

Skull Tumors

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PATHOLOGY	1
EPIDEMIOLOGY	2
CLINICAL FEATURES	2
SYNDROMES.....	2
DIAGNOSIS	2
DIFFERENTIAL DIAGNOSIS	4
TREATMENT	4
PROGNOSIS	5
TUMORS OF VERTEBRAE → see p. Onc56 >>	
GENERAL FEATURES OF BONE, CARTILAGE, SOFT TISSUE TUMORS → see p. 1197-1198 >>	

PATHOLOGY

- BONE forming tumors:**
 - OSTEOMA** (most common primary tumors of calvaria) - growths of mature dense lamellar cortical bone (outer or inner table); typical appearance - nidus of osteoid tissue in background of osteoblastic connective tissue, which is enclosed completely by reactive bone.
 - OSTEOID OSTEOMA**
 - OSSIFYING FIBROMA** - fibrous spindle cells with varying amounts of woven bone; tumor periphery is composed of mature lamellar bone.
 - OSTEOBLASTOMA** - fibrous stroma with irregular osteoid deposition.
 - OSTEOSARCOMA** (second most frequent malignant skull tumor after multiple myeloma) - malignant spindle cell stroma, which directly produces osteoid or immature bone (osteoblastic, chondroblastic, or fibroplastic form); association with prior radiation exposure, Paget disease, fibrous dysplasia, chronic osteomyelitis.
- CARTILAGE forming tumors:**
 - CHONDROMAS** (enchondroma, juxtacortical chondroma, osteochondroma) - mature hyaline cartilage; arise from cartilaginous portion of bones formed by enchondral ossification (skull base and paranasal sinuses).
 - CHONDROMYXOID FIBROMA** - chondroid and myxoid differentiation with lobular growth.
 - CHONDROBLASTOMAS** - immature cartilage cells.
 - CHONDROSARCOMA** (third most common malignant skull tumor); often associated with abnormalities of chromosomes 10 and 22; *low-grade type (myxochondrosarcoma)* - chondroid and immature cartilage deposition in areas of myxomatous change and cystic degeneration; *high-grade type (mesenchymal chondrosarcoma)* - absence of cartilage lobules and presence of fibrosarcomatous areas (groups of chondromatous cells lose their usual lobulation and begin to spindle out); both types are vimentin positive.
- CONNECTIVE TISSUE tumors:**
 - DESMOPLASTIC FIBROMA** (very rare!) - fibrous connective tissue origin marked by collagen formation.
 - FIBROSARCOMA** - varying amounts of collagen production and absence of bone, osteoid, or cartilage; *medullary subtype* has better prognosis than *periosteal subtype*.
- HISTIOCYTIC tumors** (very rare!):
 - GIANT CELL GRANULOMA** - giant cells around hemorrhagic foci, numerous spindle-shaped fibroblastic cells, and new bone formation; tumor cells are smaller than those of giant cell tumor of bone, whereas stromal cells and giant cells resemble each other.
 - NONOSSIFYING FIBROMA** - fibroblast proliferation with multinucleated giant cells.
 - XANTHOMA** - foamy xanthomatous cells.
 - EWING SARCOMA** - uniform, densely packed small cells with indistinct cytoplasmic borders and many mitotic figures; stain strongly with PAS.
 - GIANT CELL TUMOR (OSTEOCLASTOMA)** - well-vascularized tissue mass of plump, spindle, or ovoid stroma cells together with uniformly dispersed, numerous, large, multinucleated giant cells.
- Tumors of BLOOD or BLOOD VESSEL origin:**
 - EOSINOPHILIC GRANULOMA** (common) - mononuclear histiocytes* mixed with eosinophils; giant cells and areas of hemorrhage or necrosis may be observed.
*histiocytes stain positive for protein S-100; on electron microscopy, Birbeck granules (that characterize Langerhans or X cells) are noted
 - HEMANGIOMA** (10% of benign skull tumors) - non progressive brownish red lesions under skull periosteum; microscopically - capillary, cavernous, or venous blood vessels.
 - LYMPHANGIOMA** (rare) - consist of lymph vessels.
 - ANGIOSARCOMA** (hemangiopericytoma or hemangioendothelioma) - irregular anastomosing vascular channels lined by one or more layers of atypical endothelial cells and pericytes, which have anaplastic immature appearance.
- Tumors of NEUROEPITHELIAL origin:** **ESTHESIONEUROBLASTOMA**
- Tumors of SQUAMOUS CELL origin:** **SQUAMOUS CELL CARCINOMA** (nasal sinuses and temporal bone)
- Tumors of APOCRINE GLAND origin** (salivary, lacrimal glands); propensity for perineural spread.
- METASTASES** (skull is common site!); dura is effective barrier - *brain invasion is rare!*
- OTHER types:**
 - FIBROUS DYSPLASIA** - developmental anomaly - normal bone formation arrested at woven stage → lamellar bone is not formed → typical overgrowth of fibrous tissue among woven bone.
 - PAGET DISEASE** - initially increased osteoclastic activity (bone resorption) → increased osteoblastic activity (bone formation).
 - EPIDERMOID & DERMOID TUMORS** (one of most common benign skull lesions in children) see p. Onc30 >>
 - ANEURYSMAL BONE CYSTS** - large vascular spaces (lack endothelial lining) separated by trabeculae of connective tissue and bone.
 - INTRAOSSEOUS MENINGIOMAS**
 - MULTIPLE MYELOMA** - widespread osteolytic bone destruction by dense tumor cells that look like plasma cells clustered in close aggregates.

- 19% are **benign** and 81% - **malignant**.
- features of benign tumor:**
 - single, small, grossly round / oval lesion
 - peripheral sclerosis
 - intralesional calcifications
 - peripheral bone vascularity
- malignant transformation** (to osteosarcoma, chondrosarcoma, or fibrosarcoma) - in 2% **PAGET DISEASE** and 0.5% **FIBROUS DYSPLASIA** cases.
- lesion **LOCATION** is of little differential diagnostic value, but certain tendencies exist:
 - lesions of developmental origin** - strong midline propensity;
 - OSTEOMAS** - paranasal sinuses, frontal bone;
 - OSSIFYING FIBROMAS** - frontotemporal region;
 - EOSINOPHILIC GRANULOMA, OSSIFYING MENINGIOMA** - frontoparietal area;

PAGET DISEASE - skull base, usually multicentric.

cartilage tumors - skull base;

GIANT CELL GRANULOMA - sphenoid, temporal, and ethmoid areas;

HEMANGIOMAS (more common in vertebral column): *globular variety* - skull base; *sessile type* - frontotemporal region;

EPIDERMIOIDS and *DERMOIDS* - cerebellopontine angle, parasellar region, calvaria (*DERMOIDS* prefer midline).

Hyperostoses - local overgrowth of skull bones:

- induced by *INTRACRANIAL MENINGIOMAS*
- nonneoplastic

- hyperostoses may involve either outer or inner tables;
 - outer table involvement is insignificant except for possible disfigurement.
 - hyperostoses of inner table rarely grow enough to compress intracranial contents.

Hyperostosis frontalis interna - asymptomatic symmetric hyperostosis of inner table of frontal bone - common incidental finding in **women > 40 yrs**; diploe and external table are not affected; differentiate from *en plaque MENINGIOMA*.

EPIDEMIOLOGY

- account for \approx **1% of all bone tumors**.
- most manifest in **young adults!** (except *INTRAOSSSEOUS MENINGIOMA*, *PAGET DISEASE*, *MULTIPLE MYELOMA*, *SQUAMOUS CELL CARCINOMA* - affect older adults).

CLINICAL FEATURES

- Enlarging skull mass \pm pain / tenderness** (due to periosteal involvement).
 - OSTEOID OSTEOMA* - nocturnal local tenderness relieved by NSAIDs.
 - rapidly growing mass** - *DESMOPLASTIC FIBROMA*, *GIANT CELL GRANULOMA* or **malignant tumor**.
 - malignant tumors** without pain - *MULTIPLE MYELOMA*, *OSTEOSARCOMA*.
- Cranial nerve deficits** (if tumor involves skull base), e.g. visual and hearing loss.
- Dural erosion**, direct **brain compression**.
- Recurrent **sinusitis**, CSF **rhinorrhea**
 - if tumor obstructs sinus ostium \rightarrow **mucocele** (encapsulated, thick fluid collection); mucocele may erode through base of skull to compress intracranial structures.
- Subdural collections** - associated with **malignant tumors** invading dura (esp. metastatic).

SYNDROMES

Gardner syndrome:

- multiple osteomas of skull, sinus, mandible
- soft tissue fibromas of skin
- colon polyps

McCune-Albright syndrome:

- polyostotic fibrous dysplasia
- hyperpigmented skin macules
- precocious puberty

Hand-Schüller-Christian disease:

- diabetes insipidus
- exophthalmos
- bone lesions

Ollier syndrome - multiple enchondromas.

Maffucci syndrome:

- enchondromas
- dyschondroplasia
- cavernous hemangiomas of soft tissues / viscera

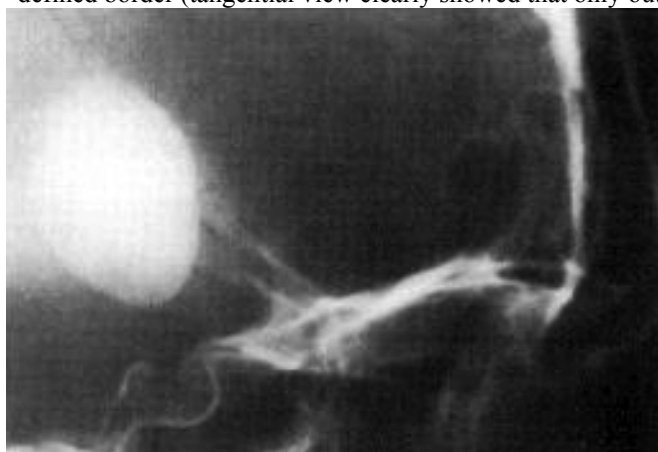
DIAGNOSIS

Plain skull radiography with special projections, **CT** (extent of intracranial extension):

- radiolucent (osteolytic)** – most tumors (benign and malignant)
 - radiopaque (osteoblastic)** – *OSTEOMA*, *OSSIFYING FIBROMA*, *INTRAOSSSEOUS MENINGIOMA*, sclerotic form of *FIBROUS DYSPLASIA*, later stages of *PAGET DISEASE*, some *METASTASES* (e.g. prostate, breast, bladder, hypernephroma).
- malignant tumors** - irregular poorly defined borders, no periosteal reaction.

OSTEOMA – condensation of cortical bone (circumscribed homogeneous bone density) which may project external to skull (exostosis) or towards cranial cavity (enostosis); arises from outer table without involvement of diploë (*SPONGY OSTEOMA* may be radiolucent; *OSTEOID OSTEOMAS* - radiolucent nidus with surrounding dense sclerosis).

Osteoma of skull vault (lateral X-ray): extracranial nature of lesion is suggested by its very well defined border (tangential view clearly showed that only outer table was affected):



OSSIFYING FIBROMA - initial lesion is radiolucent, but progressively becomes radiopaque, with sharp margins and dilated vascular channels.

INTRAOSSSEOUS MENINGIOMA - irregular bone deposition on inner and outer tables, usually in vicinity of coronal suture.

OSTEOBLASTOMA - well-demarcated nonenhancing lytic lesion with smooth calcified margins.

CHONDROMA - well circumscribed lytic lesion eroding surrounding bone; stippled calcification helps to distinguish from metastasis or chordoma.

CHONDROBLASTOMA - well-demarcated osteolytic area with varying degrees of calcification.

CHONDROMYXOID FIBROMA - radiolucent with tissue calcification.

DESMOPLASTIC FIBROMA - well-defined lytic and expansile lesions with typical soap bubble appearance; causes thinning of overlying cortex without periosteal reaction.

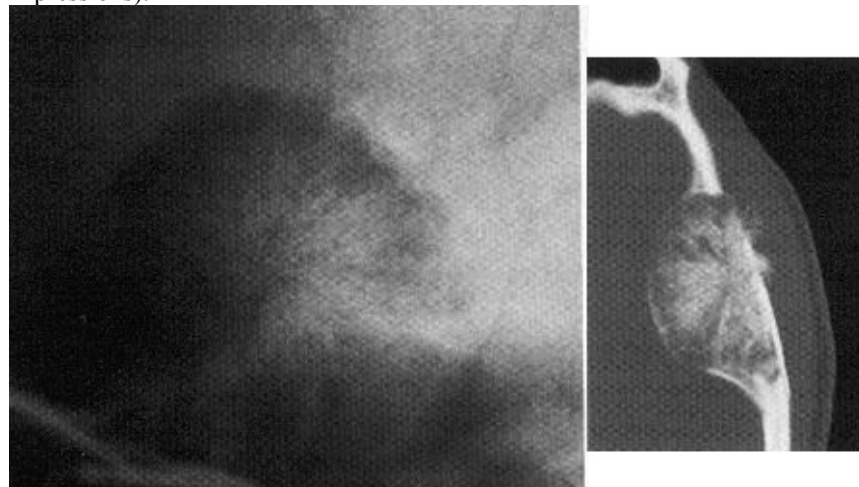
GIANT CELL GRANULOMA - radiolucent, well demarcated, multiloculated, with expansion and thinning of bone cortex; CT - isodense lesion, which may erode overlying cortical bone.

NONOSSIFYING FIBROMA, XANTHOMA - radiolucent with sclerotic margins and bony trabeculae with soap bubble appearance.

EOSINOPHILIC GRANULOMA - radiolucent, oval, well-demarcated lesion without sclerosis; appearance of punched-out defect or doughnut-shaped lesion that involves both inner and outer table; CT - soft tissue mass within area of bony destruction (central density may also be present).

HEMANGIOMA - well-defined nonenhancing lytic lesion with characteristic *honeycomb* or *trabecular* appearance; 33% show peripheral sclerosis; 10-15% show classic "*sunburst*" or "*spoke wheel*" pattern (spicules radiate from central point); intralesional calcifications are common; prominent vascular groove may be seen in vicinity (external carotid arteriography sometimes shows blush); diploe is expanded, but inner table is preserved!

Hemangioma of skull vault (A - lateral radiograph; B - CT, bone window) - well defined lucency in parietal bone has typical 'spoke wheel' appearance (due to prominent vascular impressions):



LYMPHANGIOMA - cystic bone defect.

ANEURYSMAL BONE CYST - well-demarcated lesion that arises from diploë (expands both inner and outer tables); CT - multiloculated expansile lesion with characteristic fluid level.

EPIDERMOID / DERMOID - round lytic lesion arising within diploë; may expand inner and outer tables away from each other; sharp dense sclerotic borders that involve all three layers of bone; CT - hypodense nonenhancing lesion with irregular borders.

FIBROUS DYSPLASIA - skull lucency with patches of increased density; CT - multilobulated intradiploic lesion; (can be confused with Paget disease, but occurs in younger age group); 3 different forms:

cystic form - involves mainly outer table;

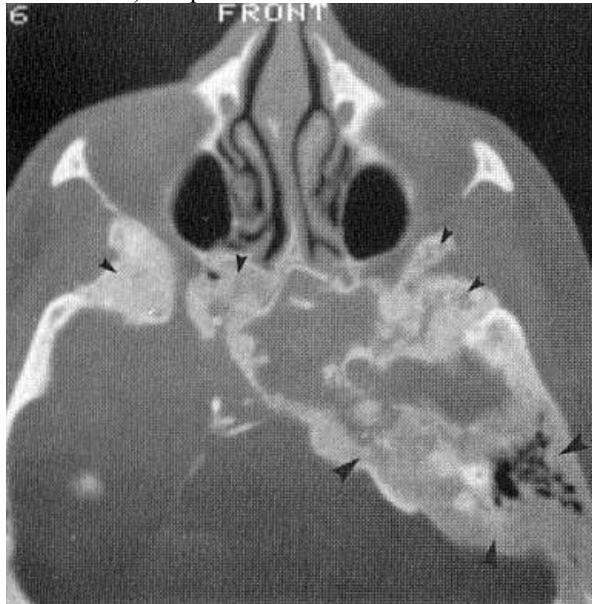
sclerotic form - characterized by bone thickening;

mixed form - manifests after third decade.

Fibrous dysplasia of orbit and ethmoid sinus (CT with bone windows):



Fibrous dysplasia of left temporal bone (*large arrowheads*) and sphenoid bone (*small arrowheads*) - expansion and sclerosis:



PAGET DISEASE - expansion of skull base by thickened abnormal bone: sharply demarcated lytic lesions (*osteoporosis circumscripta*) → enlarged, coarsened trabeculae, thickening of cortex, and nonhomogeneous patchy densities (resemble *cotton wool*) with varying degrees of bone formation and no clear edges → sclerotic-lytic appearance (can be confused with fibrous dysplasia, but occurs in older age).

CHONDROSARCOMA - no reliable radiological features (lytic and sclerotic changes within poorly defined margins).

FIBROSARCOMA - lytic lesion with thinning and widening of cortex.

EWING SARCOMA - typical *onion skin appearance* (laminated periosteal changes); CT - isodense mass surrounded by hypodense area and hyperostosis, contrast enhancing.

ANGIOSARCOMA - destructive lesion with cortical erosion and reactive ossification; CT - heterogeneous enhancement with focal necrosis.

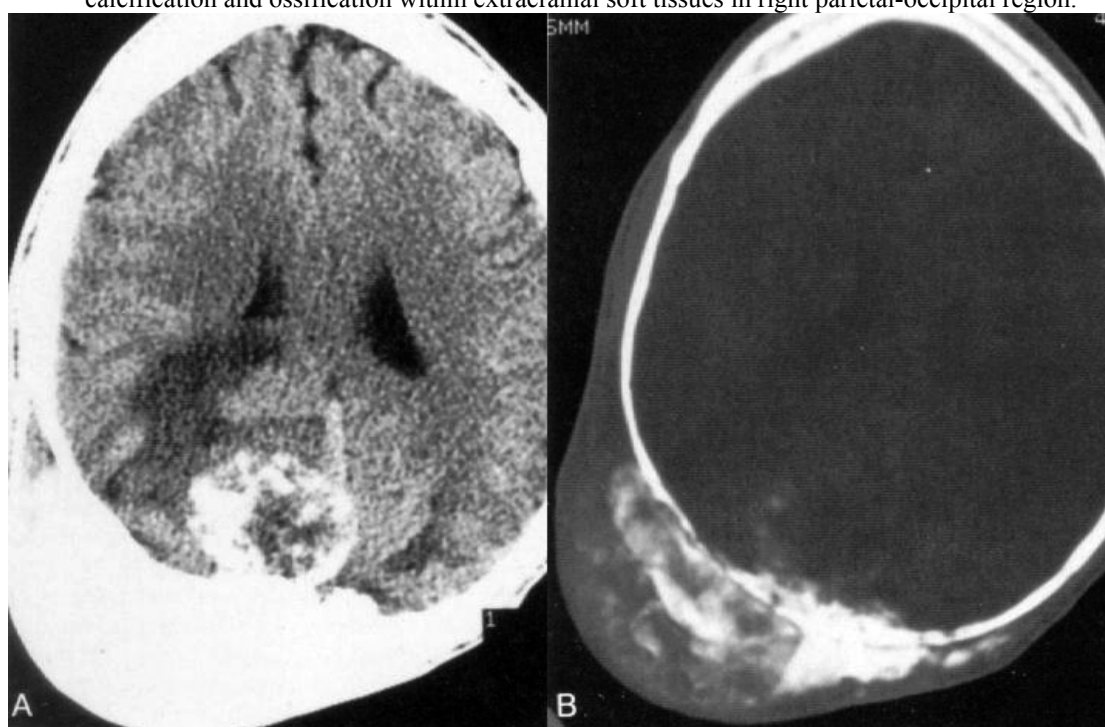
PLASMOCYTOMA/MULTIPLE MYELOMA - *multiple* lytic lesions that involve both inner and outer tables, as well as diploë from which they arise; CT - hyperdense, homogeneous enhancing lesions.

GIANT CELL TUMORS - involve sphenoid bone and commonly erode sellar region; CT - hyperdense, contrast-enhancing masses.

OSTEOSARCOMA - osteolytic soft-tissue extension; may have calcification; typical (but not frequent) appearance is *sun-ray picture*.

A. Noncontrast CT - calcified mass within medial right parietal-occipital lobes with massive extracranial soft tissue swelling.

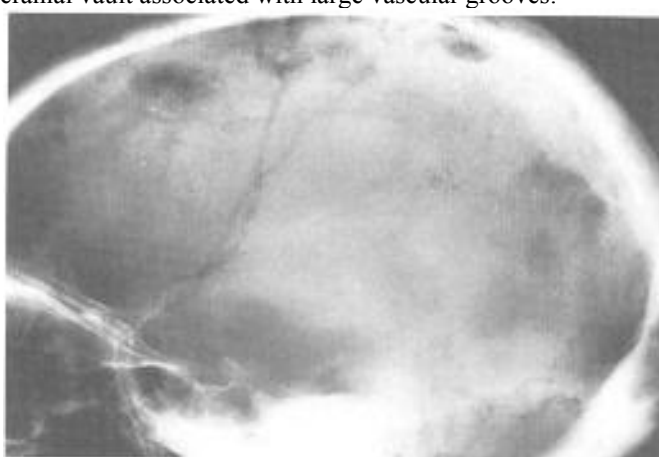
B. CT bone window - thinning and erosive changes of calvarium with several large areas of calcification and ossification within extracranial soft tissues in right parietal-occipital region.



METASTATIC NEOPLASMS:

- osteoblastic** - sclerosis and thickening (e.g. prostate, breast, bladder, hypernephroma).
- osteoclastic** - bone destruction and lucency (e.g. lung, uterus, GI tract, thyroid, melanoma, neuroblastoma).

Metastases from breast carcinoma (lateral plain skull film) - numerous irregular lytic defects in cranial vault associated with large vascular grooves:



MRI - hypointense on T1, hyperintense on T2.

- some degree of contrast enhancement is common.

Bone scanning with Tc-99m – “hot” area of increased radioisotope uptake (*OSTEOMAS*, *OSSIFYING FIBROMAS*, *OSTEOBLASTOMAS*, all *malignant tumors*).

Arteriography - high vascularity (tumors of *vascular origin*, *MULTIPLE MYELOMA*); not helpful in diagnosis of other tumors.

Biopsy - paramount importance!

Frontal mucocele (contrast MRI) - large mucocele compressing frontal lobe, with chronic inflammation of nasal mucosa obstructing nasal sinuses:



DIFFERENTIAL DIAGNOSIS

- Encephalocele, meningoencephalocele
- Venous lakes of skull, pachionian depression
- Fractures, surgical defects
- Osteomyelitis, tuberculosis, sarcoidosis, syphilis
- Hyperparathyroidism, osteoporosis, congenital hemolytic anemia

TREATMENT

No treatment is required for asymptomatic benign lesions unless diagnostic concerns exist!

- Pain control** (aspirin or NSAIDs for *OSTEOID OSTEOMA*)
- Surgical excision:**
 - benign tumors* – for symptomatic relief, cosmetic reasons, or cranial nerve decompression.
 - malignant tumors* – treatment of choice for cure (except *MULTIPLE MYELOMA*); if other means cannot control tumor expansion, surgery is still option in metastatic disease!
 - complete en bloc resection** is preferred (with extensive margins for *malignant tumors*).
 - preoperative embolization** is recommended for *ANGIOSARCOMAS* (to reduce intraoperative blood loss).
 - unresectable lesions → curettage, Gamma Knife and CyberKnife.
- Radiotherapy** - for some partially resected benign lesions with high recurrence rates (*OSSIFYING FIBROMA*, *HEMANGIOMA*, *ANEURYSMAL BONE CYST*).
Radiosurgery is primary treatment for secondary *OSTEOSARCOMA* (esp. in elderly patients), *MULTIPLE MYELOMA* (if chemotherapy fails).
 - not indicated for *ANGIOSARCOMA* and *FIBROSARCOMA*; use in *CHONDROSARCOMA* controversial.

4. **Chemotherapy** (combinations including **CISPLATIN**, **CYCLOPHOSPHAMIDE**, **CARMUSTINE**, **LOMUSTINE**) – for **OSTEOSARCOMAS**, **FIBROSARCOMAS**, **MULTIPLE MYELOMA** (first choice of treatment); efficacy in **CHONDROSARCOMA** unknown.

PROGNOSIS

Recurrence rates:

ANEURYSMAL BONE CYST - 40-50%

DESMOPLASTIC FIBROMA - 20-30%

GIANT CELL GRANULOMA - 12-16%

5-yrs survival (cure):

OSTEOSARCOMA 20-50%

CHONDROSARCOMA 10-year survival 30-80%

FIBROSARCOMA 10-year survival 40%

EWING SARCOMA 40-65%.

ANGIOSARCOMA 50%

BIBLIOGRAPHY for ch. "Neuro-Oncology" → follow this [LINK >>](#)