Cancer Association of South Africa (CANSA)

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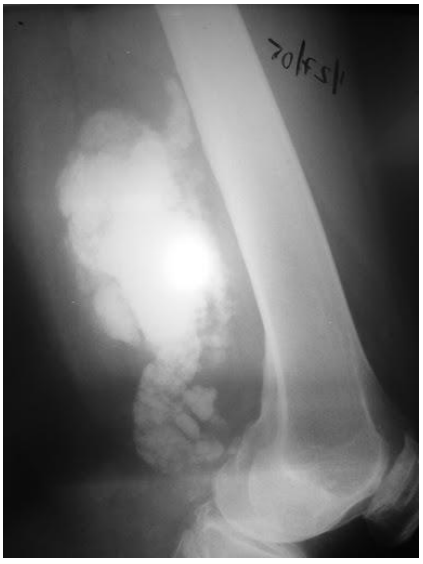
Fact Sheet
on
Extraskeletal Osteosarcoma

Introduction

Osteosarcoma is a type of cancer that produces immature bone. It is the most common type of cancer that arises in bones, and it is usually found at the end of long bones, often around the knee. Most people diagnosed with osteosarcoma are under the age of 25, and it is thought to occur more often in males than females.



[Picture Credit: Extraskeletal Osteosarcoma Picture]

Extraskeletal Osteosarcoma (ESOS)

Extraskeletal Osteosarcoma (ESOS) is a rare, fast-growing (high-grade) type of cancer (soft tissue sarcoma) that is made up of bone and cartilage cells, and forms in soft tissue near bones. It usually occurs in the thigh, buttock, shoulder, or trunk (chest and abdomen). It often recurs (comes back) after treatment and spreads to other parts of the body, including the lungs. Extraskeletal osteosarcoma usually occurs in middle-aged or older adults, and is rare in children and adolescents. It is a type of soft tissue sarcoma. Also called extraosseous osteosarcoma.

For lesions to be defined as extraskeletal, it must arise in the soft tissue and not be attached to bone or periosteum.

There are five pathologic subtypes of ESOS, similar to conventional osteosarcoma:

- osteoblastic
- chondroblastic
- fibroblastic
- telangiectatic
- small cell

Location of Extraskeletal Osteosarcoma (ESOS)

- lower extremity (thigh): 50-60%

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- upper extremity: 10-20%
- retroperitoneum: 10-15%
- trunk: 10-15%

Kito, F., Oyama, R., Noguchi, R., Hattori, E., Sakumoto, M., Endo, M., Kobayashi, E., Yoshida, A., Kawai, A. & Kondo, R. 2020.
"Extraskeletal osteosarcoma (ESOS) is a rare mesenchymal malignancy producing osteoid and bone in soft tissue without skeletal attachment. ESOS exhibits chemoresistance and poor prognosis, and is distinct from osseous osteosarcoma. The biological characteristics of ESOS are not fully understood, and patient-derived cell lines of ESOS are not available from public cell banks. Here, we established a novel cell line of ESOS and characterized its genetic and biological characteristics as well as examined its response to anti-cancer reagents. The cell line was established using tumor tissue from a 58-year-old female patient with ESOS, and named as NCC-ESOS1-C1. Phenotypes relevant to malignancy such as proliferation and invasion were examined in vitro, and genetic features were evaluated using the NCC Oncopanel assay. The response to inhibitors was monitored by screening of an anti-cancer reagent library. The cells constantly proliferated, showing spheroid formation and invasion capabilities. The NCC Oncopanel revealed the presence of actionable mutations in PIK3CA. Library screening revealed the presence of anti-cancer reagents with significant anti-proliferative effects on NCC-ESOS1-C1 at a low concentration. In conclusion, we established and characterized a novel ESOS cell line, NCC-ESOS1-C1. This cell line will be a useful resource for basic research and preclinical studies."

Incidence of Extraskeletal Osteosarcoma (ESOS)
The South African National Cancer Registry (2016) does not provide information on the incidence of Extraskeletal Osteosarcoma (ESOS).

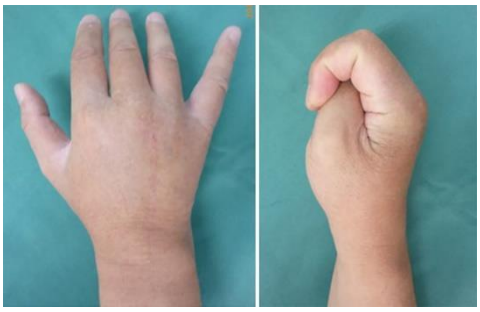
Causes and Risk Factors of Extraskeletal Osteosarcoma (ESOS)
Known risk factors for development of ESOS include:
- middle aged and elderly patients
- a history of radiation therapy
- a controversial link to trauma.

Curfman, K.R. & Morrissey, S.L. 2019.
"Extraskeletal Osteosarcoma (ESOS), a rare entity accounting for less than 2% of all soft tissue sarcomas. Known risk factors for development include: middle aged and elderly patients, a history of radiation, and a controversial link to trauma. The typical presenting symptoms, if any, are tenderness and swelling. In trauma patients, these symptoms often mask the ESOS diagnosis and are assumed to be hematoma or other traumatic diagnosis. Easy misinterpretation of what appears to be obvious traumatic injury, can lead to delays in accurate diagnosis and appropriate treatments."

Signs and Symptoms of Extraskeletal Osteosarcoma (ESOS)
Patients most commonly present with an enlarging soft-tissue mass either with or without pain. The typical presenting symptoms, if any, are tenderness and swelling. In trauma patients, these symptoms often mask

the ESOS diagnosis and are assumed to be hematoma or other traumatic diagnosis. Easy misinterpretation of what appears to be obvious traumatic injury, can lead to delays in accurate diagnosis and appropriate treatments.

[Picture Credit: Extraskeletal Osteosarcoma of the Hand]



Diagnosis of Extraskeletal Osteosarcoma (ESOS)

The diagnosis of Extraskeletal Osteosarcoma (ESOS) is generally delayed because symptoms are often absent or vague. Typically, the tumour presents as a progressively enlarging soft tissue mass associated with pain in approximately one-third of patients. Serum alkaline phosphatase levels may be elevated. Imaging studies show soft tissue masses with internal cloud-like calcifications or ossification.

Treatment of Extraskeletal Osteosarcoma (ESOS)

The initial treatment of choice of Extraskeletal Osteosarcoma (ESOS) is primarily wide margin surgical resection. Resection can be with amputation of limb salvage surgery if microscopically negative margins can be achieved.

Adjuvant chemotherapy and/or preoperative radiation therapy, although controversial, may be useful in the treatment of ESOS. Radiation therapy may be delivered by means of external beam, intraoperative, or brachytherapy.

Recent retrospective evaluation of patients with ESOS favour more polychemotherapeutic regimens in addition to wide resection, and found 5-year overall survival rates of 77% and 66%.

Heng, M., Gupta, A., Chung, P.W., Healey, J.H., Vavnrub, M., Rose, P.lS.,Houdek, M.T., Lin, P.P., Bishop, A.J., Hornicek, F.J., Chen, Y-L., Lozano-Calderon, S., Holt, G.E., Han, I., Biau, D., Niu, X., Bermthal, N.M., Ferguson, P.C., Wunder, J.S., Japanese Muscoloskeletal Oncology Group (JMOG), & Soft Tissue Osteosarcoma Interantional Collaborative (STOIC). 2020.

Purpose: The role of chemotherapy (CT) and radiotherapy (RT) for management of extraskeletal osteosarcoma (ESOS) remains controversial. We examined disease outcomes for ESOS patients and investigated the association between CT/RT with recurrence and survival.

Patients and methods: Retrospective review at 25 international sarcoma centers identified patients ≥18 years old treated for ESOS from 1971 to 2016. Patient/tumour characteristics, treatment, local/systemic recurrence, and survival data were collected. Kaplan–Meier survival and Cox proportional-hazards regression and cumulative incidence competing risks analysis were performed.

Results: 370 patients with localized ESOS treated definitively with surgery presented with mainly deep tumours (n = 294, 80%). 122 patients underwent surgical resection alone, 96 (26%) also received CT, 70 (19%) RT and 82 (22%) both adjuvants. Five-year survival for patients with localized ESOS was 56% (95% CI 51%–62%). Almost half of patients (n = 173, 47%) developed recurrence: local 9% (35/370), distant 28% (102/370) or both 10% (36/370). Considering death as a competing event, there was no significant difference in cumulative incidence of local or systemic recurrence between patients who received CT, RT, both or neither (local p = 0.50, systemic p = 0.69). Multiple regression Cox analysis showed a significant association between RT and decreased local recurrence (HR 0.46 [95% CI 0.26–0.80], p = 0.01).

Conclusion: Although the use of RT significantly decreased local recurrences, CT did not decrease the risk of systemic recurrence, and neither CT, nor RT nor both were associated with improved survival in patients with localized ESOS. Our results do not support the use of CT; however, adjuvant RT demonstrates benefit in patients with locally resectable ESOS.

Shimizu, N., Tanaka, Y., Demizu, Y., Okimoto, T. & Maniwa, Y. 2019.
Extraskeletal osteosarcoma (ESOS) arising from the mediastinum is a rare malignant tumor and associated with a poor prognosis. We present the case of a 73-year-old man with a hoarseness. Imaging studies revealed a large calcified tumor of the median mediastinum. Surgery was performed, but complete resection was impossible and approximately two thirds of the tumor was excised. The tumor was diagnosed pathologically as ESOS. Proton beam therapy has been performed on the remaining lesion, and the patient is alive without tumor regrowth after 29 months. This case report documents a mediastinum ESOS successfully treated successfully with surgery and postoperative proton therapy.

Liao, Z., Oju, M., Yang, J., Yang, Y., Zhu, L., Yang, B., Bai, X., Xing, P., Zhang, J., Xing, R., Teng, S. & Zhao, J. 2019.
"Extraskeletal osteosarcoma (ESOS) is an extremely rare malignancy with poor prognosis, accounting for 2-4% of all osteogenic sarcomas. The purpose of this study was to examine the oncological outcomes of this disease related to surgical treatment and/or combined adjuvant therapies and to analyze the associated prognostic factors in ESOS. From January 1990 to June 2016, 22 patients with primary ESOS were analyzed in this retrospective study. Overall survival (OS) and progression-free survival (PFS) rates were calculated by Kaplan-Meier methods and compared with log-rank test. 22 patients were diagnosed with ESOS, 19 showed localized diseases and 3 presented with metastatic lesions. The median age at diagnosis was 55.5 years. Surgery resection was performed for all patients, 18 of whom received adjuvant chemotherapy. The median follow-up time was 48.5 months. There were 10 cases of recurrence and 9 patients developed new metastases. The 5-year OS rate for all patients was 58%. For localized cohort, the 5-year OS rate was 62%, and the 3-year PFS rate was 31% with a median PFS of 16 months. Univariate analysis of related prognosis factors showed that larger size of tumor (>5.5 cm) and higher histologic grade emerged as significant factors associated with worse OS. The addition of combination chemotherapy has no effect found on OS or PFS in this study. In summary, for patients who presented with ESOS, larger tumor size and higher histologic grade indicate a lower OS rate. The combination chemotherapy does not improve the OS or PFS."

About Clinical Trials
Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.
Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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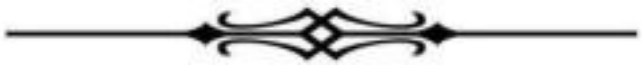

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Extraskeletal Osteosarcoma
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Extraskeletal Osteosarcoma of the Hand
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Extraskeletal Osteosarcoma Picture
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Osteosarcoma
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