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Presidential Address

The Enigma of Local Recurrence

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Abstract: Local recurrence has long been seen as a technical surgical failure to be avoided at all costs. This paper reviews the significance of local recurrence for the patient in terms of survival, using data derived from the study of extremity soft tissue sarcoma.
Key Words: Soft tissue sarcoma—Local recurrence—Microscopic margins—Survival.

Most presidential addresses begin, as is appropriate, with an expression of gratitude for the opportunity of holding such office. I am no exception. I am flattered to have participated in the preeminent Society of Surgical Oncology and for the privilege of taking a leadership role in such an association.

As you all appreciate, leadership reflects the efforts of innumerable members. To mention them individually by name runs the risk of neglecting to recognize, in a moment of stress, others equally deserving. Nevertheless, it is clear that the officers, the chairmen, and members of the committees provide a substantial strength to the organization. The support of executive secretaries, past presidents, and members of the Executive Committee all bind the organization and provide the foundation and the building blocks for the subsequent achievements that are so easily attributed, wrongly, to the President! I personally thank them all, individually and collectively.

At a time like this it is appropriate to reflect as to why one is fortunate enough to attain this position: a rather pleasant, "why me?" We are all fortunate to be members of a profession that in the main rewards us for doing what we like to do. Reflection is appropriate as we are inclined to think, "I earned it." I would suggest that most of what we achieve is a matter of luck. Luck in where, when, and to whom we were born, and luck in the genetic material with which we were endowed. In many ways, we are accidentally privileged. True, we can build on these given attributes, and persistence, diligence, and effort do help! But without these fortunate accidents of time and place, many of us would be less privileged. So I asked, "why me?" Not finding an obvious answer, I went looking for the data to see what I could learn from my predecessors!

First, is such a position an hereditary one related only to site of birth? Or, more likely, site of education? In Table 1, I have indicated the medical schools attended by the presidents of this Society since 1940. Not surprisingly perhaps, the Harvard Medical School leads that coterie, followed closely by Universities in New York State, but with an appropriate distribution throughout the nation.

I was unable to find anyone who was, as they say, an "FMG". This, then, is my singular distinction in the leadership role in the Society! No doubt, when I imagine that I might have been elected on merit, any aspirations of self-importance can be dismissed, as I recognize that this is just the natural evolution of the preoccupation in the United States with minority representation, and when you look for a minority, the more remote and obscure of origin the better!

When we examine the places of employment of the Presidents at the time they held office (Fig. 1)

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This paper is dedicated to Kristen Ann Carr, whose life was prematurely taken by the "enigma" of local recurrence.

TABLE 1. *SSO presidents–medical schools*

State	School	n
CA	UCSF	1
CT	Yale	2
DC	Howard	1
	Georgetown	1
GA	Emory	2
IL	Univ IL	1
	Chicago	1
IN	Northwestern	1
LA	Tulane	1
MA	Harvard	7
MN	Univ MN	1
NC	Duke	1
NE	Univ NE	1
NY	NYU	3
	SUNY	7
	Columbia	5
	Cornell	3
OH	Ohio State	1
OR	Univ OR	1
PA	Univ PA	1
	Temple	1
TX	Univ TX	1
VA	Univ VA	3
WA	Univ WA	1
WI	Univ WI	1

these are somewhat more diverse. In the early years, they represent the early origins of the Society, founded as it was, as an alumni group of the Memorial Sloan-Kettering Cancer Center on June 10, 1940, honoring James Ewing, pathologist and cancer treatment pioneer. It is interesting that at the first meeting after the war, held in 1947, it was decided to form a Board of Oncology, similar to, if not within, the American Board of Surgery. Little has changed in terms of the discussions over the years. The first symposium of this Society, reflected in this national meeting, was held at Memorial Sloan-Kettering Cancer Center in 1948. In 1975 the organization became the Society of Surgical Oncology,

TABLE 2. *Localized extremity soft tissue sarcoma univariate risk factors for local recurrence at five years*

	LR (%)	*p*
Presentation		
Primary	20.8	0.0001
Recurrent	39.7	
Size (cm)		
<5	19.8	0.025
5–10	27.4	
>10	27.2	
Margins		
Positive	40	0.0001
Negative	20	

Memorial Sloan-Kettering Cancer Center, July 1982–August 1994, n = 1,041.

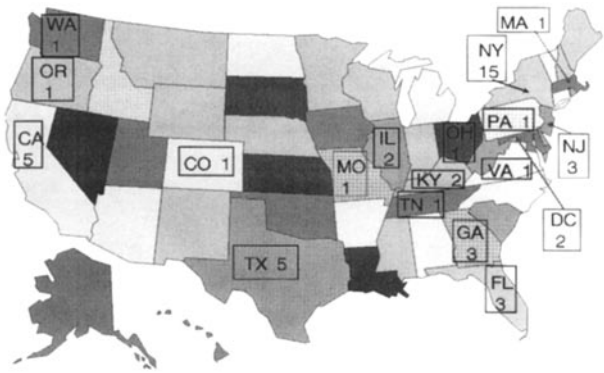

FIG. 1. States of employment of SSO Presidents at the time they held office

with increasing diversification away from an organization of graduates of the Memorial Sloan-Kettering Fellowship Program. This 21st anniversary of the Society of Surgical Oncology has, optimistically, weathered better than Old Memorial on 106th Street in New York City.

But to return to my more scientific topic: Presidential addresses are often those in which the President articulates his or her personal opinions about some aspect of "The State of the Nation." I have always felt somewhat uncomfortable with such an approach, being concerned perhaps that those who dare to speak of the future usually play little part in it! I have chosen instead to address the subject that has intrigued me, as it has many others, for some considerable time. That is the subject that I have chosen to call, "The Enigma of Local Recurrence."

I hope in this discussion to illustrate that surgeons can be interested not only in the pragmatic issues of local recurrence, but also in the philosophical significance of examining a problem in some depth along with the available data, as generated by surgeons. Because of a long-standing interest in soft tissue sarcoma, I will choose to support some of my observations with data that we have obtained from the soft tissue sarcoma database set up in 1982. That database now contains approximately 3,000 patients who have been admitted with soft tissue sarcoma spread over all sites of the body. The collection, accumulation, and analysis of these data are a reflection of the diligence of the multitude of people with whom I have been fortunate enough to work. Why choose soft tissue sarcoma to examine the question of local recurrence? Extremity sarcomas are the ideal model since the abolition of local recurrence is, in theory, simple: an amputation—a gross and gruesome solution!

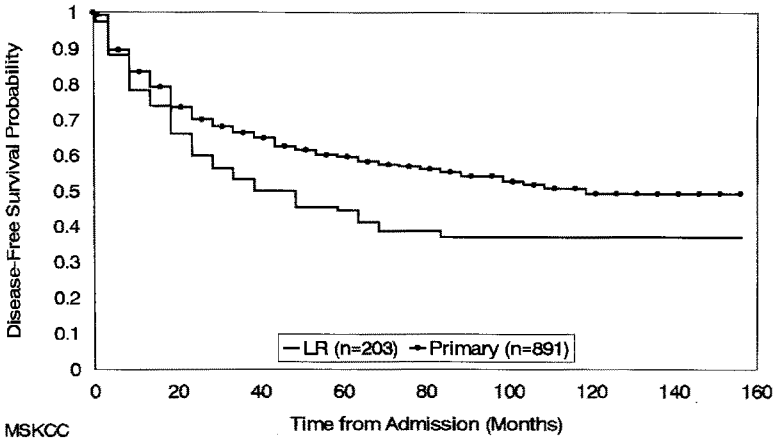

FIG. 2. Disease-free survival probability of primary localized lesions vs recurrent localized lesions. LR = local recurrence, $p = 0.0004$.

SIGNIFICANCE OF LOCAL RECURRENCE

What is the significance of local recurrence? For the surgeon it is clear: it reflects on his or her perception of his or her abilities as a surgeon to provide a complete resection with no subsequent complications. Local recurrence for the surgeon is often viewed as a surgical failure that impugns the inadequacies of the operator, and, among colleagues almost imputes the surgeon's manhood or womanhood! I believe that is quite erroneous. Surgeons, like St. George, like to slay the dragon, but, like St. George, slaying the Irish dragon by amputating the head of the Irish people, it makes little sense to amputate the limb if the dragon of metastasis survives. In the main, local recurrence is not, and should not be, a reflection on the adequacy of the surgeon. Nobody would propose a cavalier approach to a procedure that has such severe consequences. The significance for the patient, and his or her extremity is very real.

In case any of you think that by my approach to the *statistical* significance of local recurrence I am not acutely concerned with the personal and technical challenges of local recurrence, let me simply illustrate how difficult this can be. The significance of the recurrence for the patient can be devastating. A problem, once perceived as solved, recurs; a problem once simple is now complicated; a problem once overcome is now to be faced again with a drastic solution: hemipelvectomy, forequarter amputation, with and without tissue transfer and reconstruction.

What are the factors associated with local recurrence? In an analysis of 1,041 extremity patients, those who presented to our institution with a local recurrence were more likely to have a further local recurrence (1), i.e., in the next five years, the subsequent local recurrence of those patients presenting to us with a local recurrence was increased twofold. A patient with a large lesion >5 cm had about a 40% greater chance of a local recurrence than a patient with a lesion <5 cm (Table 2). It is important, however, to emphasize that one prognostic variable may be highly correlated with another but

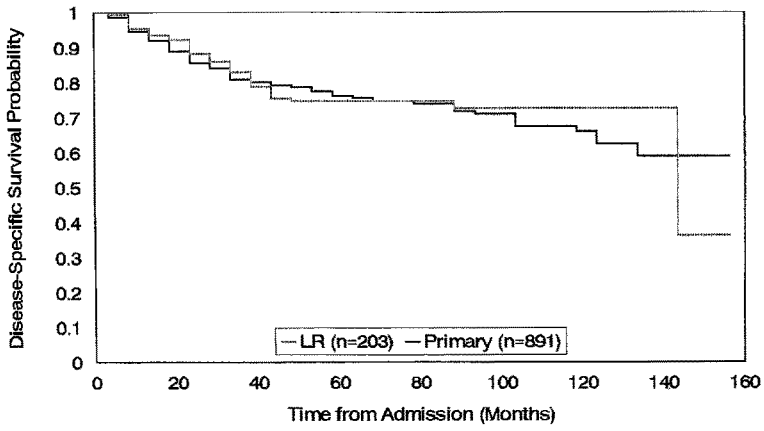

FIG. 3. Disease-specific survival probability is the same for patients with localized disease of the extremity, either as a primary lesion or with local recurrence. LR = local recurrence, p = N.S.

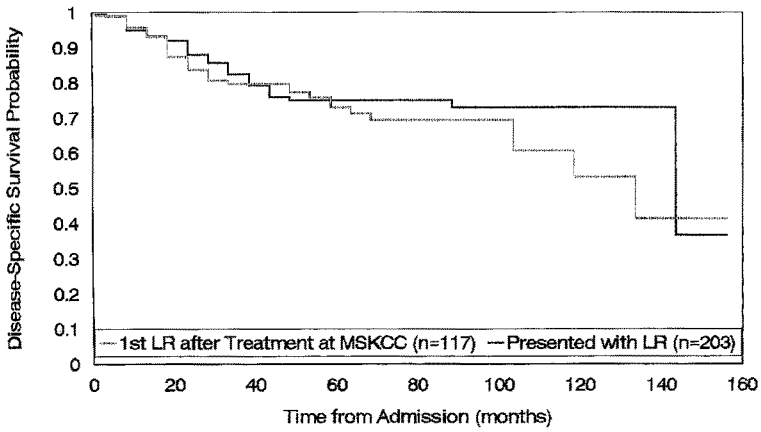

FIG. 4. Disease-specific survival curves are not different for patients with a first local recurrence after treatment at MSKCC and those with LR as a referral event. p = N.S.

may not be an independent variable. A knowledge of such interrelationships is essential.

Local Recurrence and Disease-Free Survival

What about the significance of a local recurrence in terms of disease-free survival? If we examine the patients who are referred to us with a local recurrence, as opposed to those who are referred with the primary tumor still intact or biopsied, the assumption might be that patients who are referred with a local recurrence are more difficult and more complicated patients. Another explanation, however, might be that the patient is referred with a local recurrence after the most simple studies designed to examine the presence or absence of metastatic disease have been performed. For example, a patient is not referred with a local recurrence if widespread pulmonary metastasis appears on the chest x-ray. As a result of a potential referral bias, it is therefore impossible to claim that patients referred with a local recurrence are *necessarily* a more difficult group. However, if we examine our own data, primary localized lesions can be compared with recurrent localized lesions in terms of disease-free survival (Figure 2). Patients who present with a local recurrence have a worse disease-free survival than those who do not. This is not surprising, as disease-free survival obviously includes patients who had a subsequent recurrence, and we know (Table 2) that patients who present with a local recurrence have a greater risk of subsequent recurrence, both local and distant.

Local Recurrence and Disease-Specific Survival (Tumor Mortality)

When we examine the patients referred to us with localized disease of the extremity, either as a primary lesion or with local recurrence, the disease-specific survival (tumor mortality) is the same (Figure 3). This suggests that patients who present with a local recurrence have a greater risk of further local recurrence, but this does not necessarily increase their chances of dying of the disease! Clearly, a patient who presents with a local recurrence has a greater risk of having a subsequent recurrence than a patient who presents with a pri-

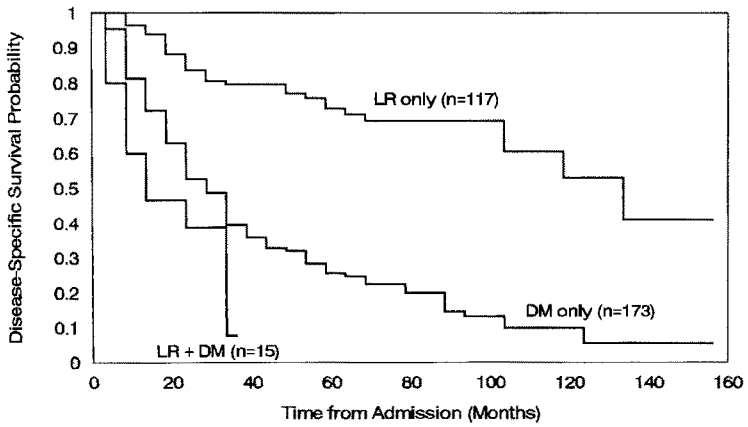

FIG. 5. For patients analyzed by *first* site of recurrence, disease-specific survival is dominated by those with metastatic disease. LR = local recurrence, DM = metastatic disease, p = 0.0001, LR vs DM; p = 0.009, DM vs. LR + DM.

mary localized lesion. But, is that a comment on our management, or a comment on biology? If we are concerned that local recurrence as a referral event is different from local recurrence after *we* have performed treatment in terms of disease specific (tumor) mortality, then we need to examine patients who present primarily to us and then have a local recurrence. Those curves should be different. Clearly, they are not (Figure 4). This is because *metastasis* is the primary cause of demise. This is the biologic reason. Presenting with a local recurrence or having a local recurrence after treatment at Memorial as a primary event affords the same risk of tumor mortality, because both now have the same risk of distant metastasis. Thus, if we look at patients who have a local recurrence as their *first* recurrence, then disease-specific survival (DSS) (tumor mortality) is effectively dependent on the development of metastatic disease (Figure 5). Why does anyone with local recurrence-*only* die of disease? Because this is recurrence by *first* recurrence, those with local recurrence have an increased risk of subsequent local and systemic relapse.

Disease-specific survival (Figure 3) is not different, but disease-free survival *is* different (Figure 2). Obviously, in disease-free survival, made up as it is of any form of recurrence, there would be a difference, whether the recurrence is local alone, metastatic alone, or local and metastatic. Clearly, while the numbers are small for those who present with local and metastatic disease (Figure 5), this raises the intriguing possibility that a local recurrence in combination with a synchronous metastatic recurrence is worse than a metastatic recurrence alone. Small solace, but some indication that local recurrence is to be avoided! Certainly, local recurrence alone is unlikely to be a significant cause of death in *extremity* sarcoma. As these curves are disease-specific (tumor mortality) survival curves, it would suggest that a local recurrence as the first event presumably goes on to be associated with a metastatic recurrence and that is the predominant cause of demise.

TABLE 3. *Localized extremity soft tissue sarcoma significant adverse prognostic factors in disease specific survival*

High grade
Size >5 cm
Deep location
Positive margins
Local recurrence at presentation
Lower extremity

Memorial Sloan-Kettering Cancer Center 1982–1994, n = 1,041.

The Influence of Tumor Grade

One might infer, therefore, that a local recurrence is a harbinger, at least for many patients, of a subsequent metastatic recurrence, and disease-specific demise. To examine this question more closely, we should analyze those patients whom we believe to be at significant risk of metastatic disease rather than those who are predominantly at risk of a local recurrence. We have spent some considerable time identifying patients who are at high risk of systemic recurrence and death (Table 3).

Careful analysis of over 1000 localized extremity lesions has shown that the prognostic factors for local recurrence and distant recurrence are different (1). Table 3 outlines factors at presentation and factors found postoperatively that influence disease-specific (tumor mortality) survival. Factors that identify patients at-risk at presentation are those with large, deep, high grade lesions of the lower extremity as well as a local recurrence at presenta-

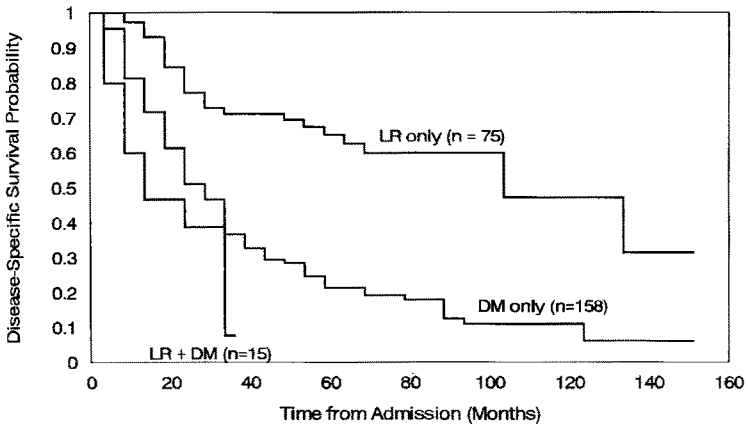

FIG. 6. Patients who have a local recurrence of a high-grade lesion as the first presentation of recurrence are more likely to have a subsequent metastasis and die of that metastasis. LR = local recurrence; DM = metastatic disease, p = 0.0001, LR vs. DM; p = 0.015, DM vs. LR + DM.

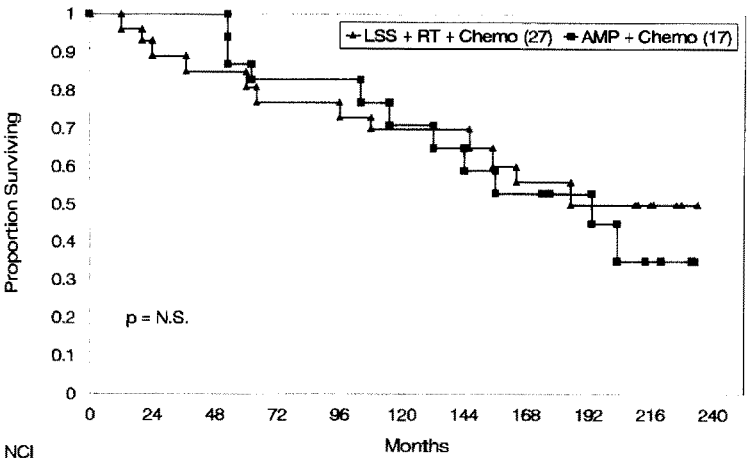

FIG. 7. Overall survival in the study from the National Cancer Institute between these two groups was not different. AMP = amputation, LSS = limb-sparing surgery, RT = radiation therapy. Redrawn from data supplied in Ref. (2).

tion. If we look only at DSS for those patients with high-grade lesions by their first recurrence presentation (Figure 6) compared with both high and low grade lesions, as seen in Figure 5, the curves are similar in shape, but worse overall, especially for the local-only group. This suggests that patients with a local recurrence of a high grade lesion as the first presentation of recurrence are more likely to have a subsequent systemic recurrence and rapid demise. Obviously those with high grade, deep lesions are most likely to have metastases, so that the metastasis curves of Figures 5 and 6 are almost identical.

Very few patients with low grade lesions actually die of an extremity local recurrence and metastatic recurrence is uncommon. When we look at low grade lesions with a local-only recurrence at presentation, they clearly do better than those who have metastases at presentation, thus emphasizing that metastasis is possible, but uncommon, in patients who have low grade lesions. This should be viewed in the context of the total number of low grade lesions, where only 6% of all primary presentations ever recur with metastases. Nevertheless, a local recurrence in a patient with a low grade lesion does increase the risk, albeit small, of a subsequent metastatic recurrence.

LOCAL CONTROL AND OVERALL SURVIVAL

The issue of the significance and impact of local recurrence on future systemic recurrence and survival has been addressed in two randomized trials. The first, from the National Cancer Institute, recently updated by Drs. Rosenberg and Yang (2), randomized patients to receive limb-sparing surgery and radiation therapy or amputation. The results of this study showed that the patients who were treated conservatively with limb-sparing surgery and radiation had a greater prevalence of local recurrence (approximately 25%), than those randomized to receive amputation, but this was not statis-

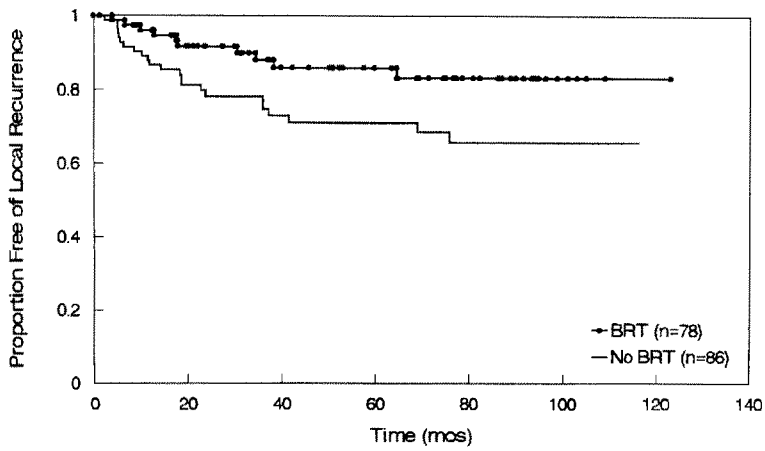

FIG. 8. There was a marked diminution in local recurrence by brachytherapy [BRT] in the randomized trial. $p = 0.02$. Reproduced with permission from ref. (3).

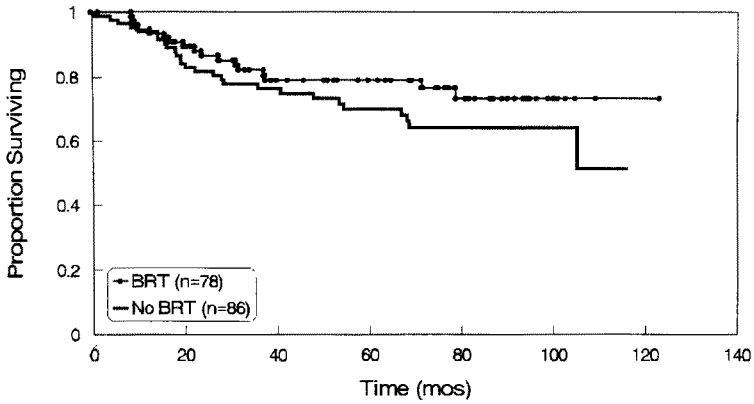

FIG. 9. Overall survival, at a median follow-up of 76 months, was not different for BRT vs. no BRT. $p = 0.28$.

tically significant. Disease-free survival for all recurrences and overall survival (Figure 7) between these two groups was not different. Thus, despite the ultimate operation designed to minimize local recurrence, i.e., amputation, there was no impact on overall survival for these patients in a randomized trial. All patients did receive chemotherapy, and it is possible that the chemotherapy was the factor that abrogated any difference and translated into survival equivalence. If this was correct, then all of the randomized trials of adjuvant chemotherapy should have been positive! They were not.

The second randomized study was our own prospective randomized trial, which examined the benefit of adjuvant radiation delivered as brachytherapy in patients who underwent a limb-sparing operation. A marked diminution in local recurrence was demonstrated (Figure 8) (3). Overall survival, at a median follow-up of 76 months, however, was not different (Figure 9). This is consistent when one examines those patients who are at significant risk of subsequent metastasis, i.e., patients with high grade lesions. It is clear that the benefit in local control with this type of adjuvant radiotherapy is to patients with high grade lesions, the group at greatest risk of tumor or disease-specific mortality (Figure 10).

These two studies are important as they address the inherent and specific concern of overall survival for patients similar in every respect at the point of entrance to the study. When randomized to receive a procedure, i.e., amputation or limb-sparing surgery and radiation therapy, to minimize local recurrence, although such a prediction can be achieved, overall survival is not significantly different in either group [Figure 9]. We can only conclude that while local recurrence is a poor prognostic factor for further local and systemic recurrence and decreased survival, decreasing local recurrence will not necessarily impact on survival where survival is dependent on the presence or absence of the development of systemic disease!

SIGNIFICANCE OF A POSITIVE MARGIN

If local recurrence is bad for the patient and the surgeon, and is associated with, and probably pred-

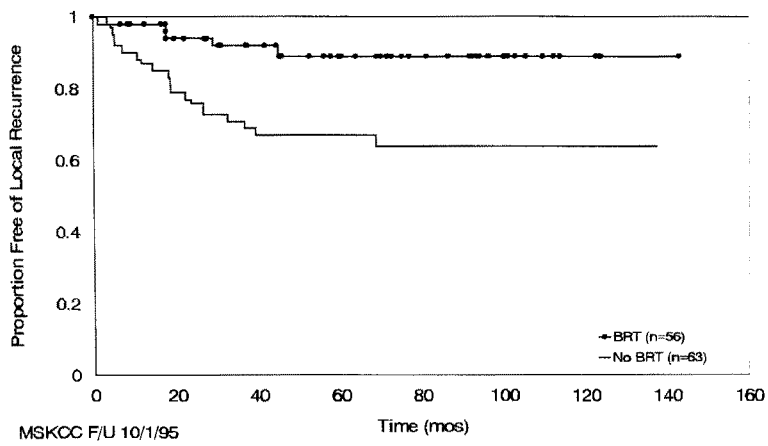

FIG. 10. The benefit of brachytherapy in local control is to high-grade lesions. $p = 0.0025$, BRT vs. no BRT. Update of data from Ref (3).

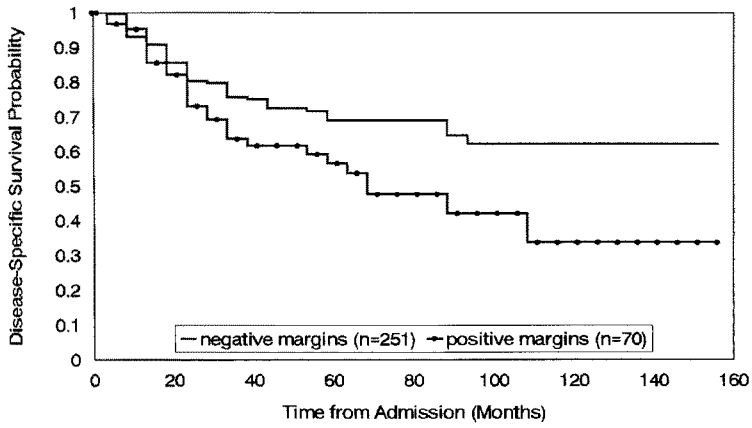

FIG. 11. Microscopic margin is a dominant factor in disease-specific survival probability for primary, high-grade, localized extremity soft tissue sarcoma. $p = 0.01$.

icates risks of death from disease, what about patients who have a positive microscopic margin? Surely, a positive microscopic margin is more likely to have local recurrence; this is clearly so (Table 2) and is a dominant factor. Patients who have a positive microscopic margin have a greater likelihood of recurrence. In fact, approximately two-fold. Disease-specific survival has a known set of preoperative (Table 3), and postoperative risk factors including positive margin. If we examine only those patients who have primary large, deep high grade lesions, then microscopic margin is a dominant factor associated with local recurrence (4) and disease-specific survival (tumor mortality) (Figure 11). A positive margin in a low grade lesion does translate into increased local recurrence (Figure 12) but not necessarily into a disease-specific death! However, the influence of a positive microscopic margin, as examined by others, while clear in terms of local recurrence, continues to be a matter of debate in regard to distant metastasis and disease-specific (tumor) mortality (4).

What then, if we try to minimize the risk of a positive margin (i.e., presumably residual microscopic disease), will that translate into lesser local or systemic recurrence? Another approach, in a non-randomized fashion, further obfuscates the problem. Of 876 patients examined with localized primary extremity sarcoma, 558 underwent definitive radical resection at our institution and 318 underwent a re-resection after undergoing excisional resection elsewhere (5). Local recurrence-free survival was the same! Five year disease-specific survival after the definitive resection, i.e., one operation, was worse than that for re-resection, i.e., two operations (Figure 13). What does that mean? Does it mean that re-resection of those patients who *could* be re-resected prevented local recurrence, or that those operated upon by a single operation at a referral institution were biologically worse? Is it conceivable that we, believing in our own infallibility, do not resect our own patients with a positive margin, but we do resect other patients with a positive margin? A sobering thought!

Multivariate analysis for disease specific survival suggested that re-resection was an independent favorable factor, emphasizing the difficulty in interpreting non-random data! Thus, re-resection did *not* impact on local recurrence, although some patients may have died of metastatic disease before local recurrence was manifest. If we look at patients who *still* have positive margins after the first operation (one operation) or after re-resection (two operations) disease-specific survival is improved by re-operation, suggesting a more biologically favorable group (Figure 14).

Obviously then, in non-random fashion, this

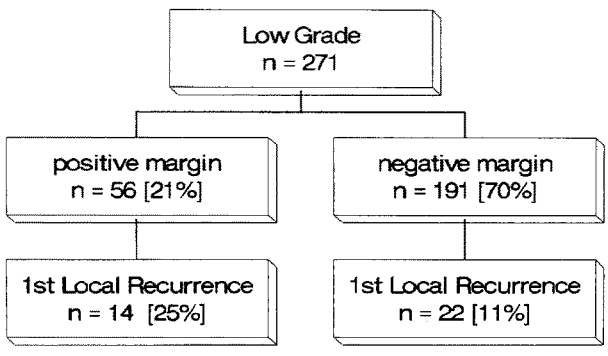

FIG. 12. Organization chart for low-grade localized extremity soft tissue sarcoma: A positive margin in a low-grade lesion does translate into increased local recurrence, but not necessarily into disease-specific death.

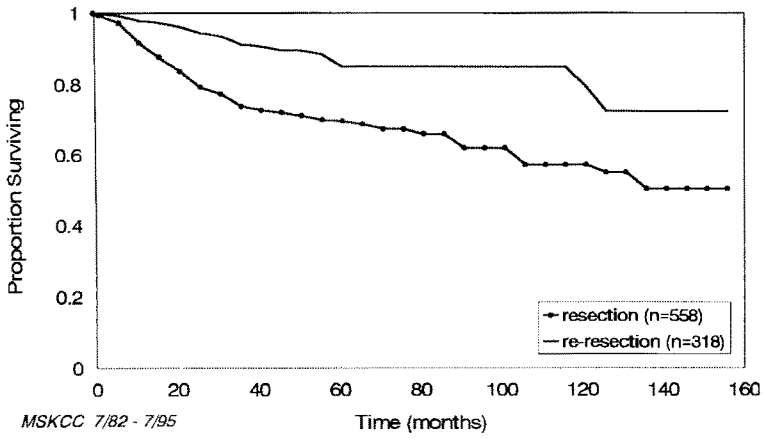

FIG. 13. Disease-specific survival for patients who presented to MSKCC from another institution and underwent a radical re-resection compared with those who underwent resection. $p = 0.0001$.

would suggest that microscopic disease, when present or suspected, should be re-resected. Unfortunately, of course, patients undergo re-resection where it is practicable. Re-resection is not practicable in those patients with a positive microscopic margin after the first maximum attempt at limb-sparing operation, other than by amputation. If we examine only those with a positive margin, re-resection was still an independent factor in metastasis-free survival. This enigma further emphasizes the importance of prospective, randomized trials to examine any issue.

The issue of a positive microscopic margin is, however, a complex one. If microscopic margin is so important to local recurrence and survival, why do *all* patients with positive microscopic margins not recur locally? Why, if 24% of single operation patients had a positive margin, did only 20% recur locally, and why, if only 8% of re-resections were still positive, did 20% recur locally? Yet, if we look at survival by margin, re-resection (i.e., a decrease in microscopic margin) did help. Presumably those patients *able* to have a re-resection had inherently a less "biologically serious" lesion than those first resected. What is the significance of such an observation? Is the definition of a positive microscopic margin imprecise, incorrect or irrelevant? We have concluded it is not irrelevant, given the powerful association with recurrence and metastasis, but how close is positive? Definitions of a positive margin vary widely in reported series.

If positive microsopic margin is so important, then we may be able to observe the consequences within the confines of our prospective randomized trial. Our recent analysis (3) suggested that patients with positive microscopic margins were appropriately equally distributed between the groups in our randomized trial. This suggests that local recurrence was the same in patients with a positive microscopic margin, whether or not they received radiation. Conversely, radiation therapy limited local recurrence in patients who had negative microscopic margins (Figure 15). Interestingly, margin status did not predict survival or disease-specific survival in the randomized trial nor did brachytherapy alter overall survival in high grade patients (Fig-

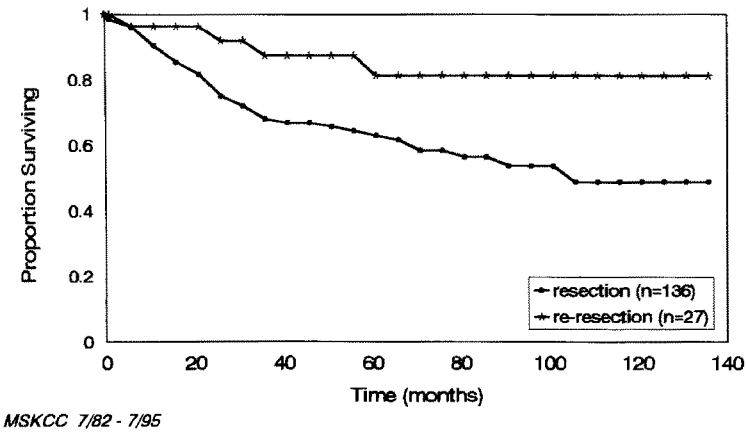

FIG. 14. Disease-specific survival in extremity soft tissue sarcoma, positive margins only, for resection vs. re-resection. $p = 0.01$.

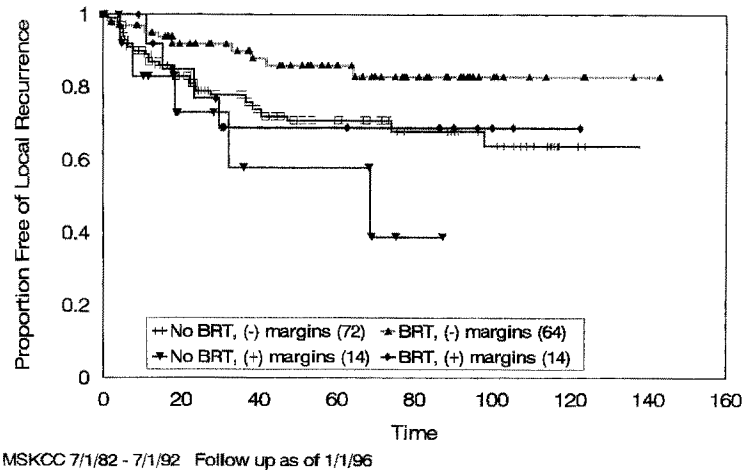

FIG. 15. Radiation therapy limited local recurrence in patients who had negative microscopic margins. $p = 0.02$.

ure 16), although the numbers are small in the positive margin group.

The only conclusion must be that the positive microscopic margin predicates greater local recurrence. Efforts to diminish local recurrence are effective but do not impact on overall or disease-specific survival. How then do we explain data for patients alive greater than five years without evidence of disease, who go on to have a subsequent distant metastatic recurrence (Figure 17)? In these patients microscopic positive margin of the original excision was a factor in metastatic recurrence (Table 4)!

Summary

It is clear that every effort should be made to minimize local recurrence, which for patient and surgeon can be a devastating event. However, once such attempts have been made, local recurrence is more likely a biological commentary than a technical failure. Such observations should never be used to justify imprecise, inaccurate or cavalier operations. Survival, however, would seem much more dependent on risk factors for metastases. Unfortunately, it appears that factors associated with a local recurrence are also associated with a distant metastasis.

Conclusions

So, what does it all mean? Does it pass the test of, "To be different, it must make a difference?" Does it make a difference? Clearly, I like to think so, but perhaps in a way that is not so obvious. The examination of the significance of local control has, I hope, been put into some perspective. In doing this, the exercise has challenged many besides myself. More importantly, the data on which this is based has set an example for countless fellows to identify a problem, however vaguely; to begin to record information designed to ask a question, and to answer

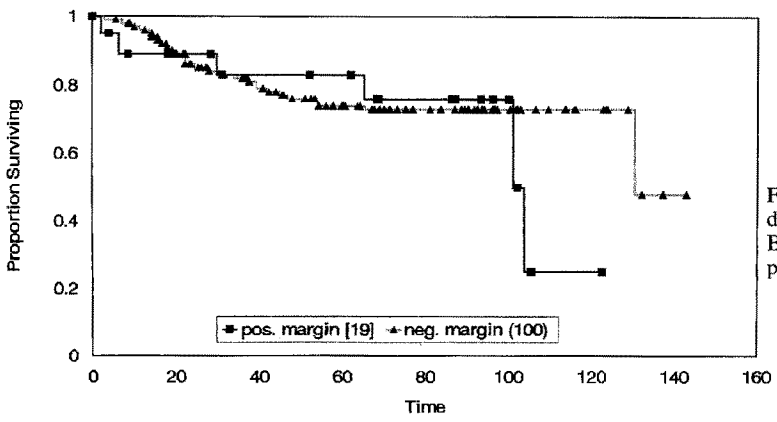

FIG. 16. Margin status did not predict survival or disease-specific survival in the randomized trial of BRT, nor did BRT alter overall survival in high-grade patients.

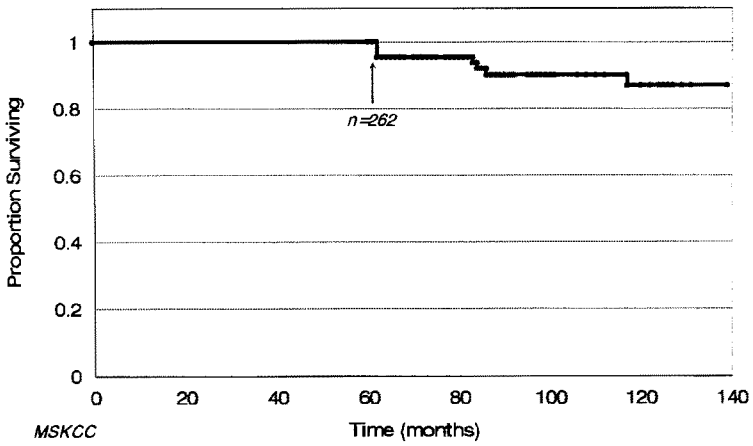

FIG. 17. Metastasis free survival in extremity soft tissue sarcoma. Patients alive > 5 years without evidence of disease, go on to have a subsequent metastatic recurrence.

it; and to undergo the realization that in the process other questions will be identified and other questions answered. Surely a worthy goal is to encourage other minds to ask more penetrating, more incisive, more thoughtful questions than we can ourselves.

But again, it does make another difference. For the patient, it is not always that we would deliver interminable life, but that we would impact upon the quality of that existence, by addressing not only the primary tumor, but the total well being of the patient. The tired and shopworn "holistic" approach is associated with those on the fringe of medicine, when in fact it has been the central theme for the majority of surgeons for decades. Why are we so frightened of embracing this mantle, or at least acknowledging that that is what we do every day, albeit within the confines of a critical, scientific approach? Is it not valuable to know the *real* risks of recurrence and survival for the patient? Or more importantly, which patient needs our efforts at aggressive treatment? Which patients are at risk for local recurrence, which, however frightening or potentially disabling, will not necessarily be a cause of their demise? How important is it to recognize and prepare for the fact that that all may not be successful, that outcome may not be favorable? Perhaps as an apologia for ourselves, we recognize that all local recurrences, all deaths, are not surgical or personal surgeon failures.

Databases such as these are valuable because they encourage the questioning and examining of apparently self-held truths, either to confirm or to deny them, or to bring us to the realization that hidden in our ever increasing mountains of computer generated figures and tables there are some truths, but not absolute truth. Even when we use the best current approach, the randomized trial, truth is a goal, not a reward! The converse is also true: my own growth and thought about these processes would not have been possible without the stimulation of fellows and colleagues and the assistance of innumerable others. To them should go any kudos for anything that I might have learned. I will have the joy of knowing that a few more people think a little more thoughtfully about this, and hopefully, about other questions. Moreover, the rewards of a life lived with gentleness and compassion can help not only the patient, but for many of us can serve as the stimulus to practice the art *and* the discipline of surgery.

I thank you all for the privilege of commentary.

TABLE 4. *Extremity soft tissue sarcoma: Multivariate analysis of disease free survival*[a]

	p Value	Risk ratio
Local		
Age	0.03	2.1
Margin	0.01	2.1
Metastatic		
Depth	0.03	4.6
Margin	0.02	2.6

Memorial Sloan-Kettering Cancer Center July 1982–July 1989; follow-up July 1994.

[a] Patients alive greater than five years.

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