Appendix

Assessment of the Surgical and Radiological MRI Questionnaires

Below we review the methods and results of validity testing for the instruments used to evaluate the distal femoral MRIs.

Methods

To assess the intrarater reliability of the surgeons using their questionnaire, ten MRI scans (the scans for five cases) were duplicated and randomly placed in the list of scans to be reviewed, thereby allowing repeat interpretations. These same ten scans were also reviewed by four fellow-level trainees in musculoskeletal oncologic surgery, to permit more robust interrater reliability.

To assess the intrarater reliability of the radiologists, they reviewed nine randomly chosen scans a second time.

Statistical Methods

To confirm that our surgical planning questionnaire was a reasonable instrument, statistical analysis included the generation of intraclass correlation coefficients for intrarater and interrater reliability among the surgeons and intrarater reliability for the radiology team. These reliabilities tested the many categorical designations in aggregate, including both global assessment of surgical plans and individual anatomic assessments.

Results

Intrarater reliability was strong for the limited set of repeat-assessment scans; the intraclass correlation coefficients, listed from most junior to most senior faculty surgeon, were 0.794 (95% confidence interval [CI], 0.692 to 0.865), 0.597 (95% CI, 0.429 to 0.725), 0.889 (95% CI, 0.829 to 0.928), and 0.832 (95% CI, 0.745 to 0.884). The interrater reliability among the four faculty surgeons for the entire group of scans was also strong, at 0.772 (95% CI, 0.736 to 0.886). The interrater reliability among the four faculty surgeons and four fellow-level trainees for the limited number of reliability scans was similar, at 0.605 (95% CI, 0.540 to 0.671).

The review of the scans by the two musculoskeletal radiologists had very strong intrarater reliability, with a mean intraclass correlation coefficient of 0.941 (95% CI, 0.770 to 0.986).

With regard to cross-validation of the two independent assessment questionnaires, the radiologists' measurements clustered in the ranges of the surgeons' measurements, in terms of distances such as tumor distance from vessels and nerves compared with the surgeons' expected margins on the same structures (Fig. E-1) and proximal length of involvement compared with proximal resection length (Fig. E-2). Notably, surgeons expected margins that were the same as or narrower than the radiologists' measured distances of tumor from neurovascular structures in all but three cases. The surgeons planned femoral resection lengths that were always beyond the length of involvement noted by the radiologists.

In addition, the surgical procedures planned on the basis of the post-chemotherapy scans reflected the surgical procedures that were actually performed in these patients. Both amputations in the group were planned and the single precarious (<1-mm) resection margin in a limb-salvage case was predicted by the post-chemotherapy MRI interpretations of the four faculty surgeons.

Discussion

We found that musculoskeletal oncologic surgeons can plan surgical procedures on the basis of MRIs with strong reliability. While validity can be difficult to measure for an instrument such as a surgical planning worksheet, the operations planned by the surgeons correlated well with the anatomic parameters measured independently by the radiologists. Furthermore, the operations planned in the study correlated grossly with the operations that the treating surgeons actually undertook, with the two amputations that took place planned on the basis of the surgeons' assessment of the post-chemotherapy scans of those patients and the single precarious margin predicted as well.

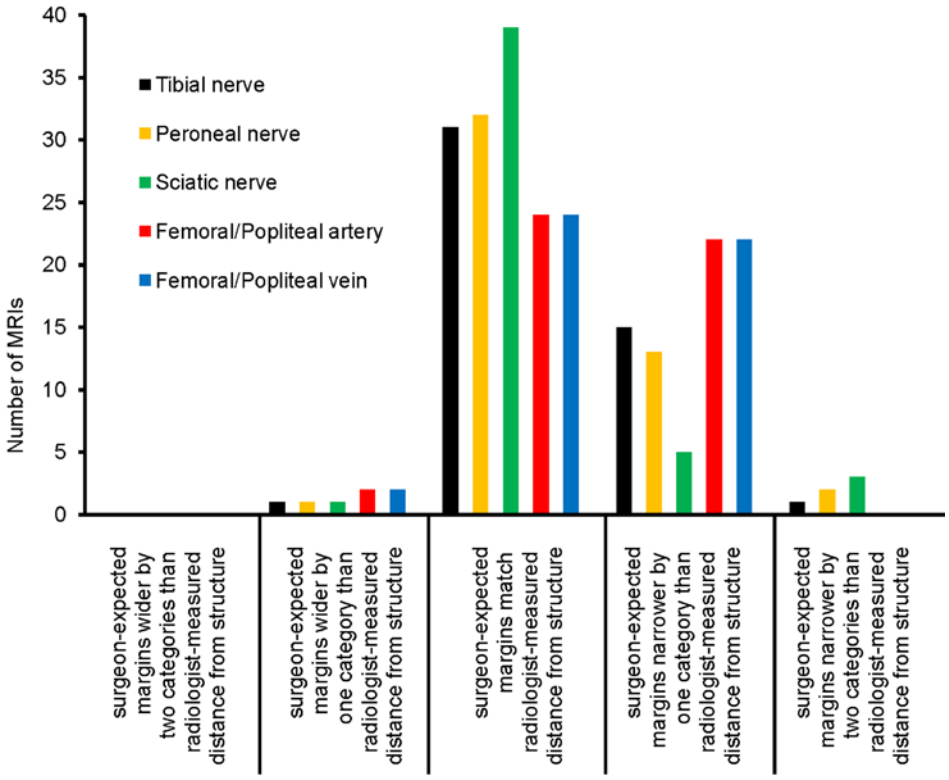

Fig. E-1

Validity figure showing the neurovascular expected-margin designations by the radiologists and surgeons. The radiologists' measurements of the proximity of tumor to critical neurovascular structures were compared with the mean expected margins designated by the four faculty surgeons. In most rating categories, the surgeon-designated margins matched the radiologist-designated distances in terms of being positive (i.e., touching or encased by tumor), narrow (1 to <10 mm), or wide (≥10 mm) margins. There was only one case for each radiologist-measured tumor-nerve distance and there were two cases for each tumor-vessel distance in which the surgeons expected wider margins (the leftmost columns).

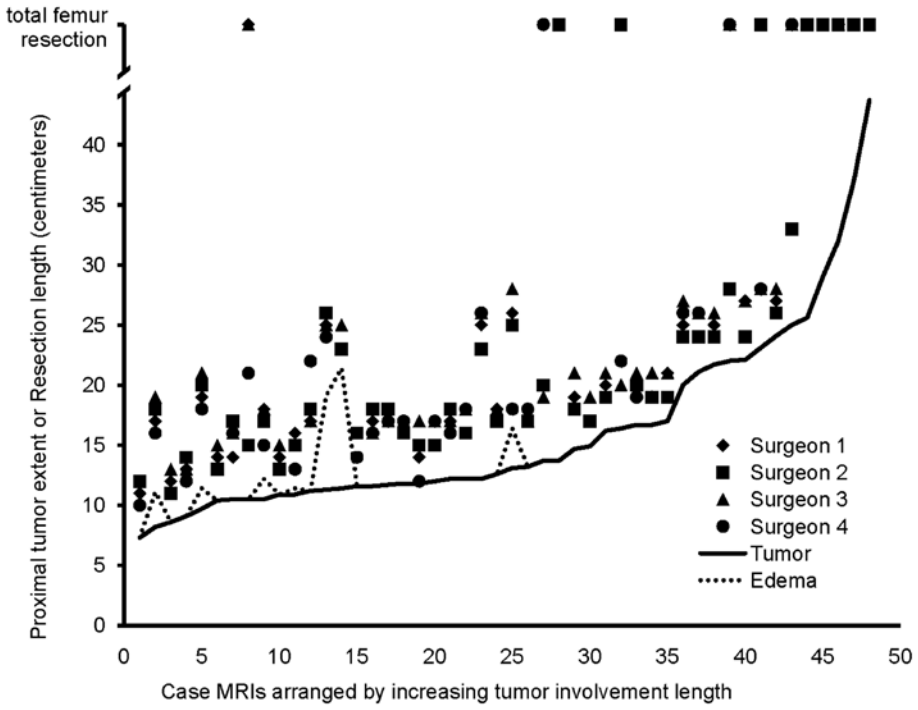

Fig. E-2

Cross-validity figure showing proximal resection length designations by the surgeons and radiologists. With cases organized according to increasing radiologist-measured length of the tumor (solid line) and edema (dotted line, where edema extended to a length beyond the tumor itself), every surgeon-designated resection length is beyond the radiologist-measured length of the tumor and edema, through normal tissue. Because surgeons designated where they planned to osteotomize the femur, their intended resection level had surgical planning inputs beyond the tumor extent alone; this was notable in some designated total femoral resections.

TABLE E-1 Characteristics of Twenty-four Consecutive Patients with a Distal Femoral High-Grade Osteosarcoma and Pre-Chemotherapy and Post-Chemotherapy Digital MRIs Available for Review

Sex	Age *(yr)*	Histological Type of Osteosarcoma	Neoadjuvant Chemotherapy*	Local Control	Percent Necrosis	Local Outcome
Male	29	Conventional	AI	Resection	100	
Female	20	Conventional	MAP	Resection	50	
Male	31	Conventional	MAP	Resection	100	
Male	31	Conventional	MAP	Resection	90	
Male	20	Conventional	MAP	Resection	95	
Male	17	Conventional	MAP	Resection	90	
Male	19	Conventional	MAP	Amputation	50	
Female	30	Conventional	MAP	Resection	80	
Male	65	Conventional	MAP	Resection	60	
Male	25	Telangiectatic	MAP	Resection	90	
Male	19	Chondroblastic	MAP	Resection	10	Local recurrence
Male	19	Chondroblastic	MAP	Resection	85	
Female	59	Chondroblastic	AP	Resection	70	
Male	20	Fibroblastic	MAP	Resection	99	
Female	5	Conventional	MAP	Resection	100	Local recurrence
Male	11	Conventional	MAP	Resection	99	Regional recurrence
Male	17	Conventional	MAP	Resection	99	
Male	10	Chondroblastic	MAP	Resection	99	
Male	11	Conventional	MAP	Resection	98	
Female	7	Telangiectatic	MAP	Resection†	35	
Male	13	Chondroblastic	MAP	Amputation	70	
Male	9	Conventional	MAP	Resection	100	
Male	13	Conventional	MAP	Resection	90	
Male	15	Conventional	MAP	Resection	80	

*AI = doxorubicin and ifosfamide; MAP = high-dose methotrexate, doxorubicin, and cisplatin; and AP = doxorubicin and cisplatin. †This case had <1-mm margins but no ink on the tumor.

TABLE E-2 Radiologists' Evaluations of Tumor Signal, Lesion Types, and Knee and Femoral Involvement on Blinded Pre-Chemotherapy and Post-Chemotherapy MRIs of Twenty-four Consecutive Patients with Distal Femoral Osteosarcoma

Parameter Rated	Pre-Chemotherapy	Post-Chemotherapy	P Value	Better*	Worse*
Tumor signal characteristics (mean ± stand. dev.) *(%)*					
Fluid signal	13.8 ± 18.1	21.7 ± 19.3	0.024	11	5
Fibrous/bone signal	82.5 ± 24.4	71.7 ± 21.8	0.048	6	11
Cartilage signal	3.8 ± 11.3	6.7 ± 19.3	0.49	2	2
Femoral skip lesion†	2	3	0.64	0	1
Pathologic fracture†	1	2	0.55	0	1
Tibial skip lesion†	1	1	1.0	0	0
Knee involvement†			0.50	3	3
Intra-articular	6	4			
Extensor mechanism	1	3			
Femoral involvement (mean ± stand. dev.) *(length in cm)*					
Proximity to knee					
Of tumor	1.8 ± 1.9	1.8 ± 1.9	0.98	8	10
Of edema	1.4 ± 1.6	1.8 ± 1.9	0.13	10	8
Proximal length					
Of tumor	16.3 ± 8.2	15.9 ± 7.3	0.63	10	12
Of edema	17.1 ± 8.0	16.3 ± 7.2	0.33	11	11

*"Better" or "worse" indicates the number of cases, of the twenty-four, that were better or worse in terms of the given parameter on the post-chemotherapy MRI compared with the pre-chemotherapy MRI. For example, "better" is less involvement or shorter tumor/edema length. For the signal characteristics, "better" indicates the number of cases with increased signal of that type and "worse" indicates those with decreased signal of that type. †Number of radiologist designations out of twenty-four.

TABLE E-3 Radiologists' Evaluations of Muscle Involvement by, and Distance from Nerves and Vessels of, Tumor and Edema on Blinded Pre-Chemotherapy and Post-Chemotherapy MRIs of Twenty-four Consecutive Patients with Distal Femoral Osteosarcoma

	Pre-Chemotherapy*		Post-Chemotherapy*				
Parameter Rated	Tumor	Edema	Tumor	Edema	P Value	Better†	Worse†
Muscle involved							
Rectus femoris	1	0	1	0	1.0	0	0
Vastus lateralis	18	1	14	2	0.20	5	1
Vastus medialis	16	3	17	2	0.89	3	3
Vastus intermedius	14	1	12	2	0.76	3	2
Sartorius	0	0	0	0	1.0	0	0
Adductor longus	2	0	2	0	1.0	0	0
Adductor magnus	4	1	4	1	1.0	1	1
Gracilis	0	0	0	0	1.0	0	0
Semimembranosus	1	0	1	0	1.0	0	0
Semitendinosus	0	0	0	0	1.0	0	0
Short head of biceps femoris	10	3	6	3	0.45	5	0
Long head of biceps femoris	0	0	1	0	0.31	0	1
Medial gastrocnemius	10	1	9	0	0.55	4	2
Lateral gastrocnemius	7	2	6	1	0.77	3	1
Distance from nerves and vessels							
Tibial nerve					Tumor: 0.70	3	4
					Edema: 0.75	8	7
Totally encased	0	1	0	3			
>50% encased	0	1	1	0			
25%-50% encased	1	4	1	3			
<25% encased	0	1	0	0			
1-5 mm from	5	3	3	4			
6-10 mm from	2	4	4	3			
>10 mm from	16	10	15	11			
Peroneal nerve					Tumor: 0.59	4	4
					Edema: 0.31	9	7
Totally encased	0	0	0	3			
>50% encased	0	1	1	0			
25%-50% encased	1	7	1	3			
<25% encased	0	1	0	1			
1-5 mm from	4	4	2	2			
6-10 mm from	3	2	6	4			
>10 mm from	16	9	14	11			
Sciatic nerve					Tumor: 0.70	1	5
					Edema: 0.43	5	5
Totally encased	0	0	0	2			
>50% encased	0	2	1	0			
25%-50% encased	1	5	0	3			
<25% encased	0	0	0	0			
1-5 mm from	3	2	4	3			
6-10 mm from	3	2	3	3			
>10 mm from	17	13	16	13			
Femoral/popliteal artery					Tumor: 0.94	6	8
					Edema: 0.40	14	4

Totally encased	0	5	1	3			
>50% encased	0	6	0	1			
25%-50% encased	5	5	4	6			
<25% encased	3	2	3	5			
1-5 mm from	7	3	8	4			
6-10 mm from	4	2	4	4			
>10 mm from	5	1	4	1			
Femoral/popliteal vein					Tumor: 0.63	5	8
					Edema: 0.28	14	4
Totally encased	0	5	1	3			
>50% encased	0	5	0	1			
25%-50% encased	4	6	5	6			
<25% encased	2	2	3	5			
1-5 mm from	9	4	9	6			
6-10 mm from	6	2	2	2			
>10 mm from	3	0	4	1			

*Number of radiologist designations out of twenty-four. †"Better" or "worse" indicates the number of cases, of the twenty-four, that were better or worse for the given parameter on the post-chemotherapy MRI compared with the pre-chemotherapy MRI. For example, "better" is less involvement or greater distance of tumor/edema from the given structure.

TABLE E-4 One Hundred and Ninety-two Surgical Procedures Planned by Four Faculty Surgeons Reviewing Pre-Chemotherapy and Post-Chemotherapy MRIs of Twenty-four Consecutive Patients with Distal Femoral Osteosarcoma

	Pre-Chemotherapy MRI	Post-Chemotherapy MRI	P Value
Type of surgery*			0.25
Safe limb salvage	53	55	
Borderline limb salvage	38	29	
Transfemoral amputation	3	7	
Hip disarticulation	2	5	
Knee articular resection*			0.16
Epiphyseal sparing	3	1	
Intra-articular	41	45	
Pseudo-extra-articular (patella and quadriceps-sparing)	25	15	
Extra-articular (sparing partial thickness of patella)	11	11	
Extra-articular (sacrificing extensor mechanism)	16	24	
Proximal resection length (mean ± stand. dev.) *(cm)*	19.5 ± 4.4 (plus 20 total femora)	18.7 ± 4.9 (plus 17 total femora)	0.39
En bloc tibial resection*	5	17	0.007
Myectomies (mean ± stand. dev.) *(% resected)*			
Rectus femoris	16.8 ± 34.7	26.0 ± 42.7	0.099
Vastus lateralis	55.4 ± 41.1	54.2 ± 42.1	0.82
Vastus medialis	61.3 ± 34.9	61.9 ± 41.9	0.90
Vastus intermedius	94.2 ± 20.2	85.4 ± 31.4	0.016
Short head of biceps femoris	68.6 ± 38.4	61.1 ± 40.9	0.15
Long head of biceps femoris	12.4 ± 26.7	14.9 ± 33.3	0.56
Sartorius	5.6 ± 22.3	12.7 ± 33.2	0.10
Semimembranosus	6.7 ± 23.3	12.6 ± 33.2	0.18
Semitendinosus	5.4 ± 22.3	12.5 ± 33.2	0.10
Gracilis	5.2 ± 22.3	12.5 ± 33.2	0.090
Adductor longus	23.0 ± 33.2	28.8 ± 39.6	0.24
Adductor magnus	36.3 ± 33.7	40.4 ± 37.9	0.38
Medial gastrocnemius	24.0 ± 27.3	27.2 ± 33.3	0.48
Lateral gastrocnemius	22.6 ± 22.6	27.7 ± 33.3	0.26
Soft-tissue coverage*			
Hamstrings rotational flap	50	36	0.042
Gastrocnemius rotational flap	20	31	0.072
Free muscle flap	2	5	0.25
Split-thickness skin graft	11	12	0.65
Neurovascular margins expected*			
Tibial nerve			0.5
Structure sacrificed	5	11	
0 mm	1	0	
1-2 mm	10	11	
3-5 mm	33	28	
6-10 mm	27	22	
11-20 mm	16	17	
>20 mm	4	7	
Peroneal nerve			0.27
Structure sacrificed	5	11	
0 mm	0	0	
1-2 mm	11	6	
3-5 mm	27	30	

6-10 mm	32	24	
11-20 mm	17	17	
>20 mm	4	8	
Sciatic nerve			0.45
Structure sacrificed	5	11	
0 mm	0	0	
1-2 mm	5	4	
3-5 mm	26	24	
6-10 mm	34	25	
11-20 mm	18	20	
>20 mm	8	12	
Femoral/popliteal artery			0.41
Structure sacrificed	11	15	
0 mm	18	15	
1-2 mm	36	25	
3-5 mm	19	20	
6-10 mm	10	16	
11-20 mm	1	4	
>20 mm	1	1	
Femoral/popliteal vein			0.42
Structure sacrificed	11	15	
0 mm	19	16	
1-2 mm	35	26	
3-5 mm	20	18	
6-10 mm	9	16	
11-20 mm	1	4	
>20 mm	1	1	

*Number of surgeon designations for each category.