Learning objectives

A systematized approach to the differential diagnosis of lytic lesions of the skull based on imaging findings.

Background

Lytic lesions of the skull have a wide range of different etiologies, ranging from normal variants to congenital, traumatic, inflammatory and neoplastic lesions, benign ones being more frequent than primary malignancies.

Some of them are incidental findings in imaging studies, while many others manifest as palpable masses, with or without associated pain.

Their true etiology may be puzzling considering their imaging features alone. Therefore, clinical information including the age of the patient, main diseases and previous physical trauma, including surgeries, is essential for the Radiologist to narrow the differential diagnosis.

Imaging approach frequently begins with radiographic and ultrasound studies, quite limited in most cases, CT and MR being complementary and the methods of choice, for the assessment of bone and associated soft tissue masses, respectively. MR is also able to depict bone marrow involvement, especially helpful at early stages [1-4, 10, 14]. Conventional angiography may be useful for both, diagnosis and treatment.

Anatomy

Osteolytic lesions of the skull may be primary, arising from the bone, or secondary to invasion, by means of distant metastases or through contiguity. The first step on their radiologic characterization is to precisely localize its origin. It is, therefore, worth an anatomy revision.

Extracranial lesions arise from the scalp, which consists of skin, fibrous and fatty tissue, galea aponeurotica and its connective tissue, as well as nerves and blood vessels connected to the ones intracranially.

Deeper lesions may arise from the calvaria with its two cortical layers, the outer and the inner table, with the marrow (diploe) between them. It is covered by the periosteum (pericranium) and lined by dura (endocranium) with its superficial and deep layers, the
periosteal and the meningeal, respectively, which are only parted to circumscribe the dural sinuses, the cerebral falx and the cerebellar tent.

The meningeal membrane divides the epidural and the subdural spaces. From superficial to deep, there is still the arachnoid and the pia mater, both delimiting the subarachnoid space, where the cerebrospinal fluid (CSF) flows.

Epidural, subdural and subarachnoid spaces are all extra-axial spaces. [5-7]

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**Fig. 1**: Diagram of a coronal section of the top of the skull, showing the layers of the scalp.

**References**: From the 20th U.S. edition of Gray’s Anatomy of the Human Body, originally published in 1918 and therefore lapsed into the public domain.

**Findings and procedure details**

Osteolytic skull lesions may have many different causes, anatomical variations being responsible for up to 60% of cases [8].
In general population, seven diagnosis include 85% of all causes - by decreasing order, dermo/epidermic cysts, hemangioma, metastasis, multiple myeloma, Langherans histiocytosis, Paget disease of bone and fibrous dysplasia [8] - most of them illustrated in these review with cases of our institution.

In adults, tumoral causes are predominant - metastasis and myeloma [8] - whereas in children, besides congenital defects, dermoid cysts and eosinophilic granuloma are the most frequent diagnosis. [8, 9, 15]

NORMAL VARIANTS

Transcalvarial Venous Channels and Venous Lakes

Transcalvarial venous channels consist of apertures in the skull through which emissary veins pass, connecting the venous sinuses of the dura mater with veins external to the skull. They look like serpiginous or linear lucencies with sclerotic borders through the skull, and are, therefore, occasionally mistaken for sutures or fractures [18].

Enlarged veins within the diploic space are known as venous lakes, corresponding to round or oval lucent foci, frequently along the inner table of the skull [19].

These normal structures show an intense enhancement after intravenous contrast administration on both, CT and MR.
Fig. 2: Typical transcalvarial venous channels and venous lakes appearing on non-enhanced CT (a) as linear lucencies through the skull with sclerotic edge and round/oval radiolucent foci with integrity of the outer calvarial table, respectively. These structures intensely enhance after gadolinium administration, as demonstrated on this T1-weighted MR image (b), which also shows a large falk meningioma.

References: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal

Arachnoid Granulations

Arachnoid granulations, also known as Pacchionian granulations, are normal anatomical structures visible in approximately 1% of patients [11], corresponding to enlarged arachnoid villi that are involved in the filtration of CSF from the subarachnoid space to the venous system.

Hypertrophic arachnoid granulations as a result of high CSF pressure may be responsible for lytic skull lesions. Most are located close to the superior sagittal sinus, appearing as rounded and sharply circumscribed lucencies with sclerotic border, seen on MR as projections within the sinus of signal intensity similar to that of CSF and on MR angiography as filling defects [11-13].
Although its relationship with headaches has been proposed in the past [12], it has not been demonstrated and should be considered asymptomatic [11-13]. Therefore, the Radiologist should learn how to promptly identify and ignore them, especially in order to differentiate them from pathology, such as dural venous thrombosis [11-13].

**Fig. 3:** Arachnoid granulation incidentally found in these non-enhanced CT scan (a) and T2-weighted MR (b) image, as a parasagittal sharply circumscribed osteolytic lesion, remodelling inner calvarial table, isointense to CSF, which remained stable over time.

**References:** Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal

**Enlarged Parietal Foramina**

Enlarged parietal foramina is an autosomal dominant inherited condition representing a benign variant of incomplete ossification of parietal bones, which are supposed to close during fetal development, by the fifth month of pregnancy.
Their imaging appearance consists of circular and symmetrical openings on both sides of the sagittal suture with variable size, up to several centimetres wide.

Although not usually associated with any medical problems, local pressure is painful, these patients being at higher risk of brain damage by local trauma [14]. Because of that and in order to avoid misinterpretation as pathological entities, it should always be reported.

**Fig. 4:** Enlarged parietal foramina. Note the bilateral and almost symmetric rounded parietal calvarial defect, with smooth and sharp margins and without any associated soft tissue or vascular malformation. The 3D reconstruction (b) provides a particularly clear visualization of this variant.

**References:** Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal

**CONGENITAL**

**Encephalocele**
Encephaloceles, occasionally misdiagnosed as dermoid cysts [16], are characterized by a protrusion of cerebral and/or meningeal tissue through a congenital defect of the skull and dura, usually located at or near the midline with an associated palpable mass [1, 17]. In some cases, the skin and dura overlying the malformation is incompletely formed resulting in direct exposure of the arachnoid layer and subsequent risk of infection [17]. Hydrocephalus due to ventricular herniation may also occur, although the prognosis is generally good [1].

As the association with systemic syndromes are describe in some cases, the exclusion of associated abnormalities is mandatory [1, 17].

Diagnosis is usually made antenatally by means of ultrasound, MR providing assessment of the contents of the herniated sac in which their classification is based on, as described in the table below. The round cranial defect with sclerotic margins may be well demonstrated on radiographs and CT. [1, 17].

<table>
<thead>
<tr>
<th>Pathologic Classification</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>Meningocele</td>
<td>CSF lined by meninges</td>
</tr>
<tr>
<td>Gliocele</td>
<td>CSF lined by glial tissue</td>
</tr>
<tr>
<td>Meningoencephalocele</td>
<td>CSF and brain</td>
</tr>
<tr>
<td>Meningoencephalocystocele</td>
<td>CSF, brain and ventricules</td>
</tr>
<tr>
<td>Atretic cephalocele</td>
<td>Small nodule of fibrous-fatty tissue</td>
</tr>
</tbody>
</table>

Pathologic classification of cephaloceles. Adapted from table 11.1 in reference 17.
Fig. 5: Encephalocele. This sagittal T2-weighted MR image demonstrates a sub-scalp occipital cystic mass with communication with the prominent interhemispheric fissure. Note the extension of the straight sinus and the tentorium through a small midline defect in the skull, with prominent superior cerebellar cistern and cisterna magna.

References: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal
Fig. 6: Encephalocele. T2-weighted MR images of another child presenting a small fluctuating mass over the posterior sagittal suture since birth, clearly depicts the herniation of the meninges and the brain tissue through a small bone defect.

References: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal

Sinus Pericranii

Sinus pericranii consists of an abnormal communication between the intracranial and extracranial venous drainages, usually congenital, manifesting as a fluctuating mass in the scalp, which varies in size according to intracranial pressure changes.

Ultrasound evaluation provides an accurate diagnosis [20]. However, contrast-enhanced CT is a more popular method, showing an enhancing epicranial mass composed of serpiginous vessels [21].

Although complication by thrombosis has been described [22], treatment has basically been recommended for aesthetic reasons. Preoperative endovascular embolization is a promising technique on preventing haemorrhage [23].
Fig. 7: Sinus pericranii. Contrast-enhanced CT scan showed an epicranian lesion grossly in the midline, composed of multiple serpiginous venous structures.
Fig. 8: The T1-weighted MR sagittal image (a) and the MR angiography (b) of the same patient as in figure 7, clearly demonstrate the intracranial communication between the scalp venous malformation and the superior sagittal sinus, consistent with sinus pericranii.

References: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal

Other rare congenital lesions include dermoid and epidermoid cysts, which are benign slow-growing intradiploic tumours believed to be secondary to aberrant epidermal or dermal inclusion in the calvarium. Their appearance is similar to CSF, dermoids usually having higher T1 signal intensity on MRI due to fatty content. Their main differential diagnosis is eosinophilic granuloma. [12]

TRAUMATIC

Posttraumatic defect
Skull defects may be posttraumatic, either surgical or as a result of high-energy trauma. Accurately evaluated by CT, usually require surgical repair [25].

**Fig. 9:** Posttraumatic frontal bone defect as a result of severe trauma in a young woman submitted to partial surgical repair years before having undergone this CT scan (a) for headache. 3D reconstruction (b) provides an exquisite anatomic detail of the bone defect.

**References:** Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal

**Leptomeningeal Cyst**

A leptomeningeal cyst is a late posttraumatic complication of 1% of skull fractures occurring under 3 years old [2], usually in parietal region [26].

Exposure of the inner table of the skull to the CSF and arachnoid pulsations subsequent to a dural tear, result in herniation of CSF or brain parenchyma into the subcutaneous tissue,
seen on both CT and MRI as a smoothly marginated skull defect with an associated cystic lesion [1, 2, 26].

Fig. 10: Leptomeningeal cyst. CT scan (a) of a 26 year-old man presenting with seizures, showed a small defect with bevelled edges in the right parietal bone with resultant mild deformity in the overlying scalp. MRI (b) demonstrated a cystic lesion insinuating into the eroded inner table, corresponding to the dilated overlying subarachnoid space.

References: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal

INFLAMMATORY

Eosinophilic Granuloma

Eosinophilic granuloma is a localized form of Langerhans cell histiocytosis, a systemic disease of unknown etiology, in which abnormal proliferation of histiocytes occurs, forming focal or diffuse clusters.
Almost exclusively affects children and young adults, who present with a palpable mass, in the parietal area in most cases [10, 27].

This entity is characterized by a well-defined lytic lesion without marginal sclerosis, invading the inner and outer tables, sometimes with a central residual bone density within it, known as "buttom sequestrum" [1, 10, 15, 27]. Its MRI signal intensity is equivalent to that of skeletal muscle, with marked enhancement after intravenous paramagnetic contrast medium administration [1, 2, 10, 15, 27].
**Fig. 11:** Eosinophilic granuloma. CT scan of a 31 year-old woman presenting with a painful swelling in the midline scalp, revealed a sharply marginated lytic bone defect with bevelled margins.

**References:** Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal

**Fig. 12:** Within the bone defect depicted in the patient of figure 11, there was a soft tissue mass, which was better evaluated by means of MR, appearing heterogeneously hyperintense on T2 (a) and gadolinium-enhancing on T1-weighted images (b). Note the mild mass effect on the adjacent dura and gyri, without invasion.

**References:** Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal

**NEOPLASTIC BENIGN**

**Hemangioma**

Hemangioma is the main cause of primary bone tumours at the skull, accounting for 10% of cases [8, 29], middle-aged women being the most affected [2, 10]. Most are single, but
may be multiple in 15% of cases [28]. Although frequently asymptomatic, may manifest as a palpable mass [9, 15, 28].

CT typically shows a well-defined lucent lesion with sclerotic margins and a reticulated internal structure radiating from the center to the periphery described as "sunburst" or "spoke-wheel" pattern [1, 2, 15, 28].

MRI better depicts the extension of the lesion and its relationship to the adjacent neurovascular structures. Hemangiomas are heterogeneously hyperintense on T2-weighted images, T1-hyperintensity being a differentiating feature. It is a strongly enhancing lesion on both, CT and MRI, after intravenous contrast medium administration [1, 2, 15, 28].

![Image](image_url)  
**Fig. 13**: Hemangioma of the skull. The slow-growing left parietal scalp swelling of a 31 year-old woman consists of an expansile lytic lesion on radiograph (a), well circumscribed, with sclerotic margins and with the typical "sunburst" pattern of bony striations on non-enhanced CT scan (b).  

**References**: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal
Fig. 14: MRI of the same patient as in figure 13 provided good visualization of the compression of the brain by the bone lesion, which showed heterogeneous T2 (a) hyperintensity and intense enhancement after gadolinium administration on T1-weighted images (b). There is no surrounding edema.

References: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal
Fig. 15: Another calvarial hemangioma in young women presenting with frontal scalp swelling, whose imaging examinations showed a bone lesion similar to that of figures 13 and 14, in a different location.

References: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal
Fig. 16: MRI demonstrated T2 (a) hyperintensity and contrast enhancement on T1-weighted images (b), although less obvious than that of the hemangioma showed in figures 12 and 13. Note the mild hydrocephalus in this patient with aqueductal stenosis.

References: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal

**Hemangiopericytoma**

Intracranial hemangiopericytoma, arisen in pericytes that originate in the meninges, account for 1% of all central nervous system tumours.

With a location similar to that of meningioma, usually occurs at an earlier age, are more aggressive, tend to recur and may metastize extracranially.

Imaging studies demonstrate bone erosion and a narrow dural attachment in most of these heterogeneously enhancing lesions. However, unlike meningioma, is not associated with calcifications. Prominent internal flow voids on T2-weighted MR images is a typical feature.
Preoperative embolization is recommended in order to reduce intraoperative haemorrhage. [30]

**Fig. 17**: Hemangiopericytoma. Non-enhanced TC scan (a) of a 4 year-old girl presenting with a marked focal scalp swelling in the midline of the parietal region, showed a soft tissue mass with bone destruction without peripheral sclerosis. Note the lobulated contour, the typical narrow base of dural attachment and the heterogeneous intense enhancement on T1-weighted MR images after gadolinium administration, which in association with the invasion of the skull, helped distinguish from a meningioma.

**References**: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal
Fig. 18: The hypervascularization of the same hemangiopericytoma as in figure 17 is also evident by the numerous intratumoral flow voids on T2-weighted MR images (a) and on the MR angiography (b).

References: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal
Fig. 19: The same lesion as in figures 17 and 18 evident on conventional angiogram by the tumor blush, supplied by the left superficial temporal, median meningeal and occipital arteries. Successful preoperative embolization verified on the control angiogram (b).

References: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal

Aneurysmal Bone Cyst

Aneurysmal bone cysts may occur in any bone, but rarely in the skull, accounting for only 3-6% of all cases [31, 32]. Most are benign but may be locally aggressive.

Its etiology is uncertain, most being primary. Although, up to one third of cases are described to be secondary to an underlying lesion [35], our case is the first reported association with a renal tumour skull metastasis.

Characteristic imaging appearance consists of an expanding osteolytic lesion containing blood-filled spaces of variable size, frequently with multiple small fluid-fluid levels representing sedimentation of red blood cells. [31-34]
Total excision is the treatment of choice, preoperative endovascular embolization significantly decreasing intraoperative bleeding [32].

**Fig. 20:** Aneurysmatic bone cyst in a 54 year-old women presenting with long-standing headache. Non-enhanced CT scan (a) demonstrated a large destructive mass in the left parietal bone, grossly lenticular with expansion of both, but predominantly the inner table of skull, with local mass effect. T2-weighted MR images (b) showed hyperintensity, consistent with its cystic nature, as well as some septations.

**References:** Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal
**Fig. 21:** T1 (a) hyperintensity of the same lesion as in figure 20. After gadolinium administration (b) the typical peripheral enhancement and the "soap-bubble" pattern, corresponding to multiple cystic cavities, are evident.

**References:** Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal
Fig. 22: Effective preoperative embolization of the aneurysmatic bone cyst described in figures 20 and 21 was performed, as demonstrated in the pre (a) and post-embolization (b) angiograms.

References: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal
Fig. 23: Macroscopic aspect after surgical excision of the same lesion as in figures 20 to 22.

References: Department of Neurosurgery, Central Lisbon Hospital Center, Lisbon, Portugal

NEOPLASTIC MALIGNANT

Multiple Myeloma

Multiple myeloma, a malignant bone marrow disorder characterized by monoclonal proliferation of plasma cells, is responsible for most primary bone lesions in advanced ages, the solitary form being designated by plasmacytoma.

Typically appear as well-defined lytic lesions, resembling punch holes, enhancing after intravenous contrast media administration, hypointense and hyperintense, respectively on T1 and T2-weighted MR images. [2, 10, 15]
Fig. 24: Uncountable lytic "punched out" lesions on the lateral skull radiograph, typical of multiple myeloma.

References: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal
Fig. 25: Myeloma lytic skull lesions on non-enhanced CT scan (a) of the same patient as in figure 24. MRI accurately depicts myelomatous infiltration with replacement of normal bone marrow as demonstrated in this T1-weighted images after gadolinium administration, showing anomalous enhancement with multiple lesions, which had a permeative pattern and T2 hyperintensity.

References: Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal

Metastases

Skull metastases mainly occur in advanced stages of elderly patients with a known primary malignancy.

Characteristic imaging features include the permeative, aggressive pattern, multiplicity with replacement of the normal diploic space, enhancement after intravenous contrast medium and T2-hyperintensity on MRI. [10, 15]
Fig. 26: Skull metastasis. Multiple expansile osteolytic lesions in a patient with long-standing rectal carcinoma. MRI features are usually similar to those of multiple myeloma lesions, namely the T2 hyperintensity (a) and the heterogeneous enhancement on T1-weighted images after gadolinium administration (b).

**References:** Department of Radiology, Central Lisbon Hospital Center, Lisbon, Portugal

**DISCUSSION**

Considering such a wide range of differential diagnosis, firstly, it might be helpful to keep the mnemonic HELP ME [1] in mind, which gathers some of the most frequent calvarial lesions with lytic or mixed lytic/sclerotic appearance.

- Hemangioma
- Epidermoid/dermoid
- Leptomeningeal cyst, Leukemia/Lymphoma
- Paget's disease, Postsurgical
Metastases, Multiple Myeloma

Eosinophilic granuloma, Encephalocele

Secondly, a careful evaluation of the margins of the lesion in conjunction with other imaging features, such as the number and the location, usually allows the Radiologist at least to state whether the lesion has benign or aggressive characteristics.

The table below, based on our results, which are basically consistent with those reported in our references, tries to generalize the main imaging findings of each lesion included in these review.

<table>
<thead>
<tr>
<th>LESION</th>
<th>NUMBER</th>
<th>LOCATION</th>
<th>BORDERS/MARGINS</th>
<th>PATTERN</th>
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<td>Parietal/Frontal</td>
<td>WD/sclerotic</td>
<td>Benign</td>
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<td>Solitary</td>
<td>Perisagittal</td>
<td>WD/sclerotic</td>
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<td>Solitary</td>
<td>Perisagittal</td>
<td>WD/sclerotic</td>
<td></td>
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<td>Encephalocele</td>
<td>Solitary</td>
<td>Perisagittal</td>
<td>WD/nonsclerotic</td>
<td></td>
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<tr>
<td>SP</td>
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<td>Perisagittal</td>
<td>WD/nonsclerotic</td>
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<tr>
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<td>WD/sclerotic</td>
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<td>Solitary</td>
<td>Parietal</td>
<td>WD/sclerotic</td>
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<tr>
<td>EG</td>
<td>Solitary</td>
<td>Parietal</td>
<td>Undefined/nonsclerotic</td>
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<tr>
<td>Hemangioma</td>
<td>Solitary</td>
<td>Parietal/Frontal</td>
<td>WD/nonsclerotic</td>
<td></td>
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<tr>
<td>ABC</td>
<td>Solitary</td>
<td>Temporal</td>
<td>WD/nonsclerotic</td>
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<td>Multiple</td>
<td>Random</td>
<td>Permeative</td>
<td>Aggressive</td>
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<tr>
<td>Metastases</td>
<td>Multiple</td>
<td>Random</td>
<td>Ill-defined</td>
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</table>

Basic imaging pattern of each lesion included in these review, based on their main imaging features.

EV-emissary veins; VL-venous lakes; AG-arachnoid granulations; EPF-enlarged parietal foramina; SP-sinus pericranii; PTD-posttraumatic defect; LMC-leptomeningeal cyst; EG-eosinophilic granuloma; ABC-aneurysmal bone cyst; MM-multiple myeloma.
To summarize, benign lesions tend to have well-defined borders with sclerotic margins, a quite predictable location, mostly near the midline, and are usually solitary. On the other hand, those with a permeative appearance, multiple and randomly distributed, are probably aggressive.

Finally, after having ruled out typical normal variants, the benign versus aggressive imaging pattern should be consistent with the specific clinical indicators, the age of the patient being the first one to be taken into account. For instance, in adults and elderly patients, metastases are by far responsible for the majority of lytic skull lesions, whereas children and young adults present more frequently one of the congenital, inflammatory, traumatic or benign neoplastic conditions mentioned above.

**Images for this section:**

**Fig. 12:** Within the bone defect depicted in the patient of figure 11, there was a soft tissue mass, which was better evaluated by means of MR, appearing heterogeneously hyperintense on T2 (a) and gadolinium-enhancing on T1-weighted images (b). Note the mild mass effect on the adjacent dura and gyri, without invasion.
Fig. 24: Uncountable lytic "punched out" lesions on the lateral skull radiograph, typical of multiple myeloma.
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**Fig. 1:** Diagram of a coronal section of the top of the skull, showing the layers of the scalp.
Fig. 19: The same lesion as in figures 17 and 18 evident on conventional angiogram by the tumor blush, supplied by the left superficial temporal, median meningeal and occipital arteries. Successful preoperative embolization verified on the control angiogram (b).
Fig. 23: Macroscopic aspect after surgical excision of the same lesion as in figures 20 to 22.
Conclusion

Although a specific diagnosis cannot often be done, a careful evaluation of the imaging appearance of lytic lesions of the skull, in conjunction with patient's age and medical history, usually allows the Radiologist to suggest the etiology as well as to recommend the adequate strategy, weather conservative or interventional.

Personal information

References