TABLE E-1 Summary of Data on the Forty-nine Patients Who Completed the Follow-up Surveys*

Age at QCT *(yr)*	Sex	Diagnosis	Lesion Site	Fracture Risk per Plain Radiographs	BMC	EA	EI	GJ	Treated?
15	F	Unicameral bone cyst	Proximal part of femur	Yes	–34.1	–83.3	–32.9	–42.7	No
15	M	Nonossifying fibroma	Distal part of femur	Yes	3	1.6	1.3	5.8	No
10	M	Unicameral bone cyst	Proximal part of femur	Yes	4.3	–15.5	–32.5	–9.8	No
17	F	Fibrous dysplasia	Proximal part of femur	No	–7.4	–11.1	–1.5	13	No
11	F	Nonossifying fibroma	Distal part of tibia	Yes	–7.2	–14.4	–8.2	–26.1	No
11	F	Nonossifying fibroma	Distal part of tibia	Yes	–7.5	–28.1	–6.5	–0.1	No
12	M	Fibrous dysplasia	Distal part of femur	Yes	0.2	–11.8	–11.3	–5.2	No
15	F	Unicameral bone cyst	Distal part of tibia	Yes	–21.1	–56.5	–24.4	–27.3	No
12	F	Nonossifying fibroma	Distal part of femur	Yes	–7	–27	–10	–15	No
16	M	Nonossifying fibroma	Distal part of femur	Yes	–6.3	–19.5	–33	–21.2	No
15	F	Enchondroma	Proximal part of femur	Yes	–11	–12	–3	–28	No
14	F	Nonossifying fibroma	Proximal part of tibia	Yes	–11	–12	–23	–21	No
10	F	Nonossifying fibroma	Distal part of tibia	Yes	–10.6	–49.9	–32.2	–37.9	No
16	F	Nonossifying fibroma	Proximal part of tibia	Yes	–9.8	–15	–35.4	–10.1	No
12	M	Nonossifying fibroma	Proximal part of tibia	No	–15	–14	–22	–13	No
19	M	Fibrous dysplasia	Proximal part of femur	Yes	–4.4	–0.6	7	3.9	No
10	M	Nonossifying fibroma	Distal part of femur	Yes	1.2	–15.9	–16.2	–6.4	No
12	M	Nonossifying fibroma	Distal part of femur	Yes	0.2	–25.7	–1.1	19.9	No
9	M	Nonossifying fibroma	Distal part of femur	Yes	–2.3	–4.8	–6.6	–14.9	No
14	M	Nonossifying fibroma	Distal part of tibia	Yes	–0.5	–9.9	10	9.9	No
12	M	Nonossifying fibroma	Distal part of tibia	Yes	5.4	1.2	8.2	6.3	No
11	M	Unicameral bone cyst	Proximal part of femur	Yes	–15.1	–15	–13.1	–8.4	No
9	M	Unicameral bone cyst	Proximal part of fibula	No	8.7	16.6	39.4	30.7	No
11	F	Fibrous dysplasia	Distal part of tibia	Yes	7.3	–7.6	–12.4	1.9	No
17	M	Nonossifying fibroma	Proximal part of tibia	Yes	3.3	5.6	–0.2	4	No
9	M	Unicameral bone cyst	Proximal part of femur	Yes	18.1	33.9	19.4	27.2	No
10	F	Nonossifying fibroma	Proximal part of tibia	Yes	–1.6	–4.4	–3.3	–2.3	No

14	M	Nonossifying fibroma	Distal part of tibia	Yes	22.1	–29.7	31.4	8.4	No
10	F	Interosseous ganglion	Proximal part of femur	No	3.6	–11.6	3.8	11.7	No
11	M	Nonossifying fibroma	Proximal part of tibia	Yes	6.4	8.4	7.9	2.7	No
9	M	Nonossifying fibroma	Distal part of tibia	Yes	0	–18.2	0	0	No
12	F	Nonossifying fibroma	Distal part of tibia	Yes	2.6	–1.4	–2.5	–1	No
12	M	Nonossifying fibroma	Distal part of femur	Yes	–16.4	–18.9	–23.4	–24	No
16	M	Nonossifying fibroma	Distal part of femur	Yes	–3.8	–33	–3.1	12	No
6	M	Unicameral bone cyst	Proximal part of fibula	No	–3.5	–4.6	–9.2	–0.8	Yes
12	F	Nonossifying fibroma	Distal part of femur	Yes	–6	–5	–2	–5	Yes
11	F	Nonossifying fibroma	Distal part of tibia	Yes	–4	–17	–9	–4	Yes
7	F	Unicameral bone cyst	Distal part of femur	Yes	–16	–58	74	66	Yes
15	F	Nonossifying fibroma	Distal part of femur	Yes	9.4	1.7	36.8	28.7	Yes
9	M	Unicameral bone cyst	Proximal part of femur	Yes	15.2	20	28.3	31.6	Yes
19	F	Neurofibroma tosis	Proximal part of tibia	No	1.5	–12	–7.4	–6.4	Yes
10	M	Nonossifying fibroma	Proximal part of femur	No	–6.2	–30.6	–12.7	–12.3	Yes
8	M	Unicameral bone cyst	Proximal part of femur	Yes	–11	–20	–30	–10	Yes
15	M	Nonossifying fibroma	Distal part of tibia	Yes	8.6	–5.4	5.7	–3.4	Yes
17	F	Fibrous dysplasia	Proximal part of femur	No	–12	–11	–12	–10	Yes
18	M	Periosteal chondroma	Proximal part of humerus	Yes	–1.2	–22.6	–0.8	7.2	Yes
10	M	Aneurysmal bone cyst	Distal part of tibia	No	3	–21	12	7.5	Yes
14	M	Nonossifying fibroma	Distal part of tibia	No	–7	–44	–35	–41	Yes
16	M	Periosteal chondroma	Proximal part of femur	Yes	–18	–11	–5	1	Yes

*QCT: quantitative computed tomography-based structural rigidity analysis. BMC: percent change in bone mineral content. EA: percent change in axial rigidity. EI: percent change in bending rigidity. GJ: percent change in torsional rigidity. Pathologic fracture was predicted by the rigidity analysis if EA, EI, or GJ was –35% or less. A skeletal lesion was considered to be at increased risk for fracture according to the criteria based on plain radiographs if the defect length was ≥3.3 cm, the defect width was ≥2.5 cm, or there was involvement of ≥50% of the cortex.

Appendix E-1: Activity Questionnaire Sent to Patients Who Had Not Undergone Surgical Treatment for the Benign Skeletal Lesion

Study of Fracture Risk in Patients with a Benign Bone Tumor
ACTIVITY QUESTIONNAIRE

Study ID:

1.	Since you were diagnosed with a benign bone tumor, has the bone with the tumor ever broken? *(Circle one number)*		
		No 0	
		Yes................................. 1	
	a.	If Yes, what were you doing when it broke? *(Circle one number)*	
			Nothing, really (lifting, reaching, standing up/sitting down, walking, etc.) 1
			Working around house or yard (vacuuming, gardening, shoveling snow, etc.) 2
			Recreational activity or exercise (biking, jogging, weight lifting, aerobics, etc.) 3
			Competitive team or individual sports (soccer, football, wrestling, skiing, tennis, etc.) 4
			Motor vehicle accident (car, motorcycle, off-road vehicle, boat, etc.) 5
2.	Has your level of physical activity or sports participation changed since you were diagnosed with a tumor in your bone? *(Circle one number)*		
		No, it's the same 0	
		Yes, I am <u>less</u> active than I used to be 1	
		Yes, I am <u>more</u> active than I used to be 2	
3.	Please circle the ONE number below that best describes your activity level <u>over the last 6 months</u>.		
		Regularly = once a week or more	
		Sometimes = once a month or less	
	10	I **regularly** participate in *<u>impact</u> activities* such as jogging, tennis, skiing, acrobatics, ballet, heavy labor, or backpacking.	
	9	I **sometimes** participate in *<u>impact</u> activities* such as jogging, tennis, skiing, acrobatics, ballet, heavy labor, or backpacking.	
	8	I **regularly** participate in *<u>active</u> activities* such as fast walking, golf, or bowling.	
	7	I **sometimes** participate in *<u>active</u> activities* such as fast walking, golf, or bowling.	
	6	I **regularly** participate in *<u>moderate</u> activities* such as moderate walking or heavy housework.	
	5	I **sometimes** participate in *<u>moderate</u> activities* such as moderate walking or heavy housework.	
	4	I **regularly** participate in *<u>mild</u> activities* such as slow walking, limited housework, or limited shopping.	
	3	I **sometimes** participate in *<u>mild</u> activities* such as slow walking, limited housework, or limited shopping.	
	2	I am **mostly** *<u>inactive</u>:* restricted to minimal activities of daily living.	
	1	I am **wholly** *<u>inactive</u>:* dependent on others; cannot leave residence.	

Appendix E-2: Treatment Questionnaire Sent to Patients Who Had Undergone Surgical Treatment for the Benign Skeletal Lesion

Study of Fracture Risk in Patients with a Benign Bone Tumor
TREATMENT QUESTIONNAIRE

Study ID:

1.	Did the bone with the benign tumor ever break or fracture before you received treatment? *(Circle one number)*		
		No .... 0 **(Skip to #2)**	
		Yes.................................. 1	
	a.	If Yes, what were you doing when it broke? *(Circle one number)*	
			Nothing, really (lifting, reaching, standing up/sitting down, walking, etc.) 1
			Working around house or yard (vacuuming, gardening, shoveling snow, etc.) 2
			Recreational activity or exercise (biking, jogging, weight lifting, aerobics, etc.) 3
			Competitive team or individual sports (soccer, football, wrestling, skiing, tennis, etc.) 4
			Motor vehicle accident (car, motorcycle, off-road vehicle, boat, etc.) 5
2.	Why did you have your bone tumor treated? *(Circle all numbers that apply)*		
		Doctor recommended it 1	
		Because of pain caused by tumor 2	
		Did not want to restrict physical activity 3	
		Did not want to return for regular follow-up clinical visits 4	
		Was worried that bone would break 5	
		Was worried that tumor would get worse 6	
		Other reason 99	
		➯ Please specify: ______________________________	
		______________________________	
3.	Date questionnaire completed: __ __ / __ __ / __ __ __ __		
	Month Day Year		

Thank you for taking the time to complete this questionnaire!

Appendix E-3: Letter Sent to Potential Participants to Solicit Consent for Enrollment in this Study

Date

Dear (patient/guardian name),

We are conducting a research study at ____________ on benign bone tumors and the associated risk of bone fracture. We hope to enroll about 60 patients in this study. We are constantly working to improve the treatment we provide, so feedback regarding your personal experience is very valuable to us.

According to our department's records, you were diagnosed with a bone tumor and underwent a quantitative computed tomography (qCT) here at ____________ to determine whether you were at risk of breaking the bone with the tumor. Consequently, we would like to ask for your participation in our study confirming the accuracy of qCT to predict fracture over a longer term. Participation involves one-time completion of the brief questionnaire enclosed. In addition, we will collect a limited amount of information about your tumor, such as size and location, and whether there was any associated pain or growth abnormality, from your medical record. All questionnaire and medical record data collected for this study will be analyzed and reported as a group, so you will not be individually identified. Participation is completely voluntary and refusal or withdrawal will not in any way affect the care that you receive at CHB, now or in the future. You will likely not directly benefit from participating in this research study; however, with your help, we hope that we will be able to treat future patients with similar tumors more effectively.

If you would like to participate in the study, please check the "Yes" box and sign the Participation Form, and return it along with the completed questionnaire, in the addressed envelope provided. If you do not want to participate, please check the "No" box and return just the form. If we do not hear back from you within two weeks, we will call you to ask if you would like to participate in this study. If you agree to participate when we call, you will be asked to provide verbal consent and then we will ask you the same questions that are on the questionnaire. This should take no more than 5 minutes of your time.

If you have any questions about the study or about your bone tumor, please feel free to contact the study nurse, __________, at ___________ or ___________. We look forward to hearing from you and hope that you find this study worth taking part in. Thank you for your time and consideration.

Sincerely,

Appendix E-4: Details of the Calculation of Cross-Sectional Structural Rigidity for Predicting the Load Capacity of Bone with an Osteolytic Defect

Any method that predicts fracture risk must be able to measure both changes in bone-tissue material properties and changes in bone geometry induced by the neoplasm. The bone-tissue modulus is a function of the bone-mineral density[33,34]. The modulus of elasticity (*E*), which is the intrinsic stiffness of the bone (in megapascals), for each pixel in the image was calculated from the apparent density with use of empirical relationships[33,34]. In order to use these density-to-modulus relationships, the bone-mineral density measured with quantitative computed tomography was adjusted by the mass ash fraction (f_{ash}) to convert bone-mineral density to apparent bone density (ρ_{app}) in grams per cubic centimeter, which represents the density of the combined mineral and organic phases of bone:

$$\rho_{app} = \frac{\rho_{ash}}{f_{ash}}$$ (Equation A1)

where $f_{ash} = 0.66$[34]. A minimum apparent density of 0.05 g/cm^2 was used as a threshold to separate bone from soft tissue. For trabecular bone, a power law relationship[33] was used:

$$E = 0.82(\rho_{app}^2) + 0.07;$$ (Equation A2)

For cortical bone, a linear relationship[34] was used:

$$E = 21.91(\rho_{app}) - 23.5.$$ (Equation A3)

The transition from trabecular to cortical bone was set at the point where the two equations intersect at 1.123 g/cm^2. The shear modulus (*G*), in megapascals, for transverse cross sections through the bone perpendicular to the primary trabecular orientation was calculated from the modulus of elasticity:

$$G = \frac{E}{2.6}.$$ (Equation A4)

Bone geometry is represented by the cross-sectional area and moment of inertia[34]. The moment of inertia describes analytically how the bone mass is distributed in space relative to a bending axis. It varies as the fourth power of the distance of the bone tissue relative to a specific bending axis. It is a vector; therefore, it has both a magnitude and a direction. The principal moments of inertia describe the magnitude and direction of the (mutually orthogonal) maximum and minimum moments of inertia for a cross section through the bone. The maximum moment of inertia corresponds to the bending axis through the bone cross section *most* resistant to bending deformation, while the minimum moment of inertia corresponds to the bending axis through the bone cross section *least* resistant to bending deformation. As an example of this principle, consider the bending of a yardstick: although the mass of the yardstick is constant, it is much easier to bend the yardstick when the bending axis is oriented along its thickness (minimum principal moment of inertia) than it is to bend the yardstick when the bending axis is oriented along its width (maximum principal moment of inertia).

Rigidity, the product of the bone tissue modulus of elasticity and bone cross-sectional geometry, describes the structural behavior of a bone and its resistance to deformation when subjected to axial, bending, or twisting loads[27]. The axial rigidity (*EA*), bending rigidity (*EI*), and torsional rigidity (*GJ*) for each transaxial cross-sectional image were calculated by summing the modulus-weighted area of *each* pixel of the bone section by its position relative to the centroid of the bone (Fig. 2):

$$EA = \sum_{i=1}^{N} E_i da$$ (Equation A5)

$$EI_x = \sum_{i=1}^{N} E_i y'^2_i \, da$$

(Equation A6)

$$GJ = \sum_{i=1}^{N} G_i \left(x'^2_i + y'^2_i \right) da$$

(Equation A7)

where *Ei* is the modulus of elasticity, which is a function of the apparent bone density (ρ_{app}) at each pixel (i); *da* is the pixel area; N is the total number of pixels forming the image; G_i is the shear modulus, which is a function of the modulus of elasticity (E_i) at each pixel (i); and x'_i and y'_i are the horizontal and vertical distances of each pixel from the modulus weighted centroid (x, y) of the bone on the cross section calculated as:

$$\overline{x} = \frac{\sum_{i}^{N} x_i E_i da}{\sum_{i=1}^{N} da}, \overline{y} = \frac{\sum_{i}^{N} y_i E_i da}{\sum_{i=1}^{N} da} .$$

(Equation A8)

where x_i and y_i are the horizontal and vertical coordinates of each pixel relative to the origin of the cross section. A is the total cross-sectional area of bone, I_x is the moment of inertia taken about the horizontal (x) bending axis in the transverse plane, and J is the polar moment of inertia.