

Fig. E-1A

Figs. E-1A through E-1F Kaplan-Meier survival curves for ninety-one children (including patients from the current report and previous reports) with primary lymphoma of bone. As noted in each of the figures, lines with vertical marks represent the survival curves. The upper and lower limits of the 95% confidence intervals corresponding to the two survival curves on each graph are demonstrated by similar lines without vertical marks. **Fig. E-1A** Survival curves demonstrating poor prognosis for patients nine years of age or less ($p < 0.05$) (dashed line).

Solitary bone versus multiple bone

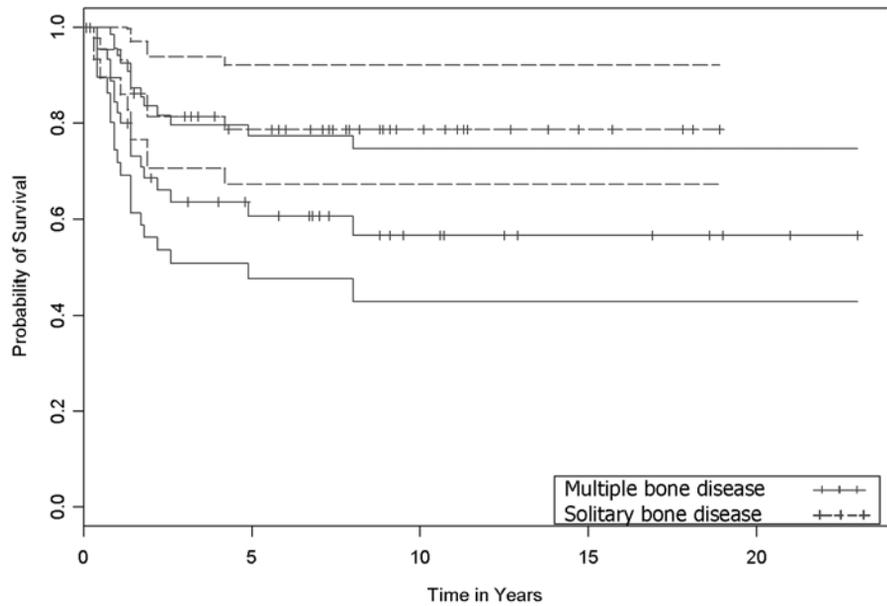


Fig. E-1B
Survival curves demonstrating poor prognosis for patients with multiple bone disease ($p < 0.05$) (solid line).

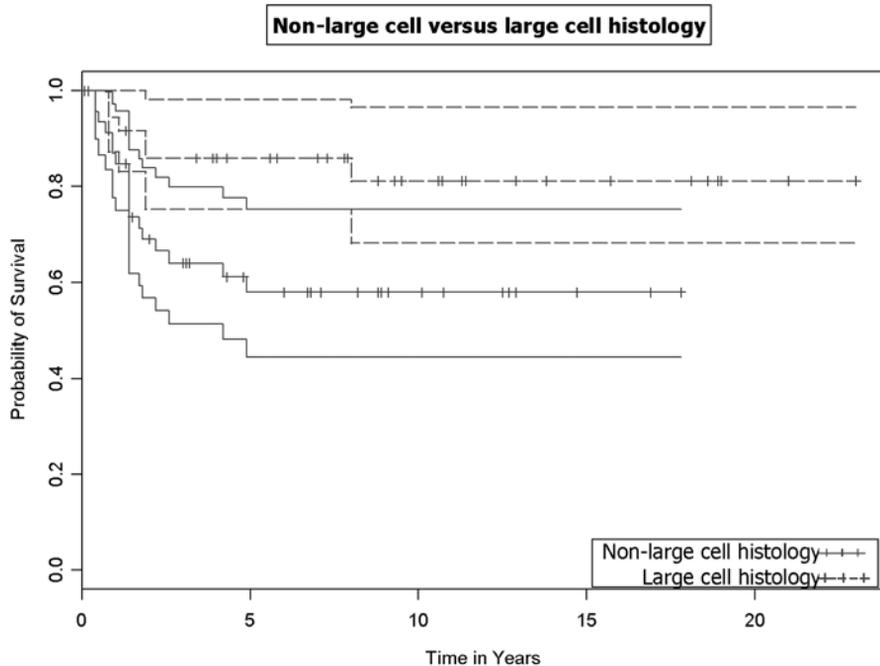


Fig. E-1C

Survival curves demonstrating poor prognosis for patients with non-large cell histology ($p < 0.05$) (solid line).

Chemotherapy versus chemotherapy with radiation therapy

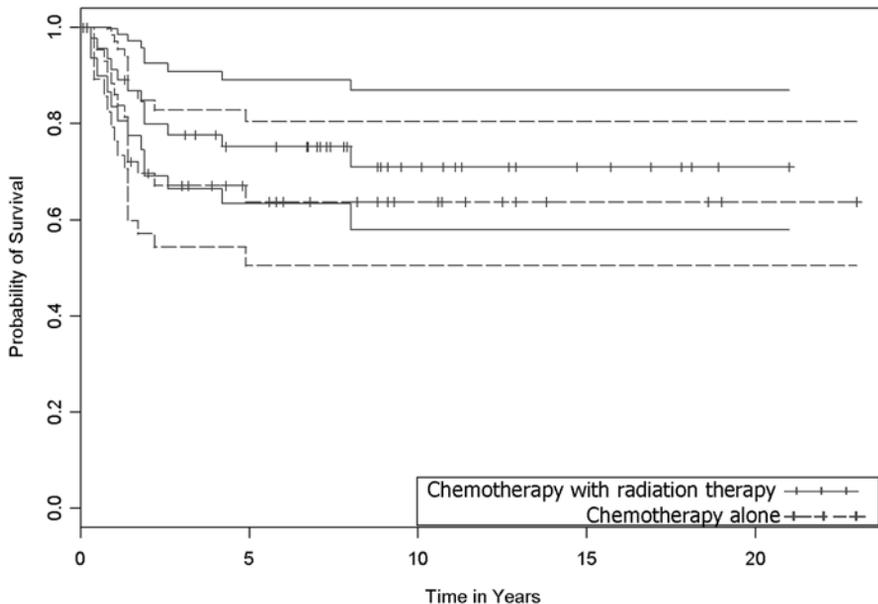


Fig. E-1D

Survival curves demonstrating similar outcomes for patients treated with chemotherapy alone (dashed line) or with chemotherapy with radiation therapy (solid line).

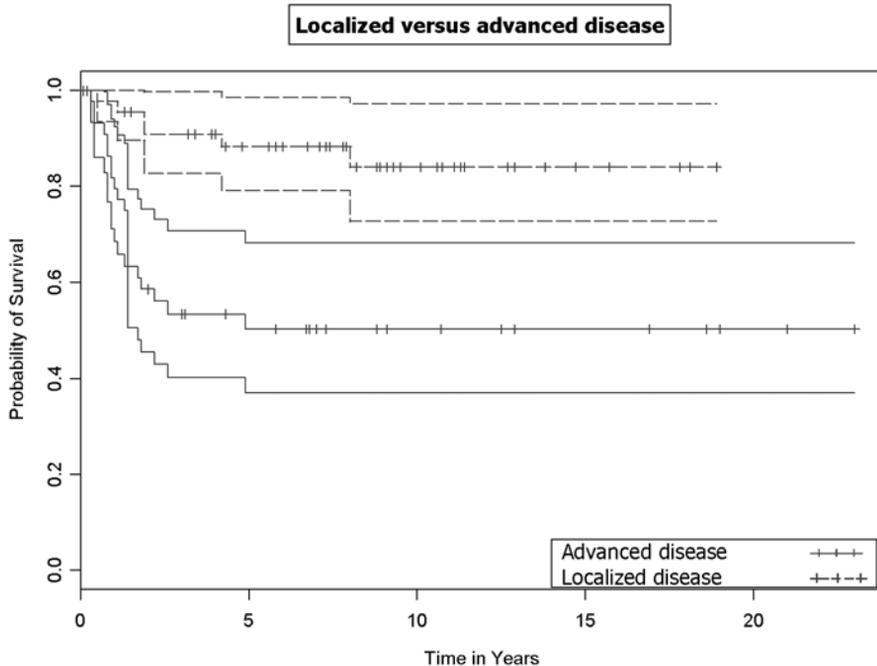


Fig. E-1E

Survival curves demonstrating good prognosis for patients with localized disease (Murphy stage I or II disease) (dashed line) compared with advanced disease (Murphy stage-III or IV disease) (solid line) ($p < 0.05$).

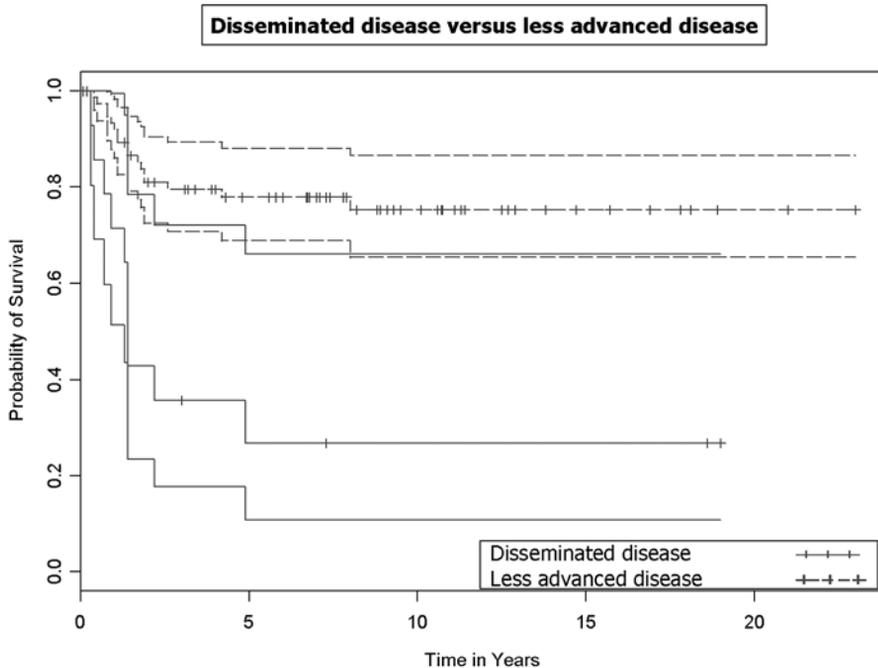


Fig. E-1F

Survival curves demonstrating poor prognosis for patients with bone-marrow involvement (disseminated, Murphy stage-IV disease) (solid line) compared with less-advanced disease (dashed line) ($p < 0.05$).

TABLE E1 Demographic and Clinical Features of Non-Hodgkin's Lymphoma Arising in Bone in Children in the Current Study

Case	Age (yr)/ Gender	Sites of Bone Involvement	No. of Sites	Presenting Symptoms	Referral Diagnosis	Delay in Diagnosis
1	11/M	L ischium, L sacroiliac joint, L pubis, R ilium	4	Leg pain for about 6 months, originally diagnosed as polymyositis, had 2 nondiagnostic bone-marrow biopsies and third biopsy was positive	Polymyositis or osteomyelitis	6 months
2	6.4/F	L humerus	1	5 day history of L elbow pain without trauma	Osteogenic sarcoma or Ewing sarcoma	<1 week
3	8.7/M	L femur, R femur, L5, L ilium	4	L thigh pain for 3 months that escalated over 3 wks, dull at first and then woke from sleep	Ewing sarcoma or osteosarcoma or lymphoma	3 months
4	16.9/M	L tibia	1	3 months of intermittent pain in L knee, with swelling, effusions, redness, heat, limp, unrelieved by acetaminophen or ibuprofen, attributed to growing pains	Osteogenic sarcoma	3 months
5	19.1/M	L ilium, L scapula, L humerus, L pubis, L tibia, R tibia, L femur, R femur, T6, T7, T8, T9	12	Followed for 2.5-3 years for migratory polyarthralgias, had abnormal bone scans and radiographs revealing lytic and osteoblastic lesions in multiple foci thought to be chronic sterile osteomyelitis, then admitted with T9 sensory level	Periodic migratory polyarthralgias or chronic sterile osteomyelitis	2.5 years
6	6.8/F	Rib 8	1	Lump on chest wall, increasing in size for 2 months	Lymphoma (known diagnosis, biopsy at outside hospital)	3 months
7	14.3/M	R femur	1	Pain in right medial knee, knee began to swell. Went to emergency room. Radiographs were negative, but magnetic resonance imaging and computerized tomography were positive one month later	Lymphoma (known diagnosis, biopsy at outside hospital)	4 months
8	13.5/F	Sacrum, ilium	2	R hip pain originally diagnosed as synovitis, pain persisted with lower back pain for several months, 15-lb (6.8-kg) weight loss	Hodgkin's disease or eosinophilic granuloma	10 months
9	16.3/M	R tibia	1	Six-month history of right tibial bone pain and swelling	Osteosarcoma	6 months
10	16.7/M	R femur	1	History of chondromalacia of right knee for 4 years, fell and fractured distal part of right femur, presented to emergency room and tumor found	Fracture	0
11	1.2/F	R femur, L femur, 3 ribs, R and L ilium	7	Several week history of irritability, decreased activity, cessation of walking, diarrhea, refusal to stand, fever and three days of vomiting. Calcium found to be 21 mg/dL	Acute lymphoblastic lymphoma or non-Hodgkin's lymphoma	1 month
12	6.6/M	L femur	1	Several month history of intermittent leg pain, night pain, and limp	Osteomyelitis or bone tumor	7 months
13	9.4/M	Mandible	1	L mandibular pain, night awakening, eventual numbness in lower middle lip and swelling of left jaw, molar eruption	Tumor	9 months
14	12.1/M	L ilium, R ischium, L2, skull	4	Nonspecific flu symptoms, leg pain thought to be pulled left groin muscle, increasing pain in hips, back, neck; began having limp, 11-lb (5.0-kg) weight loss	Lymphoma	8 months
15	15.3/F	R sternum, L scapula, rib 2, rib 6, L humerus	5	Intermittent fever, L chest pain, swelling L upper chest, L supraclavicular area, R parasternal area	Histiocytosis X	3 months

TABLE E2 Extent of Disease, Histologic Data, Treatment, and Outcomes for Non-Hodgkin's Lymphoma Arising in Bone in Children in the Current Study

Patient	Extent of Disease*	Reviewed Diagnosis and World Health Organization Classification	Initial BM/final BM†	Chemo-Therapy	Relapse	Time to Death or Last Follow-up (yr)	Outcome‡
1	Disseminated	Diffuse large B cell lymphoma	-/+	Chemo-therapy alone	N	18.6	Alive, NED
2	Disseminated	Precursor B lymphoblastic lymphoma	+/+	Chemo-therapy alone	Y (bone marrow)	1.4	Deceased, treatment induced acute myelogenous leukemia with specific chromosome deletions (del 5p, 7p, 20p), and resultant pancytopenia and death
3	Disseminated	Burkitt lymphoma	-/+	Chemo-therapy alone	Y (leukemic conversion of marrow)	0.4	Deceased, disease progression
4	Localized	Diffuse large B cell lymphoma	-/-	Chemo-therapy plus radiation	N	15.7	Alive, NED
5	Diffuse	Diffuse large B cell lymphoma	-/-	Chemo-therapy plus radiation	N	21	Alive, NED
6	Localized	Diffuse large B cell lymphoma	-/-	Chemo-therapy plus radiation	Y (mediastinum)	1.9	Deceased, progressive disease
7	Localized	Diffuse large B cell lymphoma	-/-	Chemo-therapy plus radiation	N	5.8	Alive, NED
8	Diffuse	CD 30+ lymphoma consistent with Hodgkin's disease or anaplastic large-cell lymphoma	-/-	Chemo-therapy alone	N	2	Alive, NED
9	Localized	Diffuse large B cell lymphoma	-/-	Chemo-therapy plus radiation	N	1.9	Deceased, feeding tube for cystic fibrosis complicated by peritonitis, acute respiratory distress syndrome, respiratory failure
10	Localized	Diffuse large B cell lymphoma	-/-	Chemo-therapy plus radiation	N	18.9	Alive, NED
11	Disseminated	Precursor B lymphoblastic lymphoma	+/+	Chemo-therapy alone	Y (bone, bone, lung)	4.9	Deceased, progressive disease
12	Localized	Precursor B lymphoblastic lymphoma	-/-	Chemo-therapy alone	Y (testis)	6	Alive, NED
13	Localized	Precursor B lymphoblastic lymphoma	-/-	Chemo-therapy alone	N	6	Alive, NED
14	Disseminated	Diffuse large B cell lymphoma	+/+	Chemo-therapy alone	N	19	Alive, NED
15	Diffuse	Diffuse large B cell lymphoma	-/-	Chemo-therapy alone	N	23	Alive, NED

*Localized = solitary-bone involvement without bone-marrow or systemic involvement; diffuse = multiple-bone involvement without bone-marrow or systemic involvement; and disseminated = solitary or multiple-bone involvement with bone-marrow involvement. †BM = bone-marrow examination. ‡NED = no evidence of disease.

TABLE E3 Summary of Case Series of Primary Lymphoma of Bone in Children

Study	Patients with PLB/ Patients with NHL*	Percentage of Patients with NHL*	Male: Female Ratio	Mean/ Median Age	Age Range	Large Cell: Lymphoblastic: Other*	Localized: Diffuse: Disseminated†	Chemotherapy: Chemotherapy and Radiation	Survival	Median/Mean Follow-up (Range) (yr)*
Present	15/306	4.9%	10:5	11.6/12.1	1.2-19.1	9:4:2	7:3:5	9:6	10/15	17.2/13.6 (2-23)
Coppes et al. ¹	14/450	3.1%	8:6	9.1/9.5	1.25-15	2:10:2	2:7:5	14:0	5/14	4.3/5.2 (3-8.2)
Lones et al. ²	31/1584	2.0%	20:11	11/11	3-17	14:14:3	17:14:0	14:17	26/31	9/9.9 (1.3-18.1)
Loeffler et al. ³	11/120	9.2%	6:5	13.8/14	9-17	7:4:0	9:2:0	1:10	10/11	8.4/8.1 (2.2-11.3)
Howat et al. ⁴	7/NR	NR	6:1	9.7/11.9	1.5-14.8	NR	4:0:3	1:6	4/7	7.3/6.6 (0.7-11.1)
Suryanarayan et al. ⁵	31/567	5.5%	18:13	NR	1-20	21:5:5	31:0:0	24:7	31/31	NR‡
Doll et al. ⁶	2/NR	NR	1:1	9.5/9.5	6-13	0:2:0	1:1:0	2:0	2/2	1.8/1.8 (1.5-2)
Furman et al. ⁷	11/395	2.8%	7:4	13.5/13	5.5-19	5:3:3	5:5:1	4:7	7/11	3/2.9 (0.1-7.1)
Summary	113/3422	3.3%	76:46	11.3 (mean)	1-19.1	58:42:15	76:32:14	69:53	95/122 (78%)	-

*PLB = primary lymphoma of bone, NHL = non-Hodgkin's lymphoma, NR = not reported. †Localized disease = solitary-bone involvement without bone-marrow or systemic involvement; diffuse = multiple-bone involvement without bone-marrow or systemic involvement, and disseminated = solitary or multiple-bone involvement with bone-marrow involvement. ‡In this study of thirty one patients, follow-up data could not be determined, but the maximum follow-up was reported as fifteen years, sixteen patients had less than three years of follow-up, and fifteen patients had more than three years of follow-up.