

# Cancer Association of South Africa (CANSA)



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## Fact Sheet on Chondrosarcoma

### Introduction

The skeletal system is composed of cartilage, bones and other related connective tissues (ligaments and tendons), which gives support and protection to the body. The skeleton is the body frame and thus, it gives shape to the body. Another important function of the skeleton is its involvement in locomotion. The skeleton is conveniently divided into two functional parts, namely:

- The Axial skeleton
- The Appendicular skeleton

The axial skeleton consists of the bones along the vertical axis of the body, from the head, neck, the trunk down to the sacrum. It is made up of the skull (cranium), the vertebral column, the hyoid bone, the ribs and the sternum (breastbone).

[Picture Credit: Skeleton]

The appendicular skeleton is made up of the bones of the girdles (pectoral and pelvic) and the limbs. The pectoral girdle consists of the scapula and the clavicle. Connection between the axial and appendicular skeleton is by means of the clavicle (collar bone). The pelvic girdle is composed of two innominate bones, which are joined together at the pubic symphysis. Each innominate bone consists of three fused bones, the ilium, the ischium, and the pubis. The appendicular skeleton is mainly concerned with locomotion and manipulation. (Bala).



### Chondrosarcoma

Chondrosarcoma is a rare type of cancer composed of cells that are derived from transformed cells which produce cartilage. Chondrosarcoma is a member of a category of tumours of bone and soft tissue known as sarcomas.

About 30% of skeletal system cancers are chondrosarcomas. It is resistant to chemotherapy and radiotherapy. Unlike other primary bone cancers that mainly affect children and adolescents, chondrosarcoma can present at any age.

[Picture Credit: Chondrosarcoma Left Femur]



It more often affects the axial skeleton (which consists of the skull, the vertebral column, the ribs and the sternum or breastbone) than the appendicular skeleton (consisting of the bones of the shoulder, arm, pelvis and lower extremity). The X-Ray picture on the right shows the presence of chondrosarcoma involving the left femur (thigh bone). Having stated this, chondrosarcoma is a slow-growing tumour often seen in the:

- pelvis
- thigh (femur)
- upper arm (humerus)
- shoulder blade (scapula)
- ribs

(Wikipedia; MacMillan Cancer Support).

### Incidence of Chondrosarcoma in South Africa

The National Cancer Registry (2012) does not provide any information on the incidence of chondrosarcoma in South Africa. The National Cancer Registry only provides information regarding cancer of the bone.

According to the National Cancer Registry (2012) the following number of cases of bone cancer was histologically diagnosed in South Africa during 2012:

Group - Males 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	100	1:2 864	0,27%
Asian males	2	1:4 817	0,26%
Black males	60	1:4 628	0,51%
Coloured males	10	1:1 761	0,23%
White males	28	1:1 002	0,14%

Group - Females 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	79	1:4 050	0,21%
Asian females	0	-	-
Black females	48	1:6 457	0,29%
Coloured females	8	1:2 384	0,20%
White females	23	1:1 494	0,14%

The frequency of histologically diagnosed cases of bone cancer in South Africa for 2012 was as follows (National Cancer Registry, 2012):

Group - Males 2012	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	31	35	6	9	10	2	6	0
Asian males	0	1	0	1	0	0	0	0
Black males	22	19	2	4	6	0	1	0
Coloured males	2	4	1	0	0	1	1	0
White males	3	5	1	2	9	3	1	0

Group - Females 2012	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	24	13	10	11	9	6	3	2
Asian females	0	0	0	0	0	0	0	0
Black females	19	12	7	3	2	3	0	1
Coloured females	1	1	0	2	2	0	1	0
White females	4	0	2	5	5	3	1	1

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

### Types of Chondrosarcoma

There are several types of chondrosarcoma that are named based on the way that they appear under the microscope.

These include:

- Conventional chondrosarcoma
- Clear cell chondrosarcoma
- Myxoid chondrosarcoma
- Mesenchymal chondrosarcoma
- Dedifferentiated chondrosarcoma

(The Liddy Shriver Sarcoma Initiative).

### Causes of Chondrosarcoma

As with many cancers, the cause of chondrosarcoma is not clear. However, people with certain medical conditions have an increased risk for developing chondrosarcoma.

These conditions include:

- Ollier's Disease - also known as enchondromatosis, a *non*-hereditary, sporadic, skeletal disorder characterised by multiple enchondromas that are principally located in the growth plate cartilage
- Maffucci Syndrome - a disorder that primarily affects the bones and skin. It is characterised by multiple enchondromas, which are noncancerous (benign) growths of cartilage that develop on the bones
- Multiple Hereditary Exostoses (MHE, a.k.a., osteochondromatosis) - a condition in which a person develops multiple noncancerous bone tumours called exostoses
- Wilms' Tumor – also known as nephroblastoma, which is a cancer of the kidneys that typically occurs in children, rarely in adults
- Paget's disease of bone - Paget's disease of bone or Paget disease of bone is a chronic disorder that can result in enlarged and misshapen bones. Paget's is caused by the excessive breakdown and formation of bone, followed by disorganised bone remodelling

- Diseases in children that required previous treatment with chemotherapy or radiation therapy (MacMillan Cancer Support; The Liddy Shriver Sarcoma Initiative).

### Signs and Symptoms of Chondrosarcoma

The main symptoms of chondrosarcoma are:

- Localised pain, which can be dull in nature, occurring at rest and may become worse at night. Pain may also become progressively worse.
- Local swelling.
- Walking with a limp or having restricted movement of a joint (if near the affected bone).

These symptoms can be present alone or in combination. These symptoms are often of long duration, possibly several months or years.

The average duration of symptoms before diagnosis is thought to be between 1 and 2 years. 20-30% of chondrosarcomas are painless and may only be found when a patient suffers with a fractured bone caused by a mild injury, such as from a minor fall or accident. The fracture can happen where the bone has been weakened by the tumour. This is known as a pathological fracture. (Bone Cancer Research Trust).

### Staging of Chondrosarcoma Through the TNM System

The latest edition (7th) edition of the TNM system:

T Stage	Description
T <sub>1</sub>	< 8 cm in maximum dimension
T <sub>2</sub>	> 8 cm in maximum dimension
T <sub>3</sub>	Discontinuous tumours in the same bone
N Stage	Description
N <sub>1</sub>	Nodal metastases
M Stage	Description
M <sub>1a</sub>	Lung metastases
M <sub>1b</sub>	Other distant metastases

### Stage and Grade Description

Stage	T	N	M	Grade
IA	T <sub>1</sub>	N <sub>0</sub>	M <sub>0</sub>	Low
IB	T <sub>2</sub>	N <sub>0</sub>	M <sub>0</sub>	Low
IIA	T <sub>1</sub>	N <sub>0</sub>	M <sub>0</sub>	High
IIB	T <sub>2</sub>	N <sub>0</sub>	M <sub>0</sub>	High
III	T <sub>3</sub>	N <sub>0</sub>	M <sub>0</sub>	Any
IVA	T <sub>any</sub>	N <sub>0</sub>	M <sub>1a</sub>	Any
IVB	T <sub>any</sub>	N <sub>1</sub> N <sub>any</sub>	M <sub>any</sub> M <sub>1b</sub>	Any

(OzRadOnc).

## **Grading of Chondrosarcoma**

Chondrosarcomas can be classified into the following Three histologic grades, depending on findings of cellularity, atypia, and pleomorphism:

- Grade I (low grade) – Cytologically similar to enchondroma; cellularity is higher, with occasional plump nuclei with open chromatin structure
- Grade II (intermediate grade) – Characterised by a definite and increased cellularity; distinct nucleoli are present in most cells, and foci of myxoid change may be seen
- Grade III (high grade) – Characterised by high cellularity, prominent nuclear atypia, and the presence of mitosis

The higher the grade, the more likely the tumour is to spread and metastasise. Grade I lesions rarely metastasise, whereas 10-15% of grade II lesions and more than 50% grade III lesions metastasise.

(Medscape).

## **Diagnosis of Chondrosarcoma**

Typical presentation is in the 4<sup>th</sup> and 5<sup>th</sup> decades and there is a slight male predominance of 1.5 - 2:1.

Diagnosis usually begins with a physical examination and medical history. The doctor will check for signs of disease. He or she will ask about health habits and previous illnesses and treatments.

Other tests that may be performed to diagnose chondrosarcoma include:

- X-rays use high-energy radiation to take pictures inside the body. They can show the location, size, and shape of a bone tumour
- Bone scans use a scanner and low-level radioactive material. They detect cancer cells in bones
- Computed tomography (CT) scans use a rotating x-ray camera. They take detailed, cross-sectional pictures of tissues and organs
- Magnetic resonance imaging (MRI) uses a powerful magnet and radio waves to take detailed images inside the body
- Positron emission tomography (PET) and PET/CT scans use positively charged particles (radioactive positrons) to detect subtle changes in the body's metabolism and chemical activities. It then creates images that show how the body is working, rather than its structure
- Biopsy is a procedure to remove tissue to check for cancer. Biopsies can be done using a needle or by making an incision in the skin. The doctor may remove an entire tumour during the biopsy

(Radiopaedia; Drugs.com).

## **Treatment of Chondrosarcoma**

As chondrosarcomas are very rare, they are usually treated by a team of doctors and other health care professionals at a specialist hospital. This means that one may have to travel some distance to have treatment.

The type of treatment one is given will depend on a number of things, including the position and size of the cancer, whether it has spread, the grade of the cancer, and the general health of the patient.

Some people with a chondrosarcoma will need to have a combination of different treatments. The treatments that might be used are surgery (where this is possible), chemotherapy and radiotherapy. However, chemotherapy and radiotherapy are not very effective for most chondrosarcomas and, therefore, surgery is the main treatment.

Surgery - major improvements have been made in surgery for bone cancer. In the past, it was often necessary to remove (amputate) the affected limb if chondrosarcoma was found. Now it is often possible just to remove the affected part of the bone and some of the healthy tissue around it. The bone is then replaced with a specially designed metal replacement (prosthesis) or a bone graft (bone taken from another part of the body). If the cancer affects a bone in or near a joint, the whole joint can often be replaced with an artificial one. These operations are known as limb-sparing surgery.



Unfortunately, it is not always possible to use limb-sparing surgery and, occasionally, an amputation may be the only way to treat the cancer. This is often the case when the cancer cells have spread from the bone into the nerves and blood vessels around it.

[Picture Credit: Amputation]

The type of surgery one has will depend on a number of factors. The surgeon will discuss the different types of surgery in more detail before any decision is taken about treatment.

It is often helpful to talk to someone who has had the same operation. The medical and nursing staff will be able to arrange this. In some hospitals, a counsellor may be available to discuss any concerns or worries.

Chemotherapy - chemotherapy is the use of anti-cancer (cytotoxic) drugs to destroy cancer cells. This type of treatment is not commonly used for chondrosarcoma. However, it may be helpful in certain situations.

Chemotherapy can make one feel better by relieving the symptoms of the cancer, but it can sometimes have unpleasant side effects. Any side effects that do occur can often be well controlled with medicines.

Radiotherapy - radiotherapy treats cancer by using high-energy rays to destroy the cancer cells, while doing as little harm as possible to normal cells. Radiotherapy is rarely used to treat chondrosarcomas, although it is sometimes helpful in certain situations.

Radiotherapy can cause side effects such as skin redness (erythema) and tiredness (fatigue). These side effects can be mild or more troublesome, depending on the strength of the radiotherapy dose and the length of the treatment. The radiotherapist will be able to advise on what to expect.

(MacMillan Cancer Support).

## **About Clinical Trials**

Clinical trials are research studies that involve people. These studies test new ways to prevent, detect, diagnose, or treat diseases. People who take part in cancer clinical trials have an opportunity to contribute to scientists' knowledge about cancer and to help in the development of improved cancer treatments. They also receive state-of-the-art care from cancer experts.

### Types of Clinical Trials

Cancer clinical trials differ according to their primary purpose. They include the following types:

**Treatment** - these trials test the effectiveness of new treatments or new ways of using current treatments in people who have cancer. The treatments tested may include new drugs or new combinations of currently used drugs, new surgery or radiation therapy techniques, and vaccines or other treatments that stimulate a person's immune system to fight cancer. Combinations of different treatment types may also be tested in these trials.

**Prevention** - these trials test new interventions that may lower the risk of developing certain types of cancer. Most cancer prevention trials involve healthy people who have not had cancer; however, they often only include people who have a higher than average risk of developing a specific type of cancer. Some cancer prevention trials involve people who have had cancer in the past; these trials test interventions that may help prevent the return (recurrence) of the original cancer or reduce the chance of developing a new type of cancer

**Screening** - these trials test new ways of finding cancer early. When cancer is found early, it may be easier to treat and there may be a better chance of long-term survival. Cancer screening trials usually involve people who do not have any signs or symptoms of cancer. However, participation in these trials is often limited to people who have a higher than average risk of developing a certain type of cancer because they have a family history of that type of cancer or they have a history of exposure to cancer-causing substances (e.g., cigarette smoke).

**Diagnostic** - these trials study new tests or procedures that may help identify, or diagnose, cancer more accurately. Diagnostic trials usually involve people who have some signs or symptoms of cancer.

**Quality of life or supportive care** - these trials focus on the comfort and quality of life of cancer patients and cancer survivors. New ways to decrease the number or severity of side effects of cancer or its treatment are often studied in these trials. How a specific type of cancer or its treatment affects a person's everyday life may also be studied.

### Where Clinical Trials are Conducted

Cancer clinical trials take place in cities and towns in doctors' offices, cancer centres and other medical centres, community hospitals and clinics. A single trial may take place at one or two specialised medical centres only or at hundreds of offices, hospitals, and centres.

Each clinical trial is managed by a research team that can include doctors, nurses, research assistants, data analysts, and other specialists. The research team works closely with other health professionals, including other doctors and nurses, laboratory technicians, pharmacists, dieticians, and social workers, to provide medical and supportive care to people who take part in a clinical trial.

### Research Team

The research team closely monitors the health of people taking part in the clinical trial and gives them specific instructions when necessary. To ensure the reliability of the trial's results, it is important for the participants to follow the research team's instructions. The instructions may include keeping logs or answering questionnaires. The research team may also seek to contact the participants regularly after the trial ends to get updates on their health.

### Clinical Trial Protocol

Every clinical trial has a protocol, or action plan, that describes what will be done in the trial, how the trial will be conducted, and why each part of the trial is necessary. The protocol also includes guidelines for who can and cannot participate in the trial. These guidelines, called eligibility criteria, describe the characteristics that all interested people must have before they can take part in the trial. Eligibility criteria can include age, sex, medical history, and current health status. Eligibility criteria for cancer treatment trials often include the type and stage of cancer, as well as the type(s) of cancer treatment already received.

Enrolling people who have similar characteristics helps ensure that the outcome of a trial is due to the intervention being tested and not to other factors. In this way, eligibility criteria help researchers obtain the most accurate and meaningful results possible.

### National and International Regulations

National and international regulations and policies have been developed to help ensure that research involving people is conducted according to strict scientific and ethical principles. In these regulations and policies, people who participate in research are usually referred to as "human subjects."

### Informed Consent

Informed consent is a process through which people learn the important facts about a clinical trial to help them decide whether or not to take part in it, and continue to learn new information about the trial that helps them decide whether or not to continue participating in it.

During the first part of the informed consent process, people are given detailed information about a trial, including information about the purpose of the trial, the tests and other procedures that will be required, and the possible benefits and harms of taking part in the trial. Besides talking with a doctor or nurse, potential trial participants are given a form, called an informed consent form, that provides information about the trial in writing. People who agree to take part in the trial are asked to sign the form. However, signing this form does not mean that a person must remain in the trial. Anyone can choose to leave a trial at any time—either before it starts or at any time during the trial or during the follow-up period. It is important for people who decide to leave a trial to get information from the research team about how to leave the trial safely.

The informed consent process continues throughout a trial. If new benefits, risks, or side effects are discovered during the course of a trial, the researchers must inform the participants so they can decide whether or not they want to continue to take part in the trial. In some cases, participants who want to continue to take part in a trial may be asked to sign a new informed consent form.

New interventions are often studied in a stepwise fashion, with each step representing a different “phase” in the clinical research process. The following phases are used for cancer treatment trials:

### Phases of a Clinical Trial

Phase 0. These trials represent the earliest step in testing new treatments in humans. In a phase 0 trial, a very small dose of a chemical or biologic agent is given to a small number of people (approximately 10-15) to gather preliminary information about how the agent is processed by the body (pharmacokinetics) and how the agent affects the body (pharmacodynamics). Because the agents are given in such small amounts, no information is obtained about their safety or effectiveness in treating cancer. Phase 0 trials are also called micro-dosing studies, exploratory Investigational New Drug (IND) trials, or early phase I trials. The people who take part in these trials usually have advanced disease, and no known, effective treatment options are available to them.

Phase I (also called phase 1). These trials are conducted mainly to evaluate the safety of chemical or biologic agents or other types of interventions (e.g., a new radiation therapy technique). They help determine the maximum dose that can be given safely (also known as the maximum tolerated dose) and whether an intervention causes harmful side effects. Phase I trials enrol small numbers of people (20 or more) who have advanced cancer that cannot be treated effectively with standard (usual) treatments or for which no standard treatment exists. Although evaluating the effectiveness of interventions is not a primary goal of these trials, doctors do look for evidence that the interventions might be useful as treatments.

Phase II (also called phase 2). These trials test the effectiveness of interventions in people who have a specific type of cancer or related cancers. They also continue to look at the safety of interventions. Phase II trials usually enrol fewer than 100 people but may include as many as 300. The people who participate in phase II trials may or may not have been treated previously with standard therapy for their type of cancer. If a person has been treated previously, their eligibility to participate in a specific trial may depend on the type and amount of prior treatment they received. Although phase II trials can give some indication of whether or not an intervention works, they are almost never designed to show whether an intervention is better than standard therapy.

Phase III (also called phase 3). These trials compare the effectiveness of a new intervention, or new use of an existing intervention, with the current standard of care (usual treatment) for a particular type of cancer. Phase III trials also examine how the side effects of the new intervention compare with those of the usual treatment. If the new intervention is more effective than the usual treatment and/or is easier to tolerate, it may become the new standard of care.

Phase III trials usually involve large groups of people (100 to several thousand), who are randomly assigned to one of two treatment groups, or “trial arms”: (1) a control group, in which everyone in the group receives usual treatment for their type of cancer, or 2) an investigational or experimental group, in which everyone in the group receives the new intervention or new use of an existing intervention. The trial participants are assigned to their individual groups by random assignment, or randomisation. Randomisation helps ensure that the groups have similar characteristics. This balance is necessary so the researchers

can have confidence that any differences they observe in how the two groups respond to the treatments they receive are due to the treatments and not to other differences between the groups.

Randomisation is usually done by a computer program to ensure that human choices do not influence the assignment to groups. The trial participants cannot request to be in a particular group, and the researchers cannot influence how people are assigned to the groups. Usually, neither the participants nor their doctors know what treatment the participants are receiving.

People who participate in phase III trials may or may not have been treated previously. If they have been treated previously, their eligibility to participate in a specific trial may depend on the type and the amount of prior treatment they received.

In most cases, an intervention will move into phase III testing only after it has shown promise in phase I and phase II trials.

Phase IV (also called phase 4). These trials further evaluate the effectiveness and long-term safety of drugs or other interventions. They usually take place after a drug or intervention has been approved by the medicine regulatory office for standard use. Several hundred to several thousand people may take part in a phase IV trial. These trials are also known as post-marketing surveillance trials. They are generally sponsored by drug companies.

Sometimes clinical trial phases may be combined (e.g., phase I/II or phase II/III trials) to minimize the risks to participants and/or to allow faster development of a new intervention.

Although treatment trials are always assigned a phase, other clinical trials (e.g., screening, prevention, diagnostic, and quality-of-life trials) may not be labelled this way.

### Use of Placebos

The use of placebos as comparison or “control” interventions in cancer treatment trials is rare. If a placebo is used by itself, it is because no standard treatment exists. In this case, a trial would compare the effects of a new treatment with the effects of a placebo. More often, however, placebos are given along with a standard treatment. For example, a trial might compare the effects of a standard treatment plus a new treatment with the effects of the same standard treatment plus a placebo.

### Possible benefits of taking part in a clinical trial

The benefits of participating in a clinical trial include the following:

- Trial participants have access to promising new interventions that are generally not available outside of a clinical trial.
- The intervention being studied may be more effective than standard therapy. If it is more effective, trial participants may be the first to benefit from it.
- Trial participants receive regular and careful medical attention from a research team that includes doctors, nurses, and other health professionals.
- The results of the trial may help other people who need cancer treatment in the future.
- Trial participants are helping scientists learn more about cancer (e.g., how it grows, how it acts, and what influences its growth and spread).

### Potential harms associated with taking part in a clinical trial

The potential harms of participating in a clinical trial include the following:

- The new intervention being studied may not be better than standard therapy, or it may have harmful side effects that doctors do not expect or that are worse than those associated with standard therapy.
- Trial participants may be required to make more visits to the doctor than they would if they were not in a clinical trial and/or may need to travel farther for those visits.

### Correlative research studies, and how they are related to clinical trials

In addition to answering questions about the effectiveness of new interventions, clinical trials provide the opportunity for additional research. These additional research studies, called correlative or ancillary studies, may use blood, tumour, or other tissue specimens (also known as 'biospecimens') obtained from trial participants before, during, or after treatment. For example, the molecular characteristics of tumour specimens collected during a trial might be analysed to see if there is a relationship between the presence of a certain gene mutation or the amount of a specific protein and how trial participants responded to the treatment they received. Information obtained from these types of studies could lead to more accurate predictions about how individual patients will respond to certain cancer treatments, improved ways of finding cancer earlier, new methods of identifying people who have an increased risk of cancer, and new approaches to try to prevent cancer.

Clinical trial participants must give their permission before biospecimens obtained from them can be used for research purposes.

### When a clinical trial is over

After a clinical trial is completed, the researchers look carefully at the data collected during the trial to understand the meaning of the findings and to plan further research. After a phase I or phase II trial, the researchers decide whether or not to move on to the next phase or stop testing the intervention because it was not safe or effective. When a phase III trial is completed, the researchers analyse the data to determine whether the results have medical importance and, if so, whether the tested intervention could become the new standard of care.

The results of clinical trials are often published in peer-reviewed scientific journals. Peer review is a process by which cancer research experts not associated with a trial review the study report before it is published to make sure that the data are sound, the data analysis was performed correctly, and the conclusions are appropriate. If the results are particularly important, they may be reported by the media and discussed at a scientific meeting and by patient advocacy groups before they are published in a journal. Once a new intervention has proven safe and effective in a clinical trial, it may become a new standard of care. (National Cancer Institute).

### **Medical Disclaimer**

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