

[Case Report]

**MULTIPLE AND INCIDENTALLY FOUND CANCERS DETECTED BY
¹⁸F-FDG POSITRON EMISSION TOMOGRAPHY/CT
AT ONE EXAMINATION**

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Abstract : During the initial 8 months period of ¹⁸F-FDG PET/CT examination in our institution eleven cases of double cancers were detected. Eight cases were simultaneous second cancers and 3 cases are consecutive cancers. All cases are clinical ones and were referred from both outside hospitals and our own hospital. ¹⁸F-FDG PET/CT examination were utilized either to determine the extent of tumor or to stage the cancer or to detect recurrent tumors during the follow-up period.

During the 8-months period 964 cases were studied. Therefore, the detection rates of simultaneous and consecutive cancers are 0.83% and 0.31% respectively. All together the detection rate of double cancer was 1.14%.

To gain the general conception of double cancers the authors reviewed the autopsy registry of Japanese Society of Pathology during the four years from 2000 through 2003, and tabulated the combination of primary and second cancers. Frequently found combination of cancers were cancers of the thyroid, lung, stomach, liver, biliary tract, colon, rectum, and prostate.

¹⁸F-FDG PET/CT examination seems to be very useful in the management of cancer patients in terms of whole patient care.

Key words : Positron Emission Tomography, PET, Double cancer, Multiple cancer, PET/CT

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INTRODUCTION

Double cancers or multiple cancers are well known to the pathologists and clinical oncologists. They are usually found incidentally or during the follow-up of cancer patients in clinical practice. Pathologists find multiple cancers at the time of autopsies.

Small cancers, however, are not easily found by conventional high technology modalities such as CT, MRI, US and Gallium scintigraphy.

Recently ^{18}F -FDG Positron Emission Tomography (hereafter, PET) became available clinically, and it is being utilized even for mass screening of cancer¹⁻⁶⁾ because of its capability to detect smaller cancers in its earlier stage than before. It is said that even a tumor as small as 5 mm in diameter could be found in some cases. PET is utilized clinically to ascertain the extent of tumor or staging in cancer management.

Normal and pathologic FDG uptake is discussed by Kostakoglu *et al.*⁷⁾ and Nakamoto and his associates⁸⁾.

The combined machine of PET and CT (hereafter, PET/CT) enhanced the accuracy in diagnosis because of its exactly fused images of both PET and CT, enabling easy localization of lesions^{9,10)}.

We found eight simultaneous double cancers and three consecutive cancers during the initial evaluation of the first cancer or follow-up study of the initial cancer or evaluation of malignancy of the first tumor at one examination of ^{18}F -FDG PET/CT during the initial eight months after the installation of the PET/CT in our institution.

Herein we report double cancer or second cancer found by whole body screening using ^{18}F -FDG PET/CT, and also review the results of annual autopsy registry of double cancer gathered by Japanese Society of Pathology¹⁸⁾.

MATERIALS AND METHOD

In 2004 five units of PET scanners were installed in our institution. Two of five scanners are PET/CT scanners (Discovery LS, GE Medical Systems, Milwaukee, Wis.). Other three scanners are Advance NXi. Clinical studies were carried out by PET/CT scanners. Namely, PET/CT scanners are used to assess the metabolic activity of malignant tumor or extent of a tumor.

The patients were prepared by fasting for more than six hours.

PET imaging was performed 60 minutes after the administration of 210 to 230 MBq of FDG. The patients were requested to lie quietly on a reclining couch for about 60 minutes without moving any muscles as much as possible after the administration of FDG. Blood glucose levels were checked before the administration of FDG.

The initial technical parameters for CT of the PET/CT are as follows: The CT of PET/CT is a 4-channel multidetector row CT. The beam pitch is 1.5 : 1 (equivalent to the slice pitch of 6 : 1 in a single helical CT). The gantry rotation time of 0.5 seconds, table speed of 30 mm per gantry rotation, 120 kVp, and 300 mA. The technique was then changed from July, 2004 as follows: Auto mA control system was introduced and kVp was elevated to 140 kVp and the tube current ranged from 50 to 169 mA depending on the thickness or density of the part of the body. The gantry rotation time and the table speed are same as they were before.

PET images and fused PET-CT images were evaluated regarding malignant nature and extent of the tumor. SUV of tumors were measured on the PET image whenever possible. SUV stands for the "standardized uptake value." We measured SUV by encircling the entire FDG high uptake area (so-called hot spot) in the MIP images and the value was expressed in the maximum values, as Jinnouchi¹¹⁾ recommended. Both 3 dimensional (3D) black and white images and color images were evaluated by certified radiologists.

RESULTS

During the period of April through November, 2004 the second cancers were found in 11 patients. Those second malignant tumors in 8 cases were found during the assessment of the first tumors. Cases were referred from both outside hospitals and our own hospital for the assessment of extent of tumor or confirmation of malignancy. Two tumors were suspected to have the possibility of malignancy, so FDG PET examination was carried out. They turned out to be submandibular tumor and parotid tumor, but the second incidentally found tumors were cancer of the colon and rectum. Two concurrent tumors were found during the search of suspected malignancy (Table 1).

As to the detection time of a second cancer, simultaneous detection was in 8 cases, and consecutive detection was in 3 cases. During the period of initial 8 months in PET/CT studies 964 cases were examined. Therefore, the detection rate of simultaneous double cancer was 0.83%, and the detection rate of consecutive cancer was 0.31%. The overall detection rate of double cancer was 1.14%.

Eight cancers were found by PET alone, but the remaining three patients were diagnosed as cancer by CT of PET-CT, contrast-enhanced (CE) CT or cystoscopy and biopsy.

False negative cases on FDG PET are a case of thyroid cancer, a case of HCC and a case of the urinary bladder. The combination of PET study and CT were very useful in detection of cancers, which were not revealed by that time.

A few cases of incidentally found cancers will be illustrated.

Case 1. A 61-year-old man presented with the chief complaint of backache. X-ray of the thoracic spine showed suspected metastasis in the thoracic vertebrae. The patient was then referred to the PET Center for evaluation of malignancy.

Table 1. Survey of Double Cancer or Incidental Second Cancer

Case #	Age	Sex	First Cancer or Dis. + or - on PET (SUV)	Second Cancer/+ or - on PET (SUV)	Modality of positive finding for 2nd Ca	Note: Detectability by PET, (Pathology of 1st. Cancer)
1.	61	M	Ca thyroid/+ (SUV 16.5)	Malignant lymphoma, lower thoracic spine region/+ (20.4)	PET	Concurrent detection of two cancers
2.	75	M	Ca tongue/+ (6.6)	FMH testis & LN meta/+ (11.1, testis; 16.9, Rt. ing. LN)	PET	SUV (10.6 at Rt. Buttock, 6.2 at Lt. fem. LN)
3.	70	F	F/U of P.O. Ca tongue (w/d SCC)/-, No recurrence	Ca (TCC) of bladder/-(missed detection)	CT & Cystoscopy, TUR-BT TCC	FN on PET re. ca bladder
4.	79	F	Ca of Rt. Hypopharynx/+ (12.9)	Follicular Ca thyroid/-(not detected)	CT of PET-CT, Low density mass on CT	FN on PET re. ca thyroid
5.	73	M	Ca of Lt. Hypopharynx/+ (30.1)	HCC/-(not detected)	CT of PET-CT and CE CT	FN on PET re. HCC, + Lt. cervical LN (16.0)
6.	73	M	Ca Lt. lung (SCC)/+ (8.6)	Ca sigmoid (Ca in adenoma)/(11.6)	PET	
7.	68	M	Ca lung (SCC)/+ (15.9)	Ca (SCC) of esophagus/+ (5.5)	PET	Endoscopy: Advanced ca esophagus
8.	79	M	F/U of PO Ca larynx/- No recurrence	Ca of colon (ascending)/+ (11.9)	PET	
9.	79	F	F/U of PO Ca Rt breast/- No recurrence	Ca of colon (ascending)/+ (23.5)	PET	
10.	79	M	Lt. Submandibular tumor/+ (5.1)	Ca sigmoid colon/+ (8.5)	PET	(Pleomorphic Adenoma submand. gland.)
11.	63	M	Rt. Parotid tumor/+ (4.2)	Ca rectum/+ (25.7)	PET	(Chronic Sialoadenitis of Rt. Parotis)

FN: False negative. Ca: Carcinoma. re: regarding. SUV is expressed in maximum value. F/U: Follow-up

^{18}F -FDG PET revealed high uptake of FDG in the region of thoracic vertebrae (SUV 20.4) and also in the thyroid gland (SUV 16.5) (Fig. 1A and 1B).

Aspiration biopsy of the thyroid gland showed adenocarcinoma of the thyroid gland. Pathology of the lesion after thyroidectomy was papillary adenocarcinoma. The lesion in and around the lower thoracic vertebrae turned out to be malignant lymphoma.

Case 2. This 73-year-old man with carcinoma of the left lung was examined with FDG PET/CT to assess the extent of the lesion and staging. FDG PET revealed high uptake of FDG in the sigmoid colon in addition to the high uptake in the bilateral hilar lymph nodes. The SUV values of the left hilar node and the

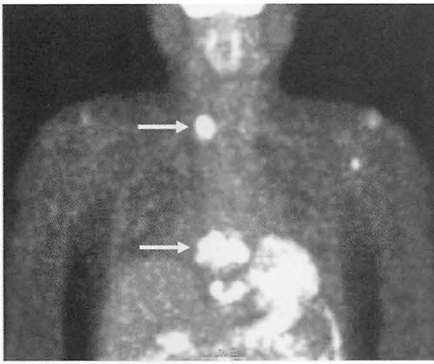


Fig. 1A

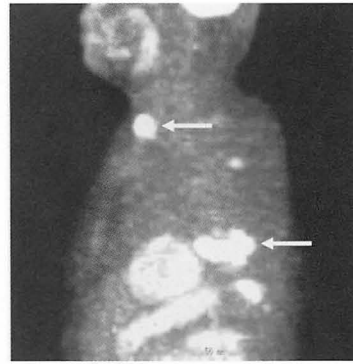


Fig. 1B

Fig. 1. Carcinoma of the thyroid gland and malignant lymphoma.

1A: Frontal image. Note the very high uptake of FDG in the right lobe of the thyroid (SUV 16.5) and in the region of the lower thoracic spine (SUV 20.4).

1B: Lateral image. The high uptake of FDG in the region of the lower thoracic spine projects further anteriorly and posteriorly from the thoracic vertebra.

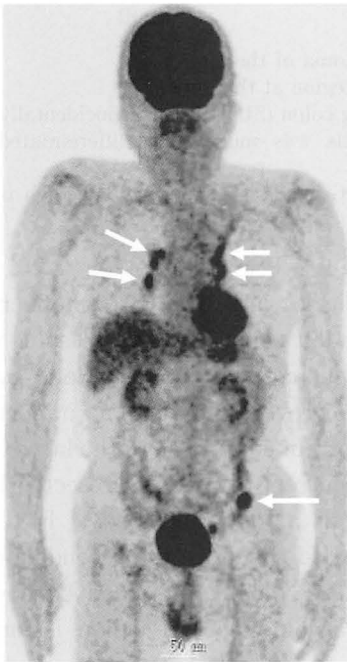


Fig. 2A

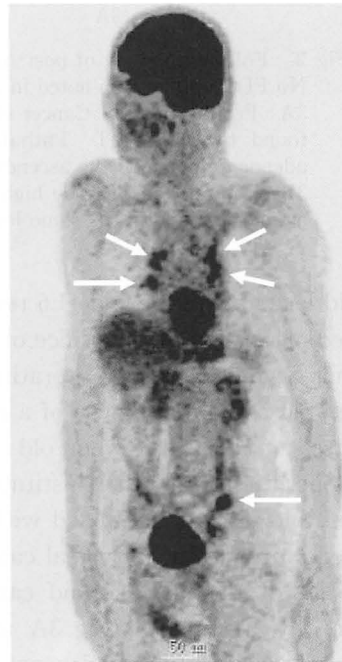


Fig. 2B

Fig. 2. Carcinoma of the left lung with bilateral hilar node metastases and carcinoma of the sigmoid colon. This 73-year-old man presented with the complaint of cough and wheezing. Chest X-ray showed atelectatic lesion in the left upper lobe.

2A: Frontal image. FDG PET showed high uptake in bilateral hilar nodes and sigmoid region.

2B: Oblique image. The high uptake of FDG in the sigmoid region seen in the frontal image stays in the same sigmoid location.

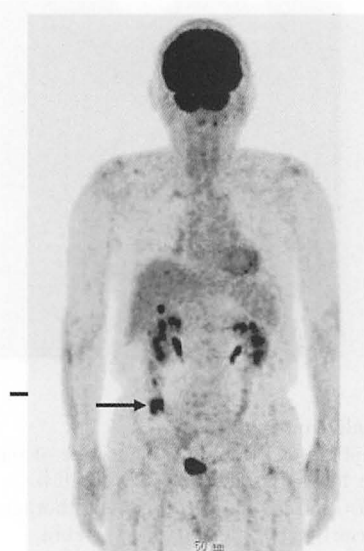


Fig. 3A

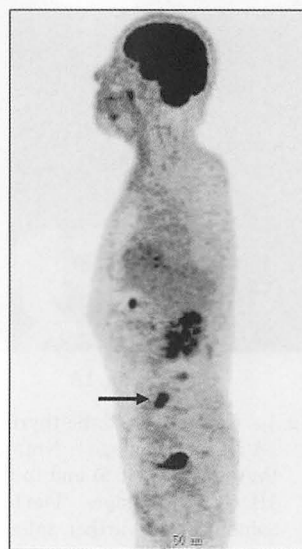


Fig. 3B

Fig. 3. Follow-up study of post-operative carcinoma of the larynx.

No FDG uptake was noted in the laryngeal region at this time.

3A: Frontal image. Cancer of the ascending colon (SUV 11.9) was incidentally found by FDG-PET. Pathological diagnosis was moderately differentiated adenocarcinoma of the ascending colon.

3B: Lateral image. The high uptake of FDG in the ascending colon region is again identified in the same location.

sigmoid lesion were 8.7 and 11.6 respectively (Fig. 2A and 2B). Bronchofiberscopy revealed narrowing of the orifice of B1+2 of the left upper lobe and brushing of the bronchus revealed Class V, keratinizing squamous cell carcinoma. Endoscopy of the sigmoid colon and biopsy of a polypoid tumor revealed carcinoma in adenoma.

Case 3. This is a 79-year-old man with recurrent carcinoma of the larynx after initial operation in another institution. The recurrent tumor was resected in our hospital and he was examined with FDG PET as a follow-up study. FDG PET revealed no recurrent laryngeal cancer but revealed cancer of the ascending colon. The SUV of this new second cancer was 11.9. Namely a second cancer was detected by FDG PET (Fig. 3A and 3B). Pathology of the colon lesion was moderately differentiated adenocarcinoma.

DISCUSSION

As stated above multiple cancers or double cancers were occasionally found at the time of autopsy by pathologists. Clinical oncologists also encounter second or multiple cancers. Up to now, however, no concrete single examination modality existed to show multiple cancers at one examination. FDG PET is now possible to

survey the almost whole body except the very distal portion of the legs and is capable to detect cancers as if it is a one-stop shopping. This fact is often quoted and the slogan of "PET first in cancer management" is being spread. Clinical usefulness is reported in several literatures¹²⁻¹⁶.

In our initial experience of FDG PET/CT in 8-month-period we found 11 second cancers. This fact is important to manage cancer patients because we have to treat the whole body of patients.

In order to find the frequent combination of cancers in one individual patient, the registry of multiple cancers at Japanese Society of Pathology was consulted. We reviewed the registry of four fiscal years; between years 2000 and 2003. Because of numerous sites of cancers we categorized to one group in some disease groups. They are as follows. The site of neurologic tissue included cerebrum, cerebellum, brain stem, spinal cord, meninges, and so forth. Pharynx: epipharynx, mesopharynx, hypopharynx, nasopharynx, pharyngoesophageal junction. Lung: lung, trachea, bronchus. Liver and biliary tract: liver, bile duct, gallbladder, papilla vater. Colon and rectum: colon, rectum, cecum, appendix. Bone marrow and lymphatic system: bone marrow, spleen, lymph node.

The number of cases of each cancer group in four years was summed up and tabulated (Table 2). This table illustrates numerous combination of cancers, but there are several heavily tied combination of cancerous diseases. Some of second cancers, such as carcinoma of the prostate, seemed prone to occur in aged patients.

The frequently found second cancers in patients with cancers of lung, liver group, bone marrow group and pancreas are cancers of the thyroid, stomach, colon group and prostate. The concurrent double cancers of the first cancer of the colon and rectum noted at the registry of Pathology are cancers of the thyroid gland, stomach and prostate.

FDG PET reflects the metabolic activity of a disease. It picks actively growing cancer in its earlier stage and therefore is very useful to determine the malignant nature and the extent of a disease. However, FDG PET shows inflammatory lesions also as does the Gallium scintigraphy.

Another interesting point of differential diagnosis is that atheroma can uptake FDG¹⁷. The exact localization of FDG will help in the differential diagnosis.

The definitive diagnosis depends on the tissue diagnosis by pathologists, but the FDG PET leads the selection of further examination or treatment methods. It detects hidden second cancer also. This is beneficial also to the patients to consider and select treatment methods by patients themselves.

CONCLUSION

Eleven second cancers were incidentally found by FDG PET/CT during the period of eight months in our institution. FDG PET is very useful in the management of cancer patients in terms of whole patient care.

Table 2. Double Cancer, From the Registry of Double Cancer Diagnosed by Autopsy. Japanese Society of Pathology. Period : Year 2000 through 2003

Primary Site 1 Primary Site 2	Thyroid	Paranasal sinuses	Neurologic tissue	Tongue	Pharynx	Oral cavity	Larynx	Esophagus	Lung	Breast	Stomach	Liver and Biliary tract	Small intestine	Colon and Rectum	Bone marrow, Lymph. System	Kidney, Renal pelvis	Pancreas	Ureter, Bladder, Urethra	Prostate	Uterine cervix	Uterine body	Ovary
Thyroid		4	8	4	7	4	2	9	136	37	84	137	7	49	109	39	47	12	20	11	8	18
Paranasal sinuses	0		0	0	0	0	0	0	2	0	0	1	0	0	0	0	0	0	1	0	0	0
Neurologic tissue	1	0		0	0	0	0	0	2	1	2	2	1	1	4	0	3	0	1	0	0	0
Tongue	0	0	0		3	0	0	7	5	0	1	2	0	0	2	0	0	0	1	0	0	0
Pharynx	0	0	0	0		0	0	16	11	1	5	2	0	2	2	1	2	1	0	0	0	0
Oral cavity	0	0	0	3	2		0	9	15	0	5	3	0	2	4	0	0	0	0	0	0	0
Larynx	2	1	0	1	1	0		11	22	0	9	8	0	5	7	2	1	2	4	0	0	0
Esophagus	3	1	3	0	21	2	3		46	3	35	22	0	9	11	3	27	7	6	1	1	1
Lung	13	0	3	1	3	3	9	31		12	72	70	3	29	74	13	31	18	22	3	1	4
Breast	3	1	2	1	2	2	0	5	41		31	38	0	14	30	2	17	0	0	4	7	13
Stomach	8	4	8	4	12	1	4	107	281	15		225	2	69	98	18	65	15	51	7	3	6
Liver and Biliary tract	5	0	1	1	4	2	1	21	80	12	72		5	31	63	13	36	8	14	2	1	3
Small intestine	1	0	0	0	0	0	0	5	8	3	2	9		3	8	1	2	0	0	0	0	0
Colon and Rectum	13	2	4	0	7	1	5	50	177	11	174	159	10		119	20	69	21	35	8	8	9
Bone marrow, Lymph. System	2	0	3	1	3	1	1	7	42	9	44	27	1	7		4	15	2	15	5	0	3
Kidney, Renal pelvis	4	1	3	1	1	2	0	4	53	2	34	40	1	25	33		20	20	16	0	1	0
Pancreas	1	2	1	0	2	0	1	6	12	4	23	20	0	7	14	1		8	9	1	0	2
Ureter, Bladder, Urethra	1	0	2	1	1	0	0	4	57	2	28	24	4	15	17	37	10		13	1	0	0
Prostate	9	5	4	6	11	9	5	41	331	0	193	177	4	76	165	35	83	49		0	0	0
Uterine cervix	3	0	1	0	0	1	0	2	13	6	9	26	0	10	14	5	6	7	0		1	1
Uterine body	0	0	1	0	0	0	0	0	2	3	2	5	0	1	3	0	1	2	0	0		6
Ovary	0	0	0	0	0	0	0	0	4	4	4	5	0	8	2	1	4	1	0	1	2	
Others	5	0	5	1	3	1	0	3	38	9	32	23	2	9	36	9	8	8	12	4	1	0

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REFERENCES

1. Yasuda S, Ide M, Fujii H, Nakahara T, Mochizuki Y, Takahashi W, Shohtsu A. Application of positron emission tomography to cancer screening. *Brit J Cancer*, **83**: 1607-1611, 2000.
2. Ide M. Cancer screening using FDG-PET (in Japanese). *Jpn J Diag Imaging (Gazo-Shindan)*, **23**: 1190-1197, 2003.
3. Uno K. Cancer screening. *In*: Ito M, et al, eds. *Frontiers in high technology practice of cancer diagnosis and therapy*. CAFI, Tokyo, 69-75, 2004.
4. Jinnouchi S. Data of PET screening. *In*: Jinnouchi S, ed. *FDG-PET Manual*. 1st ed. Inner Vision, Tokyo, 62, 2004.
5. Moriyama N. Evaluation of cancer screening and expectation in future: Summary of results at Research Center for Prevention and Screening of Cancer at National Cancer Center one year after its opening (in Japanese). *New Medicine in Japan (Shin-iryō)*, No. 374, 82-84, Feb., 2006.
6. Chen YK, Kao CH, Liao AC, Shen YY, Su CT. Colorectal cancer screening in asymptomatic adults: The role of FDG PET scan. *Anticancer Res*, **23**: 4357-4362, 2003.
7. Kostakoglu L, Hardoff R, Mirtcheva R, Goldsmith SJ. PET-CT fusion imaging in differentiating physiologic from pathologic FDG uptake. *RadioGraphics*, **24**: 1411-1431, 2004.
8. Nakamoto Y, Tatsumi M, Hammoud D, Cohade C, Osman MM, Wahl RL. Normal FDG distribution pattern in the head and neck: PET/CT evaluation. *Radiology*, **234**: 879-885, 2005.
9. Gutzeit A, Antoch G, Kühl H, Egelhof T, Fischer M, Hauth E, Goehde S, Bokisch A, Debatin J, Freudenberg L. Unknown primary tumors: Detection with dual-modality PET/CT-Initial experience. *Radiology*, **234**: 227-234, 2005.
10. Hany TF, Steinert HC, Goerres GW, Buck A, Schulthess GK. PET Diagnostic accuracy: Improvement with in-line PET-CT system: Initial results. *Radiology*, **225**: 575-581, 2002.
11. Jinnouchi S. Method of PET screening. *In*: Jinnouchi S, ed. *FDG-PET Manual*. 1st ed. Inner Vision, Tokyo, 17, 2004.
12. Pannu HK, Bistow RE, Cohade C, Fishman EK, Wahl RL. PET-CT in recurrent ovarian cancer: Initial observations. *RadioGraphics*, **24**: 209-223, 2004.
13. Kazama T, Faria SC, Varavithya V, Phongkitkarun S, Ito H, Macapinlac HA. FDG PET in the evaluation of treatment for lymphoma: Clinical usefulness and pitfalls. *RadioGraphics*, **25**: 191-207, 2005.
14. Ito M, et al., eds. *Frontiers of Clinical PET*. Published by Research Institute of Frontier Medical Technologies, Tokyo, August, 2004.
15. Ito M, et al., eds.: *Frontiers of Practice of Diagnosis and Therapy of Cancer by high technologies: From PET to Particle Radiotherapy*. Published by CAFI, Tokyo, December, 2004.
16. Watanabe K, Matsuzawa T, Ishii K, Ito M, eds. *Progress in Researches and Clinical Practice of PET; Cancer and Brain*. Published by Southern Tohoku Research Institute

- for Neuroscience, Koriyama, Japan, March, 2005.
17. Tatsumi M, Cohade C, Nakamoto Y, Wahl RL. Fluorodeoxyglucose uptake in the aortic wall at PET/CT: Possible finding for active atherosclerosis. *Radiology*, **229**: 831-837, 2003.
 18. Japanese Society of Pathology: Registry of Double Cancer. Year 2000 through 2003 In Autopsy Registry of Japanese Society of Pathology.