Radiofrequency and atypical cartilaginous tumours

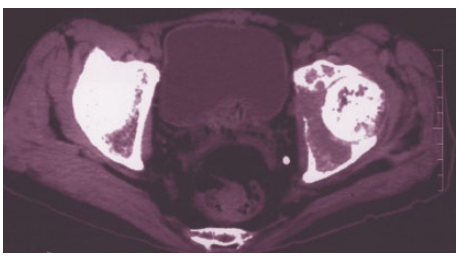
Surgery is the mainstay of treatment in patients with rare atypical cartilaginous tumours in the long bones, although a role for radiofrequency ablation in the management of these challenging-to-treat lesions has been established. With difficulties in establishing diagnosis and malignant potential, along with uncertainty surrounding outcomes, there has been recent interest in radiofrequency treatments. In a further development to the technique, this study group from **Groningen (The Netherlands)** sought to assess the influence of multiple needle placements and longer application of radiofrequency on the proportion of tumours that are successfully ablated.[1] The authors present a prospective review of 24 patients, all with a diagnosis of atypical cartilaginous tumours in the long bones, each of whom underwent CT-guided radiofrequency ablation (RFA) followed by curettage with adjuvant phenolization three months later. The material retrieved was assessed for viable tumour. In addition, gadolinium-enhanced MRI was performed before curettage check for residual tumour. Complete tumour ablation was achieved in 71% of cases. Where multiple needles were used, complete ablation was achieved in 83% of tumours ⩾ 30 mm. There was incomplete ablation in 8% of patients. Post-ablation gadolinium-enhanced MRI findings agreed with the histological results in 17 out of 23 cases, and there was a negative predictive value of 83%. As a result, the authors concluded that RFA could be used as an alternative to curettage when treating atypical cartilaginous tumours in the long bones. Multiple needle placement, in addition to longer duration of the ablation procedure, was an effective measure in achieving complete ablation in tumours ⩾ 30 mm. Diaphyseal tumours are more amenable for RFA treatment, possibly because of the heat sink effect (more heat loss to surrounding tissue is plausible in metaphyseal bone if the thinness of the cortex and the higher vascularity of the metaphysis are considered). Gadolinium-enhanced MRI could help guide post-ablation follow-up.

Survival after recurrence in osteosarcoma: a report from the Children's Oncology Group X-ref

Survival following treatment for paediatric malignancy has steadily improved over recent years, and continues to do so. However, in those children with a diagnosis of primary osteosarcoma, survival has been largely unchanged for the last 30 years. This group from **Los Angeles, California (USA)** have closely examined the factors that influence survival after a first relapse of osteosarcoma.[2] The authors used the survival after recurrence (SAR) data for 431 patients, all with relapsed osteosarcoma, as the primary outcome measure for this retrospective analysis from registry data. They found that the overall SAR at five years was 17.7%, and that 20.6% of localized patients and 9.0% of metastatic patients survived beyond five years after their first relapse. A long SAR in patients with relapsed osteosarcoma was associated in their model with younger age (adolescent and young adult patients showing a shorter SAR than children), the extent of disease at diagnosis (patients with primary metastatic disease have shorter SAR), site of relapse (a combination of bone and lung, in particular, being associated with poor outcome), and time to relapse (two years or more being favourable). Histological response was significantly associated with time to relapse, but was not predictive of SAR. Ethnicity, primary site of tumour, race, and gender were also not significantly related to SAR. Interestingly, the presence of a local recurrence was also not significantly associated with SAR. However, this may be because the number of events was so low that association may not be apparent in the models. In summary, patients with relapsed osteosarcoma were more likely to survive after first relapse if they were less than 18 years old, had localized disease at diagnosis, relapsed two or more years after diagnosis, and did not have a combination relapse (bone/lung). Unfortunately, the limitations of the available data meant that the authors were unable to assess the impact of post-relapse surgical management and/or chemotherapy on outcome, which is a suitable avenue for further research.

Perioperative chemo-/radiotherapy in primary soft-tissue limb sarcoma

There are several options in the management of soft-tissue sarcoma. Despite our wide experience with these lesions, and their relative frequency in the case of musculoskeletal tumours, the role of radiotherapy (RTx) and chemotherapy (CTx) in primary soft-tissue limb sarcoma patients is not precisely defined. In order to better understand the roles of these treatment modalities, a group from **Milan (Italy)** have retrospectively analyzed local registry data regarding 3752 consecutive primary soft-tissue limb sarcoma patients treated within a 20-year time span from three European centres and one North American centre.[3] As with all treatments for which there is no strong or universally accepted evidence base, the treating centre and tumour histology significantly influenced the chances of any particular patient being administered RTx and CTx during the study period. In this series, the use of RTx was associated with a better local outcome, especially in patients with myxoid liposarcoma, vascular sarcoma, and myxofibrosarcoma, without being associated with overall patient survival. CTx was not an independent prognostic factor for outcomes of osteosarcoma treatment in all patients. Propensity score analysis of the data showed that there was a trend towards a 5% survival benefit associated with CTx administration observed in a propensity score-matched analysis. These findings are consistent with the published literature, although in the case of this series, the difference did not reach statistical significance. The major weaknesses of this analysis (despite the large numbers) are the retrospective design and the fact that the choice of administering CTx or RTx was made independently in each centre. In addition, because the study enrolled only patients treated with surgery, patients progressing under neoadjuvant CTx and not operated on would have been excluded, thus biasing the results in favour of the CTx group.



The 'whoops' procedure in stage III soft-tissue limb sarcoma

Soft-tissue sarcomas are difficult to treat successfully as a result of their heterogeneity. This becomes more evident when tumours are encountered incidentally and excised in an unplanned or incomplete manner, usually by an inexperienced surgical team who have failed to make the diagnosis in preoperative assessment. This particularly comes to light when tumours present at an advanced stage where a high risk of relapse is present. Conflicting evidence exists regarding the approach to these incidental tumours, in terms of whether unplanned excision and subsequent

re-excision or planned primary excision yields the best results. A group from **Toronto (Canada)** have used data collected prospectively in a tertiary tumour service.[4] All patients with stage III soft-tissue limb sarcomas treated between 1989 and 2010 were identified and their records were examined for details of their diagnosis and treatment. Of this initial cohort, 500 patients were identified for inclusion in the study, 94 of whom were referred with incomplete excisions being performed outside the study centre. Of these 94 patients, 83% had tumour at the margins of the re-excision specimens. Rates of reconstructive surgery were higher in this group than in those who underwent primary planned excision. The rates of local recurrence, metastasis-free survival, and overall survival were no different between the two groups. Similar functional outcomes were found as well. This study suggests that, overall, survival is not influenced by the excision of soft-tissue sarcomas in a planned or more opportunistic manner, although surgical morbidity may be higher in those treated with incomplete excision in the first instance. However, this does not, based on the data used in this study, appear to give rise to inferior oncological outcomes in the longer term. Clearly, the ideal option is for patients to have a planned complete excision at a tumour centre; however, all is not lost if patients undergo a 'whoops' procedure first.

Machine learning and chondrosarcoma survival models

Machine learning, a form of artificial intelligence that conducts intensive computational interrogation with large data sets, is becoming increasingly common in complex surgical planning. There are a number of different algorithms but, in principle, machine learning uses permeations of potential models (either neural or non-neural) to establish the best fitting predictive model for any given condition. The techniques have been around for a long time, and form the basis of computer optical character recognition. Within orthopaedic oncology, machine learning has begun to be used in predicting patient outcomes in primary bone tumours. In this study from **Boston, Massachusetts (USA)**, a group examined the use of a machine learning system to predict the five-year survival in patients with chondrosarcoma, and also investigated the feasibility of delivering this system through a web-based portal suitable for everyday clinical use.[5] The group took data related to 1554 patients diagnosed with chondrosarcoma from the Surveillance, Epidemiology, and End Results (SEER) Registry, all of whom had primary diagnoses between 2000 and 2010. A raft of data related to diagnosis and treatment were collected on the SEER registry and survival at one, three, five, and ten years was calculated (92%, 82%, 76%, and 54%, respectively). From this data, four predictive models were constructed using boosted decision tree, support vector machine, Bayes point machine, and neural network models. The discrimination and predictive abilities of each model were then assessed. The authors found that discrimination and predictive ability were generally very good across the models, but that the Bayes point machine model was most successful in accurately predicting patient outcome. This model was then published in an accessible web-based app. As yet, the model remains unvalidated; however, as it is used more often and fed more data, it should give rise to an increasingly accurate, user-friendly model capable of informing patients and clinicians as to their overall prognosis and their potential outcomes.

Survival and prognostic factors in conventional central chondrosarcoma

Chondrosarcoma, while a rare tumour in the grand scheme of malignancy, is one of the more common primary bone lesions seeking treatment in specialist centres. In general, the treatment strategy relies on the familiar principle of thorough surgical excision for optimal outcomes. A study from **Munich (Germany)** seeks to address this deficiency in the evidence by examining data from 87 consecutive chondrosarcomas, in order to determine whether surgical margins or tumour localization is most closely related to overall survival.[6] In this cohort, wide resection was achieved in 62% of cases, with the remainder undergoing a less thorough surgical clearance. All patients were followed up for evidence of local recurrence or the discovery of a distant metastasis. The authors report a five-year local recurrence-free survival of 75%, which showed significant association with both localization and excisional margins. Furthermore, the quality of surgical margins and the presence of local recurrence, where it occurred, did not influence overall survival in multivariate analysis. Unsurprisingly, pelvic, metastatic, and higher-grade disease fared worse in the longer term. This study suggests that high-grade chondrosarcomas of the pelvis in the elderly patient are likely to fare the worst of any, and that these need to be treated aggressively. However, the authors do not give any guidance as to how treatment should be modified in these high-risk cases, meaning that more work needs to be done to further refine this data and create evidence to support specific treatment strategies in these patients.

Intraoperative imaging of surgical margins of canine soft-tissue sarcoma using optical coherence tomography

The complete excision of a tumour, as assessed by the histological margins, is essential in the successful treatment of any malignancy. The importance of complete excision has been underlined in almost every paper that assesses outcomes following musculoskeletal tumour management. The current standard of care for surgical margin evaluation is the histological assessment of surgical margins following formalin fixation. Optical coherence tomography (OCT) is a rapid non-invasive imaging technique that has shown high sensitivity for intraoperative surgical margin assessment in human breast cancer clinical trials, but is not currently used in musculoskeletal tumour surgery. This veterinary article from **Urbana, Illinois (USA)** correlates normal and abnormal histological features with OCT images for surgical margins from excised canine soft-tissue sarcoma (STS) and seeks to establish image evaluation criteria for identifying positive surgical margins.[7] OCT imaging of two to four areas of interest on the resected specimen were performed. Following imaging, these areas were marked with surgical ink and trimmed for histopathology evaluation. Results showed that different tissue types had different and characteristic appearances on OCT, which closely correlate with low-power histology images. OCT has the potential to be used to identify positive surgical margins immediately following resection of STS.

Systemic treatment for unresectable chondrosarcoma

Chondrosarcoma remains one of the more common primary bone malignancies presenting to specialist units, and typically responds well to surgical treatment. It is, however, a difficult diagnosis to make, and many patients are unsuitable for surgical treatment. In these patients, prognosis is generally poor and systemic chemotherapy remains the mainstay of treatment. In order to assess the response of chondrosarcoma to modern non-surgical regimens, this group from **Leiden (The Netherlands)** analyzed data from all four major sarcoma centres in The Netherlands and assessed the progression-free survival (PFS) of the four treatment strategies in use. A total of 112 patients were included in the study, representing the four main chondrosarcoma types.[8] In short,

the results for the systemic treatment of chondrosarcoma are poor. Conventional chondrosarcoma PFS was found to be 6.7 months, with shorter survival for the remaining subtypes. This useful data shows that chondrosarcoma continues to respond poorly to chemotherapy, despite the range of newer protocols available. Prospective studies are required to develop a regimen to treat these lesions in order to improve survival. Furthermore, the heterogeneity between treatment strategies means that meaningful data is hard to come by. More data is needed here.

The role of surgical margins in chondrosarcoma

■ Surgery is the mainstay of treatment for chondrosarcoma, and the surgical margins of the excision, as with many musculoskeletal tumours, are the key to successful treatment. The minimal size of that margin has been defined by a team from **Birmingham (UK)**, who have investigated the role of margin size in local recurrence-free survival for limb or pelvic chondrosarcoma, and the role of any local recurrence in disease-free survival.[9] The research team collected and interpreted data regarding 341 cases of limb and pelvic chondrosarcoma, adding significantly to the number of reported cases. The group found a 23% local recurrence rate and established that pelvic location, pathological fracture, surgical margin, and grade of lesion were factors for local recurrence. Multivariate analysis showed that surgical margins and pelvic location were positive factors for local recurrence, whereas grade 1 or 2 lesions were negative factors. Disease survival, disease grade, pathologic fracture, and local recurrence were factors for disease-specific survival. The paper concludes that surgical margins affect the rate of local recurrence in all cases, but that local recurrence affects disease survival only in grade 2 or 3 lesions. The group goes on to recommend a 4 mm margin in all tumour excision, as biopsies are unreliable in grading tumours. However, the authors do not explore whether this is possible or not in larger lesions, particularly in the pelvis.

Bone sarcomas: ESMO-PaedCan-EURACAN Clinical Practice Guidelines for diagnosis, treatment, and follow-up

■ Finally, we would draw readers' attention to the recently published 2018 European Society for Medical Oncology (ESMO) guidelines for bone sarcoma treatment for anyone wanting to refresh their knowledge.[10]

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