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Extrathoracic Location and “Borderline” Histology are Associated with Recurrence of Solitary Fibrous Tumors After Surgical Resection

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Abstract

Background—Most solitary fibrous tumors (SFTs) are cured by complete resection, but many recurrent and metastatic SFTs do not respond to treatment and are fatal. Malignant histology, defined by England’s pathologic criteria, is strongly associated with recurrence, but some benign SFTs still behave aggressively. Several studies have suggested that extrathoracic SFTs have a worse prognosis. We reviewed thoracic and extrathoracic SFTs from our institution to determine if extrathoracic location is associated with recurrence, independent of malignant histology.

Methods—With IRB approval, we retrieved patient pathology reports from the Johns Hopkins Surgical Pathology database between 1991 and 2011 and included 83 SFT patients in our analysis. Patient history and outcomes were obtained from the medical record and primary care physicians. Predictors of recurrence were analyzed by univariate and multivariate analysis and survival determined by the Kaplan–Meier method.

Results—Of the 83 patients, 59 had extrathoracic SFTs in neurologic ($n = 24$), extremity or head/neck ($n = 13$), or visceral/intraabdominal ($n = 22$) sites. A total of 74 SFTs were classified benign and 9 as malignant. Of the 14 recurrences, 13 occurred in extrathoracic SFTs; only 7 were classified as malignant. Multivariate analysis confirmed that malignant histology had the strongest association with recurrence, but extrathoracic location also independently predicted recurrence. A total of 20 benign SFTs possessed 1 or more of England’s criteria but to an insufficient degree for malignant classification. These “borderline” SFTs were more likely to recur than benign SFTs without these features.

Conclusions—Extrathoracic and “borderline” SFTs with any of England’s criteria have a higher risk of recurrence.

Solitary fibrous tumors (SFTs) are rare spindle-cell neoplasms that classically present as well-circumscribed, pleural-based masses arising from mesenchymal soft tissue and grow slowly over years.¹ However, SFTs have now been reported in essentially every anatomic location.^{2–10} SFTs typically contain multiple histologic features, arranged in a “patternless” architecture: highly fibrous collagen meshwork, pockets of cellularity, and vascularized sections with irregular, thin-walled blood vessels. Immunohistochemistry markers help distinguish SFTs from related neoplasms; most SFTs express CD34, BCL2, CD99, and vimentin and do not express desmin, cytokeratins, and S100.^{8,11,12} Surgical resection is the mainstay of treatment, and recurrence-free survival (RFS) generally exceeds 90 % with complete resection.^{6,13,14} However, about 10 % of SFTs will recur locally or distantly, often more than 10 years after surgery.^{7,8,15–18} While many local recurrences can be controlled with resection, widespread disease is often fatal because of the poor response of SFTs to chemotherapy.^{16,18–21} Identification of SFTs at high risk of local and metastatic recurrence would avoid unnecessary surveillance radiation and anxiety for those patients likely to be cured.

The best-described predictor of recurrence in SFTs is malignant histology, defined by pathologic criteria developed by England et al.^{15,16} In 82 patients with pleural SFTs exhibiting these criteria (hypercellularity, >4 mitotic figures/10 high-power fields (hpf), pleomorphism/atypia, infiltrative growth pattern, necrosis, hemorrhage), 55 % of the patients succumbed to recurrence, metastasis, or invasion. However, even among malignant tumors, outcomes are still unpredictable; up to 50 % of patients will be cured with resection, while at least 25 % will die from widespread SFT, most within 2 years.^{4,9,15,17,22–26} Equally puzzling, a small number of benign tumors recur locally or metastasize.^{4,6,7,17,27} These SFTs often acquire malignant criteria on recurrence, such as a higher mitotic rate or nuclear atypia.^{17,23,27}

Prognostic factors apart from frankly malignant histology would be helpful to identify additional high-risk SFTs. Distinguishing benign and malignant SFTs can be challenging, as some SFTs possess foci of increased cellularity, giant cells, necrosis, or mitoses <4/10 hpf; these “borderline” abnormalities generally are not considered high-risk features.^{2,7,9,15,24,25,27–30} Whether “borderline” findings are associated with recurrence has not been evaluated. Additionally, several studies suggest that extrathoracic SFTs have a worse prognosis than thoracic SFTs, with recurrence rates as high as 80 %, while others described similar recurrence risk regardless of location.^{2,4,5,7,9,10,18,25,28,29,31–35} The utility of other potential prognostic factors including large tumor size, positive surgical margins, and age has been similarly inconsistent between series.^{6,17,35,36} Therefore, we reviewed thoracic and extrathoracic SFTs from our institution to determine clinical and pathologic factors associated with recurrence.

METHODS

Under an IRB-approved protocol, we queried the prospectively maintained surgical pathology database at The Johns Hopkins Hospital for patients with SFT between 1991 and 2011. Following review of pathology reports, patients were excluded from analysis if the most likely diagnosis was not SFT. For patients where SFT was likely but uncertain, slides were rereviewed by a sarcoma pathologist to confirm SFT. Historical, pathologic, and treatment data were extracted from electronic and paper medical records. Each report was reviewed for official classification (benign or malignant) and any mention of specific England's criteria (hypercellularity, mitoses, pleomorphism/atypia, infiltrative growth pattern, necrosis, hemorrhage). Each SFT was categorized as "benign with no atypical features" (no England's criteria were reported), "borderline" (1 or more England's criteria were noted, but the final classification was "benign") or "malignant." Recurrences (based on imaging or biopsy) and deaths were obtained from medical records, primary care physicians, or query of the Social Security Death Index.

Statistical Analysis

Continuous variables were compared using unpaired *t* tests or 1-way ANOVAs followed by Tukey's post-test, and categorical variables were compared using 2-sided Fisher exact tests or Chi square tests (Graphpad Prism version 4.0). Predictor variables of age, size, tumor location (thoracic or extrathoracic), pathologic classification (benign with no atypical features, borderline, or malignant), and positive/close (<1 mm) surgical margins were modeled by logistic regression to identify associations with recurrence (SAS software). RFS and overall survival (OS) were plotted using the Kaplan–Meier method and survival curves compared by log-rank test. A *p* value of <0.05 was considered statistically significant.

RESULTS

We retrieved 117 surgical pathology reports, consolidated 19 redundant specimens, and excluded 15 patients with a non-SFT diagnosis; 83 patients were included in final analysis.

Demographic and Historical Characteristics

Few significant differences were identified in patient characteristics based on SFT location or histology (Table 1). Patients with extrathoracic SFTs were younger (median age, 55 vs 63 years; *p* = 0.02), presented more frequently with local symptoms (85 vs 25 %; *p* <0.0001), were less likely to have a smoking history (39 vs 75 %; *p* = 0.004), and were more likely to have a positive family history of cancer or autoimmune disease (32 vs 8 %; *p* = 0.03) relative to patients with thoracic SFTs. The entire population showed relatively high prevalence of smoking (49 %), comorbid benign soft tissue lesions (14 %), and autoimmune disease (12 %), including four patients on immunosuppressive therapy at the time of diagnosis. Also, 23 % of patients possessed another cancer diagnosis, including twelve patients with previous cancers, five of whom had received chemotherapy or radiation, and six patients developed multiple cancers during the follow-up period. There were three patients who developed SFTs near sites of prior radiation, arising from the pleura (breast

radiation), thyroid (radium to adenoids), and T-spine (thymus radiation). In addition, 25 % of patients had a positive family history for cancer or auto-immune disease.

Pathologic Data

As shown in Fig. 1a, 24 patients had thoracic and 59 had extrathoracic SFTs. Among extrathoracic SFTs, 24 occurred in neurologic sites (N), 13 arose in head, neck or extremity soft tissue (ST), and 22 originated from visceral organs, intra-abdominal or retroperitoneal soft tissue (V). There were 74 SFTs classified as benign and 9 as malignant (Fig. 1b). Of the 74 benign SFT reports, 20 mentioned 1 or more of England's criteria and were classified as borderline. These findings included foci of hypercellularity ($n = 16$), 0–4 mitoses/10 hpf ($n = 5$), atypia ($n = 4$), or necrosis ($n = 7$). Extrathoracic SFTs had a higher rate of malignant histology compared with thoracic SFTs (15 vs 0 %; $p = 0.06$) (Table 1). Borderline SFTs were found in thoracic and extrathoracic locations (38 vs 19 %; $p = 0.09$). No extrathoracic subgroup had a significantly higher proportion of malignant SFTs; however, 3 of the 5 retroperitoneal SFTs were malignant (Table 2).

We recorded tumor size, immunostaining, and margin status and looked for associations with location and histology (Tables 1, 2). SFTs ranged from 0.5 to 32 cm with malignant tumors significantly larger than benign tumors (median, 7.5 vs 4.6 cm; $p = 0.0024$). All tumors presented as solitary lesions, except for one patient who presented with multiple benign retroperitoneal SFTs. 88 % of pathology reports included immunostaining with CD34 and/or Bcl2 to aid the diagnosis, but 33 % of thoracic tumors were diagnosed based on histology alone. While most SFTs were CD34 or Bcl2 positive, 7 of 58 extrathoracic tumors were CD34 negative while all thoracic tumors with CD34 testing were positive. Finally, positive/close margins were quite common in all locations (extrathoracic 37 % vs thoracic 25 %; $p = 0.32$) with the highest rate in soft tissue tumors (69 %).

Recurrence

A total of 14 patients recurred with an overall median follow-up time of 3.1 years (range, 0–15.4 years) (Fig. 1c); median time to recurrence (TTR) for all SFTs was 1.9 years. Of the 14 recurrences, 13 occurred in extrathoracic SFTs, with a higher recurrence rate compared with thoracic tumors (22 vs 4 %; $p = 0.06$), and a lower RFS (Fig. 1d). Also, 10 patients recurred locally, while 4 patients developed metastases, including the only thoracic recurrence. Malignant SFTs had a higher recurrence rate than all benign tumors (78 vs 9 %; $p < 0.0001$) and significantly lower RFS (Fig. 1e). However, 7 of the 14 recurrences occurred in benign SFTs, with 4 of these in borderline cases. Borderline tumors had a higher recurrence rate (20 vs 6 %; $p = 0.08$) and lower RFS compared with benign tumors without atypical features (Fig. 1e). Median TTR was decreased in malignant and borderline SFTs compared with benign tumors (malignant, 1.4 years; borderline, 1.2 years; benign, 5.8 years). The highest rate of recurrence occurred in the neurologic subgroup (N 33 % vs ST 15 % vs V 14 %; $p = 0.22$) (Table 2).

On univariate analysis, extrathoracic location, borderline histology, and malignant histology were associated with recurrence (Table 3), while positive/close surgical margins, larger tumor size, and age were not. Multivariate analysis was performed to separate the effects of

location and histology. Extrathoracic location was independently associated with recurrence (odds ratio, 5.1; $p = 0.16$), although histologic classification had a stronger association with recurrence, including malignant (odds ratio, 68.4; $p = 0.0001$) but also borderline (odds ratio, 10.3; $p = 0.01$).

Of the 14 recurrent patients, 2 had confirmed histologic evolution between primary and recurrent tumor. One patient's initial SFT was borderline, with bright Bcl2 staining, focal CD34 staining, and rare mitoses, but evolved on recurrence to bright CD34 and Bcl2 staining, hypercellularity, and >4 mitoses/10 hpf. The second patient's SFT was initially benign, yet recurrent tumor was malignant with a high mitotic index. Of the 14 recurrences, 7 lacked histologic evolution on recurrence, while comparison with initial pathology was not documented in remaining patients.

Treatment and Survival

Surgical resection alone was performed in 78 % of patients, and they remained free from disease; patients who recurred and/or received additional therapy are detailed in Table 4. Because of the small numbers of patients, treatment effect on recurrence was not evaluated. Of 15 confirmed deaths, only 2 patients with extrathoracic, malignant, metastatic SFT died of the disease, and OS (all-cause) did not differ based on location or pathology classification (Fig. 1e, f).

DISCUSSION

Most SFTs are curable with surgery, but for patients with aggressive SFTs, outcomes can be as devastating as high-grade sarcomas. Identification of SFTs more likely to recur, metastasize, or transform to a high-grade sarcoma would help tailor clinical surveillance and adjuvant therapy. England's criteria identify many high-risk SFTs, but some benign tumors still recur. Prior studies of additional prognostic markers have been limited by few recurrences, inconsistent criteria for "malignant" classification, and brief follow-up time. In this retrospective analysis of 83 SFT patients, although our statistical power remains limited by low recurrence numbers, we found that extrathoracic location and histologic classification (malignant and "borderline") were associated with recurrence, while age, tumor size, and margin status were not. Tumor size and margin status were associated with malignant histology (Table 1), suggesting that previously reported links between tumor size, positive margins, and recurrence may have been confounded by higher-risk histology. Similarly, in previous studies reporting increased recurrence in extrathoracic SFTs, the relative impact of histology vs location was unclear.^{6,37} In 2 large SFT series including pathologic classification, worse local RFS was suggested in extrathoracic SFTs, but the second study found no significant difference in time to metastasis after controlling for histology.^{6,35} However, these extrathoracic SFTs, particularly abdominal/pelvic tumors, had a shorter time to local recurrence and more frequently metastasized to distant sites.³⁵ Interestingly, CNS SFTs are particularly prone to recurrence, although the difficulty in achieving R0 resection likely contributes to worse outcomes.^{3,30,38}

In our patients, extrathoracic SFTs recurred more frequently than thoracic tumors, independent of malignant histology, size, or margin status (Table 3). As a tertiary referral

center, it is possible that the higher recurrence rate might be exaggerated relative to other series given the large number of extrathoracic tumors in our study, particularly CNS SFTs. However, no difference in recurrence rates or positive margins were seen in neurologic tumors relative to other extrathoracic subgroups, and when CNS SFTs were omitted from analysis, extrathoracic SFTs still recurred more frequently (13 vs 4 %; $p = 0.40$).

We also found that extrathoracic SFTs were more likely to have atypical histologic features. Extrathoracic SFTs were more likely than thoracic to be malignant, and all SFTs lacking typical CD34 expression occurred in extra-thoracic sites, particularly the visceral/intraabdominal subgroup. The loss of CD34 has been reported in some malignant SFTs, but only 2 of the CD34-negative tumors in our study were malignant.^{11,23,24,39} Two patients with ex-trathoracic SFTs showed histologic evolution with altered CD34 expression and increased mitoses between initial and recurrent tumors. With higher risk of recurrence and tendency to possess adverse histologic features, even without meeting criteria for malignancy, our data supports previous studies suggesting that extrathoracic location portends a worse prognosis.

In both thoracic and extrathoracic SFTs, we confirmed that malignant histology, defined by England's histologic criteria, remains the most powerful predictor of recurrence. However, application of the criteria requires pathologist expertise and adequate tumor sampling. Of the 74 benign SFTs, in our study, 20 possessed some foci of cellularity, necrosis, or mitoses $<4/10$ hpf, but were not considered malignant. The sole recurrent thoracic SFT in our study contained "areas of necrosis and scattered mitoses up to 2/ 10 hpf," but "no definite morphologic features of malignancy"; this tumor recurred 7 years later with widespread lung and bone metastases. The concept of a "borderline" SFT has been described previously, but our study provides evidence that "borderline" SFTs are more likely to recur compared with benign tumors without any atypical features.⁹

Findings of hypercellularity, vascularity, hemorrhage, and necrosis, as well as increased risk of recurrence, were classic characteristics of hemangiopericytomas (HPCs) prior to the merger of SFT/HPC in the 2002 WHO classification.⁴⁰ Interestingly, a recent retrospective study of combined CNS SFT/HPCs showed that a grading system based on high-risk pathologic features (necrosis, mitoses, hypercellularity) predicted PFS and OS, whereas histologic classification (SFT/HPC) and extent of surgery (subtotal/complete resection) did not correlate.³⁸ A review of 110 SFT/HPC cases found that increased mitoses and necrosis predicted time to metastasis; pleomorphism and hypercellularity were not predictive.³⁵ Our results support consideration of SFT/HPC as a pathologic and clinical continuum and development of pathology-based risk-stratification models.

In our series, two initially benign-appearing SFTs evolved malignant features in subsequent recurrences, which have also been described elsewhere.^{17,23,27} One explanation could be existence of a few cells with atypical genetics that were left behind after resection or micrometastasized. Supporting this concept are "dedifferentiated" SFTs wherein "classic" histologic patterns lie adjacent to high-grade sarcomatous areas, frequently with loss of CD34 staining and p53 and p16 overexpression in the high-grade portion.^{4,39} However, recent sequencing data from 51 benign and malignant SFTs including extrathoracic locations

showed a conserved gene fusion event between NAB2-STAT6, leading to transcriptional activation of EGR1, suggesting a common biologic basis.⁴¹ It remains unknown whether HPCs also possess this fusion protein. Further understanding of the activity of downstream targets of NAB2-STAT6, or the induction of subsequent mutations, may help to explain the differences in histologic appearance, dedifferentiation, and clinical behavior within the SFT/HPC spectrum.

In summary, SFTs/HPCs must be recognized as a spectrum of neoplasms with highly disparate clinical outcomes. While frankly malignant SFTs carry the worst prognosis, our study supports that extrathoracic and “borderline” SFTs with any of England’s criteria should be considered higher-risk tumors. As prospective validation of retrospective data will be challenging in rare tumors, at our institution we recommend surveillance imaging for up to 10 years, increasing the screening interval after 2 years, based on the plateaus of RFS (Fig. 1d, e). Prompt local management of recurrent SFTs is paramount, given the paucity of effective systemic therapy. Continued investigation of SFT pathophysiology is vital for development of molecular and genetic prognostic markers as well as targeted therapies.

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FIG. 1.

Recurrence and survival based on location and histologic classification of solitary fibrous tumors. **a** Anatomic distribution of 83 solitary fibrous tumors (SFTs). **b** Histologic classification of 83 SFTs within thoracic and extrathoracic subgroups. **c** Number of recurrent SFTs by location, histologic classification, and pattern of recurrence (local or metastatic). **d** and **e** Kaplan–Meier analysis of the percent of SFTs free from recurrence over time. Log-rank test assessed for significant differences based on location and histologic classification. Median time to recurrence: malignant, 1.4 years; borderline, 1.2 years; benign, 5.8 years. **f** and **g** Kaplan–Meier analysis of overall survival, with log-rank test comparing differences based on location and histology.

TABLE 1

Association of demographic, historical, and pathologic features of solitary fibrous tumors with location and histology

	All N = 83	Thoracic N = 24	Extrathoracic N = 59	p Value (thoracic vs extrathoracic)	All benign N = 74	Benign (no atypical features) N = 54	Borderline (benign with atypical features) N = 20	Malignant N = 9	p Value ("all benign" vs malignant)
<i>Demographic</i>									
Median age (range), years	58 (18–87)	63 (42–84)	55 (18–87)	0.02 ^a	57 (18–87)	55.5 (18–86)	61 (36–87)	62 (37–83)	0.82
Gender				0.63					0.29
Male	39 (47 %)	10	29		33	21	12	6	
Female	44 (53 %)	14	30		41	33	8	3	
Race				0.89					0.50
White	61 (73 %)	18	43		55	37	18	6	
Black	13 (16 %)	4	9		12	10	2	1	
Other	9 (11 %)	2	7		7	7	0	2	
<i>Presentation</i>									
Asymptomatic, detected by imaging	27 (33 %)	18	9	<0.0001 ^a	26	18	8	1	0.26
Local symptoms	56 (67 %)	6	50		48	36	12	8	
Associated paraneoplastic syndrome	5 (6 %)	2	3	0.62	4	3	1	1	0.44
<i>Clinical history</i>									
Smoking	41 (49 %)	18	23	0.004 ^a	36	21	15	5	0.74
Personal history of benign soft tissue lesions	12 (14 %)	4	8	0.74	11	8	3	1	1
Personal history of cancer	19 (23 %)	5	14	1	17	10	7	2	1
Previous exposure to chemotherapy/radiation	10 (12 %)	3	7	1	10	8	2	0	0.59
Personal history of autoimmune disease	10 (12 %)	3	7	1	9	5	4	1	1
Family history of cancer or autoimmune disease	21 (25 %)	2	19	.03 ^a	17	14	3	4	0.22
<i>Pathologic data</i>									
Median size (range), cm	5 (0.5–32)	6.5 (0.8–19.5)	4.5 (0.5–32)	0.11	4.6 (0.5–19.5)	5 (0.8–16.5)	4.5 (0.5–19.5)	7.2 (2.5–32)	0.0024 ^a
<i>Histologic classification</i>									
Benign, no atypical features	54 (65 %)	15	39	0.80					

	All N = 83	Thoracic N = 24	Extrathoracic N = 59	p Value (thoracic vs extrathoracic)	All benign N = 74	Benign (no atypical features) N = 54	Borderline (benign with atypical features) N = 20	Malignant N = 9	p Value ("all benign" vs malignant)
Borderline, atypical features	20 (24 %)	9	11	0.09					
Malignant	9 (11 %)	0	9	0.06					
Immunostaining									
Histology only	10 (12 %)	8	2	0.0005 ^a	10	9	1	0	0.59
CD34				0.33					0.21
Positive	66 (80 %)	15	51		59	40	19	7	
Negative	7 (8 %)	0	7		5	5	0	2	
Not recorded	10 (12 %)	9	1	<0.0001 ^a	10	9	1	0	0.59
BCL2				1					0.31
Positive	41 (49 %)	5	36		35	22	13	7	
Negative	2 (2 %)	0	2		1	1	0	5	
Not recorded	40 (48 %)	19	21	0.0005 ^a	38	31	7	2	0.16

All data are numbers of patients unless otherwise indicated

^aSignificant p values

TABLE 2

Pathologic features and recurrences of location subgroups of solitary fibrous tumors

<i>Pathologic data</i>	Thoracic N = 24	Neurologic N = 24	Soft tissue N = 13	Visceral/intra-abdominal N = 22	p values (significant pairs)
Median size, (range), cm	6.5 (0.8–19.5)	3.25 (0.5–6.5)	6.5 (1–15)	5.9 (3.2–32)	0.001 (Visc vs neuro <0.0001 ^a)
Histologic classification					
Benign, no atypical features	15	14	11	14	0.26
Borderline, with atypical features	9	7	0	4	0.47
Malignant	0	3	2	4	0.89
Immunostaining					
Histology only	8	0	1	1	0.43
CD34					0.02 (visc vs neuro 0.04 ^a)
Positive	15	23	12	16	
Negative	0	1	0	6	
Not recorded	9	0	1	0	
Bcl2					0.82
Positive	5	16	6	14	
Negative	0	1	0	1	
Not recorded	19	7	7	7	
Positive/close margins (<1 mm)	6 (25 %)	9 (38 %)	9 (69 %)	4 (18 %)	0.01 ^a (soft tissue vs visc 0.004 ^a)
<i>Recurrence</i>					
Any recurrence (% of all tumors in location)	1 (4 %)	8 (33 %)	2 (15 %)	3 (14 %)	0.22
Local (% of recurrent tumors in location)	0 (0 %)	7 (88 %)	2 (100 %)	1 (33 %)	0.12
Metastatic (% of recurrent tumors in location)	1 (100 %)	1 (13 %)	0 (0 %)	2 (66 %)	
Recurrences with positive/close margins (% of recurrent tumors in location)	0 (0 %)	4 (50 %)	2 (100 %)	0 (0 %)	Thoracic: 1; neuro: 0.41 soft tissue: 1; visc: 1

^a Significant p values

TABLE 3

Clinical factors associated with recurrence of SFTs by univariate and multivariate analysis

Variable	Univariate		Multivariate	
	Odds ratio (95 % CI)	p Value	Odds ratio (95 % CI)	p Value
Age >55 years	1.3 (0.4–4.3)	0.77		
Gender (F)	1.4 (0.4–4.6)	0.77		
Extrathoracic location	6.5 (0.8–52.8)	0.06	5.1 (0.5–49.7)	0.16
Benign histology with atypical features (borderline)	4.3 (0.86–21)	0.08	10.3 (1.7–62.2)	0.01
Malignant histology	59.5 (8.4–420.9)	<0.0001	68.4 (8.2–572.4)	0.0001
Tumor size >10 cm	0.98 (0.2–4.0)	1		
Positive/close margins	1.6 (0.5–5.2)	0.54		

TABLE 4
Outcomes of SFT patients with recurrent tumors or who received local or systemic therapy in addition to surgery

Patient ID	Location	Histology	Treatment course	Outcome	TTR (years)	Follow-up (years)
17	Cerebellum	Borderline	Received stereotactic XRT on recurrence	NED	1.5	10.6
26	Retroperitoneum	Malignant	Resected, 6 cycles adjuvant AI	NED		10
33	Pancreas	Benign, no atypical features	Resected, adjuvant chemoradiation with gemcitabine for pancreatic adenocarcinoma component	NED		8.1
34	Brain, dura	Benign, no atypical features	Declined therapy on recurrence	Active disease	1	4.4
38	Frontal lobe	Benign, no atypical features	Partial resection, received stereotactic XRT to residual disease, recurrent edema/mass, resected	NED		6.8
40	Orbit	Benign, no atypical features	Recurrent three times after initial resection, resected, opted for no further therapy	Active disease	2.3	6.8
47	Orbit	Borderline	Partially resected, local growth three years later, resected, developed 2 small satellite nodules	Active disease	5.8	5.9
51	Kidney	Malignant	2 cycles AI for widespread disease	Died of disease	0.3	0.5
54	Temporal fossa	Borderline	Recurrent 6 years after resection, resection for 6 subsequent recurrences. Received adjuvant XRT after most recent resection	NED	0.7	5
58	Cerebellum	Malignant	Subtotal resection, received adjuvant XRT. Intracranial recurrence, resected. Developed leptomeningeal metastases, received palliative XRT	Died of disease	0.4	0.9
59	Soft tissue, arm	Malignant	Positive margins after initial resection, received adjuvant XRT. Recurred, resected with positive margins. Refused amputation	Active disease	2.6	3.6
61	Spine, C2	Malignant	Subtotal resection initially, recurred	NED	1.1	2.1
62	Orbit	Malignant	Recurrent 4 years after initial resection, received stereotactic XRT. 4 subsequent recurrences, resected each time	NED	2.2	3.2
66	Soft tissue, neck	Malignant	Resected, recurred and resected, adjuvant XRT	NED	4.5	7.6
68	Retroperitoneum	Malignant	Received neoadjuvant XRT, followed by resection with intraoperative XRT. Recurred with lung metastasis, resected	NED	1.4	2.4
73	Retroperitoneum	Malignant	Resected and received adjuvant XRT	NED		1.4
82	Pleural	Borderline	Resected, recurred with multiple metastases to bones and contralateral lung. Treated with cryoablation	Active disease	4.5	7.7
83	Kidney	Benign, no atypical features	Resected, metastatic recurrence to pancreatic head and liver, pathology malignant. Resected, no adjuvant therapy	NED	8.6	8.9

NED no evidence disease, XRT radiation, AI adriamycin/ifosfamide chemotherapy