Preface

The management of bone and soft tissue sarcomas

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The management of bone and soft tissue sarcomas has evolved tremendously over the last 25 years. Amputation as the sole treatment has given way to a multidisciplinary approach that relies on the expertise of surgical, medical and radiation oncologists who are valiantly supported by imaging specialists, cytopathologists, geneticists and molecular biologists. Together, the advances in surgical technique and instrumentation, adjuvant therapy and basic knowledge of tumour biology has resulted in a dramatic improvement in the control of local and systemic disease. For a class of malignancy that accounts for less than 1% of all neoplasms, the improvement in disease free survival from less than 20% to over 75% is one of the most encouraging of all cancers. In developing newer and more aggressive therapies, many advances have been matched by controversies which have stimulated further quests to minimise over-and undertreatment.

With such dramatic improvements in survival there has been greater demands on the Orthopaedic Oncologist to perform more limb sparing surgery. In the late 70's major complication rates from attempted limb salvage was as high as 30%, and many patients eventually underwent amputation. However, with a better understanding of the effects of adjuvant chemotherapy and radiotherapy as well as more judicious use of soft tissue reconstructive techniques, the frequency of neurovascular or wound complications has markedly diminished. Additionally, the risk now of local recurrence is similar for limb sparing or ablative surgery without any increase in the mortality of patients who undergo limb salvage. Today, most patients would be offered the option of limb sparing surgery as the primary surgical option.

Musculoskeletal tumour surgery has been well supported by the research and developments in the prosthetic industry. Improved biomaterials and prosthetic designs have enhanced the longevity of implants, many of which are essential for mobile reconstructions. Furthermore, improvements in bone banking techniques and the use of allografts have added greater scope to the surgical options for reconstruction which now include biological and non-biological methods and a combination of the two. Further advances are still being sought in regard to the fixation and articulation of the prosthesis. Paediatric limb prostheses are now being built which allow elongation of the limb to avoid large limb length descrepancies that were previously common amongst children undergoing limb sparing surgery.

One of the most important advances in sarcoma management has been in the field of medical imaging. After plain radiographs, magnetic resonance imaging has had the greatest impact on delineating the tumour. Through this modality, the intramedullary, cortical and extraosseous extent of tumour can be accurately mapped, and the lesion's proximity to vital structures can be clearly appreciated. The sensitivity of this modality permits far better planning of surgical margins which not only decreases local recurrence but also improves the potential for limb sparing surgery. MRI is well supported by nuclear medicine which with its advances in functional imaging can now identify tumour through its own metabolic activity rather than the response of the surrounding tissue to tumour presence.

Radiotherapy has had a major impact on the local control of soft tissue tumours, and its use is now routinely combined with surgery. Together, surgery and adjuvant radiotherapy can prevent local recurrence in up to 90% of cases. While the use of radiotherapy is not new, its importance in preventing local recurrence without an impact on survival is only now being accepted. Conventional radiotherapy via an external beam is commonly used. Alternative or supplemental techniques include intraoperative irradiation and brachytherapy which allow more localised delivery of radiation. Improved understanding of tumour and radiation biology has helped to minimise the serious local side-effects of earlier times.

Chemotherapy has had a major impact on the survival of patients with bone sarcomas. Modern chemotherapy which includes methotrexate in various combinations with adriamycin, ifosfamide or cisplatinum is responsible for 5 year survival rates of over 75%. Initially, chemotherapy was used in the post-operative setting but now, chemotherapy is an essential part of the presurgical management (neo-adjuvant) of bone sarcomas. Neoadjuvant chemotherapy is helpful in reducing the size of the tumour, decreasing the associated oedema of adjacent tissues and for developing a fibrotic capsule around the tumour which is helpful during the dissection of the tumour. Furthermore, the use of preoperative chemotherapy allows an assessment of its effect when the surgical specimen is examined histologically which permits post-operative regime modification.

By contrast, chemotherapy has been extremely disappointing in the management of soft tissue sarcomas. Major institutional studies of single agent or combination chemotherapy have not demonstrated convincing evidence for an effect on overall survival. Various methods have been tried which include intravenous and intraarterial routes, sometimes in combination with regional hyperthermia which has resulted in significant local complications. While such aggressive methods have limited local recurrence when combined with surgery, there has been virtually no effect on survival.

The role of surgical extirpation of pulmonary metastases is currently being investigated. The rationale for pulmonary metastasectomy is that in approximately 50% of cases who metastasise, single lesions are noted. This implies that if the lesion is removed, the potential for cure remains. Several studies have demonstrated a survival benefit in patients with limited numbers of lesions. While primary tumour characteristics such as size and grade have been shown to be of importance in the behaviour of the tumour, the characteristic of the metastasis appears to be of prime importance for the survival of those who have metastases and who have undergone pulmonary metastasectomy. Stricter indications for this modality is currently being undertaken.

Cyto- and molecular genetics will occupy very important roles in the future of sarcoma management. Already an entire catalogue of chromosomal aberrations have been described for bone and soft tissue tumours. Many of these aberrations involve the translocation of genetic material from one chromosome to another and some have been shown to be unique to specific tumours such as synovial sarcoma, myxoid liposarcoma, Ewing's sarcoma and alveolar rhabdomyosarcoma. A more accurate identification of these tumours may assist in determining and testing different chemotherapeutic agents, as at present, the difficulty in establishing histological diagnoses may be one reason for the apparent lack of efficacy of chemotherapy in soft tissue sarcomas. Despite the number of chromosomal aberrations noted, few have been shown to have prognostic significance (ring chromosomes and additional genetic material on chromosome 19). The identification of the products of fusion genes from the translocation of genetic material from one chromosome to another and the availability of routine methods for performing laboratory analyses will have a major impact on the way tumours are diagnosed, classified and treated.

Without doubt the most important evolution in the management of bone and soft tissue tumours has been the concept of centralised treatment. It has been shown in numerous reports that centralised management which includes imaging, biopsy, surgery and chemotherapy results in better local control of tumour and fewer complications for patients. Each year, a major proportion of limbs are lost because of inappropriately performed biopsies carried out by surgeons who do not regularly treat tumours. The recurrence rates for tumours biopsied outside a tumour centre is signficantly higher than for those performed at a tumour centre. By developing centres of excellence for the treatment of musculoskeletal tumours, the risks to the patients are minimised and the potential for limb salvage are maximised. As these tumours represent only 1% of all cancers, the frequency at which most doctors will encounter such a lesion may only amount to 2 to 3 per lifetime, thus not providing the doctor with enough experience to manage the tumours adequately. Centralised management ensures that the expertise is maintained and the indications for specific techniques are developed. The *sine qua non* of centralised management is education of the referral source.

With each new development there has been a reassuring tide of questions which have tested the indications and applicability of it use, and which have forced critical analyses of that technique. Some of the major questions which remain controversial include

a) Limb salvage or amputation?
b) Simple or complicated reconstructions?
c) Should radiation therapy be included after all surgery for soft tissue sarcomas?
d) When is radiation therapy indicated and how should it be delivered in soft tissue sarcoma?
e) Should patients with soft tissue sarcoma receive off-protocol chemotherapy?
f) Is there an advantage for intraarterial chemotherapy as opposed to intravenous administration?
g) What criteria should be employed in selecting pa-

tients for soft tissue sarcoma chemotherapy?
h) Should there be a chemotherapy protocol for adults and another for children?
i) Should patients with pulmonary metastases receive chemotherapy?
j) How aggressive should pulmonary metastasectomy be?
k) How can the lack of consensus between pathologists be resolved?
l) To what extent should laboratory tests be performed to identify the histotype of tumours?
m) Is tumour histology and grade of soft tissue sarcomas important in the preoperative planning and surgery?
n) Is the lack of centralisation a failure of the referring source or the centre's ability to educate?
o) How can centralisation of tumour management be achieved?
p) Is the failure to refer to a centre negligent?

This symposium is directed to all those who have a specific interest in the management and study of musculoskeletal tumours. It is hoped that this meeting will provide a forum for discussion that may lead to some resolution of controversies that abound in this field and to the discarding of age old myths. The fruition of this symposium represents a concerted effort in both countries to expand the oncology network which in turn, may lead to greater collaboration between groups. The contents of this book are meant to shed some light on recent advances in clinical and basic science research and to give some insight into the current practice of sarcoma management.

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