.9	0.057	5.7
Brt(mean)	24/54=44.4	9/45=20.0	0.050	5.0

false-positive rate of 26.7%. In that case, the maximum value of R was 0.249 bit and percentage of R/H(x) was 25.0%.

3. Computer diagnosis

In order to improve the diagnostic accuracy by a computer analysis, combination of Vp (index) and other criteria was investigated. However, other criteria also showed a similar tendency as Vp (index). Therefore, by such a combination, only 2 cases were newly found as true positive and there was no case to be added to the true-negative group.

The best result of computer diagnosis obtained by combination of Vp (index) and other criteria, compared with mammography and echography on the same material, is shown in Table 4. Each of

Table 4. Results of computer diagnosis of breast thermograms compared with mammography and echography on the same material

	True-positive (%)	False-positive (%)	H (x) (bit)	R (bit)	R/H (x) (%)
Computer diagnosis of thermograms	47/54=87.1	12/45=26.7	0.994	0.290	29.1
Mammography	51/53=96.2	6/19=31.6	0.833	0.330	39.7
Echography	40/50=80.0	1/9 =11.1	0.616	0.199	32.3

H(x) and R of mammography and echography are calculated based on the assumption that the true-positive and false-positive rates obtained for their examination are the single operating points on their ROC curves. The true-positive rate, false-positive rate, R, and R/H(x) for the computer diagnosis were 87.1%, 26.7% 0.290 bit, and 29.1%, respectively.

Discussion and Conclusion

The results shown in Table 2 confirmed the general truth that the mean temperature difference between hot area on one breast and the corresponding area on the other breast of the malignant group is larger than that of the benign or normal group.

In recent years, various investigators[5)9)22)-26)] have used thermal pattern and temperature difference as the diagnostic criteria for the purpose of increasing the accuracy in breast thermogram interpretation. Barash et al.[16)] considered vein pattern (Vp), vein temperature (Vt), background temperature (Bt), and areolar temperature (At) as diagnostic criteria and showed that Vp and Bt were more significant than Vt and At. On the other hand, Feasey et al.[9] attempted a blind reading using similar criteria in the detection of breast cancer and concluded that no criterion could distinguish between the benign and malignant groups. Reasons for the discrepancy between these conclusions are not readily apparent. Therefore, in the present study, the ability of each criterion, using the breast thermogram processing system developed with reference to their criteria, was analysed by the methods of ROC curve and information capacity. ROC curve for each criterion represents that the further up and to the left the curve is located, the greater is the ability of the criterion. As shown in Fig. 3 and 4, ROC curves with the exception of Vp (index) were located rather low and hardly showed any significant difference from each other. R, H(x), and R/H(x) were calculated at the single operating points that represent the maximum amount of information on ROC curves for various criteria. Its results, except for Vp (index), were not good, as given in Table 3, and gave rise to the same conclusion as made by Feasey et al.,[9] but the new criterion, Vp (index), used in the present study gave a better distinction between the malignant and benign or normal groups. The results of Vp (index) showed the same tendency as those of Vp by Barash et al.[16] It may safely be said, therefore, that the vein pattern is a very important factor in the diagnosis of breast thermograms. However, further investigation on the methods of quantifying the vein pattern will be necessary.

Application of a computer to quantify the interpretation of breast thermograms has been reported by several investigators,[11)-15)] of whom only Ziskin et al.[13] and Ooi and Miki[14] have given the results of computer diagnosis. Ziskin et al.[13] reported that their computer system yielded an overall accuracy of 85% for the entire test material, but did not give detailed results in their report. Ooi and Miki[13] obtained true-positive rate of 62% and false-positive rate of 13% in a study of 49 patients, of whom 23 had benign lesions and 26 had malignant tumors. These results were found to ride approximately on the ROC curve for Vp (index) given in Fig. 4. On the other hand, R, H(x), and R/H(x), which were calculated on the assumption that their results are a single operating point on the ROC curve obtained from their study, were 0.191, 0.997 bit, and 19.2%, respectively. The best results obtained in the present study, as shown in Table 4, are better than the above results, but these results cannot be compared directy because the patient materials studied are small samples and probably not similar.

The point to which special attention should be paid may be that the present study had a false-positive rate of 26.7%, which seems to be high. While false-negative rates are important, false-positive rates have been a greater problem. As individual tumors differ in their biological conditions and therefore their heat production, active benign diseases often show positive thermograms. On the other hand, cancers do not invariably show positive thermograms. If only symptomatic patients are examined, the false-positive rate will increase. Consequently, various diagnostic criteria being used by many investigators, which are based on the simple difference in temperatures, will not give a better separation between active benign and malignant diseases as indicated in Table 3.

While the value of true-positive rate, in general, increases by changing the diagnostic-criterion level employed, the value of the false-positive rate also increases further. A wide variation in the reported diagnostic accuracy of breast thermography can be considered from the such reasons. At present, the greatest drawback of breast thermography is the lack of specific diagnostic criteria for cancer and, unfortunately, no solution for it has as yet been found. Several authors[6)-9)] have stated that thermography is not a suitable method for breast cancer detection because the diagnostic accuracy is lower than that of clinical examination or mammography but it would be too hasty a conclusion. As shown in Table 4, the diagnostic accuracy of thermography compared with mammography and echography is never too low, and thermography has the advantage that it is relatively cheap, atraumatic, and involves no exposure to radiation. To make use of these advantages, efforts in search for better diagnostic criteria should be continued. At the same time, each ability of various criteria being used by many investigators should be evaluated by the methods of ROC curve and information capacity, as employed in the present study. In this respect, application of a computer is the most suitable method because it makes possible to evaluate the abilities of various criteria using the same material. The combination of significant criteria obtained from the above evaluation, even if each of the criteria is nonspecific for cancer, will improve the overall diagnostic accuracy.

For that purpose it will be necessary to standardize the method for performing breast thermography and to increase the number of patients examined. In relation to this standardization, Lapayowker et al.[26] have reported an attempt to codify diagnostic criteria of breast thermography and to specify certain operating characteristics and conditions. The Anglo-Dutch study group has also recomended a procedure for breast examination[27] but there are a few differences between these recomendations. In particular, the difference in the position of the hands will be an important problem to be considered.

The conclusion on the value of thermography for breast cancer detection is to be made after further investigation.

From the results described above, the quantitative diagnosis of breast thermogram by a computer was found to be a significant method. However, the problem to be considered in the present processing system will be that the assignments of the processed area for each criterion and of the threshold of temperature level for Vp are rather subjective. The overall accuracy of computer diagnosis may vary more or less by different assignments. By considering problems discussed above, the present processing system will be improved in the near future.

This study was supported in part by a Grant-in-Aid for Cancer Research from the Ministry of Health and Welfare, Japan, which is gratefully acknowledged.

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