

Activities of Tissue Registry and Tumor Registry in NAGASAKI Area

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In Nagasaki area, registry of malignant tumor patients found in hospitals and clinics in the city has been conducted by the Nagasaki City Medical Association with the cooperation of Radiation Effects Research Foundation (RERF) since 1957.

The method of diagnosis is various such as 1) autopsy, 2) microscopy, 3) cytologic diagnosis, 4) endoscopic examination findings, 5) operation, 6) radiography, 7) clinical findings, 8) death certificate and 9) others. The number of cases collected during the period of 19 years up to 1975 amounts to 41,780.

On the other hand, tissue registry was started in September 1975. In this Registry, all hospitals in Nagasaki Prefecture and RERF where specimens and tissues are obtained and examined for diagnostic and therapeutic purposes are invited to participate. The purpose of the Tissue Registry is to register as many cases as possible occurring in the residents of Nagasaki prefecture and to promote diagnosis, treatment, early detection, and prevention of tumors by analyzing the collected data.

Prior to the establishment of the Tumor Registry, it was agreed to provide the best possible tissue diagnosis, clarify incidence and site of tumors, and to provide a central depository where useful and confirmed diagnosis are available as a source of data for medical studies related to tumors.

Fortunately, financial assistance was given to the establishment the Tissue Registry through RERF in accordance with a provision of the contract between the National Cancer Institute and the National Academy of Sciences, USA and thus the operation of the Tissue Registry has become available.

At commencement of this project, we established two sub-committees; Pathology Committee and Statistics Committee.

PATHOLOGY COMMITTEE

The Tissue Registry was commenced with the neoplasm tissues of 1973. From among the paraffin blocks preserved at various institutions, those specimens of benign or malignant tumor and of the diseases of probable precancer condition are registered.

Microscopic specimens are stained with H-E or with special stain as required. Diagnosis of specimens is made by a group of four committee members. For the cases on which the diagnosis is not in unanimous agreement (about 3-5%), the diagnosis is decided at the weekly discussion meeting by all the 12 members. Those cases with established diagnosis are recorded in the registry card one by one.

STATISTICS COMMITTEE

The procedure for coding of basic information on patients, clinical diagnosis (ICD)¹⁾ and histological diagnosis of tumors (ACS and SNOP)²⁾³⁾, has been established. The work involves preparation of code sheets, coding, confirmation of the accuracy of data, exchange of information on exposure distance, death date, etc., with RERF. Punch cards and magnetic tapes of data have been prepared with the cooperation of RERF, and classification and statistical analysis of the registry data are being made for utilization in research and education.

On the occasion of this opportunity, we wished to review the relationship between young Tissue Registry and almost 20 years old Tumor Registry in search of the direction of future activities.

I. TUMOR REGISTRY

Local cancer registry is conducted in 17 prefectures and 2 cities in Japan.

The method of diagnosis for the cases registered in Nagasaki City from 1957 to 1970 was autopsy in 15.9%, microscopy and cytologic diagnosis in 34.6%, operation in 10.0%, radiography in 9.1%, clinical diagnosis in 17.9%, death certificate in 12.8%.

Malignant neoplasm (MN) of stomach was diagnosed by autopsy in 11.4%, microscopy and cytologic diagnosis in 26.5%, operation in 14.5%, radiography in 16.3%, clinical diagnosis in 16.9%, and death certificate in 14.0%. MN of cervix uteri was diagnosed by autopsy in 4.7%, microscopy and cytologic diagnosis in 76.1%, operation in 4.4%, radiography in 0.1%, clinical diagnosis in 13.5%, and death certificate in 1.1%. There was a contrast between MN of stomach and cervix uteri.

Incidence and mortality of malignant neoplasms

1) *Number of patients and incidence of malignant neoplasm by year since 1957*

There is a tendency of gradual increase. When this is observed by age group, the peak is in the age group of 60-64 for both male and female. (Table 1)

Table 1. The Number of Patients and Incidence of Malignant Neoplasms (Nagasaki City)

Year	Total	1957	1958	1959	1960	1961	1962	1963	1964	1965
Population	7092697	321827	331080	336471	345335	350230	376048	395652	399258	407541
Number of Patients	14152	435	492	515	575	590	630	617	702	813
Incidence (-/10 ⁵ pop.)	199.5	135.5	148.6	153.3	166.7	168.6	167.6	156.2	175.9	199.8
Year		1966	1967	1968	1969	1970	1971	1972	1973	1974
Population		412266	417343	418970	418810	422474	425279	430338	440048	443457
Number of Patients		888	865	985	889	965	972	993	1124	1102
Incidence (-/10 ⁵ pop.)		215.5	207.4	235.6	212.7	228.7	228.7	230.9	255.5	248.8

2) *The order of malignant neoplasms in incidence by sex*

Table 2-1 & Table 2-2 shows the annual means of the incidence of malignant neoplasms from 1957 to 1975. Malignant neoplasm of stomach is the top in ranking for both male and female.

3) *The order of malignant neoplasms in mortality by sex*

As compared with Table 2-1 & 2-2, pancreas and esophagus are ranked higher for male, and the order of No.3 and No.4 is reversed for female. There are many other changes in the order of malignant neoplasms. (Table 3-1 & 3-2)

Table 2-1. The Number of Patients and Incidence of Malignant Neoplasms

Order	Diagnosis	Incidence	
		No.	-/10 ⁵
1	Malignant neoplasm of stomach	2845	83.9
2	Malignant neoplasm of trachea, bronchus and lung	786	23.2
3	Malignant neoplasm of liver and intrahepatic bile ducts specified as primary	355	10.5
4	Secondary malignant neoplasm of respiratory and digestive systems	346	10.2
5	Malignant neoplasm of rectum and rectosigmoid junction	252	7.4
6	Malignant neoplasm of large intestine, except rectum	238	7.0
7	Malignant neoplasm of pancreas	207	6.1
8	Malignant neoplasm of prostate	185	5.5
9	Lymphosarcoma and reticulum-cell sarcoma	164	4.8
10	Malignant neoplasm of bladder	137	4.0

Table 2-2. The Number of Patients and Incidence of Malignant Neoplasms

Female (Population 3693223)

Incidence

Order	Diagnosis	No.	-/10 ⁵
1	Malignant neoplasm of stomach	1930	52.3
2	Malignant neoplasm of cervix uteri	1160	31.4
3	Malignant neoplasm of breast	648	17.6
4	Malignant neoplasm of trachea, bronchus and lung	346	9.4
5	Other malignant neoplasm of uterus	256	6.9
6	Malignant neoplasm of thyroid gland	241	6.5
7	Secondary malignant neoplasm of respiratory and digestive systems	219	5.9
8	Malignant neoplasm of rectum and rectosigmoid junction	197	5.3
9	Malignant neoplasm of gall bladder and bile ducts	194	5.3
10	Malignant neoplasm of large intestine, except rectum	190	5.1

Table 3-1. The Number and Rate of Mortality

Male (Population 3399474)

Mortality

Order	Diagnosis	No.	-/10 ⁵
1	Malignant neoplasm of stomach	1999	59.0
2	Malignant neoplasm of trachea, bronchus and lung	651	19.2
3	Malignant neoplasm of liver and intrahepatic bile ducts, specified as primary	338	10.0
4	Secondary malignant neoplasm of respiratory and digestive systems	289	8.5
5	Malignant neoplasm of pancreas	179	5.3
6	Malignant neoplasm of esophagus	167	4.9
7	Malignant neoplasm of rectum and rectosigmoid junction	166	4.9
8	Malignant neoplasm of large intestine, except rectum	149	4.4
9	Lymphosarcoma and reticulum-cell sarcoma	145	4.3
10	Malignant neoplasm of prostate	136	4.0

Table 3-2. The Number and Rate of Mortality

Female (Population 3693223)

Mortality

Order	Diagnosis	No.	-/10 ⁵
1	Malignant neoplasm of stomach	1345	36.4
2	Malignant neoplasm of cervix uteri	462	12.5
3	Malignant neoplasm of trachea, bronchus and lung	268	7.3
4	Malignant neoplasm of breast	208	5.6
5	Secondary malignant neoplasm of respiratory and digestive systems	192	5.2
6	Malignant neoplasm of gall bladder and bile ducts	181	4.9
7	Malignant neoplasm of ovary, fallopian tube and broad ligament	137	3.7
8	Malignant neoplasm of rectum and rectosigmoid junction	134	3.6
9	Malignant neoplasm of liver and intrahepatic bile ducts, specified as primary	112	3.0
10	Malignant neoplasm of pancreas	111	3.0

and lymphosarcoma, and the occurrence is frequent in the 40's to 60's though the peak is not definite because of the small number of cases.

5) *Comparison of the malignancy between clinical and morphological diagnosis -1st Diagnosis-*

Among the 337 cases of malignant neoplasms of stomach by histological diagnosis,

Table 5. Number of Primary Malig. of Breast by Sex, by Morphology and by Age

SEX	TOTAL	MORPHOLOGY	TO TAL	AGE													
				00-	05-	10-	15-	20-	30-	40-	50-	60-	70-	80-	UNK		
M	1	Duct carcinoma, infiltrating	1							1							
F	100	Undifferentiated carcinoma	1										1				
		Papillary carcinoma	1						1								
		Squamous cell carcinoma	1						1								
		Adenocarcinoma															
		Papillary adenocarcinoma	1							1							
		Duct carcinoma, infiltrating	91					2	9	34	22	18	3				3
		Medullary carcinoma	2							2							
		Lobular carcinoma	2												2		

Table 6. Number of Primary Malig. of Cervix Uteri by Sex, by Morphology and by Age

SEX	TOTAL	MORPHOLOGY	TO TAL	AGE													
				00-	05-	10-	15-	20-	30-	40-	50-	60-	70-	80-	UNK		
F	194	Carcinoma, in situ	2								1	1					
		Squamous cell carcinoma	182							19	47	49	33	23	4		7
		Adenocarcinoma	3							1	1	1					
		Clear cell carcinoma	1														1
		Adenosquamous cell carcinoma	6							2	2	1					1

Table 7. Number of Primary Malig. of Lymph Nodes by Sex, by Morphology and by Age

SEX	TOTAL	MORPHOLOGY	TO TAL	AGE													
				00-	05-	10-	15-	20-	30-	40-	50-	60-	70-	80-	UNK		
M	40	Malignant tumor	1														1
		Malignant lymphoma, type unknown	9							1	3	2	2	1			
		Lymphocytic lymphosarcoma	4									2	2				
		Lymphoblastic lymphosarcoma	4					1	1				1	1			
		Reticulum cell sarcoma	18					1	3	3	2	7	2				
		Hodgkin's disease	4							3			1				
F	21	Malignant tumor	1														1
		Malignant lymphoma, type unknown	8							1	2	1	2	2			
		Lymphoblastic lymphosarcoma	3								3						
		Reticulum cell sarcoma	8							1	2	3	1				1
		Hodgkin's disease	1								1						

290 cases (86.5%) by clinical diagnosis were in agreement. Likewise, agreement was seen in 67 out of 101 cases of breast (66.3%), 131 out of 194 cases of cervix uteri (67.5%), and 43 out of 51 cases of lymph nodes (70.5%).

B. *Relationship between Tissue Registry and Tumor Registry*

1) *Overlapping of Tissue Registry cases with Tumor Registry cases for patients living in Nagasaki City & outside of City*

As shown in Table 8, the Tissue Registry cases of 1973 were cross-checked with the Tumor Registry cases of 19 years. 1,085 cases were registered in both registries and 1,380 cases were not in Tumor Registry. This may have resulted from the fact that, while Tissue Registry covered the entire prefecture for collection of specimens, Tumor Registry was limited to Nagasaki City and outskirts. As shown in total, 997 unmatched cases were out of city, and additional 151 in city cases were registered.

Table 8. Overlapping of Tissue Registry Cases with Tumor Registry Cases

Tumor R.	Tissue R.											
	M				F				Total			
	Total	In	Out	Unk	Total	In	Out	Unk	Total	In	Out	Unk
Total	881	273	445	163	1584	611	698	275	2465	884	1143	438
Matched	398	237	65	96	687	496	81	110	1085	733	146	206
Unmatched	483	36	380	67	897	115	617	165	1380	151	997	232

Most of unmatched cases are out of city

Table 9. Tumor Registry Cases

Total	in 31021	out 10408	unk 351	total 41780
1957	990	713	4	1707
58	1062	741	1	1804
59	1160	739	2	1901
60	1247	780	2	2029
61	1291	790	3	2089
62	1438	693	6	2137
63	1618	608	5	2231
64	1742	565	8	2315
65	2011	491	10	2512
66	2161	416	14	2591
67	1893	491	21	2405
68	1902	539	23	2464
69	1738	480	15	2233
70	1959	471	19	2449
71	1927	436	25	2388
72	1841	420	27	2288
73	1928	387	104	2419
74	1845	353	34	2232
75	1268	290	28	1586

2) *Tumor Registry cases*

As shown in Table 9, 1,700 to 2,500 cases are registered per year.

3) *Comparison of address between Tissue Registry cases and Tumor Registry cases*

Among the Tissue Registry cases that were also registered in Tumor registry, malignant tumor was found in 733 cases in city, and the address of these cases was compared with the residence at time of initial diagnosis in Tumor Registry. As shown in Table 10, only 14 cases had different address. Among the 146 cases registered as out of city in Tissue Registry, 20 cases were registered otherwise in Tumor Registry. This may be due to the difference in time of registry since Tumor Registry has been conducted for a long time.

4) *Comparison of diagnosis in Tissue Registry and Tumor Registry (for agreed cases)*

Among the 1,085 cases, 63 cases (5.8%) has been diagnosed to have malignant and benign neoplasm in Tumor Registry but they were found to be negative in Tissue Registry. Malignant neoplasms were present in 12 cases involving breast in 7 cases, malignant lymphoma in 3 cases, prostate in 1 case and large intestine in 1 case in Tumor Registry. The other 51 cases were benign in Tumor Registry.

Excluding these 63 cases, the remaining 1,022 cases were examined whether their diagnosis agree or disagree between the two registries. Table 11-1 shows the result. First

Table 10. Comparison of Address Between Tissue Registry Cases and Tumor Registry Cases (Matched cases)

in city in Tissue R.				Out of city in Tissue R.				Unk. in Tissue R.			
Tumor				Tumor				Tumor			
Total	In	Out	Unk	Total	In	Out	Unk	Total	In	Out	Unk
733	719	10	4	146	19	126	1	206	87	34	85

Table 11-1. Comparison of Diagnosis Between Tissue Registry Cases and Tumor Registry Cases

Diag. of Tissue R.	Tumor Diagnosis (1st diagnosis)						
Total	Total		M		F		
Total	Agreed/Disag.	1022	799/223	390	288/102	632	511/121
In City	Total		M		F		
∕	782	623/159	287	219/ 68	495	404/ 91	
Out	Total		M		F		
∕	156	112/ 44	68	45/ 23	88	67/ 21	
Unk	Total		M		F		
∕	84	64/ 20	35	24/ 11	49	40/ 9	

diagnosis in Tumor Registry means the diagnosis by the first diagnostic method in the order of priority. The rate of agreement was 78.2% in total, 74.0% in male and 80.9% in female.

Then it was checked if the diagnosis in Tissue Registry agree or disagree with any of the first diagnosis through the third diagnosis in Tumor Registry. Table 11-2 shows the result. The rate of agreement is higher as a matter of course. It is 83.3% in total, 80.3% in male and 85.1% in female.

The diseases (ICD) of which diagnosis disagreed in over 50% of cases between the two registries are listed in Table 11-3.

Table 11-2. Comparison of Diagnosis Between Tissue Registry Cases and Tumor Registry Cases

Diag. of Tissue R.	Diag. of	Tumor Diagnosis (any diagnosis)					
		Total		M		F	
Total Agreed/Dis.		1022	851/171	390	313/ 77	632	538/ 94
In	∕	782	667/115	287	239/ 48	495	428/ 67
Out	∕	156	117/ 39	68	49/ 19	88	68/ 20
Unk	∕	84	67/ 17	35	25/ 10	49	42/ 7

Table 11-3. ICD of Disagreed Cases (over 50%) for 1st Diagnosis
* for any diagnosis

145.	Malignant neoplasm of other and unspecified parts of mouth
148.	Malignant neoplasm of hypopharynx
152.	∕ small intestine including duodenum
171.*	∕ connective and other soft tissue
195.*	∕ ill-defined sites
196.*	Secondary and unspecified m. n. of lymph nodes
197.*	Secondary m. n. of respiratory and digestive systems
198.*	Other secondary m. n.
201.*	Hodgkin's disease
204.*	Lymphatic leukemia
207.*	Other and unspecified leukemia
211.	Benign neoplasm of other parts of digestive system
212.	Benign neoplasm of respiratory system
219.*	Other Benign neoplasm of uterus
221.	Benign neoplasm of other female genital organs
239.*	Benign neoplasm of eye

Method of Diagnosis in Tumor Registry

: 1. Autopsy 2. Microscopy 3. Cytologic Diagnosis 4. Endoscopic Examination Findings 5. Operation 6. Radiography 7. Clinical Findings 8. Death Certificates 9. Others.

5) *Method of diagnosis in cases of agreed diagnosis*

First diagnosis in Tumor Registry by other than microscopic examination was seen in only 13 cases out of 799 cases as shown in Table 12-1.

Also, as shown in Table 12-2, any diagnosis in Tumor Registry by other than histological diagnosis was seen in 15 cases out of 851 cases.

6) *Method of diagnosis in cases of disagreed diagnosis*

The method of diagnosis in 223 cases whose first diagnosis in Tumor Registry disagreed with the diagnosis in Tissue Registry is shown in Table 13-1. Diagnosis by other than histological diagnosis was seen in 24 cases showing some increase compared with the previous cases. As to any diagnosis, 15 cases out of 171 cases were diagnosed by other than histological diagnosis. (Table 13-2)

Table 12-1. Methods of diagnosis in Cases of Agreed Diagnosis

Method of Diagnosis on 1st Diagnosis in Tumor Registry							
Agreed		Autopsy	Surgical	Operation	X-Ray	Clinical	D.C.*
Total	799	49	737	7	1	3	2
M	288	29	253	4	1	1	
F	511	20	484	3	2	2	
In	623	37	578	4	1	2	1*
Out	112	12	95	3		1	1*
Unk	64		64				

*184 Malignant neoplasm of other and unspecified female genital organs

*203 Multiple myeloma

Table 12-2. Methods of Diagnosis in Cases of Agreed Diagnosis

Method of diagnosis on Any Diagnosis in Tumor Registry							
Agreed		Autopsy	Surgical	Operation	X-Ray	Clinical	D.C.
Total	851	51	785	7	1	4	3*
M	313	29	277	4	1	1	1
F	538	22	508	3		3	2
In	667	38	619	4	1	3	2
Out	117	13	99	3		1	1
Unk	67		67				

3 cases of D.C.* 184 Malignant neoplasm of other and unspecified female genital organs

197 Secondary malignant neoplasm of respiratory and Digestive systems

203 Multiple myeloma

The fact that 1st diagnosis in 32 cases and any diagnosis in 28 cases by autopsy disagreed with the diagnosis in Tissue Registry is due to the difference in the site of tumor and the difference between primary and secondary in most cases. Complex malignant neoplasm was observed in a few cases.

Table 13-1. Methods of Diagnosis in Cases of Disagreed Diagnosis

Method of Diagnosis on 1st Diag. in Tumor Registry							
Disagreed	Autopsy	Surgical	Operation	X-Ray	Clinical	D.C.	
Total	223	32*	167	4	4	9	7
M	102	17	76	1	3	2	3
F	121	15	91	3	1	7	4
In	159	27	115	2	3	7	5
Out	44	5	32	2	1	2	2
Unk	20		20				

* 143 m.n. of gum
 154 m.n. of rectum and rectosigmoid junction
 162 m.n. of trachea
 171 m.n. of connective and other soft tissue
 185 m.n. of prostate
 191 m.n. of brain
 196 Secondary and unspecified m.n. of lymph nodes
 197 Secondary m.n. of respiratory and digestive systems
 198 Other secondary malignant neoplasm
 200 Lymphsarcoma and reticulum cell sarcoma
 201 Hodgkin's disease
 225 Benign n. of brain and other parts of nervous system
 m. n. malignant neoplasm

Table 13-2. Methods of Diagnosis in Cases of Disagreed Diagnosis

Method of Diagnosis on 1st Diag. in Tumor Registry							
Disagreed	Autopsy	Surgical	Operation	X-Ray	Clinical	D.C.	
Total	171	28	128	2	2	6	5
M	77	16	58		1		2
F	94	12	70	2	1	6	3
In	115	25	82		1	4	3
Out	39	3	29	2	1	2	2
Unk	17		17				

7) *Frequency of malignant neoplasm*

As shown in Table 14, the frequency of malignant neoplasm was in the order of stomach MN, metastatic MN of lymph nodes, malignant lymphoma in male, and MN of cervix uteri, MN of stomach, MN of breast in female.

8) *Complex MN*

Among the 2,465 cases, complication of MN and MN was observed in 3 cases and complication of MN and benign neoplasm in 14 cases.

Table 14. Diagnosis by Sex Group of Tissue Reg. Cases
(In the order of frequency of malignant neoplasms)

Total		M		F	
1. Stomach (P-M)	331	1. Stomach (P-M)	207	1. Cervix Uteri (P-M)	178
2. Cervix Uteri (P-M)	178	2. Lymph Nodes (M-M)	53	2. Stomach (P-M)	124
3. Lymph Nodes (M-M)	102	3. Lymph Nodes (P-M)	41	3. Breast (P-M)	99
4. Breast (P-M)	99	4. Rectum, Rectosigmoid junction, Anal Canal & Anus, NOS (P-M)	39	4. Lymph Nodes (M-M)	49
5. Lymph Nodes (P-M)	65	5. Skin (P-M)	35	5. Lymph Nodes (P-M)	24
6. Rectum, Rectosigmoid junction Anal Canal and Anus, NOS(P-M)	61	6. Urinary Bladder (P-M)	26	6. Connective tissue & other soft tissue (M-M)	22
7. Skin	60	7. Large Intestine (P-M)	24	7. Rectum, Rectosigmoid junction, Anal Canal and Anus, NOS (P-M)	22
8. Retroperitoneum, Peritoneum & Intra-abdominal sites (M-M)	43	8. Retroperitoneum (M-M)	23	8. Retroperitoneum, Peritoneum & Intra-abdominal sites (M-M)	20
9. Connective tissue & other soft tissue (M-M)	39	9. Esophagus (P-M)	19	9. Other parts of Uterus (P-M)	19
10. Urinary Bladder (P-M)	33	10. Connective tissue & other soft tissue(M-M)	17	10. Thyroid Gland & Thyroglossal Duct (P-M)	19

P-M: primary malignancy

M-M: metastatic malignancy

CONCLUSION

By the combined use of Tissue Registry, the criteria of diagnosis by pathologists can be standardized and histopathological diagnosis can be made more accurately. This may give a greater significance to geopathological studies. This may also provide important information for clinical diagnosis, determination of prognosis and decision of therapy.

Tumor Registry and Tissue Registry can be used for follow-up of patients and sometimes valuable cases can be found. Moreover, Tissue Registry serves as the library of neoplasm tissue specimens and these specimens are useful as educational materials.

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