Pathology Teaching in an Integrated Pre-clinical Medical School Curriculum and Adaptations to COVID-19 Restrictions

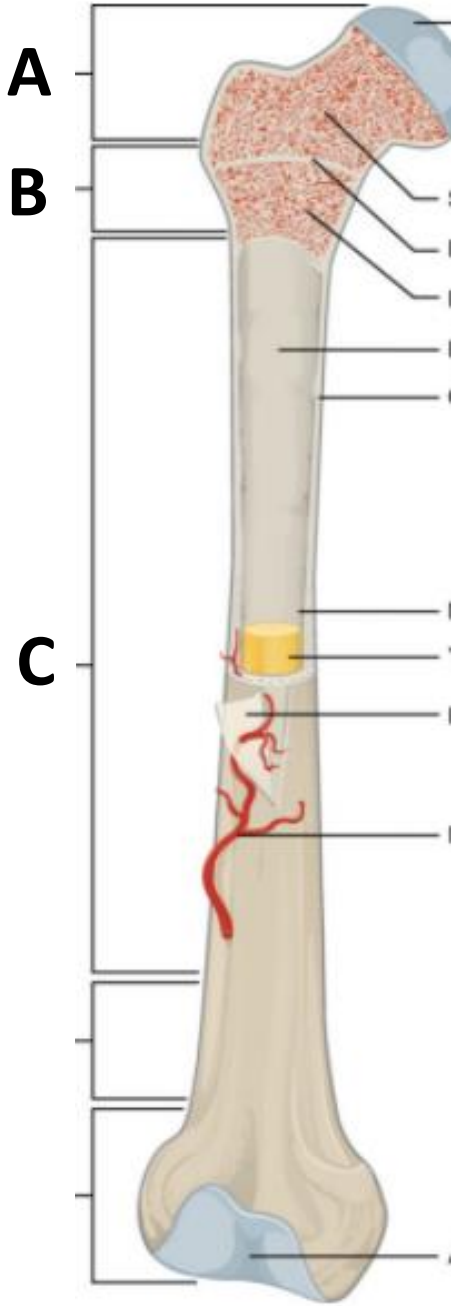
Supplemental Appendix 1: Example Case Analysis Used in Large Group Online Format

Bone/Soft Tissue Cases

October 20, 2020

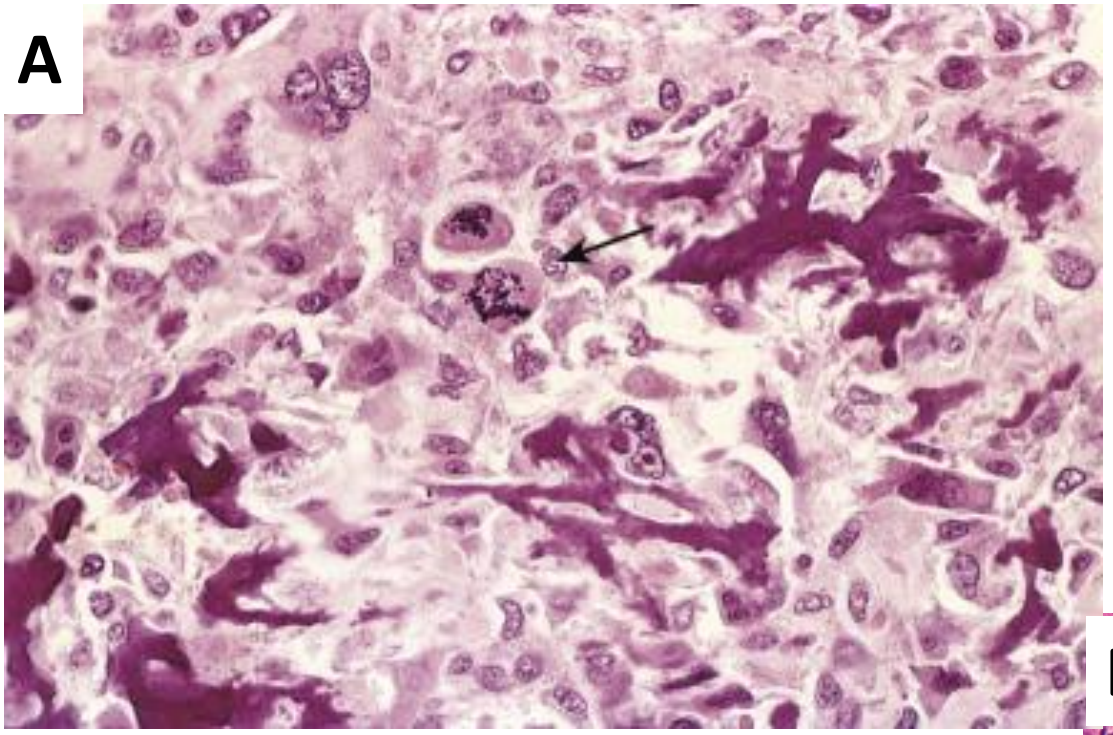
POLL QUESTIONS
Pre-Test

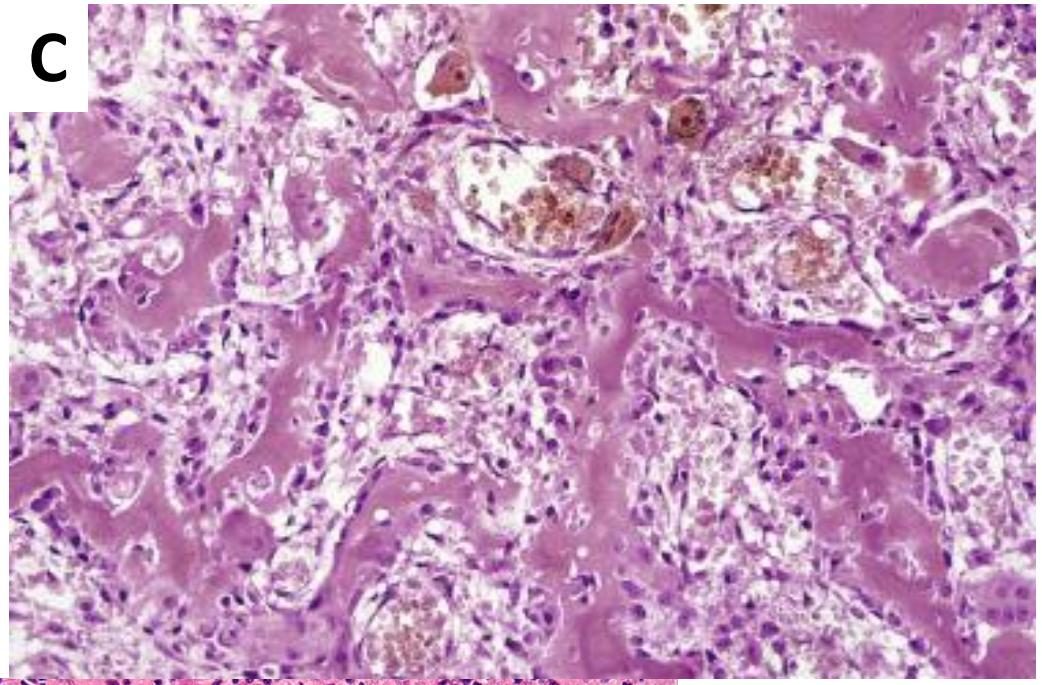
Pre-Test Poll 1

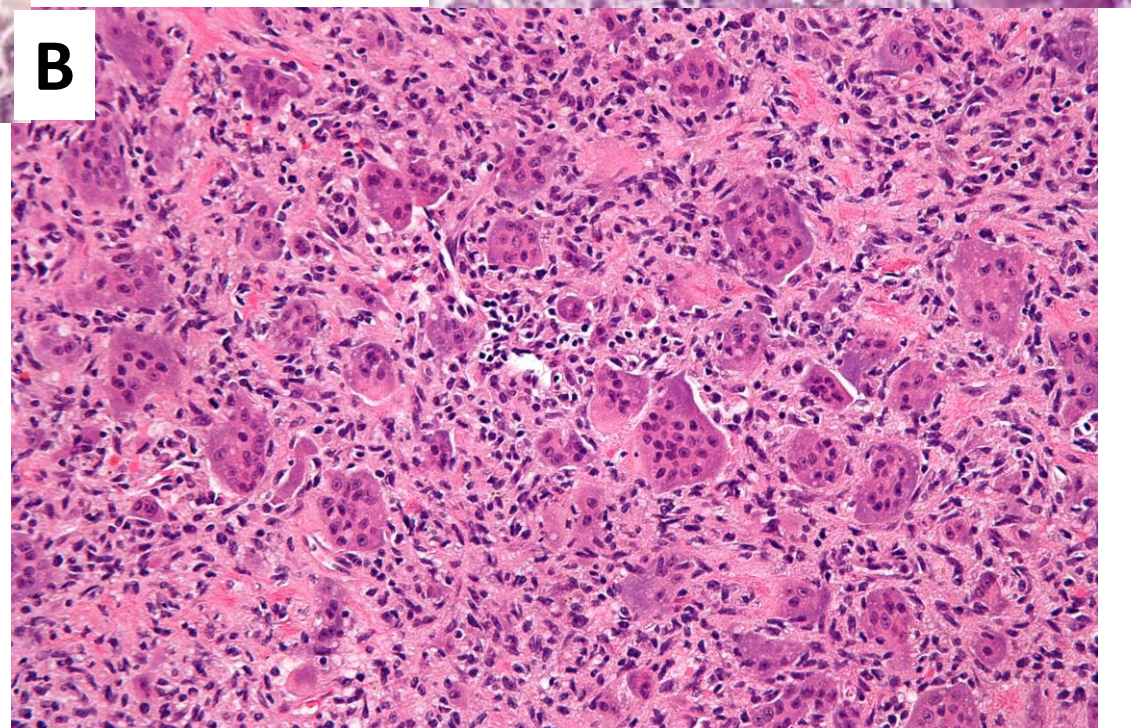


POLL QUESTION:
Which of the following represents the metaphysis?
A
B *
C

Pre-test Poll 2







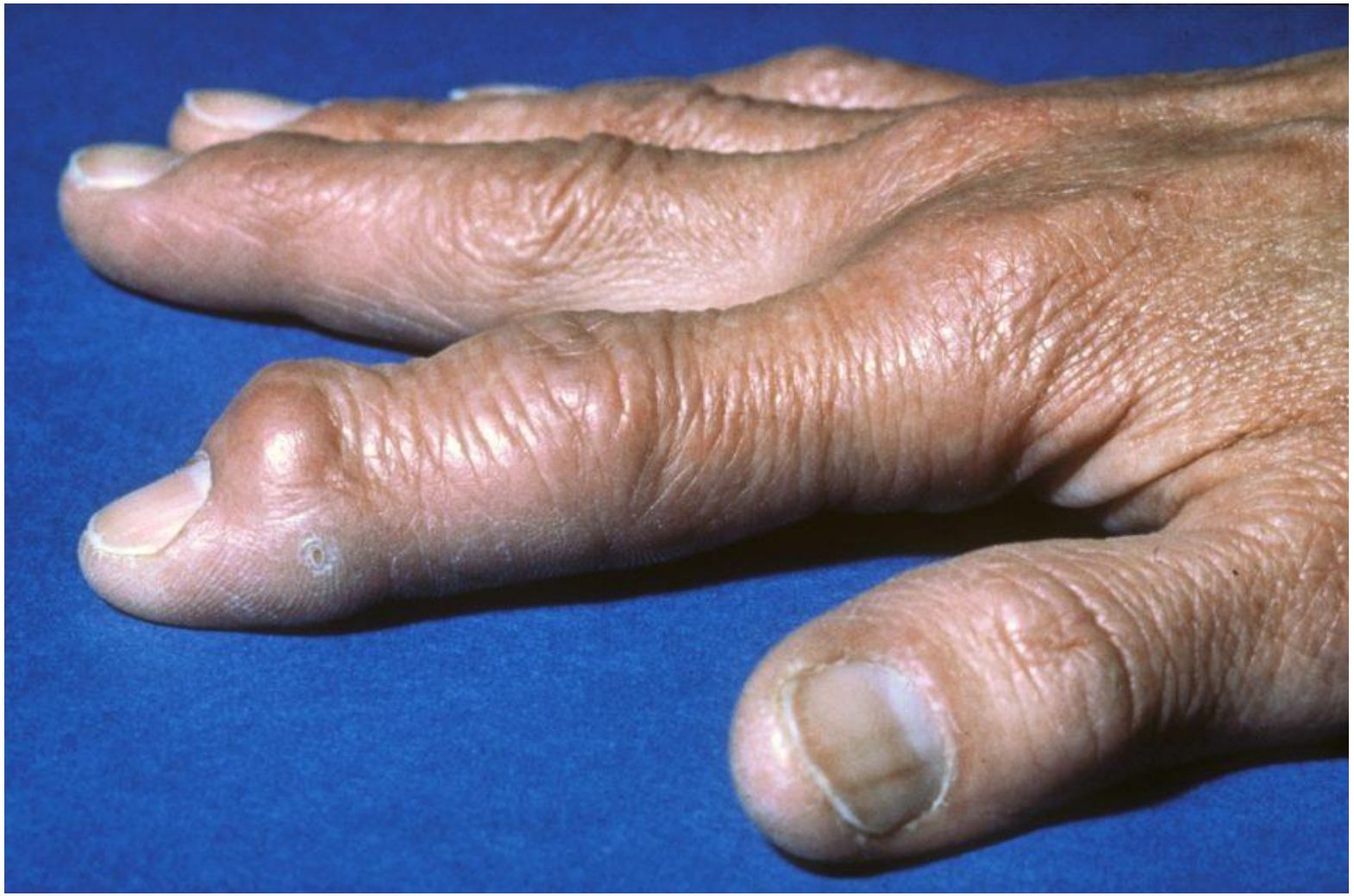
POLL QUESTION:
The histologic features in which of the photos is most consistent with osteoid osteoma?

A

B *

C

Pre-test Poll 3



POLL QUESTION:
Which of the following is present on this patient's hand?
Aschoff node
Bouchard node
Charcot node
Dupuytren node
Heberden node *

Okay – let’s get started on the Cases…….

Case 1

CLINICAL SUMMARY

A 10 year old male was brought to the emergency room after soccer practice with acute pain in his right leg above the knee. He could not bear to put weight on the leg due to pain. He had been complaining of pain in the leg for several months, sometimes awaking him from sleep at night. There had been no swelling or redness, and no pattern to the pain in relationship to activity.

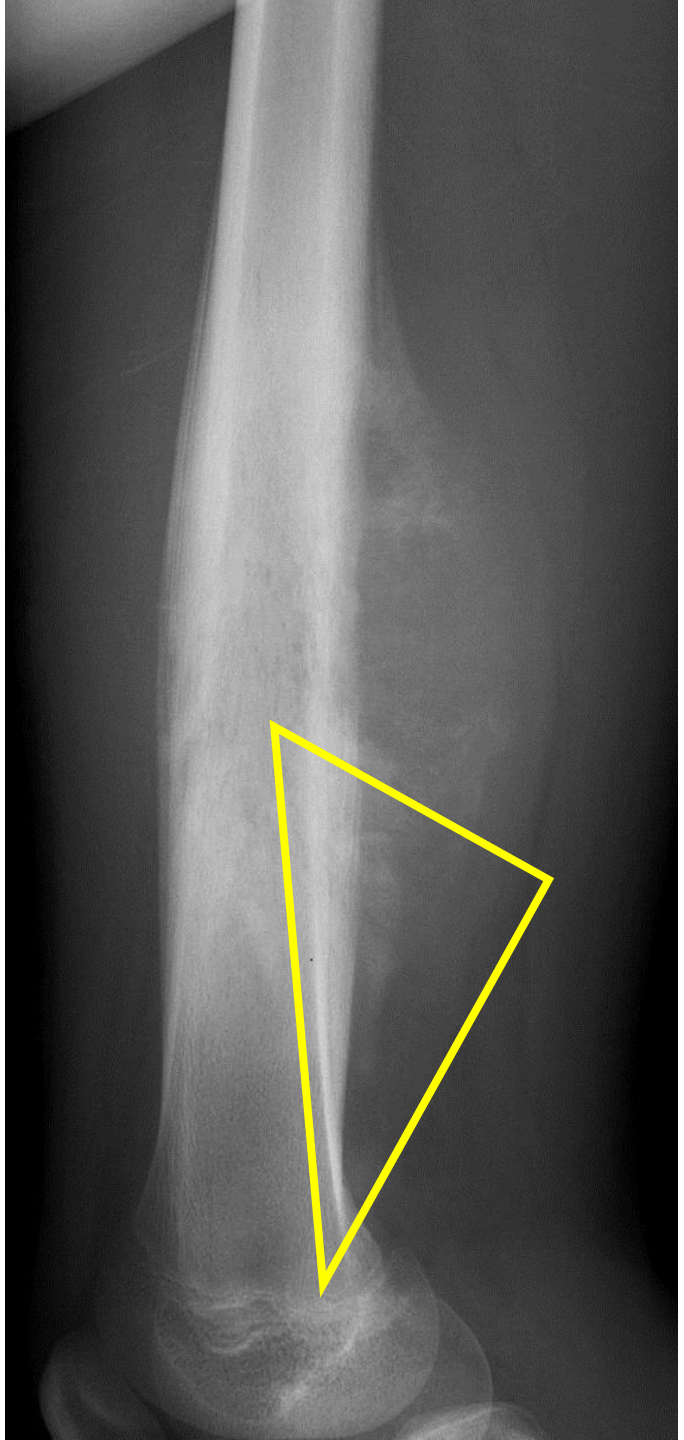
Continue

Tests and Procedures

A x-ray was done which showed a lesion in the metaphysis of the femur. (The x-ray at left is from a similar patient.)

X-ray distal femur

Identify the lesion in the bone. There is bone destruction with a somewhat motheaten appearance and periosteal reaction (and lifting of the periosteum - Codman triangle).



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The differential diagnosis might include chrondosarcoma, Ewing sarcoma, osteochondroma, osteoid osteoma, and osteosarcoma. Enter your top choice and explain your reasoning.

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The IMAGING (lesion that shows bony destruction) along with the patient AGE and history (leg PAIN) and put a malignant process (osteosarcoma and Ewing sarcoma) at the top of my list. And those are the two most common bone sarcomas in children. The LOCATION of the tumor in the metaphysis favors this being osteosarcoma (as Ewing sarcoma most often arises in diaphysis. Also, osteosarcoma is the most common malignant primary bone tumor in children.

Chondrosarcoma, the other malignancy listed, most often occurs in adults (40-60 yrs), affects axial skeleton (pelvis, shoulder).

Osteochondroma and osteoid osteoma are lesions that could occur in this age range and both arise in metaphysis, however these are benign lesions and the imaging features are those of a malignant process.

PATHOLOGY

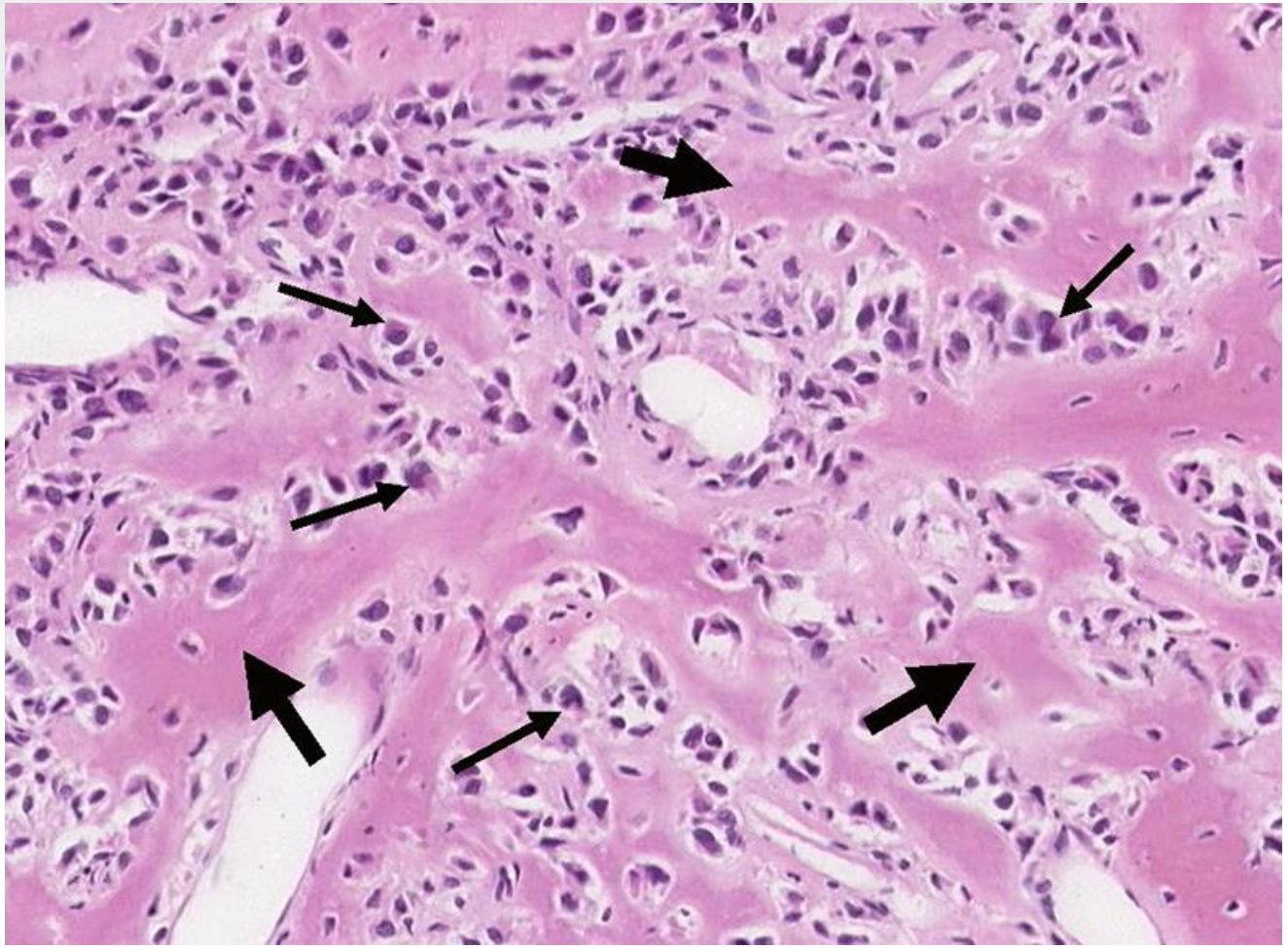
An open biopsy was performed and diagnosed as osteosarcoma. **Review the biopsy specimen.** Chemotherapy was instituted and three months later, limb conserving surgery was performed and the distal femur was resected.

Continue

BIOPSY SPECIMEN (before treatment)

Thin arrows identify some of the numerous hyperchromatic neoplastic cells.

Thick arrows identify new osteoid laid down by the neoplastic cells



PATHOLOGY

An open biopsy was performed and diagnosed as osteosarcoma. **Review the biopsy specimen.** Chemotherapy was instituted and three months later, limb conserving surgery was performed and the distal femur was resected.

Examine the resection specimen (gross and microscopic). Be able to identify and describe the morphologic findings in the resected femur and discuss their etiology and pathogenesis.

Note that the amputation was performed after chemotherapy, which was intended to kill tumor cells, so the histology in the resected specimen does not resemble the initial biopsy.

Compared with the original tumor, indicate in the box below approximately what percentage of the tumor cells you think has been killed by the therapy and explain why this information is important?

Distal Femur

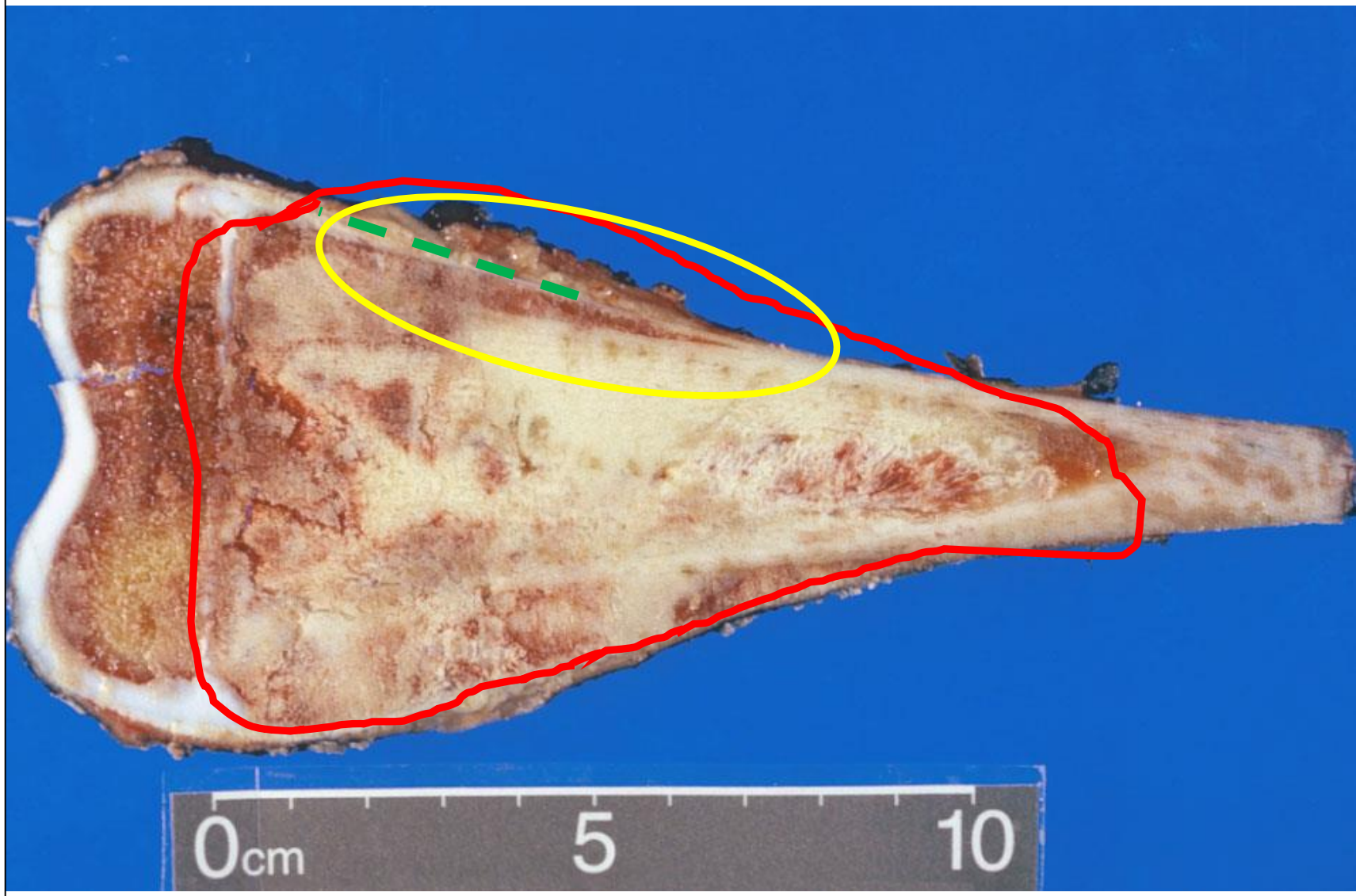
<u>On gross image identify:</u>

-normal bone and joint architecture

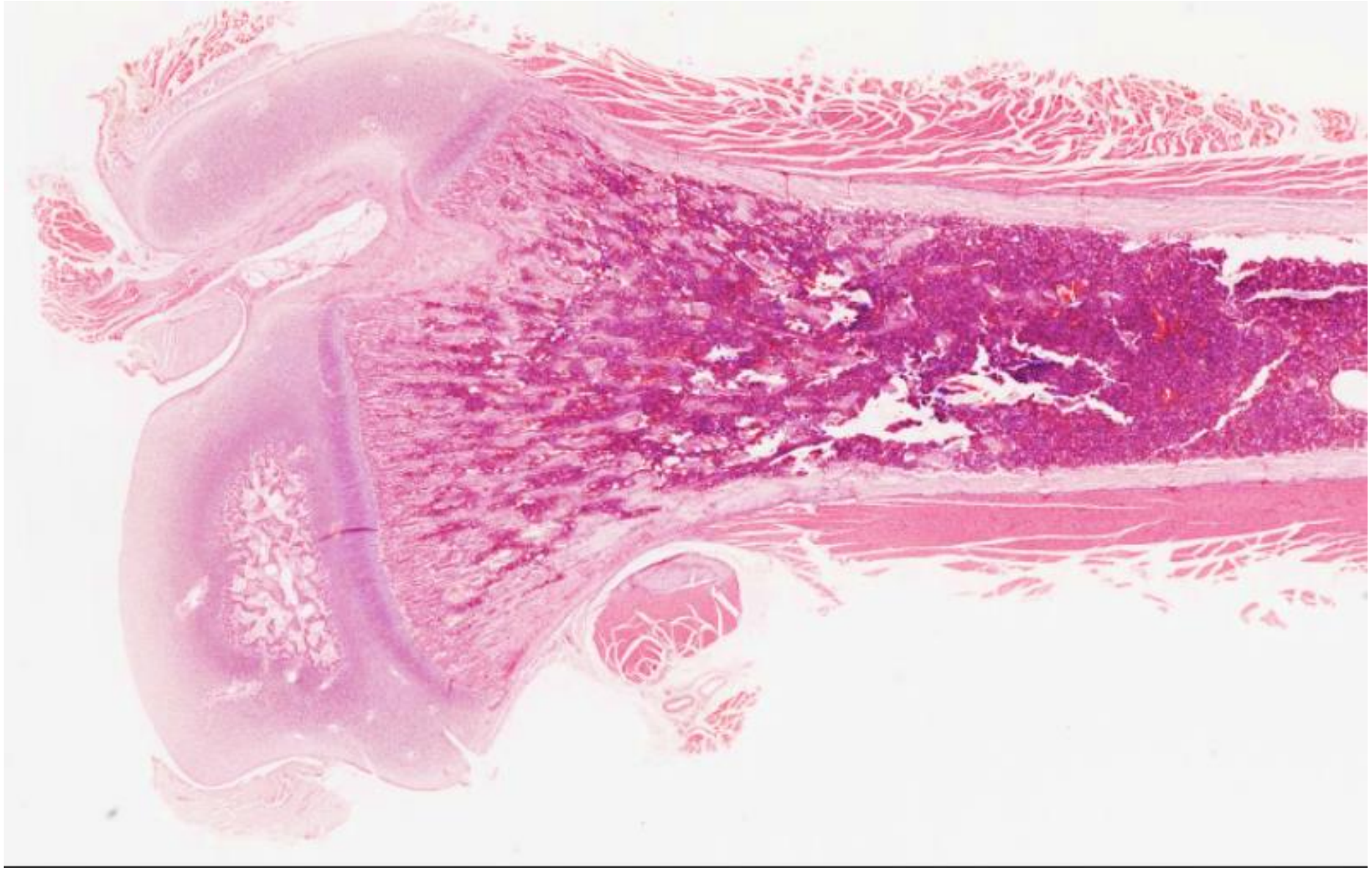
-extent of the tumor (where is it located?) tumor = **red**

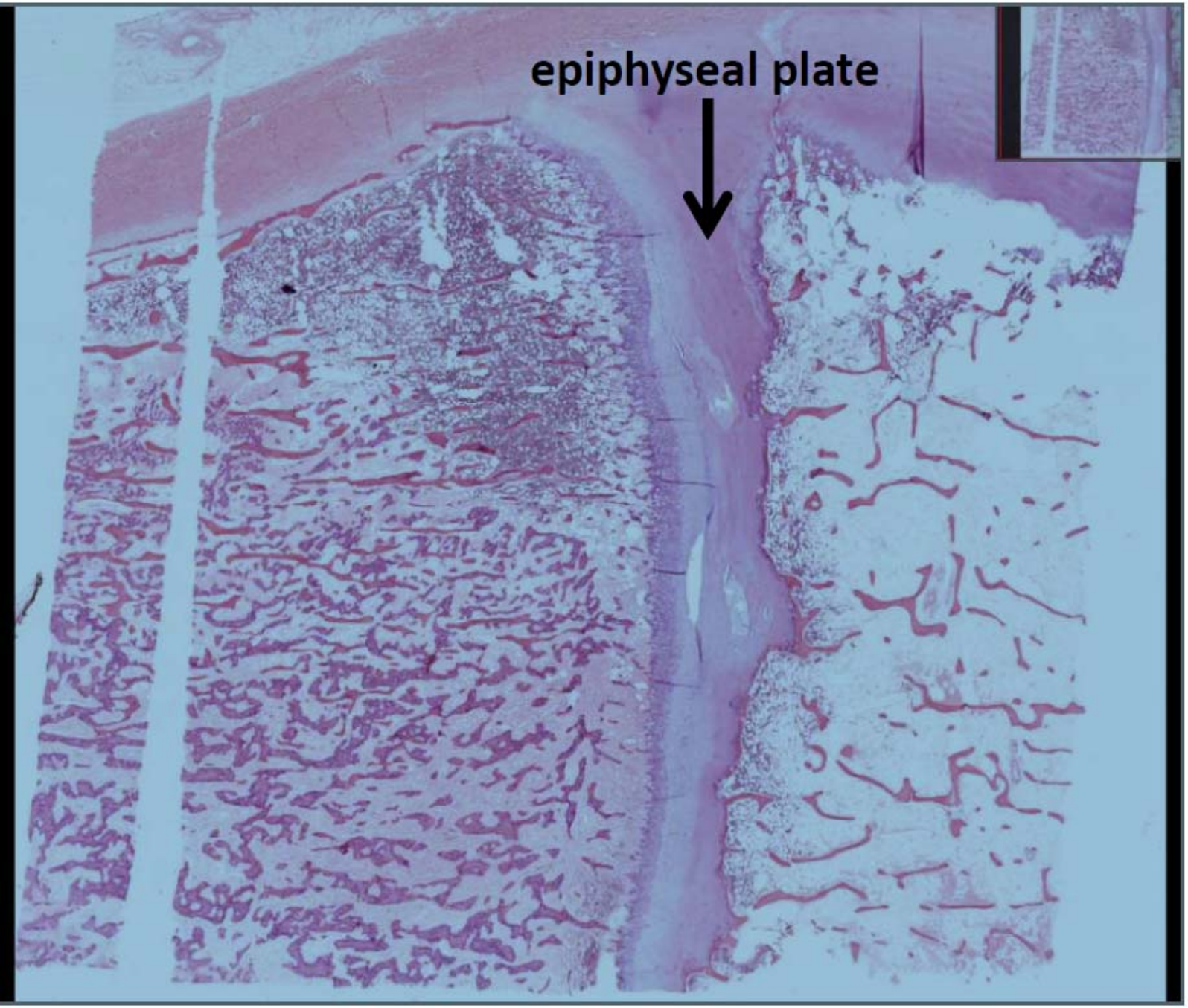
-Codman's triangle (tumor lifting the periosteum) **Green line**

Generally the sarcoma is bulky, gritty, gray-white and may contain cysts and areas of degeneration. The lesions frequently destroy the surrounding cortex and may lift the periosteum in the typical Codman triangle seen on x-ray. They spread extensively in the medullary canal.

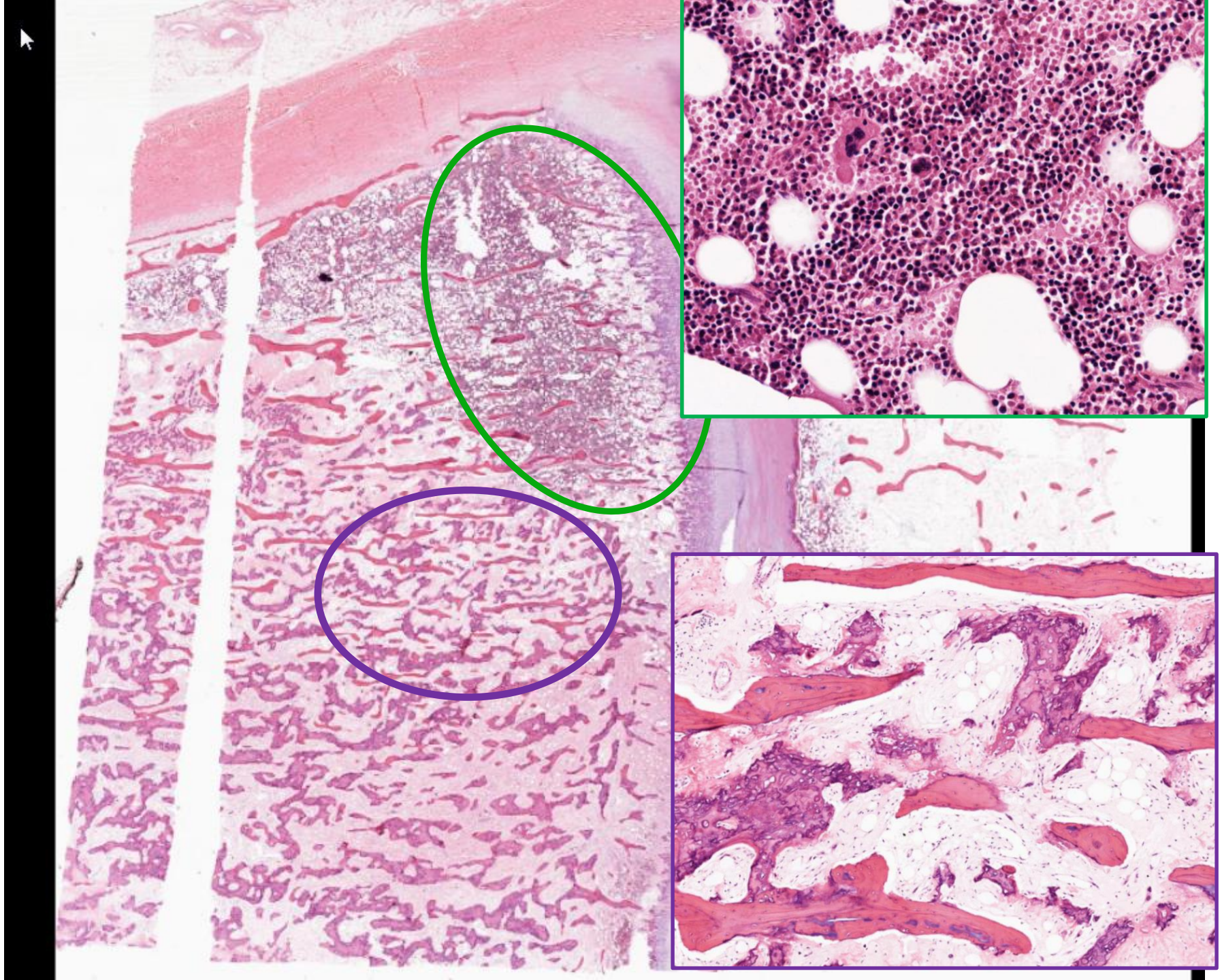


Normal Comparison





First virtual slide ("Resection specimen with epiphyseal plate" – POST TREATMENT)

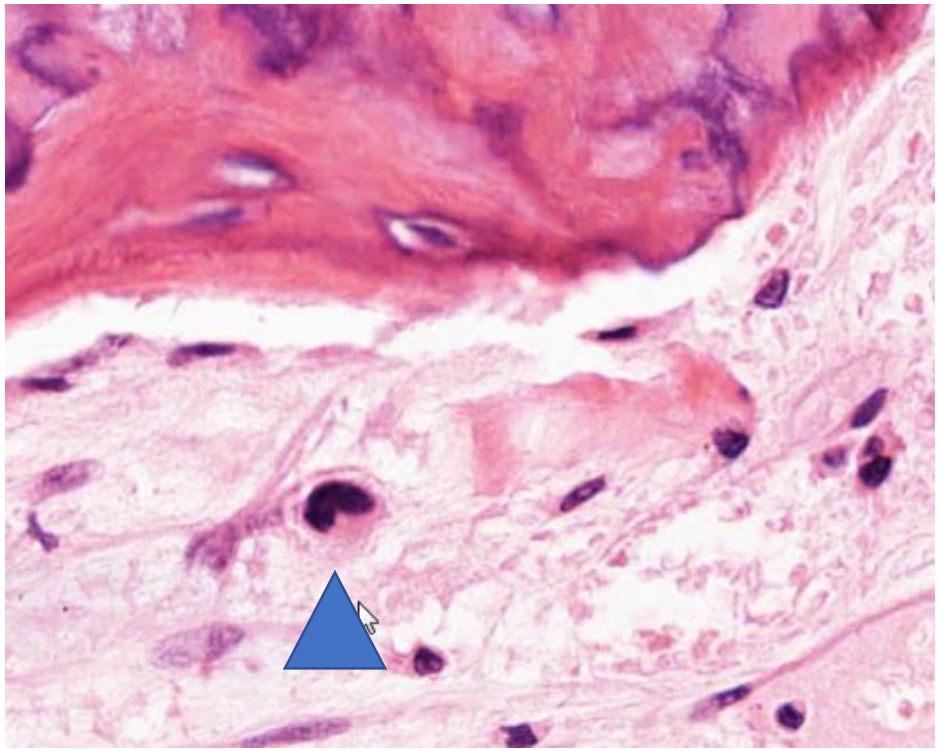


<u>On first virtual slide ("Resection specimen with epiphyseal plate" – POST TREATMENT)</u> <u>identify:</u>

-the epiphyseal plate

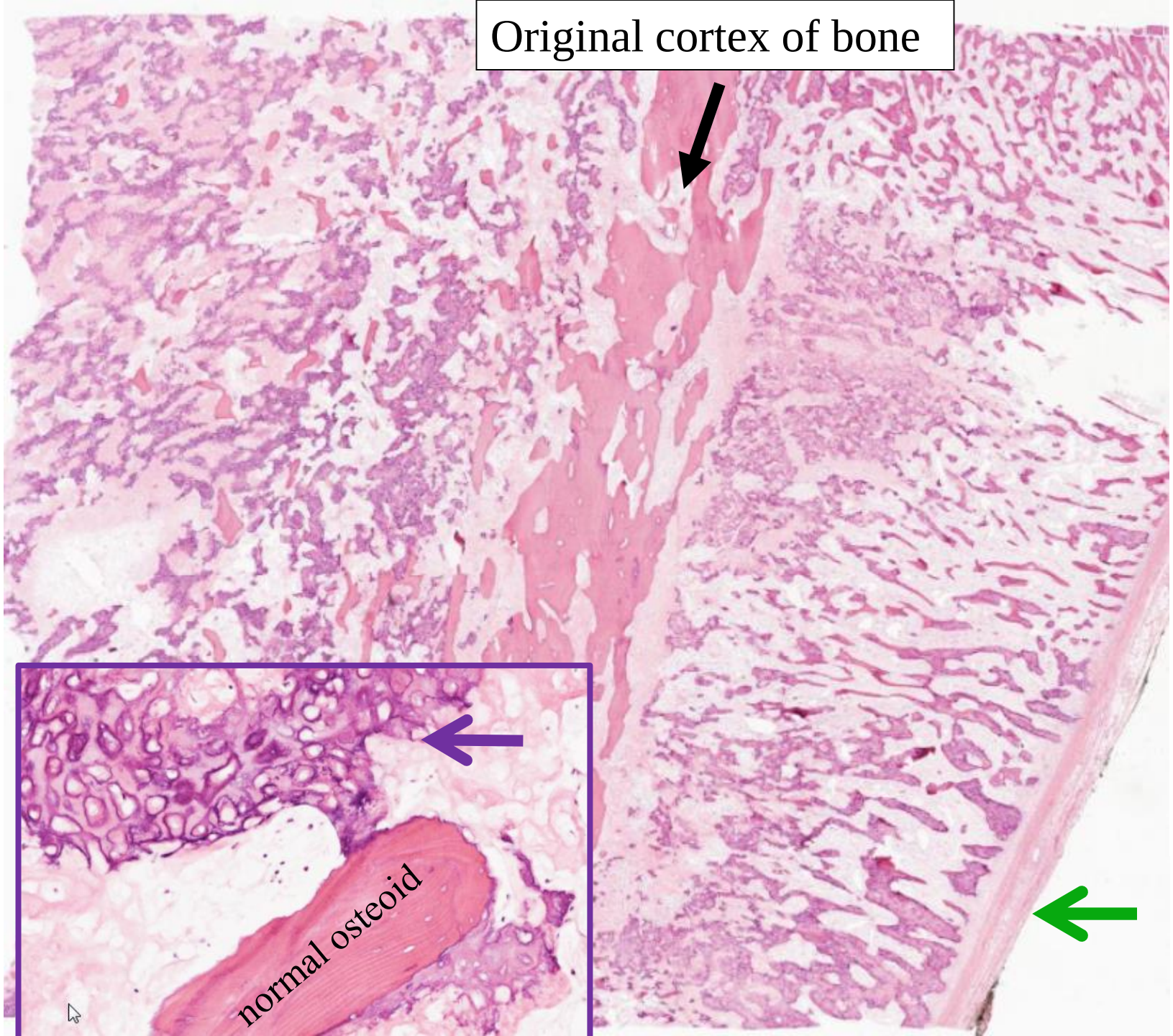
-residual bone marrow - **green oval**

-treated tumor (BELOW) which contains some residual original mature bony trabeculae (**arrow heads**) as well as abnormal osteoid (**thin arrows**) that had been laid down by the tumor. **Purple circle.**



Scattered large atypical hyperchromatic cells are seen within and between the osteoid. (**blue arrow head**).

The microscopic characteristics include osteoid formation. The neoplastic bone has a coarse, lacelike architecture frequently, or may be laid down in broad sheets. Neoplastic cells vary greatly in size and shape, and giant cells may be formed. The epiphysis in the gross photo is on the left side. The epiphysis in the microscopic slide is on the right. This case as with most resections has had chemotherapy prior to resection. However, normal elements of the cartilagenous epiphyseal plate are present, and some normal marrow is present. There is residual neoplasm with very large and atypical osteocytes within the non-lamellar atypical osteoid.



<u>On second virtual slide ("Resection including cortex of bone") identify:</u>

-residual mature bone that probably represents the original cortex (black arrow)

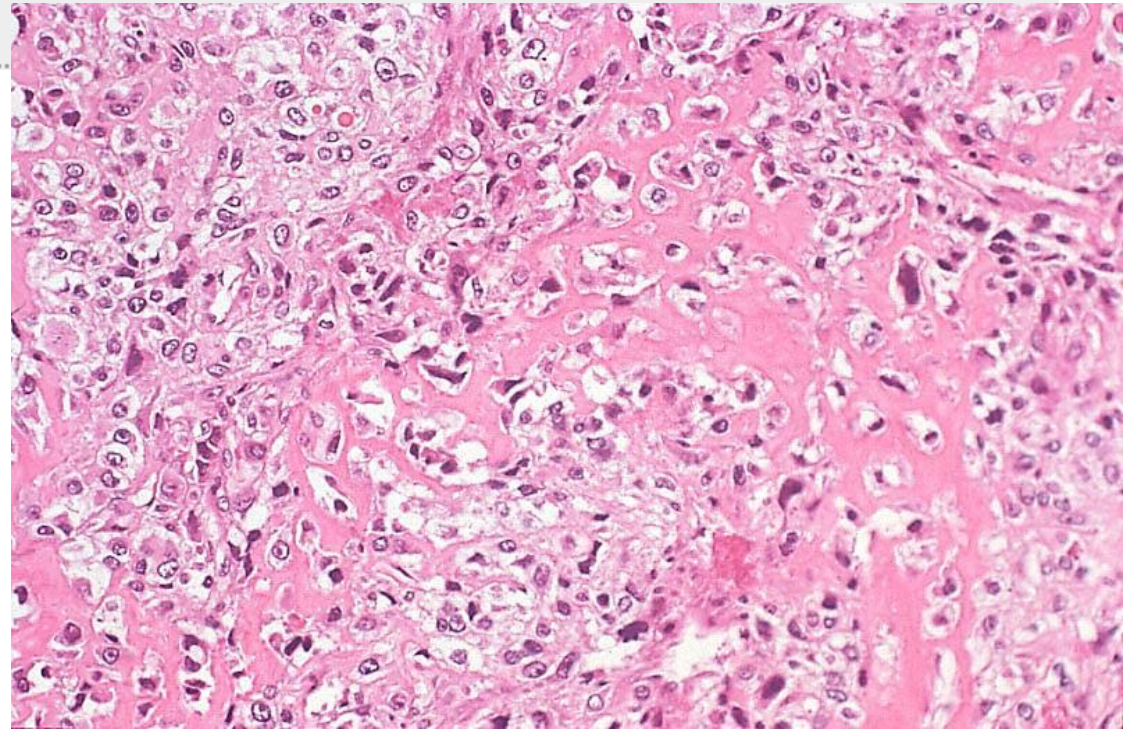
-periosteal surface (**green arrow**)

-poorly <u>formed new osteoid</u> that was formed by the tumor (purplish color – **purple arrow**)

-Note that for the most part the abnormal osteoid has <u>empty spaces</u> where tumor cells once resided; however, as noted in the previous slide, there are occasional residual atypical cells (large hyperchromatic cells with prominent nucleoli).

Compared with the original tumor, indicate in the box below approximately what percentage of the tumor cells you think has been killed by the therapy and explain why this information is important?

There is approximately 90% tumor necrosis (per Dr. Tanas). A favorable response and prognosis is associated with 90% necrosis.

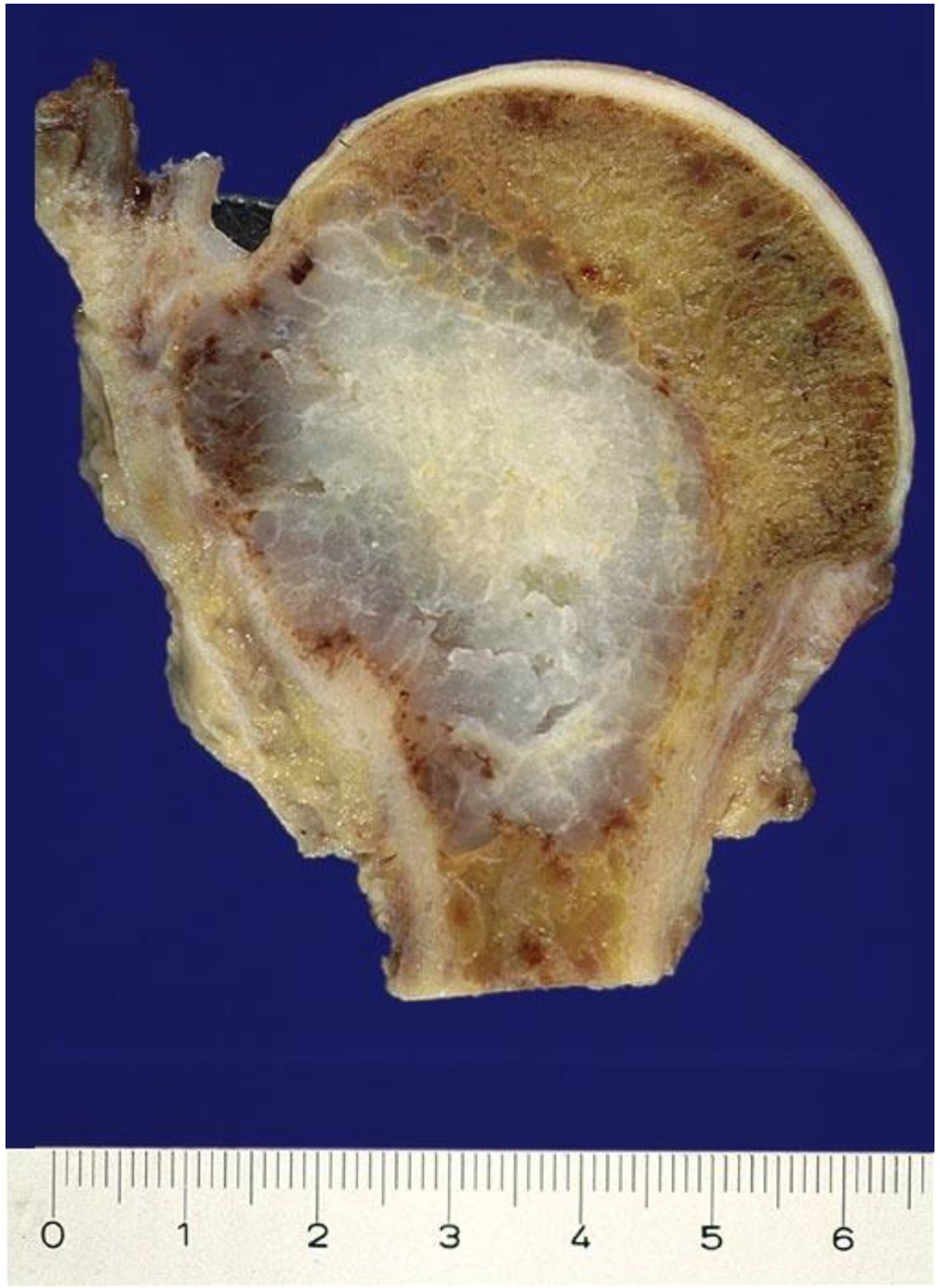


CLINICAL-PATHOLOGIC CORRELATION

Review the Supplemental Images.

Chondrosarcoma, humerus

This is an example of a different sarcoma arising in bone - a malignant cartilage producing neoplasm. Nodules of hyaline and myxoid cartilage proliferate and can engulf and destroy bone. Note how this also breaks through the cortex of bone similar to the osteosarcoma, a feature that can be identified radiographically and suggests a malignant process.



CLINICAL-PATHOLOGIC CORRELATION

Review the Supplemental Images.

In the box below answer the following questions:

1) Briefly discuss the treatment and prognosis of osteosarcoma, especially with respect to this patient.

2) Briefly compare and contrast the primary bone-forming tumors (osteoid osteoma, osteoblastoma, and osteosarcoma) with respect to age, distribution (what bones are most often involved), location within the bone, and behavior.

1) Briefly discuss the treatment and prognosis of osteosarcoma, especially with respect to this patient.

Osteosarcoma is treated with a multimodality approach that consists of (1) neoadjuvant chemotherapy, (2) surgery, and (3) chemotherapy. The amount of chemotherapy-induced necrosis found at surgical resection is an important prognostic finding. These aggressive neoplasms spread a hematogenous route to the lungs. Although the prognosis has improved substantially since the advent of chemotherapy, with 5-year survival rates reaching 60% to 70% in patients without detectible metastases at initial diagnosis, the outcome for patients with metastases, recurrent disease, or secondary osteosarcoma is still poor.

2) Briefly compare and contrast the primary bone-forming tumors (osteoid osteoma, osteoblastoma, and osteosarcoma) with respect to age, distribution (what bones are most often involved), location within the bone, and behavior.

Osteoid Osteoma: a benign tumor occurring most commonly in patients aged 10-20. It is a well-circumscribed tumor that involves the cortex of the bone. It mostly affects the metaphysis of long bones (femur and tibia) and can present with pain. It is < 2 cm.

Osteoblastoma: is essentially on a continuum with osteoid osteoma – it's a benign tumor, most commonly occurring in the vertebral column in the in patients aged 10-20. Histologically, it is identical to osteoid osteoma, but is larger in size (>2 cm) and more often found in the medulla of bone, not cortex.

Osteosarcoma: is a malignant bone tumor. It's typically found in the metaphysis of the distal femur, the proximal tibia, and the humerus in children aged 10-20. It's characterized by outward, destructive growth and lifting of the periosteum with some characteristic radiographic findings on x-ray (Codman's Triangle or sunburst pattern).

POLL QUESTIONS
Post-Test
(same questions as beginning)

Note: the second “Case” for this session was osteoarthritis (not shown) – hence one question related to that on Poll