

Chondrosarcoma

Malignant cartilage-producing tumors of bone

Classification · Pathogenesis · Morphology · Prognosis

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Learning objectives

- Classify the major chondrosarcoma subtypes and recognize their distinct presentations.
- Relate EXT1/EXT2, IDH1/IDH2 and CDKN2A alterations to their stated disease contexts.
- Identify radiologic, gross and histologic evidence of cartilage-producing malignancy.
- Explain how grade and skeletal location influence recurrence, metastasis and treatment.

Defining feature of chondrosarcoma

Malignant tumor that produces cartilage

- Cartilaginous matrix defines the phenotype of this bone malignancy.
- The presence of cartilage alone does not establish malignancy: Benign cartilage tumors also exist.

Matrix-producing malignancies

Osteosarcoma

- Malignant bone tumor
- Produces neoplastic bone or osteoid matrix

Chondrosarcoma

- Malignant bone tumor
- Produces cartilaginous matrix

Chondrosarcoma as second to osteosarcoma among malignant matrix-producing bone tumors.

Cartilage matrix: What is being produced?

Schematic cartilage lacunae and chondrocytes



Interpretation

- A cartilage matrix contains chondrocytes in lacuna-like spaces.
- Histologic interpretation requires architecture and cytologic features, not matrix recognition alone.
- This drawing is conceptual; It does not depict an actual tumor.

Four major chondrosarcoma subtypes

Subtype	Key distinguishing source feature
Conventional	Hyaline cartilage-producing; dominant subtype
Clear cell	Large cells with clear cytoplasm; often epiphyseal
Dedifferentiated	Low-grade cartilage tumor plus high-grade noncartilaginous component
Mesenchymal	Primitive small round cells with islands of cartilage

Conventional subtype predominates

Approximately 90% of chondrosarcomas are conventional

- This group chiefly drives the typical epidemiologic and anatomic description.
- Nonconventional subtypes must not be forced into the conventional age–site profile.

Typical demographic profile

Conventional chondrosarcoma

- Usually presents in the fourth decade or later.
- Men are affected about twice as often as women.

Selected nonconventional subtypes

- Clear-cell and mesenchymal variants can present in the teens or 20s.
- Distinct age distribution may influence the morphologic differential.

Usual skeletal distribution

- Axial skeletal sites are prominent in conventional disease.
- Pelvis, shoulder region and ribs are characteristic locations.
- Distal extremities are rarely involved, unlike many benign enchondromas.

Site as a diagnostic clue

Conventional chondrosarcoma

- Often located in pelvis, shoulder or ribs.
- Concerning in the setting of pain and progressive growth.

Benign enchondroma

- Frequently occurs in tubular bones of hands and feet.
- May be found incidentally without pain.

Anatomic predilection is supporting context, not a stand-alone histologic diagnosis.

Two origins of conventional disease

Primary (de novo) tumor

Secondary tumor in an existing cartilage lesion

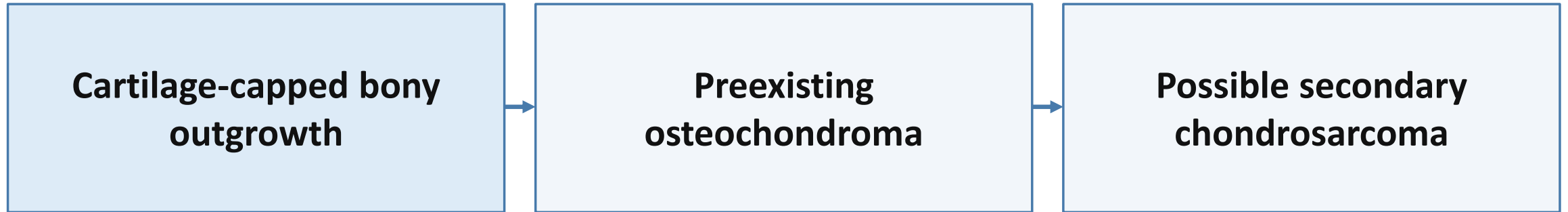
- Conventional chondrosarcoma may arise without an identified benign precursor.
- A subset develops in association with an enchondroma or an osteochondroma.

Secondary chondrosarcoma

Approximately 15% of conventional cases arise secondarily

- Recognized antecedents include enchondroma and osteochondroma.
- This proportion refers to conventional chondrosarcoma as, not all variants.

Osteochondroma and secondary risk



- Secondary malignancy is rare in the overall osteochondroma population.
- The background is especially relevant in multiple hereditary exostoses.

Enchondroma and secondary risk



- Sporadic solitary enchondromas rarely undergo sarcomatous transformation.
- Enchondromatosis is a more important risk setting.

Enchondromatosis syndromes

Ollier disease

- Multiple enchondromas.
- Nonhereditary enchondromatosis syndrome.

Maffucci syndrome

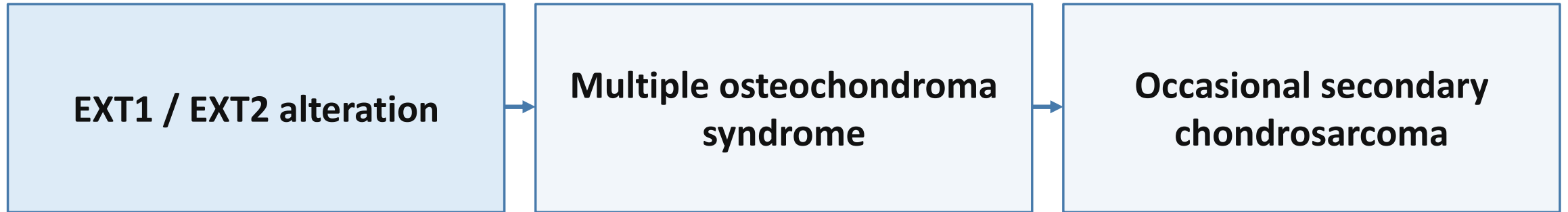
- Multiple enchondromas.
- Also associated with spindle-cell hemangiomas and other neoplasms.

Pathogenesis is genetically heterogeneous

No single driver explains all chondrosarcomas

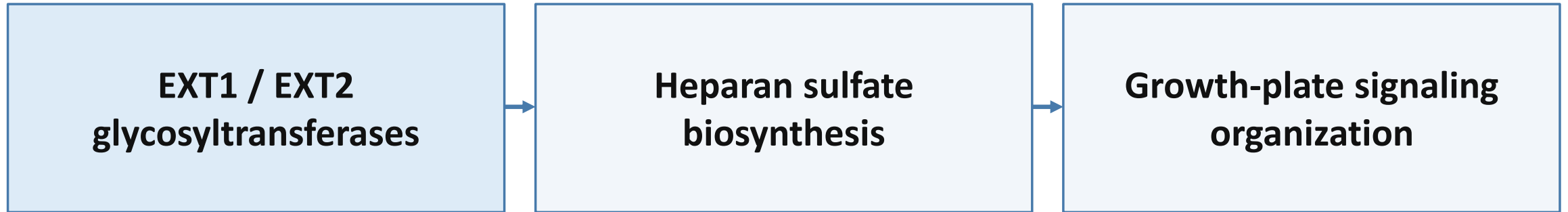
- Recurrent molecular alterations include EXT1/EXT2, IDH1/IDH2 and CDKN2A silencing.
- Their frequency, context and interpretation differ; Avoid treating them as universal diagnostic tests.

EXT1 / EXT2-associated setting



- The source links these alterations to chondrosarcoma in multiple osteochondroma syndrome.
- The gene products participate in matrix-associated glycosylation pathways.

Why EXT function matters in precursors



- In osteochondroma, reduced EXT function can disturb chondrocyte polarity and signaling.
- Do not infer a single deterministic EXT-to-sarcoma pathway from this context.

IDH-related tumor setting

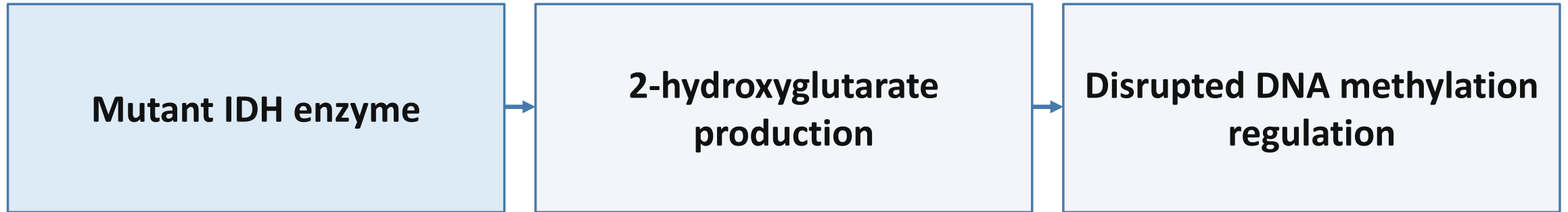
IDH1 / IDH2 mutation

**Chondromatosis-related
tumors**

**Also found in sporadic
chondrosarcoma**

- An IDH alteration identifies a molecular association, not by itself a malignancy grade.

IDH gain of function: Precursor context



- This mechanistic sequence for enchondroma.
- Consequences for differentiation, proliferation and survival are context-dependent; This is not a complete transformation model.

CDKN2A epigenetic silencing

CDKN2A locus methylation



CDKN2A silencing

- Source identifies the silencing event, without a claimed diagnostic sensitivity or predictive therapeutic role.

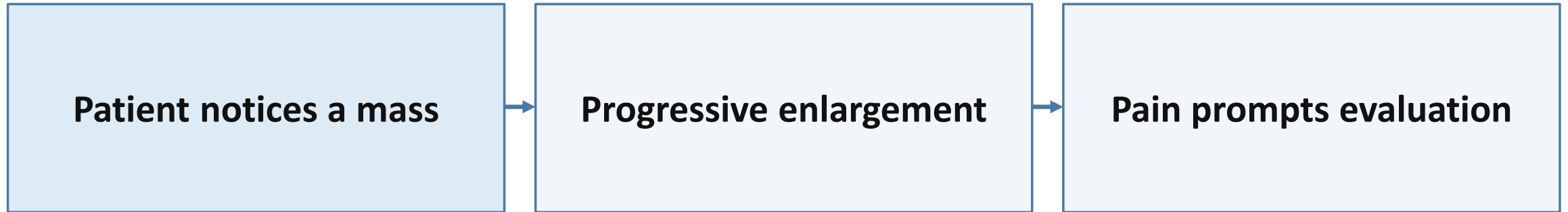
Interpreting molecular alterations

Finding	Robbins context	What it does not prove
EXT1 / EXT2	Multiple osteochondroma-associated lesions	Not present in every chondrosarcoma
IDH1 / IDH2	Chondromatosis-related and sporadic lesions	Does not alone distinguish benign from malignant cartilage
CDKN2A methylation	Common sporadic tumor alteration	Not a quantified universal prognostic marker

Clinical presentation: Pain and enlargement

- Typically presents with a painful mass.
- Progressive enlargement is a characteristic clinical pattern.
- Pain and growth must be integrated with lesion location, imaging and morphology.

Clinical reasoning begins with a time course



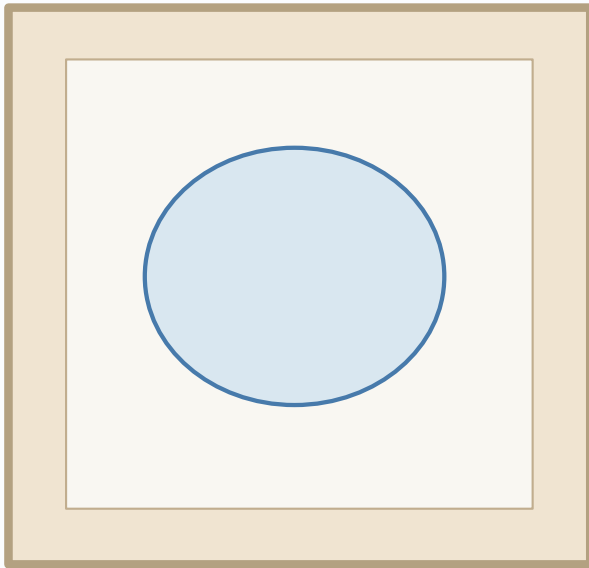
- The usual complaint reflects a progressively expanding cartilage-producing lesion.
- A clinical history alone cannot establish histologic grade.

Imaging evidence of cartilage matrix

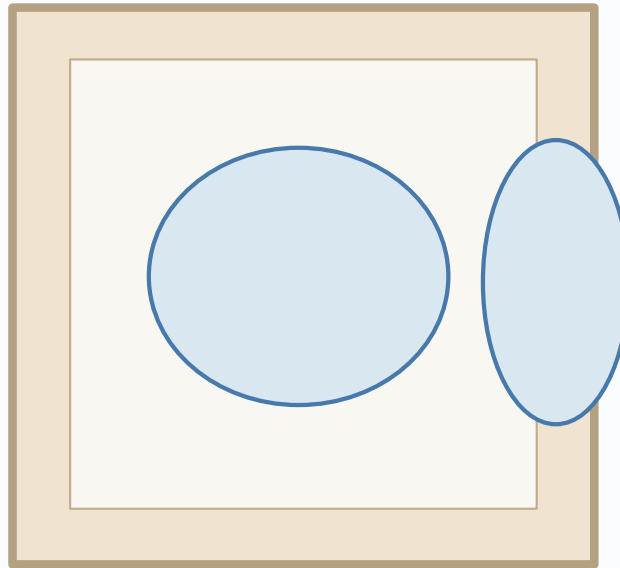
- Calcified tumor matrix produces flocculent densities on imaging.
- Mineralization supports a chondroid matrix-producing lesion.
- Cortical reaction or destruction helps assess local aggressiveness.

Slow-growing lesion: Reactive cortex

Cortex retained



Cortex breached



Interpretation

- A retained or thickened cortex can occur with a slowly growing, low-grade tumor.
- Cortical disruption and extracortical extension are more concerning features.
- Both panels are explanatory representations, not patient scans.

The cortex records tumor behavior

Slow-growing low-grade disease

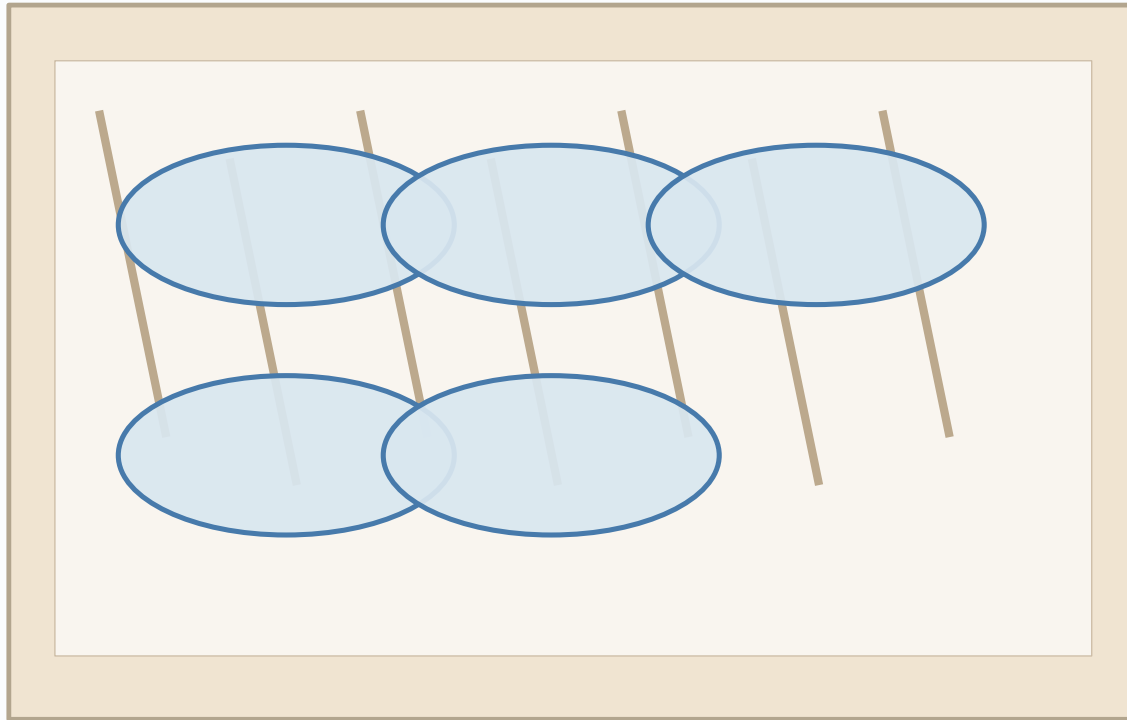
- May induce reactive cortical thickening.
- Can remain locally confined in appearance.

Aggressive high-grade disease

- Cortical destruction is characteristic.
- Extension into soft tissues may produce a mass.

From medullary growth to tissue invasion

Cartilaginous lobules permeate marrow



Pre-existing bony trabeculae are entrapped

Interpretation

- Tumor permeates marrow and surrounds existing bone trabeculae.
- Extracortical extension may involve adjacent muscle or fat.
- Apparent lobulation does not exclude infiltrative behavior.

Imaging clues and pathologic interpretation

Observed feature	Interpretation supported by the source
Flocculent matrix densities	Mineralization within chondroid matrix
Reactive cortical thickening	May accompany slower low-grade growth
Cortical destruction	Evidence of aggressive local behavior
Soft-tissue mass	Extracortical tumor extension

Why axial site matters in management

- Pelvis and other axial sites can make local disease control difficult.
- Local recurrence is particularly problematic in limb girdles and axial skeleton.
- Anatomical site modifies prognosis beyond histologic grade alone.

Gross appearance: A nodular cartilage tumor

- Conventional tumors may be bulky.
- Cut surfaces show nodules of glistening gray-white, translucent cartilage.
- Gross appearance may suggest a cartilage-producing tumor but cannot establish grade by itself.

Two gross matrix textures

Firm / translucent cartilage

- Glistening gray-white cartilage nodules.
- Cartilage matrix forms the major tumor substance.

Gelatinous / myxoid matrix

- Focally softer, gel-like material.
- Myxoid matrix may ooze from the cut surface.

Gross secondary changes

- Focal calcification may interrupt otherwise translucent cartilage.
- Central necrosis may create cystic spaces.
- These components contribute to gross and imaging heterogeneity.

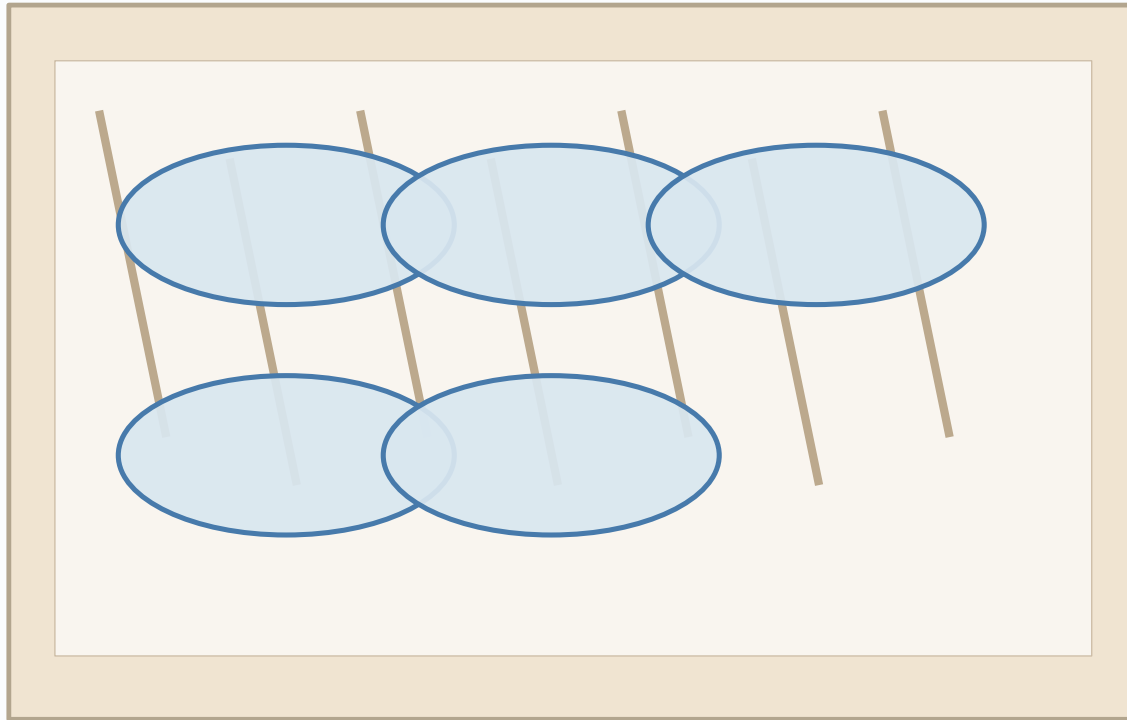
Gross tumor extension



- Extracortical growth is frequent in established conventional tumors.
- Interpret the full margin and surrounding tissue interface.

Permeative growth within marrow

Cartilaginous lobules permeate marrow



Pre-existing bony trabeculae are entrapped

Interpretation

- Cartilage surrounds pre-existing bony trabeculae.
- Permeation is an architectural clue to malignant cartilage-producing growth.
- Native diagram intentionally omits true microscopic textures.

Entrapped trabeculae: Why they matter

- Malignant cartilaginous tissue may infiltrate the marrow space.
- Pre-existing bony trabeculae become enclosed by the neoplastic cartilage.
- This architectural finding complements cellularity and nuclear atypia.

Benign enchondroma versus malignancy

Enchondroma

- Well-circumscribed nodule of hyaline cartilage.
- Cortex usually intact; Peripheral reactive bone may surround lesion.

Chondrosarcoma

- Cartilage can permeate marrow and surround trabeculae.
- Cortical destruction and extracortical growth may occur.

Why cellular atypia is not the whole diagnosis

- Benign cartilaginous tumors can show some increased cellularity or atypia in syndromic settings.
- A low-grade chondrosarcoma may have only modest cytologic abnormalities.
- Tumor architecture, imaging, symptoms and location therefore matter together.

Conventional histologic grade is multidimensional

Cellularity

Cytologic atypia

Mitotic activity

- Grades 1–3 correlate with biologic behavior and prognosis.
- The source does not specify numeric scoring cutoffs for the three variables.

Grade 1 chondrosarcoma: Subtle cytology

- Typically has low cellularity.
- Neoplastic chondrocytes possess plump vesicular nuclei and small nucleoli.
- Cytologic blandness must be interpreted together with infiltrative growth.

Grade 3 chondrosarcoma: Overt malignancy

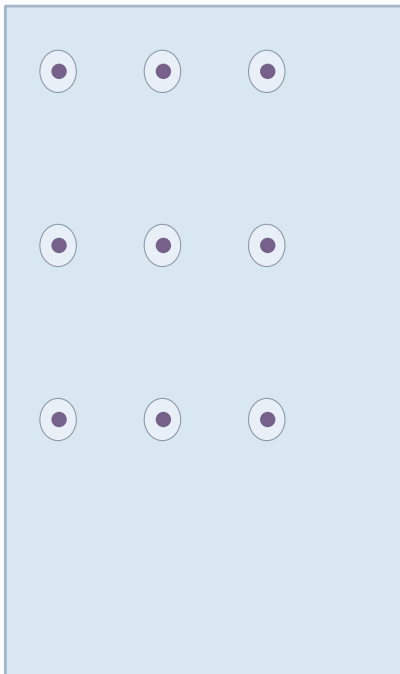
- High cellularity is typical.
- Extreme nuclear pleomorphism is present.
- Mitotic figures are frequent; Risk of hematogenous metastasis is much higher.

Grade 2: Between the textbook poles

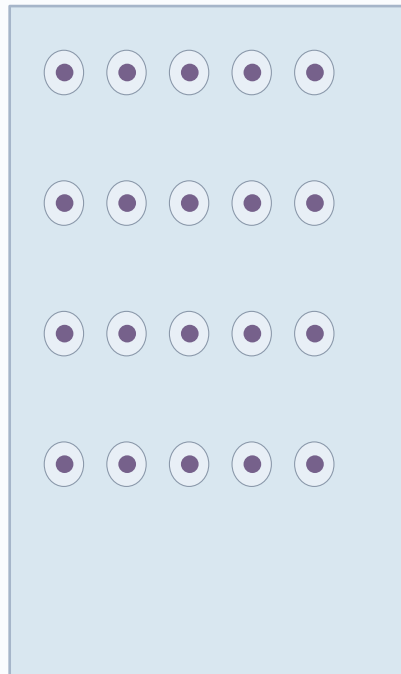
- Conventional chondrosarcoma is graded 1, 2 or 3.
- The extracted Robbins passage provides detailed descriptors for grades 1 and 3, but not an independent grade-2 scoring algorithm.
- Intermediate-grade assignment requires complete histologic assessment rather than interpolation from a schematic.

Cellularity and atypia across grades

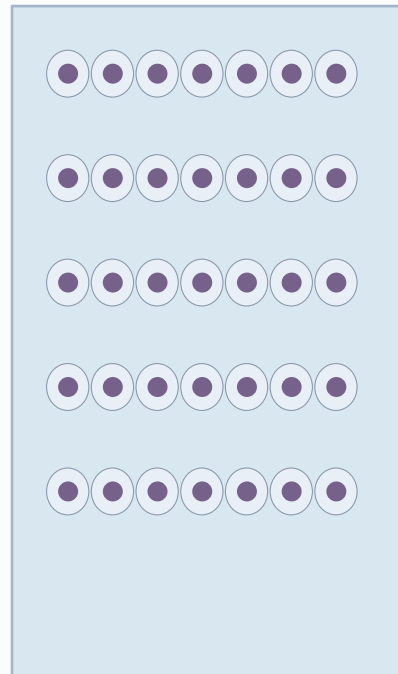
Grade 1



Grade 2



Grade 3



Interpretation

- The conceptual panels show increasing cellularity and nuclear variation.
- They are schematic, not WHO grading micrographs or quantitative thresholds.
- Grade is assigned on actual sampled tumor morphology.

Low versus high grade: Linked domains

Grade 1 pattern

- Low cellularity and relatively mild cytologic atypia.
- May show reactive cortical change on imaging.

Grade 3 pattern

- Marked pleomorphism and many mitoses.
- Aggressive cortical destruction and metastatic potential.

Dedifferentiated variant: Two components

Low-grade chondrosarcoma

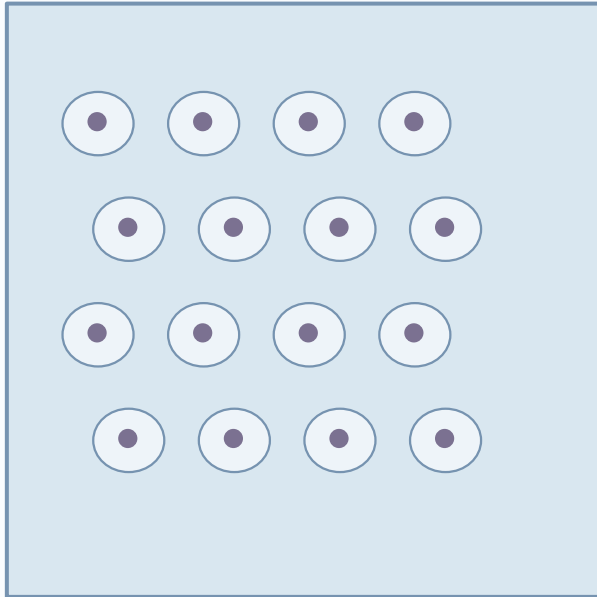
**Abruptly distinct second
component**

**High-grade
noncartilaginous sarcoma**

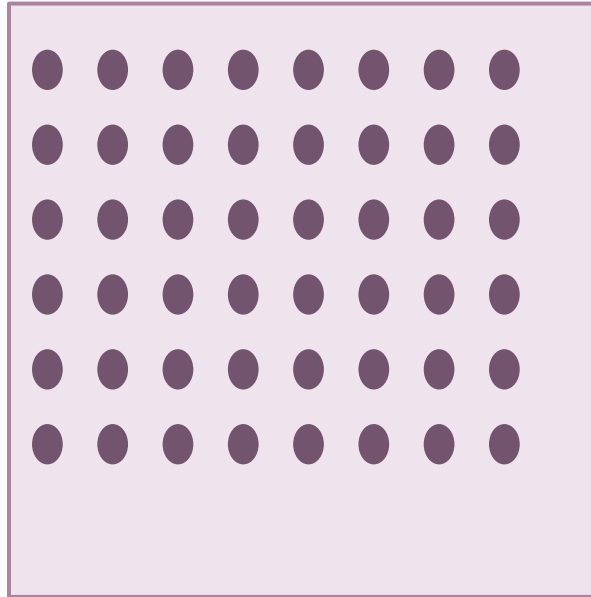
- The defining feature is juxtaposition of differentiated cartilage and high-grade noncartilage tissue.

Dedifferentiated morphology is biphasic

Cartilaginous component



Noncartilaginous high-grade cells



Interpretation

- The two components differ in matrix production.
- Sampling only the cartilage component could miss the high-grade component.
- This is a conceptual sampling pitfall, not a source-specific diagnostic algorithm.

Clear-cell variant: Distinct profile

Clinical / anatomic pattern

- May occur in teens or 20s.
- Arises in epiphyses of long tubular bones.

Microscopy

- Sheets of large atypical chondrocytes with clear cytoplasm.
- Osteoclast-type giant cells and intralesional bone formation.

Clear-cell morphology: Multiple tissue elements

- Abundant clear cytoplasm in large atypical tumor cells.
- Numerous osteoclast-type giant cells.
- Bone formation within the lesion: Part of its described morphology.

Mesenchymal subtype: Age and architecture

Clinical context

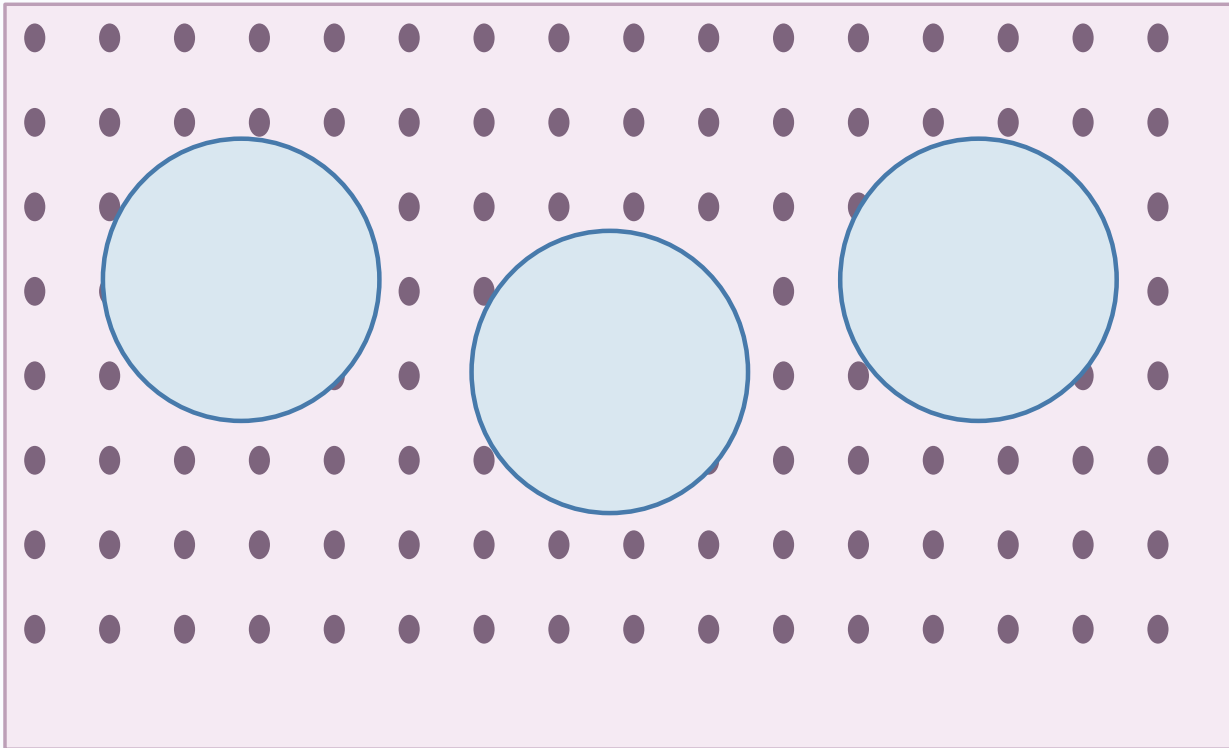
- Often affects younger patients, including teens or 20s.
- Unlike conventional disease, age distribution is not dominated by older adults.

Microscopy

- Islands of differentiated hyaline cartilage.
- Primitive small-round-cell sheets around the cartilage.

Mesenchymal pattern: Cartilage islands

Cartilage islands in primitive-cell background



Interpretation

- Well-differentiated hyaline cartilage appears as discrete islands.
- Sheets of primitive-appearing small round cells surround those islands.
- This schematic is not a bona fide H&E section.

Subtype recognition: One decisive pattern

Subtype	Distinguishing tissue feature
Conventional	Infiltrative hyaline/myxoid cartilage; graded 1–3
Dedifferentiated	Low-grade cartilage component plus high-grade noncartilage tumor
Clear cell	Large clear-cytoplasm chondrocytes, giant cells and bone
Mesenchymal	Small round cells with discrete hyaline cartilage islands

Integrated diagnosis is more than one feature

- Identify chondroid matrix and the growth pattern.
- Examine the interface with marrow, cortex and adjacent tissues.
- Assess cytologic atypia, cellularity and mitoses.
- Integrate grade with age, site and imaging phenotype.

Key benign–malignant comparison

Features favoring enchondroma

- Well-defined intramedullary cartilage nodule.
- Preserved cortex, possibly a thin reactive bony rim.
- Often incidental in small tubular bones.

Features favoring chondrosarcoma

- Painful progressively enlarging mass.
- Permeation around trabeculae.
- Potential cortical destruction or soft-tissue extension.

Limits of a small biopsy or isolated image

- The sampled region may not represent all tumor components.
- Grading depends on evaluable tumor morphology and the interface with host bone.
- An isolated image cannot reliably demonstrate the patient's symptoms, full cortical behavior or site.

Histologic grade predicts behavior



- Source directly associates grade with outcome, including metastasis and survival.
- Site influences consequences of local failure.

Grade 1: Local recurrence remains relevant

Approximately 10% local recurrence

- Grade 1 tumors rarely metastasize.
- Despite excellent overall survival, recurrent disease can cause major morbidity.

Grade 1: Excellent reported survival

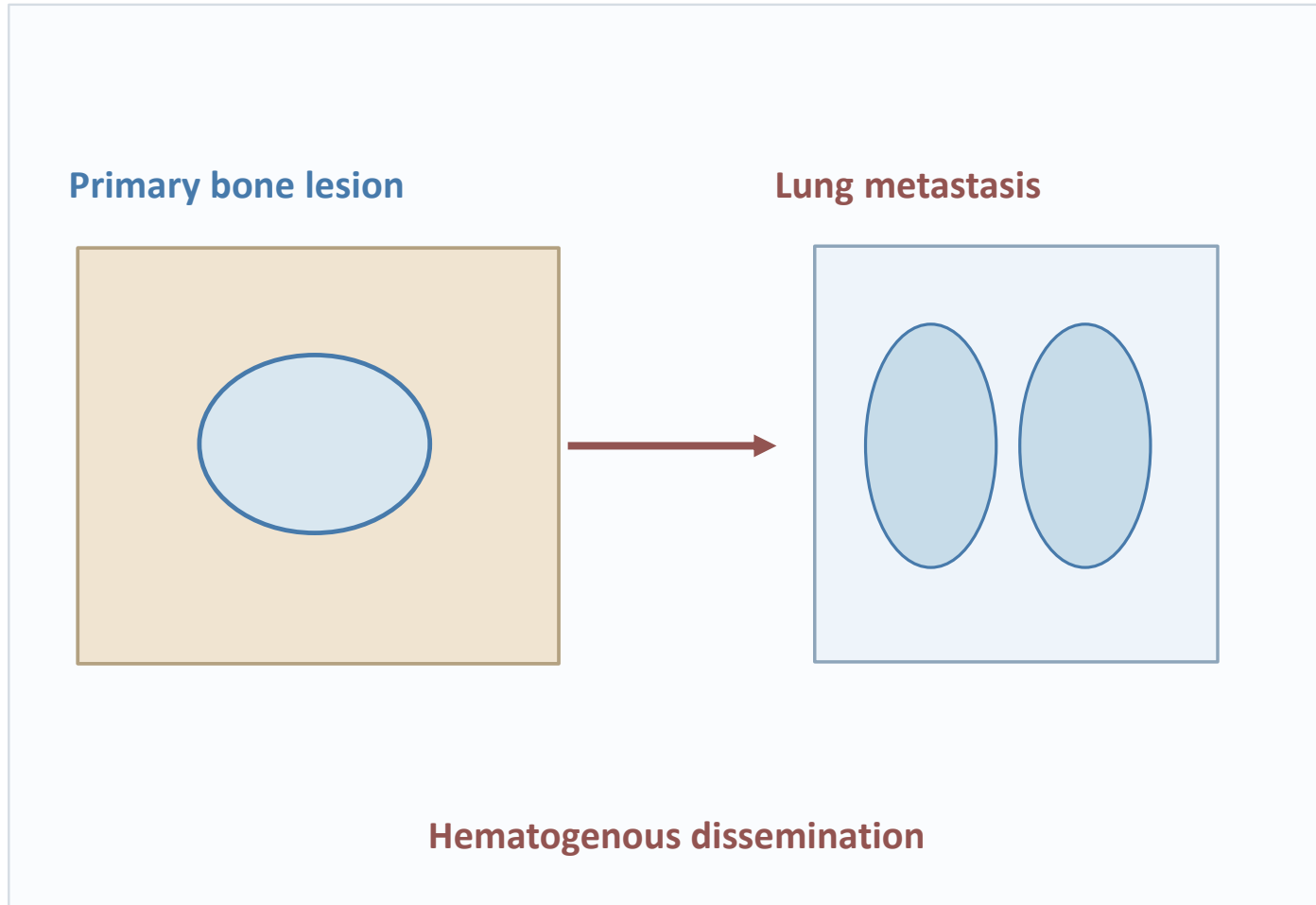
Five-year survival close to 100%

- This is the textbook estimate for grade 1 disease; It is not a prediction for an individual patient.
- Clinical location and local control still matter.

Local recurrence is not uniformly harmless

- Axial and limb-girdle sites are especially challenging for local control.
- Mortality in grade 1 disease can result from local recurrence.
- Grade alone does not capture surgical accessibility and risk.

Grade 3: Hematogenous metastasis



Interpretation

- Most grade 3 tumors spread through the bloodstream.
- The lungs are a particularly important metastatic site.
- This pathway is schematic and does not encode metastasis rates.

Grade 3: Markedly poorer outcome

Five-year survival less than 50%

- Textbook estimate for grade 3 tumors.
- Most grade 3 chondrosarcomas disseminate hematogenously, especially to the lungs.

Terminology in low-grade extremity disease

Grade 1 chondrosarcoma

- Traditionally indicates a low-grade malignant cartilaginous neoplasm.
- Textbook notes that metastasis is rare.

Atypical cartilaginous tumor

- Proposed label for grade 1 lesions of long bones of extremities.
- Emphasizes their favorable behavior at this anatomic site.

Terminology is site-dependent; Do not extend the same prognosis to equivalent-appearing axial tumors.

Treatment tracks tumor risk and location

Grade 1, selected sites

**Possible intralesional
curettage**

**Higher grade /
nonappendicular sites:
Wide excision**

- Surgery is the principal treatment.
- Site, grade and appropriate case selection govern treatment extent.

Surgery: Selective local versus wide treatment

Selected grade 1 case

- Curettage may be appropriate in selected cases.
- Requires careful assessment of local risk.

Higher-grade or axial/nonappendicular case

- Wide surgical excision is the described approach.
- The anatomic challenge of achieving margins is clinically relevant.

Case 1: Painful expanding pelvic mass

Hypothetical vignette

An older adult has progressive pelvic pain and an enlarging lesion. Imaging suggests calcified cartilage matrix, cortical destruction and extension into adjacent soft tissue.

Interpretation prompts

- Which subtype is most compatible with this age–site profile?
- What features indicate aggressive local behavior?

Case 1: Interpretation

Reasoning from provided findings

- Conventional chondrosarcoma is compatible with the older age and pelvic location.
- Flocculent mineralization supports chondroid matrix; Cortical destruction and soft-tissue extension signify aggressiveness.
- Grade still requires microscopic assessment; Imaging alone cannot assign grade 3.

Case 2: Epiphyseal lesion in a young adult

Hypothetical vignette

A patient in their early 20s has a cartilage-producing tumor centered in the epiphysis of a long bone. Histology shows large cells with clear cytoplasm and osteoclast-type giant cells.

Interpretation prompts

- Which subtype best integrates the site and morphology?
- Which additional described tissue component might occur?

Case 2: Interpretation

Reasoning from provided findings

- Clear-cell chondrosarcoma best fits the epiphyseal origin and large clear-cytoplasm chondrocytes.
- Intralesional bone formation is another described microscopic feature.
- The conventional older-adult axial-site pattern should not be imposed on this subtype.

Case 3: A low-grade extremity lesion

Hypothetical vignette

A long-bone cartilage tumor has low cellularity and subtle atypia. Imaging shows limited local aggressiveness and microscopic sampling raises grade 1 conventional chondrosarcoma.

Interpretation prompts

- What alternative site-dependent term does Robbins discuss?
- What prognosis and local issue should be explained?

Case 3: Interpretation

Reasoning from provided findings

- Atypical cartilaginous tumor is the source-discussed alternative terminology for grade 1 lesions in long bones of extremities.
- Metastasis is rare and the estimated five-year survival approaches 100%, but local recurrence remains possible.
- An equivalent low-grade lesion in an axial site requires greater attention to difficult local control.

Synthesis: Grade, site and clinical action

Domain	Low-grade setting	Aggressive setting
Architecture	May have permeation despite bland cytology	Often more destructive and infiltrative
Cytology	Low cellularity; relatively mild atypia	Marked pleomorphism; frequent mitoses
Biologic risk	Mainly local recurrence	Hematogenous dissemination, especially lung
Operative strategy	Selected grade 1 lesions: curettage	Higher-grade/nonappendicular: wide excision

Final diagnostic synthesis

- A malignant cartilage-producing bone tumor is identified by matrix, growth pattern and clinical–radiologic context.
- Conventional, clear-cell, dedifferentiated and mesenchymal variants have distinct morphology.
- EXT1/EXT2, IDH1/IDH2 and CDKN2A changes are contextual—not universal grading substitutes.
- Grade and anatomic site jointly inform recurrence, metastatic potential and surgery.

Principal reference and editorial limitations

Robbins, Cotran & Kumar

Pathologic Basis of Disease, 11th edition (2026)

Chapter 26 — Bones, Joints, and Soft Tissue Tumors, pp. 1080–1084

Source note: extracted Markdown interleaves the chondrosarcoma morphology text with the next section. The relevant continuation was recovered and included.

All tissue, cell, radiologic and metastasis drawings are native, editable teaching schematics, not diagnostic specimens.