

**SERVIZIO SANITARIO REGIONALE
EMILIA - ROMAGNA**
Istituto Ortopedico Rizzoli di Bologna
Istituto di Ricovero e Cura a Carattere Scientifico



“Synovial chondrosarcoma: a single Institution experience”


<u>Study code</u>	<u>SynoChondroS</u>
Sponsor's Name and Address:	Istituto Ortopedico Rizzoli Via di Barbiano 1/10 40136 Bologna Italy
Study Number/Version/Date:	Vers 1.0 16 May 2018
Coordinating Center:	IRCCS Istituto Ortopedico Rizzoli Pathology Unit Via Pupilli 1 40136 Bologna, Italy
Coordinating Investigator and address:	Marco Gambarotti MD Phone: 051-6366.652 Email: marco.gambarotti@ior.it
Methodology:	Experimental study with biological material (Single institution case series review of clinical and histological data)
Type:	Academic
Founding:	None
Principal Investigator Signature	I confirm that I've read this protocol and I accept to run the study in compliance with what is stated in the protocol and with the ICh-GCP and all applicable law Marco Gambarotti MD Firma  _____

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BACKGROUND

Chondrosarcoma of the synovium (also called synovial chondrosarcoma) is an exceedingly rare entity. It can arise de novo or as a malignant transformation of synovial chondromatosis. In the latter situation, synovial chondrosarcoma can arise on a pre-existing synovial chondromatosis or co-exist with a synovial chondromatosis. The rate of malignant transformation of synovial chondromatosis is very rare (about 5% of cases), generally after several recurrences, many years after the first diagnosis.

Several case reports and reviews of synovial chondrosarcoma are described in the literature¹⁻⁵. Radiologically, synovial chondrosarcomas may show aggressive features; however the differential diagnosis between synovial chondromatosis and synovial chondrosarcoma can be challenging. Histologically, features in favour of malignancy are hypercellularity, loss of clustering of the chondrocytes, myxoid change of the matrix, necrosis, and infiltration of bone and soft tissues with permeative margins⁵.

Although the majority of synovial chondrosarcomas behave as low-grade conventional chondrosarcomas, metastasis can develop in about 29% of cases⁴. For this reason, a wide surgical treatment is recommended and the differential diagnosis with synovial chondromatosis is very important, as the latter is generally treated with a more conservatory surgical approach.

OBJECTIVE OF THE STUDY

The aim of the present study is to review all the cases with a diagnosis of synovial chondrosarcoma treated at the Rizzoli Institute from 1982, retrospectively examining all the clinical, radiological, and histological features of these tumors, in order to better understand their characteristics and to identify the best therapeutic approach.

STUDY DESIGN

This is a single institution cases series review of histological, radiological and clinical data

POPULATION

Inclusion criteria

- 1) Male and female patients treated at Rizzoli Institute from 01 January 1982 to 31 December 2017
- 2) Diagnosis of synovial chondrosarcoma

- 3) Age \geq 18 years
- 4) Histological slides / formalin-fixed paraffin-embedded tissue tumor (FFPE) blocks from archive available to perform the histology analysis
- 5) Written informed consent prior to any study-specific analysis and/or data collection

Exclusion criteria

- 1) Patients with histological diagnosis different from synovial chondrosarcoma

MATERIAL AND METHODS

We will retrieve from the archives of the Rizzoli institute all the cases with a histological diagnosis of synovial chondrosarcoma.

We expect to find approximately ten cases.

We will review all the medical records, radiological imaging, and histological slides of these cases.

STATISTICS

To the case series will be applied a descriptive statistic.

ENROLLMENT PROCEDURE

Patients considered eligible will be included in the study, after providing a written informed consent.

Due to the high incidence of mortality of the disease under investigation, it would be possible that some eligible subjects will be deceased.

DATA COLLECTION

Clinical data will be retrieved by patient charts.

A protocol-specific CRF reporting the results of the review will be provided.

A CRF is required and should be completed for each included subject.

ETHICS AND QUALITY ASSURANCE

The clinical trial protocol and its documents will be sent before initiating the study to the competent Authorities and Ethics Committees of each participating country for its approval.

The responsible investigator will ensure that this study is conducted in agreement with either the most updated Declaration of Helsinki and all the international and local laws that apply to clinical trials and to patient protection.

The protocol has been written, and the study will be conducted according to the principles of the ICH Harmonized Tripartite Guideline for Good Clinical Practice (ref: <http://www.emea.eu.int/pdfs/human/ich/013595en.pdf>).

INFORMED CONSENT

All patients will be informed, by the investigator, of the aims of the study, the possible risks and benefits that will derive from the study participation.

The Investigator must clearly inform that the patient is free to refuse participation in the study and that can withdraw consent at any time and for any reason.

They will be informed as to the strict confidentiality of their patient data, but that their medical records may be reviewed for trial purposes by authorized individuals other than their treating physician.

The informed consent procedure must conform to the ICH guidelines on Good Clinical Practice. This implies that "the written informed consent form should be signed and personally dated by the patient or by the patient's legally acceptable representative".

The Investigator must also sign the Informed Consent form, and will keep the original at the site and a copy of the original must be handed to the patient.

The competent ethics committee for each Institution participating to the study must validate local informed consent documents before the study can be opened. It will be emphasized that the participation is voluntary and that the patient is allowed to refuse further participation in the study whenever he/she wants. This will not prejudice the patient's subsequent care.

Due to the high incidence of mortality of the disease under investigation, it would be possible that some potential eligible subjects will be deceased.

GENERAL PRINCIPLES FOR HUMAN BIOLOGICAL MATERIAL (HBM) COLLECTION

Human biological material (HBM) collection involves the collection and storage of biological material, residual biological material or derivatives in compliance with ethical and technical requirements.

Biological material (FFPE blocks of tumor sample) are already stored in the Bone Biobanks at Istituto Ortopedico Rizzoli Pathology Department.

The biological material will be used and stored according with the sample characteristic and applicable regulation.

- The Istituto Ortopedico Rizzoli will have a designated person responsible for collection and will act as a communication point
- The collected HBM should be documented, i.e. the amount remaining and its location. act as a communication point
- IDH1 and IDH2 analysis will be performed the Pathological Anatomy dept. of the Treviso's Hospital under Prof. Angelo Paolo Dei Tos responsibility

CONFIDENTIALITY

In order to ensure confidentiality of clinical trial data as disposed the national and European applicable regulation, data will be only accessible for the trial Sponsor and its designees, for monitoring/auditing procedures, the Investigator and collaborators, the Ethics Committee of each corresponding site and the Health Authority.

Investigator and the Institution will allow access to data and source documentation for monitoring, auditing, Ethic Committee revision and inspections of Health Authority, but maintaining at all times subject personal data confidentiality as specified in the "Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995".

The Investigator must guarantee that patient anonymity is kept at all times and their identity must be protected from unauthorized persons and institutions.

All patients included in the study will be identified with a numeric code, so that no identifiable personal data will be collected (pseudo anonymization)

The Investigator must have and conserve a patients' inclusion registry where it figures the personal data of the patient: name, surname, address and corresponding identification code into the study, this register will be kept on the Investigator File.

PUBLICATION OF RESULTS

The results from this study will be published or shown at scientific conferences. The final publication of the study results will be written by the Principal Investigator.

REFERENCES

- [1] Ng VY, Louie P, Punt S, Conrad EU. Malignant Transformation of Synovial Chondromatosis: A Systematic Review. *Open Orthop J.* 2017 May 31;11:517-524.
- [2] Biazzo A, Confalonieri N. Synovial chondrosarcoma. *Ann Transl Med.* 2016 Aug;4(15):280.
- [3] Zamora EE, Mansor A, Vanel D, Errani C, Mercuri M, Picci P, Alberghini M. Synovial chondrosarcoma: report of two cases and literature review. *Eur J Radiol.* 2009 Oct;72(1):38-43.
- [4] Campanacci DA, Matera D, Franchi A, Capanna R. Synovial chondrosarcoma of the hip: report of two cases and literature review. *Chir Organi Mov.* 2008 Dec;92(3):139-44.
- [5] Bertoni F, Unni KK, Beabout JW, Sim FH. Chondrosarcomas of the synovium. *Cancer.* 1991 Jan 1;67(1):155-62.