TECHNICAL REPORT
RERF TR 4-87
業 績 報 告 書

RECLASSIFICATION OF LEUKEMIA AMONG A-BOMB SURVIVORS BY FRENCH-AMERICAN-BRITISH (FAB) CLASSIFICATION
1. CONCORDANCE OF DIAGNOSIS IN NAGASAKI CASES BY RERF MEMBERS AND A MEMBER OF FAB COOPERATIVE GROUP
FRENCH-AMERICAN-BRITISH(FAB) 分類による被爆者白血病の再分類
1．放影研血液学者と FAB 分類提唱者の診断の一致率，長崎

TATSUKI MATSUO, M.D. 松尾辰樹
MASAO TOMONAGA, M.D. 朝長万左男
JOHN M. BENNETT, M.D.
KAZUTAKA KURIYAMA, M.D. 栗山一孝
FUMIO IMANAKA, M.D. 今中文雄
ATSUSHI KURAMOTO, M.D. 蔵本 淳
NANAO KAMADA, M.D. 鎌田七男
MICHITO ICHIMARU, M.D. 市丸道人
STUART C. FINCH, M.D.
ANTHONY V. PISCIOTTA, M.D.
TORANOSUKE ISHIMARU, M.D. 石丸寅之助

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放影研 RERF RADIATION EFFECTS RESEARCH FOUNDATION
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Research Project 研究課題 4-82

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FRENCH-AMERICAN-BRITISH(FAB)分類による被爆者白血病の再分類 1．放影研血液学者とFAB分類提唱者の診断の一致率，長崎

TATSUKI MATSUO, M.D. (松尾辰樹)[1]; MASAO TOMONAGA, M.D. (朝長万左男)[4,8]; JOHN M. BENNETT, M.D.[5,9]; KAZUTAKA KURIYAMA, M.D. (栗山一孝)[8]; FUMIO IMANAKA, M.D. (今中文雄)[1]; ATSUSHI KURAMOTO, M.D. (蔵本 淳)[6,10]; NANAO KAMADA, M.D. (鎌田七男)[6,11]; MICHITO ICHIMARU, M.D. (市丸道人)[6,8]; STUART C. FINCH, M.D.[3]; ANTHONY V. PISCIOTTA, M.D.[7,12]; TORANOSUKE ISHIMARU, M.D. (石丸寅之助)[2]

RERF Departments of Clinical Studies[1], Epidemiology[2], Chief of Research[3], Part-time Professional Staff[4], Visiting Scientist[5], Consultant[6], Former Vice-Chairman[7]; Atomic Disease Institute, Nagasaki University School of Medicine[8]; University of Rochester Cancer Center[9]; Departments of Internal Medicine[10] and Hematology[11], Research Institute for Nuclear Medicine and Biology, Hiroshima University; Medical College of Wisconsin[12]

放影研臨床研究部[1]，疫学部[2]，研究担当理事[3]，非常勤研究員[4]，来所研究員[5]，顧問[6]，元副理事長[7]；長崎大学医学部原研内科[8]；Rochester 大学癌センター[9]；広島大学医学部原医研内科[10]，同血液[11]；Wisconsin 医科大学[12]

SUMMARY

The concordance rate for the French-American-British (FAB) reclassification diagnoses of atomic bomb-related cases of leukemia in Nagasaki was determined by a group of RERF hematologists and one of the members of the FAB cooperative group. The peripheral blood and/or bone marrow smears from 193 persons with leukemia or related disorder were reviewed. There was 85% agreement in the identification of leukemia types and subtypes. There was almost complete agreement for the diagnosis of non-FAB disorders (chronic myeloid leukemia and others) resulting in overall concordance of 88.2%. The conclusion from this remarkably high rate of concordance is that it is feasible to accurately apply the FAB classification system to the cases of A-bomb-related leukemia. These preliminary observations suggest that the previously established leukemia types for about a quarter of the cases of acute leukemia and related disorders should be changed.

要 約

長崎の被爆者白血病症例のFAB再分類による診断の一致率について，放影研の血液学者らとFAB分類提唱者のひとりとの間で検討した．対象は末梢血，骨髄塗沫標本など放影研に何らかの標本が現存する白血病及び白血病関連疾患の193例である．白血病病型とそのsubtypeを含む病型の診断一致率は85%であり，FAB分類が対象としない病型(慢性骨髄性白血病，その他)についてはほぼ全例診断は一致した．全体の最終診断との一致率は88.2%である．この一致率は十分高いものと思われ，放影研における被爆者白血病の分類にFAB分類システムを適用しても正確性をもちうると考えられる．今回の観察から急性白血病と関連疾患の大まかな病型について旧診断の約4分の1に診断変更の必要があることがわかった．

Approved 承認 12 May 1987

Printed 印刷 September 1987

INTRODUCTION

The purpose of this study was to determine the feasibility of reclassifying the A-bomb-related leukemias of Hiroshima and Nagasaki in accordance with the most modern classification criteria. A question arose as to whether the Wright or May-Grunwald Giemsa-stained leukemia slides, without the benefit of special stains, were adequate for the reliable identification of adult T-cell leukemia (ATL) cells and the cell types described in the FAB classification system.[1-4]

In order to achieve the objective, the accuracy of reclassification was determined by means of comparing the diagnoses made by one (JMB) of the members of the FAB cooperative group with those made by the RERF hematologists. All participants of the study were experienced hematologists.

In previous reports,[5,6] all leukemias in A-bomb survivors are defined in accordance with the classical nomenclature which has prevailed throughout the world during the past 50 or more years. Morphological appearance of the blood and bone marrow, histochemical responses, peripheral blood findings, and the clinical presentation have been the modalities most frequently employed in determining a particular type of leukemia. At the inception of the leukemia study of A-bomb survivors, rather rigid criteria were established to assure diagnostic consistency and continuity.[7] Over the years, hematologists have had few problems with the diagnosis of chronic myeloid leukemia, but uncertainties frequently have been expressed concerning classification of the preleukemia disorders and certain acute leukemias.

Development of the FAB classification of the acute leukemias and related disorders during the past 10 years represents a major advance in leukemia classification.[1-4,8] The system is clearly defined on the basis of morphological, ultrastructural, cytochemical, surface marker, and chromosomal changes. The various types of leukemia relate well to the clinical presentation, prognosis, and response to therapy. Furthermore, the system provides reasonable criteria for identification of various myelodysplastic syndromes (MDS)[8] which previously were considered as poorly defined preleukemic disorders. Another important recent advance in the leukemia field has been the identification

緒　言

この研究は広島，長崎の被爆者白血病を最新の分類法で再分類できるかどうかを検討するため行われた．標本はほとんどライト又はメイ-グルンワルド・ギムザ標本で特殊染色の併用なしに，成人T細胞白血病やFAB分類[1-4]に出てくる病型を正確に同定するのに適しているかどうか疑問と思われた．

そこで放影研における血液研究者の診断とFABグループのひとり(JMB)の診断を比較することで，再分類の正確性を検討することとした．参加した血液学者はすべて，白血病診断に十分の経験を有する者である．

以前の報告[5,6]における被爆者白血病の病型は，50年以上もの間，広く用いられた古典的命名法によるものであった．したがって，ある白血病の病型を決める際には，末梢血及び骨髄の形態，細胞化学所見，末梢血所見，及び臨床経過が判定基準としてよく用いられた．被爆者の白血病研究が始まった時期には診断の正確度を高め継続性を保つためにかなり厳密な診断基準が確立されていた．[7] しかし，この診断基準は慢性骨髄性白血病診断の際にはほとんど問題はないが，急性白血病の一部と前白血病の分類に関してはあいまいであることがしばしばあった．

急性白血病とその関連疾患におけるFAB分類の提唱は過去10年の白血病分類上の最も大きな進歩であった．[1-4,8] この分類法は，形態，電顕，細胞化学，表面マーカー，染色体所見に基づいており，明確な定義がなされている．この分類はまた臨床像，予後，治療反応性とも関連している．更に，以前ほとんど定義されていなかった様々な前白血病に対し，myelodysplastic syndrome(MDS)[8]としてしかるべき分類がなされた．白血病の分野でもう一つの重要な進歩は，長崎を多発地域に含む成人T細胞白血病の

of ATL which is endemic in the Nagasaki area.[9] Therefore, it seemed important to reclassify leukemias which have occurred in the A-bomb survivors of Hiroshima and Nagasaki according to the most recent classification. Furthermore, it seemed quite likely that reclassification, based on the FAB system, might provide new insight regarding the pathogenesis of radiation-induced leukemia.

MATERIALS AND METHODS

The materials for review consisted of any, or all, of the peripheral blood smears, bone marrow aspiration smears, and pathology sections preserved at RERF for persons with leukemia who were exposed within 8,990 m of the hypocenter in Nagasaki. Of the 344 cases registered at RERF, 193 (56.1%) had histological material available for study. These slides were reclassified by experienced RERF hematologists and by a member of the FAB cooperative group, according to the FAB classification. The clinical records and other information were reviewed only if diagnostic agreement was not reached on the basis of the morphological findings. Classifications of the chronic leukemia and ATL were based on established morphological criterion.[9,10] After comparing the diagnoses between the two parties, the concordance rate for each type of leukemia was determined. In disagreements, the final diagnosis was established by discussing the morphological features during their double-headed microscopic examination, and by reviewing the clinical records.

RESULTS

Diagnostic review was completed for 180 of the 193 cases. The slides of 13 cases were in such a poor state of preservation that a final diagnosis could not be reached even after reviewing clinical records. Final diagnosis was not agreed upon for two cases. The concordance rate for all diagnoses, excluding the two with basic disagreement, is shown in Table 1. There was agreement in 102 (85.0%) of 120 diagnoses of acute leukemias and MDS that are classifiable under the FAB classification. Agreement was reached in 93 (86.9%) of 107 cases for which the FAB subtype also could be determined in the final diagnosis. Diagnoses of non-FAB leukemias which include chronic myeloid leukemia (CML), chronic lymphocytic leukemia (CLL), hypoplastic leukemia, and ATL agreed in 55 (94.8%) of

疾患概念の確立である.[9] これらの状況から，広島，長崎の被爆者白血病を最新の分類法に基づいて再診断することは重要と思われた．更にこのFAB分類に基づいた再分類により，放射線誘発白血病の発症に関して新しい知見が得られることも可能と思われた．

対象及び方法

対象は，長崎において爆心地から8,990m以内で被爆した白血病症例として登録された344例のうち，現在，放影研に何らかの標本（末梢血，骨髄血，病理標本）が保存されている193例（56.1%）である．再診断はFAB分類により，経験を積んだ血液学者らとFABグループのひとりとの合意の上で行われた．形態の所見に基づいて合意が得られなかった場合にのみ，臨床記録やその他の情報を参考に再検討した．慢性白血病及び成人T細胞白血病は確立した形態基準の知見に基づいて診断を下した.[9,10] 二者間で診断を比較した後，各病型について一致率を検討した．診断不一致の場合は，診療記録を参考に，二者の同時鏡検による形態的特徴の検討を行い，双方の合意の上で最終診断を決定した．

結　果

対象193例のうち180例について検討し，13例については標本の保存が不良のため，臨床記録を検討したけれどついに診断に到らなかった．また2例については最終診断の合意をみなかった．この基本的に合意の得られなかった2例を除いたすべての診断の一致率を表1に示す．FAB分類が対象とする急性白血病及びMDSに関しては，120例中102例（85.0%）において一致をみた．最終診断がsubtypeについてまで可能であった107例では，93例（86.9%）について一致した．FAB分類対象外の慢性骨髄性白血病，慢性リンパ球性白血病，低形成性白血病，成人T細胞白血病等に関しては58例中55例（94.8%）で一致し，

58 cases. The concordance rate for all leukemia cases was 88.2%.

全症例における一致率は88.2%であった.

TABLE 1 CONCORDANCE OF DIAGNOSES BETWEEN RERF HEMATOLOGISTS AND A MEMBER OF FAB COOPERATIVE GROUP
表1 放影研血液研究者とFAB分類提唱者のひとりとの診断の一致率

Category	Cases Reviewed	Cases of Concordance	Concordance (%)
FAB	120	102	85.0
FAB subtype classifiable	107	93	86.9
Non-FAB	58	55	94.8
Total	178	157	88.2

Agreement between the diagnoses of leukemia established previously and the FAB reclassified diagnoses by type of leukemia is shown in Table 2. About half of the 14 cases of acute lymphocytic leukemia (ALL) previously diagnosed were reclassified into another type. This included four cases of which the diagnoses were changed to acute myeloid leukemia (AML). On the other hand, about the same number were reclassified from acute granulocytic leukemia (AGL) to ALL. The net result of these changes is a slight increase in identification of cases of ALL. AML was decreased by more than 10% due to the new categorization for eight cases of MDS and six cases of hypoplastic leukemia which previously had been diagnosed as AGL. There was little change in the diagnosis of CML. Reclassification of ATL included most of the cases of leukosarcoma, more than half of the CLL cases, two cases of ALL, and one acute monocytic leukemia (AMoL).

各白血病型について今回のFAB再分類による最終診断と旧診断名の一致について示したのが表2である. 旧診断の急性リンパ球性白血病14例の約半数が他の病型へと再分類され, そのうち4例は急性骨髄性白血病であった. 一方, ほぼ同数の症例が旧診断の急性顆粒球性白血病から急性リンパ球性白血病へと再分類され, 総計として急性リンパ球性白血病の症例数はやや増加した. また旧診断急性顆粒球性白血病からは更にMDS 8例, 低形成性白血病6例などが新たに診断され, そのために急性骨髄性白血病の症例数は10%以上減少することになった. 慢性骨髄性白血病の診断変更は極めて少なかった. 以前に診断された白血肉腫症例のほとんど, 慢性リンパ球性白血病例の半数以上, 及び急性リンパ球性白血病の2例と, 急性単球性白血病の1例が成人T細胞白血病へ診断変更された.

The distribution of the reclassified leukemias by high dose (> 100 rad) and low dose (0-99 rad) groups are shown in Tables 3a-c. These data are not suitable for statistical analysis because of the small number in each group, but it should be noted that the frequency of MDS is high and that of ATL is low in the high dose group (Table 3a). All FAB subtypes, except M_7, were present in the AML low dose group, and all subtypes except M_3 and M_6 were present in the high dose AML group (Table 3b). There appeared to be no remarkable differences in FAB subtypes of ALL between the high and low dose groups (Table 3c).

再分類による各病型の分布を高線量群(>100rad)と低線量群(0−99rad)に分けて示したのが表3a-cである. 各群の症例数が少ないため統計解析には適さないが, 高線量群においてMDSの比率が高く, 逆に成人T細胞白血病の比率が低いことが注目される(表3a). 急性骨髄性白血病では, 低線量群でM_7を除くすべてのFAB subtypeがみられ, 高線量群ではM_3及びM_6を除くすべてのsubtypeがみられる(表3b). 急性リンパ球性白血病では低線量群と高線量群の間にFAB subtype上の明らかな違いはないようである(表3c).

TABLE 2 CONCORDANCE OF PREVIOUS DIAGNOSIS TO RECLASSIFICATION

表2 再分類診断に対する以前の診断の一致数

Previous diagnosis	Reclassification																			Total
	L_1	L_2	L_3	M_1	M_2	M_3	M_4	M_5	M_6	M_7	AML	AL	MDS	Hypo L	CML	ATL	CLL	Leu. L	No Dx	
ALL	4	3	0	2	0	0	0	1	0	0	0	0	0	0	0	2	1	0	1	14
ASL	0	3	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	5
AGL	1	5	1	17	22	10	4	1	2	1	5	0	8	6	0	0	0	1	8	92
AMMoL	0	0	0	0	1	1	5	0	0	0	0	1	1	0	0	0	0	0	0	9
AMoL	0	0	0	0	1	2	0	4	0	0	1	0	1	0	0	1	0	0	0	10
EL	0	0	0	0	0	0	1	0	3	0	0	0	1	0	0	0	0	0	0	5
CML	0	0	0	0	0	0	0	0	0	0	1	0	1	0	18	0	0	0	1	21
Leuk. S	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	21	0	0	2	25
CLL	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	2	0	1	9
Total	5	11	1	20	24	13	10	7	6	1	7	2	12	6	18	30	3	1	13	190

ALL: Acute lymphoid leukemia, ASL: Acute stem cell leukemia, AGL: Acute granulocytic leukemia, AMMoL: Acute myelomonocytic leukemia, AMoL: Acute monocytic leukemia, EL: Erythroleukemia, CML: Chronic myeloid leukemia, Leuk. S: Leukosarcoma, CLL: Chronic lymphocytic leukemia, AML: Acute myeloid leukemia, AL: Acute leukemia, MDS: Myelodysplastic syndrome, Hypo L: Hypoplastic leukemia, ATL: Adult T-cell leukemia, Leu. L: Leukemic lymphoma, No Dx: No diagnosis.

ALL：急性リンパ性白血病，ASL：急性幹細胞白血病，AGL：急性顆粒球性白血病，AMMoL：急性骨髄単球白血病，AMoL：急性単球白血病，EL：赤白血病，CML：慢性骨髄性白血病，Leuk. S：白血肉腫，CLL：慢性リンパ球性白血病，AML：急性骨髄性白血病，AL：急性白血病，MDS：骨髄形成異常症候群，Hypo L：形成不全性白血病，ATL：成人T細胞白血病，Leu. L：白血病性リンパ腫，No DX：診断なし．

Figures in the square indicate cases of concordance of previous diagnosis to reclassification ignoring the subtypes.

囲み数字は subtype を除く再分類診断に対する以前の診断の一致例を示す．

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TABLE 3a RECLASSIFIED LEUKEMIA GROUPS AND T65D
表3a 白血病群再分類と T65D

T65D in rad	AML	ALL	MDS	CML	ATL	CLL	Hypo L	Other	No Dx	Total
0-99	81	12	7	13	28	3	5	2	9	160
>100	10	4	4	5	1	0	0	1	4	29
Total	91	16	11	18	29	3	5	3	13	189

See Table 2 for abbreviations. 略語については表2を参照

TABLE 3b FAB SUBTYPE (AML) AND T65D
表3b FAB subtype(急性骨髄性白血病)と T65D

T65D in rad	M_1	M_2	M_3	M_4	M_5	M_6	M_7	Total
0-99	19	19	13	9	6	6	0	72
>100	1	5	0	1	1	0	1	9
Total	20	24	13	10	7	6	1	81

TABLE 3c FAB SUBTYPE (ALL) AND T65D
表3c FAB subtype(急性リンパ性白血病)と T65D

T65D in rad	L_1	L_2	L_3	Total
0-99	3	8	1	12
>100	2	2	0	4
Total	5	10	1	16

DISCUSSION

The optimum techniques for diagnosis and classification of acute leukemias include not only morphology but also cytochemistry (peroxidase, esterase, and platelet peroxidase) and both ultrastructural and surface marker identification (TdT, CALLA). Many hospitals now resort to the FAB classification system, since it is based primarily on morphology and cytochemistry (peroxidase and esterase), and neither ultrastructural nor surface marker techniques are available. The concordance rate for the diagnosis of acute leukemia among academic hematologists using the FAB system has been reported to be in the range of 80%-90%.[11] It also has been reported that the

考 察

急性白血病の診断と分類は現在では形態学のみならず，ペルオキシダーゼ，エステラーゼ，血小板ペルオキシダーゼなどの細胞化学及び電子顕微鏡学的手段，更には TdT，CALLA などの表面マーカーに基づいて行われるのが望ましい．しかしながら，一般病院においては電子顕微鏡及び表面マーカーは使用できないことが多いため，FAB 分類は主に形態とペルオキシダーゼ及びエステラーゼの細胞化学に基づく分類法となっている．この分類法による血液学者らの急性白血病についての診断一致率は80%～90%といわれる．[11] 一方，形態のみに基づく診断ではその

concordance rate without cytochemistry is about 70%. Addition of cytochemistry improves the rate up to 90%, and almost complete if immunophenotyping is employed.[12] Unfortunately, when most of the radiation-induced leukemia cases occurred in Nagasaki, many of the more sophisticated techniques were unavailable so that most of the diagnoses were established on the basis of morphology and limited cytochemistry (peroxidase). Confirmation of leukemia type and evaluation of the accuracy of diagnosis now can be determined only by means of comparing diagnoses made independently by skilled hematologists. In fact, the concordance rate for the diagnoses of various types of leukemia by the RERF hematologists and JMB was as high as those obtained using good cytochemistry in addition to morphology.[12] These observations provide strong support for the validity of reclassification of the radiation-related acute leukemias using the FAB classification, even under the limited circumstances which have been noted above. These results also provide an impetus for proceeding with the FAB reclassification of leukemia cases in Hiroshima.

Previous diagnoses under major leukemia categories were changed in 25.4% in the current review, even excluding those changed from leukosarcomas to ATL. The changes in diagnosis between ALL and AML were mainly due to the difference in the morphological criteria between the FAB classification and those diagnosed previously. Establishment of the diagnostic criteria for ATL is most important, since it comprises 16% of the leukemias reviewed in Nagasaki. ATL may have to be excluded from the category of radiation-induced leukemia since its annual incidence among A-bomb survivors is constant and the overall incidence does not appear to be related to radiation dose (unpublished data). Furthermore, it has now become apparent that most cases of CLL, atypical ALL, and leukosarcoma that have been reported previously in Nagasaki correspond to ATL. This indicates that reclassification is essential for accurate leukemia comparison between Hiroshima and Nagasaki, as well as for characterization of radiation-induced leukemia. It should be noted, however, that the previously reported high frequency of radiation-induced CML in Hiroshima would be changed little through reclassification, as judged by the

一致率は70%程度であり，細胞化学を併用することで90%に上昇し，表面マーカーの追加によりほぼ完璧に一致することが報告されている.[12] 長崎の被爆者白血病症例では，当時まだ技法が開発されておらず残念ながら一部の症例についてのみ組織化学標本（ペルオキシダーゼ）あるいはその所見が利用可能であり，多くの場合，形態のみに基づいて診断を下さねばならない．このような条件下で診断が正確に行われているか否かを知るには，それぞれ経験のある血液学者によって別個になされた診断の一致率を検討するしかない．放影研の血液学者とJMBの診断一致率は，細胞化学を形態観察に併用した場合の一致率に匹敵するものであった.[12] この結果から，上述の限られた診断条件でも，FAB分類を用いて十分正確に被爆者急性白血病を再分類できると思われる．この結果は広島症例の再分類の施行を促すものである．

今回の再分類により，白血肉腫から成人T細胞白血病への診断変更を除いても，主な白血病分類の旧診断の25.4%が診断変更を余儀なくされた．急性リンパ球性白血病と急性骨髄性白血病の間の診断変更は，主に旧分類とFAB分類の形態上のcriteriaの違いによるものと思われる．成人T細胞白血病の診断基準の確立は極めて重要であり，この疾患は実に長崎検討例の16%を占めた．被爆者からの成人T細胞白血病の年間発生率は一定しており，その発生頻度は被曝線量に相関していない（未発表データ）ことから，成人T細胞白血病例は放射線誘発白血病から除外されるべきかもしれない．また，長崎における慢性リンパ球性白血病，異型急性リンパ球性白血病，白血肉腫のほとんどが実は成人T細胞白血病であることも明らかになった．このことから，全体としての被爆者白血病の特異性を明らかにするためにも，また広島と長崎の症例を正確に比較するためにも，再分類が不可欠と思われる．しかしながら今回の長崎の再分類の経験から，広島において過去に慢性骨髄性白血病が多発したことは，再分類によっても動かし難い事実

experience in Nagasaki. The striking difference in the incidence of CML between the two cities may continue to be a problem in relation to the biologic response to radiation exposure.

Few problems were encountered in the application of the FAB classification system to the leukemia material in Nagasaki. All cases were classified by the FAB system and all subtypes were represented with the exception of M_3 and M_6 AML which were not observed in the high dose group. However, this observation is considered important since about half of secondary leukemias following chemotherapy have been reported to be unclassifiable by the FAB classification system.[13] This difference suggests that leukemogenesis of A-bomb-induced leukemia is different from the secondary type of leukemia which occurs following the prolonged administration of anticancer drugs.

Each leukemia subtype in the FAB classification is closely associated with a specific chromosome aberration.[14] Furthermore, there is increasing evidence for a close relationship between these chromosome aberrations and certain oncogene chromosomes. It is quite possible that FAB reclassification of all A-bomb-related leukemia and the reassessment of the A-bomb dosimetry[15] will provide new information concerning radiation leukemogenesis at the oncogene level.

であろう．この両市間の慢性骨髄性白血病の発生頻度の明らかな違いは原爆放射線の生物学的効果の未解決の問題として残るようである．

FAB 分類は長崎の被爆者白血病によく適合し，全くの分類不能例はなかった．すべての例が FAB システムで分類可能であり，高線量群に M_3 及び M_6 の subtype がみられないほかは，すべての subtype が見られた．抗癌剤使用後の二次性白血病の約半分が，FAB システムでは分類不能であったということが一方で報告されているので，[13] このことは重要な事実と考えられる．この相違は原爆放射線と抗癌剤の長期間使用による白血病誘発のメカニズムそのものの違いによるものかもしれない．

FAB 分類の各 subtype と特殊な染色体異常が密接に関連していることが，現在までに知られてきている．[14] 更に，ある種の癌遺伝子とこれらの染色体異常の間に密接な関連があるとする研究が増えてきている．被爆者白血病をすべて再分類し，最新の線量[15] を導入して検討することで，癌遺伝子レベルにおける放射線の白血病誘発について新たな示唆を得ることが可能と思われる．

APPENDIX LIST OF RECLASSIFICATION OF LEUKEMIA CASES, NAGASAKI
付録　白血病症例の再分類，長崎

MF#	Previous Dx	RERF Dx	JMB Dx	Final Dx
[redacted]	AGL	M_2	M_2	M_2
	AGL	L_2	L_2	L_2
	AGL	L_2	L_2	L_2
	AGL	No Dx	No Dx	No Dx
	AGL	M_2*	RAEB	RAEB
	AGL	M_1	AML	AML
	AGL	M_2	M_5*	M_2
	Leuk. S	ATL	ATL	ATL
	AGL	AML	AML	AML
	Leuk. S	ATL	ATL	ATL
	AGL	M_2	M_2	M_2
	AGL	M_7	M_7	M_7
	AGL	M_3	M_3	M_3
	AGL	No Dx	No Dx	No Dx
	AGL	No Dx	No Dx	No Dx
	AGL	No Dx	No Dx	No Dx
	CML	CML	CML	CML
	Leuk. S	No Dx	No Dx	No Dx
	AGL	M_2	M_2	M_2
	AGL	M_1	M_1	M_1
	AGL	L_2	L_2	L_2
	Leuk. S	ATL	ATL	ATL
	AGL	AML*	MDS	MDS
	AGL	M_1	L_2*	M_1
	AGL	No Dx	No Dx	No Dx
	Leuk. S	ATL	ATL	ATL
	CML	CML	CML	CML
	AGL	M_4	M_4	M_4
	AMMoL	No Dx*	AL	AL
	AGL	M_3	M_3	M_3
	ALL	L_2*	L_1	L_1
	AGL	M_2	M_2	M_2
	CLL	ATL	ATL	ATL
	AGL	M_2	M_2	M_2
	AGL	M_2	M_4*	M_2
	Leuk. S	ATL	ATL	ATL
	Leuk. S	ATL	ATL	ATL
	AGL	M_3	M_3	M_3
	ALL	L_2	M_1*	L_2
	Leuk. S	ATL	ATL	ATL
	ASL	AL	AL	AL
	AGL	M_1	M_1	M_1

MF#	Previous Dx	RERF Dx	JMB Dx	Final Dx
[redacted]	CLL	CLL	CLL	CLL
	Leuk. S	ATL	ATL	ATL
	CML	CML	CML	CML
	ALL	M_1	M_1	M_1
	Leuk. S	ATL	ATL	ATL
	AGL	M_3	M_3	M_3
	AGL	L_2	L_2	L_2
	AGL	M_2	M_2	M_2
	Leuk. S	ATL	ATL	ATL
	CML	CML	CML	CML
	AGL	M_3	M_3	M_3
	CLL	No Dx	No Dx	No Dx
	AMMoL	M_4	M_4	M_4
	AGL	M_3	M_3	M_3
	EL	M_6	M_6	M_6
	AGL	No Dx	No Dx	No Dx
	CML	CML	CML	CML
	CML	CML	CML	CML
	AGL	M_3	M_3	M_3
	AGL	M_1	M_1	M_1
	AMML	M_2	M_2	M_2
	AMoL	M_5	M_5	M_5
	AGL	Hypo L	Hypo L	Hypo L
	AGL	M_1	M_1	M_1
	AMoL	M_3	M_3	M_3
	AGL	M_4	AML	AML
	CML	CML	CML	CML
	Leuk. S	M_6	M_6	M_6
	Leuk. S	M_1	M_1	M_1
	AGL	M_5*	M_1	M_1
	AGL	M_1	M_1	M_1
	AGL	Hypo L	Hypo L	Hypo L
	CML	CML	CML	CML
	AGL	No Dx	No Dx	No Dx
	ALL	L_1	L_1	L_1
	CML	CML	RAEB*	CML
	AGL	M_2	M_2	M_2
	CLL	CLL	CLL	CLL
	AGL	M_2	M_2	M_2
	AGL	M_2	M_2	M_2
	AGL	Hypo L	Hypo L	Hypo L
	AGL	RAEB	RAEB	RAEB

(Continue 続く)

APPENDIX (Continued 続き)

MF#	Previous Dx	RERF Dx	JMB Dx	Final Dx
[redacted]	Leuk. S	No Dx	No Dx	No Dx
	CML	CML	CML	CML
	AMMoL	M_4	M_4	M_4
	CML	CML	CML	CML
	AGL	RAEB	RAEB	RAEB
	AMMoL	M_4	M_4	M_4
	Leuk. S	ATL	ATL	ATL
	CML	CMMoL	CMMoL	CMMoL
	AGL	L_1*	M_1	M_1
	ASL	L_2	L_2	L_2
	AGL	AML	AML	AML
	CML	CML	CML	CML
	CLL	ATL	ATL	ATL
	CML	No Dx*	AML	AML
	Leuk. S	ATL	ATL	ATL
	CML	No Dx	No Dx	No Dx
	AGL	No Dx	No Dx	No Dx
	AGL	Hypo L*	L_3	L_3
	AGL	M_2	M_2	M_2
	AGL	M_2	M_2	M_2
	CLL	ATL	ATL	ATL
	ASL	L_2	L_2	L_2
	ALL	ATL*	CLL	CLL
	AGL	M_2	M_2	M_2
	EL	M_6	M_6	M_6
	AGL	M_1	M_1	M_1
	CML	CML	CML	CML
	AMoL	M_3	M_3	M_3
	ASL	M_5	M_5	M_5
	CLL	ATL	ATL	ATL
	AGL	L_1	L_1	L_1
	Leuk. S	ATL	ATL	ATL
	ALL	ATL*	L_2	L_2
	AMMoL	M_4	CMMoL	CMMoL/M_4
	ALL	ATL	ATL	ATL
	Leuk. S	ATL	ATL	ATL
	AGL	RAEB*	M_6	M_6
	ALL	M_5	M_5	M_5
	ASL	L_2	L_2	L_2
	AGL	M_2	M_1*	M_2
	Leuk. S	ATL	ATL	ATL
	CML	CML	CML	CML
[redacted]	AGL	RAEB-T	RAEB-T	RAEB-T
	CML	CML	CML	CML
	AMoL	M_4	M_4	M_4
	Leuk. S	ATL	ATL	ATL
	AGL	M_2	M_2	M_2
	AGL	M_2	M_2	M_2
	AMML	M_4	M_4	M_4
	CML	CML	CML	CML
	AL	No Dx*	AL	AL
	AMoL	AL*	ATL	ATL
	AGL	M_5	M_5	M_5
	AGL	CMMoL*	M_4	M_4
	AMoL	AML	AML	AML
	ALL	No Dx	No Dx	No Dx
	CLL	ATL	ATL	ATL
	ALL	L_1	L_1	L_1
	AGL	Hypo L	Hypo L	Hypo L
	AMoL	M_5	M_5	M_5
	AGL	M_1	M_1	M_1
	AGL	M_2	M_2	M_2
	ALL	ATL	ATL	ATL
	EL	RAEB	RAEB	RAEB
	AGL	M_1	M_1	M_1
	AGL	M_4	M_5	M_4/M_5
	AGL	M_4	M_4	M_4
	AGL	M_5	M_5	M_5
	AGL	M_1	M_1	M_1
	AGL	Leuk L	Leuk L	Leuk L
	AGL	M_2*	RAEB-T	RAEB-T
	AGL	M_2	M_2	M_2
	AGL	M_1	M_1	M_1
	AMoL	M_5	M_5	M_5
	Leuk. S	ATL	ATL	ATL
	ALL	L_2	L_2	L_2
	EL	M_6	M_6	M_6
	AGL	RAEB	RAEB	RAEB
	AGL	M_1	M_1	M_1
	AGL	M_3	M_3	M_3
	AGL	M_6	M_6	M_6
	Leuk. S	ATL	ATL	ATL
	AGL	M_2	M_2	M_2
	AGL	M_1	M_1	M_1

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APPENDIX (Continued 続き)

MF#	Previous Dx	RERF Dx	JMB Dx	Final Dx
[redacted]	Leuk. S	ATL	ATL	ATL
	EL	M_4	M_4	M_4
	AGL	M_4	M_4	M_4
	AMMoL	M_3	M_3	M_3
	AGL	M_1	M_1	M_1
	AGL	M_2	M_2	M_2
	CML	CML	CML	CML
	ALL	M_1	M_1	M_1
	AGL	CML*	M_2	M_2
	AGL	M_3	M_3	M_3
	AGL	RAEB-T	RAEB-T	RAEB-T
	AMMoL	RA	RA	RA
	AGL	Hypo L	Hypo L	Hypo L
[redacted]	AMoL	RAEB	RAEB	RAEB
	Leuk. S	ATL	ATL	ATL
	AGL	Hypo L	Hypo L	Hypo L
	AGL	M_2	M_2	M_2
	AGL	L_2	L_2	L_2
	AGL	M_1	M_1	M_1
	AGL	M_3	M_3	M_3
	AMoL	M_2	M_2	M_2
	CLL	ATL	ATL	ATL
	CML	CML	CML	CML
	ALL	L_1	L_1	L_1
	Leuk. S	ATL	ATL	ATL

Dx: Diagnosis, AGL: Acute granulocytic leukemia, ALL: Acute lymphocytic leukemia, ASL: Acute stem cell leukemia, AMMoL: Acute myelomonocytic leukemia, AMoL: Acute monocytic leukemia, EL: erythroleukemia, CML: Chronic myeloid leukemia, Leuk. S: Leukosarcoma, CLL: Chronic lymphocytic leukemia, AL: Acute leukemia, Hypo L: Hypoplastic leukemia, ATL: Adult T-cell leukemia, Leuk L: Leukemic lymphoma, RA: Refractory anemia, RAEB: Refractory anemia with excess of blasts, RAEB-T: Refractory anemia with excess of blasts in transformation, CMMoL: Chronic myelomonocytic luekemia, MDS: Myelodysplastic syndrome, *: Major disagreement case.

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