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Non-invasive diagnosis of intracranial aneurysms


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Abstract  Patients need to be examined for intracranial aneurysms if they have had a subarachnoid hemorrhage. The preferred technique in this situation is CT angiography. Screening can be done for familial forms or for elastic tissue disorders, for which the first line investigation is magnetic resonance angiography. These non-invasive methods have now taken over from conventional angiography that was reserved for the pretreatment phase. A good technical knowledge of these imaging methods, their artifacts and misleading images enables reliable detection of intracranial aneurysms and for an accurate report to be returned to clinicians.

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Seventy-five per cent of spontaneous subarachnoid hemorrhages (SAH) or cerebral-meningeal hemorrhages are due to rupture of an intracranial aneurysm for which patients should be examined on an urgent basis. A family history in a first-degree relative, or a risk factor such as elastic tissue disease or polycystic renal disease should prompt screening for unruptured intracranial aneurysms. In all of these situations it is important to know how to detect an intracranial aneurysm, choose the best non-invasive imaging technique depending on the patient’s clinical state, understand the technical settings for each modality and the diagnostic pitfalls to be avoided and finally to know which information is important to provide to the clinician in the report.

**General information**

**Pathophysiology**

An intracranial aneurysm is a local dilation of an intracranial artery. In the vast majority of cases it is an acquired lesion. Intracranial aneurysms are rare in children and very rare in the neonatal period [1]. The pathophysiology of their development remains extremely controversial.

It has been suggested that genetic factors are involved because of the presence of familial forms and multiple sites have been found [2]. Involvement of environmental factors such as hypertension, chronic alcoholism and the patient being an active smoker are well documented in the development of intimal intracranial artery wall lesions [3–5]. An intimal abnormality due to disturbance of local blood flow [6] occurring in genetically predisposed patients is believed to cause fragmentation of the internal elastic layer and the media, from which the aneurysm develops.

In addition to "degenerative" saccular aneurysms, other more rare forms of aneurysm also exist (Fig. 1):

- "true" aneurysms with a wall:
  - non-dissecting fusiform aneurysms, which may be congenital or "degenerative", secondary to arterial wall disease (atheroma, hypertension),
  - high flow rate aneurysms associated with arteriovenous malformations due to increased blood flow in the afferent arteries;
- pseudo-aneurysms which do not have a wall:
  - mycotic aneurysms due to a leukocyte infiltrate which destroys the arterial wall and complicates 5% of cases of endocarditis: these aneurysms are fusiform or (more rarely) saccular, irregular in outline and in particular are located distally and spare the circle of Willis,
  - dissecting aneurysms which are typically fusiform or fusiform-saccular and occur after intimal damage leading to the formation of a secondary channel between the limiting elastic interna and the media,

![Figure 1](image)

**Figure 1.** Different forms of intracranial aneurysm. Aneurysms with a wall (a, b, c) and without a wall or pseudo-aneurysms (d, e, f), seen on catheterized angiography. a: left motor cortex saccular aneurysm; b: left multi cortex fusiform aneurysm; c: peri-callosal and calloso-marginal low flow aneurysms associated with an arterio-venous malformation; d: mycotic aneurysm of segment M2 of the middle cerebral artery; e: dissecting left carotid artery aneurysm; f: post-traumatic aneurysm of the carotid siphon associated with direct carotid cavernous fistula (opacification of the cavernous sinus around the carotid siphon from the superior ophthalmic vein anteriorly and inferior petrous sinus posteriorly).
traumatic aneurysms, as a result of injury from sudden deceleration or a cranio-cerebral wound directly inflicting lesions on the arterial wall. These are pseudoaneurysmal sacs without a wall per se.

This review is restricted to "degenerative" saccular aneurysms.

Epidemiology

The prevalence of intracranial aneurysms varies depending on whether the study is prospective or retrospective and on the study population. The prevalence ranges from 0.8 to 4.6% in the general population, depending on the series, with a female predominance (sex-ratio 2.2–2.4) [7]. Risk factors for intracranial aneurysm are age, being female, an active smoking habit and hypertension [8,9]. Rare familial forms are found: for a given patient, these forms are defined by the presence of at least two first-degree relatives with intracranial aneurysms. Screening is indicated in these situations [2,10]. These aneurysms are not transmitted on a mendelian basis and this reflects genetic heterogeneity. Intracranial aneurysms are also more common in autosomal dominant polycystic renal disease and hereditary connective tissue disorders such as type IV Ehlers-Danlos syndrome, type I neurofibromatosis and fibromuscular dysplasia [8].

Site

Intracranial aneurysms develop preferentially in the arterial part of the circle of Willis (70 to 90% depending on the studies) (Fig. 2): 20 to 36% in the anterior communicating artery and anterior cerebral artery; 11 to 40% in the carotid siphon, end of the carotid artery and origin of the posterior communicating artery; 15 to 31% in the middle cerebral artery and 10 to 30% are located in the cerebro-basilar arterial system (primarily at the end of the basilar artery and at the origin of the postero-inferior cerebellar artery). Multiple aneurysms are present in 15 to 20% of cases [11,12]. It is essential with carotid siphon aneurysms to establish the specific segment from which the aneurysm has developed. Some aneurysms develop in the intra-cavernosan segments and do not carry a risk of subarachnoid hemorrhage if they rupture. On the other hand those which develop in segment C1 and C2 are subarachnoid, as is the case for localized carotid caval, superior pituitary, peri-ophthalmic, posterior communicating and anterior choroid aneurysms) (Fig. 3). If it is suspected that an aneurysm may be extra-dural, a T2 weighted coronal image may be useful as this shows the upper limit of the intra-cavernosal carotid artery (Fig. 4).

Method of presentation

The feared method of presentation of intracranial aneurysms is subarachnoid hemorrhage due to rupture of

Figure 2. The most common locations for degenerative saccular aneurysms illustrated in real time MRA. a: overall MRA, caudal view; b: anterior communicating artery aneurysm; c: left carotid artery termination aneurysm; d: aneurysm of the bifurcation of the middle cerebral artery; e: aneurysm at the origin of the left postero-inferior cerebellar artery; f: aneurysm of the termination of the basal artery.
the aneurysmal sac. Headaches associated with meningeal hemorrhage are sudden in their onset, developing within a minute and occurring with no prodrome. The term “thunderclap headaches” is used. These are severe from the outset and continuous and are often associated with nausea and vomiting. Sudden onset headaches may be the presenting feature of an aneurysm, which is not necessarily ruptured, in which case the term “sentinel headaches” is used which describes a pre-rupture state with fissuring of the aneurysm. Circle of Willis imaging is therefore recommended for sudden onset headaches, even without overt SAH.

Cranial nerve paralysis or localizing focal neurological signs can be seen and are caused by the mass effect of a large aneurysm (classically a posterior communicating artery aneurysm compressing the third cranial nerve pair), migration of an embolism from an aneurysmal thrombus or intra-parenchymal bleed and, more rarely, from late onset cerebral ischemia as a result of vasospasm, the incidence of which peaks 4–12 days after rupture. The main manner

Figure 3. Carotid siphon aneurysms. a: oblique MRA view in real time of the right internal carotid artery. Terminal segment of the internal carotid artery (ICA): segment C1 (1). Ophthalmic segment of the ICA: segment C2 (2). Clinoid segment of the ICA: segment C3 (3). Horizontal cavernous segment of the ICA: segment C4 (4). Ascending cavernous segment of the ICA: segment C5 (5). Segments 3, 4 and 5 are the cavernous ICA; b: location of carotid siphon aneurysms (A: cavernous aneurysm; B: carotid-caval aneurysm; C: superior hypophyseal aneurysm; D: peri-ophthalmic aneurysm; E: carotid-posterior communicating artery aneurysm; F: anterior choroid aneurysm. PC: posterior communicating artery. Shaded: cavernous sinus).

Figure 4. Superior hypophyseal artery aneurysm. MRA 3D TOF SS shows an aneurysm of the left carotid siphon which has developed at the junction of segments C2 and C3 (a). In a carotid siphon aneurysm the risk of subarachnoid hemorrhage is only present with aneurysms located in C1 and C2. The T2 weighted coronal image (b) shows whether a portion of the aneurysm has developed outside of the cavernous sinus towards segment C2, in the subarachnoid area. This shows that the superior part of the aneurysm (arrow) is located above the roof of the cavernous sinus (distal dural ring or foramen of Kobayashi), shown by the dotted line and therefore located in the subarachnoid area.
in which intracranial aneurysms are discovered nowadays is as an incidental finding because of increased diffusion on imaging sections.

**Indications for imaging**

Thunderclap headaches are a formal indication for urgent cerebral imaging. Unenhanced cerebral CT is the most commonly carried out investigation to exclude SAH and although the sensitivity of cerebral CT is high in the acute phase, a normal cerebral CT does not obviate the need for a lumbar puncture particularly if it is performed over 6 hours after symptoms have developed [13–15]. If MRI is accessible, FLAIR, T2* susceptibility weighted imaging (SWI) can be used instead of unenhanced CT and is more sensitive to diagnose meningeal hemorrhage [16,17].

Screening may be offered in cases of autosomal dominant polycystic renal disease, hereditary.connective tissue disorders (type IV Ehlers-Danlos syndrome, type I neurofibromatosis, fibromuscular dysplasia) or if at least two first-degree relatives have intracranial aneurysms [2,18].

**Imaging methods**

**Conventional angiography**

Conventional cerebral angiography offers excellent spatial resolution and provides a dynamic study of the entire cerebral vasculature. It is still the reference technique to identify intracranial aneurysms. Using 3 dimensional acquisitions it provides a very accurate characterization of the morphology of the aneurysm, its shape, contours and regularity, measurement of sac size and particularly dimensions of the neck of the aneurysm and the anatomy of the artery involved and its neighboring branches. Conventional angiography, however, is an invasive investigation [19], which is less commonly accessible, expensive and involves irradiation to the patient and doctor. For this reason it is currently not performed for a positive diagnosis of aneurysm but rather is performed in order to plan treatment, or only in the initial stage under general anesthesia before endovascular stenting. The large reduction in the number of conventional diagnostic angiographies performed has been due to the development of non-invasive CT and MR angiography techniques.

**Cerebral CT angiography**

Investigation technique

Cerebral CT angiography is a non-invasive technique, which is very quick to perform, can be carried out on an urgent basis and can be used to supplement unenhanced CT which has diagnosed subarachnoid hemorrhage. The iodine contrast medium is injected via an automatic injector (40 to 80 mL of contrast medium at 3 mL/second) and a region of interest is placed in an infrapetrous internal carotid artery. If the density at that point reaches the threshold value (100 HU), the image is acquired automatically.

The image volume should cover the brain from the occipital foramen to the vertex in order not to miss aneurysms developing at the origin of the posterior inferior cerebellar arteries and distal pre-callosal aneurysms. The volume examined is then reconstructed in thin sections in an axial plane. Three-dimensional maximum intensity projection (MIP) or volume rendering (VR) reconstructions can produce angiographic views. In order to optimize image quality reconstructions can be centered on a single arterial vessel.

The performance of CT angiography in detecting intracranial aneurysms

The sensitivity and specificity of cerebral CT angiography to diagnose an intracranial aneurysm are 92.8 to 100% and 83 to 100% respectively [11,20–24]. Performance varies depending on the equipment used and type of population studied (all-comers or patients with meningeal hemorrhage). The risk of missing an aneurysm is between 5 and 10%, although this sensitivity varies depending on the size of the aneurysm. Sensitivity appears to be poorer in aneurysms under 3 mm in size (64 to 74.1%) [23,25] and also appears to vary depending on the site of the aneurysm. Therefore the main false negative results are for aneurysms in intraosseous, petrous or carotid siphon segment. Several studies have shown VR analysis to be superior to MIP in these sites (Fig. 5).

CT angiography offers excellent detection sensitivity but appears to be more limited in specific planning for a treatment procedure. Detection of arterial branches arising from the aneurysmal sac, neck or close to the aneurysm, the dimensions of the sac and neck are obtained more reliably from conventional angiography [26,27].

**Magnetic resonance angiography (MRA)**

Main MRA imaging techniques for the circle of Willis

3D TOF MRI angiography is based on a 3D T1 weighted echo gradient compensated for flow to emphasize the vascular signal in relation to the stationary proton signal in surrounding tissues. The image appearance depends on:

- the RT of the image;
- the image tilt angle;
- the T1 weighted appearance of tissues located within the volume investigated.

Short repetition time echo gradient images are performed to saturate all of the protons bound in a plane of the image section. The short repetition time reduces regrowth of maximal fixed spin longitudinal magnetization and as a result measurable transverse magnetization. In other terms, the bound proteins result in a very low or even zero image and only protons contained in circulating blood vessels which are not pre-excited display maximum longitudinal magnetization resulting in measurable maximal transverse magnetization and a strong image appearance.

It is useful to use presaturation bands in order to counteract the signals from vessels proximal to the volume selected. This principle involves the technique of applying a series of successive impulses to prevent any regrowth of longitudinal magnetization and therefore extinguishes the image before it penetrates a region of interest. For circle of Willis MRA, two presaturation bands are positioned in the superior sagittal sinus and torcular, thereby selectively excluding the image from veins.
In order to reduce out-of-phase effects due to the coils when embolized aneurysms are being monitored the ET needs to be reduced to under 3 msec. This improves the sensitivity of the circulating arterial network or recanalization of the aneurysmal sac, which appears as a flow hyperintensity.

The utility of 3D TOF with gadolinium enhancement

As the vascular appearance obtained at real time is generated by flow effects themselves, it is easy to understand the difficulties which this technique experiences when studying structures with very turbulent flow (giant aneurysms) or slow flow (stenoses). Intravoxel out-of-phase and circulating spin saturation effects cause drops in the signal, artefactually increasing a degree of stenosis or leading to an incorrect diagnosis of partially thrombosed aneurysm. An injection of a half dose of gadolinium chelate can recover the signal in these borderline cases by a T1 shortening effect. Then, the image is therefore not depending on flow effects but only on the presence of gadolinium within the vessels (Figs. 6 and 7).

Optimizing the investigation volume

MRI angiography must be adapted to the protocol required for the patient: in the management of an acute phase CVA and optimizing the 3D TOF sequence parameters can achieve an image acquisition time of approximately 2 minutes. In screening from aneurysm the acquisition sequence can last for up to 9 minutes in order to obtain multi-slab coverage from the postero-inferior cerebella arteries (PICA) to the peri-callosal arteries with high spatial resolution (Figs. 8 and 9) [28]. Increasing the image acquisition volume when circulating spin gradually loses its image appearance, requires several interlinked image acquisition volumes to be used: this is the principal of "multi-block" overlap or "multi-slabs" in which in general 3 slabs are required to correctly cover the occipital foramen to the peri-callosal vessels [25] (Fig. 10). A 30% slab coverage avoids a loss in vascular signal at the interface between two slabs. If this overlap is inadequate a signal loss artifact at the slab junction known as a venetian artifact (with reference to the venetian stores) may hinder interpretation (Fig. 8).

Post-treatment

Angiographic reconstructions are obtained by selecting information in the volume containing the most intense image before summing these (MIP software). Ideally the analysis is performed axis-by-axis after separating out and isolating the different arterial vessels in the circle of Willis. Wherever it possible, this axis-by-axis reconstruction should endeavor to separate out and exclude the subcutaneous and orbital hyperintense fat and then isolate and analyze the vessels individually [29].

One of the pitfalls of this image is its sensitivity to short T1 weighted environments (blood, fat, post-pituitary), which appear hyper intense on a TOF view and they interfere with the analysis (false vascular images). Vessel by vessel analysis and using the basic sections can overcome this pitfall.

Quality criteria for MRA

When an MRA 3D TOF report for the circle of Willis is produced, it is simple to provide an assessment of MRA quality. The visualized arteries are a good quality criterion in terms of spatial definition: seeing an ophthalmic artery or anterior
choroid artery indicates that the examination can be used to study structures between 0.5 and 1 mm in size.

The first volume section must pass beneath the occipital foramen and visualize the vertebral arteries as they pass through the dura mater. The final section is located above the arterial bend in the corpus callosum (Fig. 10).

Diagnostic performance with 3D TOF MRA
The sensitivity and specificity of 3D TOF MRA to identify an intracranial aneurysm over 3 mm in size are 87 to 100% and 86 to 100% respectively [30]. The results are better with 3 Tesla MRI than with 1.5 Tesla MRI because of greater spatial resolution. At 3 Tesla, the sensitivity and specificity to detect aneurysms under 5 mm in size are 98 and 94% respectively [28].

Apart from a positive diagnosis of aneurysm, MRA should be used to investigate for irregular scalloped, ‘‘pustular’’ appearances of the wall suggestive of fissure or rupture. The artery or arteries with malformations need to be described together with the appearance of the neck (wider or narrower), shape of the aneurysm (base of origin wider than depth: poor candidate for embolization) and the presence or absence of an artery arising from the sac [31].

A final key factor to investigate is whether the aneurysm is single or multiple (20% of cases) beginning with an examination of the equivalent contralateral arterial segment (mirror aneurysm).

The specific case of monitoring aneurysms treated by remobilization
MRA has a very important role to play in monitoring embolized aneurysms and provides excellent correlation with angiographic results to identify recanalization of the aneurysmal sac [32–35]. It is the recommended investigation to monitor aneurysms treated by embolization [36]. The technical settings for the imaging need to be adjusted in order to minimize artifacts due to the presence of platinum coils (shortening the echo time with an ET of under 3 msec). Some groups propose routine gadolinium enhancement to increase the sensitivity to identify recanalization of the aneurysm [37].
Figure 7. Improved visualization of the aneurysmal sac on real time MRA with gadolinium enhancement. Seventy-two-year old male patient with a fusiform basilar artery aneurysm presenting with lower limb paresis, dysarthria and swallowing difficulties. Heterogeneous appearance of the sac on FLAIR imaging (a). Note the absence of a homogeneous hyper intensity in the aneurysmal sac on the unenhanced real time MRA sections (b), which may suggest partial thrombosis. After enhancement with a half dose of gadolinium chelate (c) the sac is fully filled excluding the possibility of a partially thrombosed aneurysmal sac. The outlines of the aneurysm together with its morphology and dimensions are difficult to assess on MIP reconstructions (d); this information becomes available after enhancement (e).

Figure 8. Positioning of a real time MRA image volume for the circle of Willis. Correct position (a) and incorrect position (b). The investigation field should include caudally, the origin of the inferior cerebella arteries (lower arrows), and cranially, the branches of the division of the peri-callosal arteries (upper arrows), outside of the imaging field. This coverage requires the use of several slabs which need to be 30% overlapped; if overlapping is insufficient, a band of signal loss (dotted arrows in b) is seen at the intersection of the slabs and may create an artefactual stenosis.
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Figure 9. MRA coverage defect. Subarachnoid hemorrhage predominantly in the posterior fossa. This is attributed to rupture of a 3 mm aneurysm at the termination of the basilar artery shown on the global postero-anterior view (a) of the real time MRA and on the selective posterior anterior view of the basilar artery (dotted arrow) (b). On catheterized angiography, selective opacification of the left vertebral artery (c) confirms the presence of the aneurysm (dotted arrow) and particularly reveals an 8 mm aneurysm at the origin of the PICA (continuous arrow), not seen on MRA as it is outside of the field of vision.

Conclusion

Subarachnoid hemorrhage, thunderclap headaches, and a history of an intracranial aneurysm in a first-degree family member are indications for 3D TOF MRA to investigate for an aneurysm. Whilst conventional angiography remains the reference method, 3D TOF MRA at 1.5 Tesla provides a sensitivity of over 90% for aneurysms over 3 mm in size in a non-invasive manner without as complicated a technical procedure. Joint examination of 3D maximum intensity projection (MIP) reconstructions and unprocessed sections offers a sensitivity of over 90% and a specificity of 100% [31]. The volume rendering (VR) 3D TOF reconstruction technique appears to offer better detection and improved assessment of intracranial aneurysms plan MIP reconstructions [38]. There does not appear to be a significant difference in sensitivity between CT angiography and MRA [39]. Three millimeters appears to be a cut off below which the sensitivity of 1.5 Tesla MRA falls rapidly regardless of the reconstruction technique used. Diagnostic performance is better at 3 Tesla, including aneurysms under 5 mm in size.

TAKE-HOME MESSAGES

- MRA and CT angiography are taking over from digital angiography to detect aneurysms, the latter being reserved for the treatment stage for managing intracranial aneurysms.
Clinical case

Questions

1. What do you think about this MRA (Fig. 11), performed for sudden onset headache?
   1 – it is a real time MRA
   2 – there is no aneurysm in the anterior circulation
   3 – coverage is correct
   4 – coverage is incorrect

2. The field of vision of a circle of Willis MRA:
   1 – changes with the indication
   2 – is from the protuberance to the corpus callosum
   3 – can be increased by volume addition
   4 – includes branches of the external carotid artery

3. What do you conclude from this MRA (Fig. 12):
   1 – artifact
   2 – cavernous sinus aneurysm
   3 – peri-ophthalmic aneurysm

Answers

Q1: 1, 2, 4. Defective cranial coverage that may miss a pericallosal aneurysm (seen on Fig. 13).
Q2: 1, 3, 4. Field of vision beneath the occipital foramen to below the bend of the corpus callosum. The superficial temporal branches of the external carotid arteries are included in the field of vision and are usually very clearly seen.
Q3: 1. The substances on short T1 imaging such as fat, a hematoma (methemoglobin), with gadolinium enhancement, produce a strong image, which is difficult

Figure 11. Imaging for sudden onset headache.

4 – posterior communicating aneurysm
4. The sensitivity of MRA to diagnose aneurysm
   1 – is 90%
   2 – is 70% of the lesions less than 3 mm in size
   3 – increases with reconstruction artery by artery
   4 – increases the reconstruction artery by artery in VR compared to MIP

5. What are the indications for gadolinium enhancement on a TOF MRA?
   1 – investigation for angiitis
   2 – giant aneurysm
   3 – arterial obstruction
   4 – basal meningioma

Figure 12. MRA.
Figure 13. Same patient as Fig. 11.

to saturate. The post-MIP processing software cannot distinguish this appearance from an appearance of circulating blood and shows it on the angiography reconstructions hindering examination of the circle of Willis or leading to incorrect interpretations. In this case the H1 hyperintensity of the anterior clinoid fat is seen (cross).

Q4: 1, 2, 3, 4.

Q5: 1, 2, 3, 4. In a meningioma of the base of the cranium enhancement can quantify stenosis due to a tumor, as a result of compression or invasion.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


