Abstract

Purpose: In about 15% of patients with SAH no causative vascular lesions can be found in acute imaging with CTA and DSA. Usually, repeat DSA is mandatory and bears the usual risk of invasive angiography. The present study attempts to assess the diagnostic impact of 3D rotational angiography in order to avoid repeat DSA.

Materials and Methods: From January 2004 to December 2012, 649 patients with an acute non-traumatic SAH were examined. 91 patients with negative initial imaging diagnostics concerning the bleeding source were included in this study. These patients underwent a second angiography scan: 61 in 4-plane technique, and 30 with 2-plane technique and additional 3D DSA. Two cohorts were compared: patients with repeat angiography in conventional 4-plane technique from 2004 to July 2008 and 2-plane technique with additional 3D rotational DSA from 2008 to 2012. Statistical significance was verified by means of Fisher’s exact test.

Results: In the second DSA scan, 4 aneurysms in 4 patients (4/91; 4.4%) were found and treated subsequently. Within the first 4.5 years of this study, 401 patients with SAH were treated and 61 of them underwent repeat angiography (15.2%) compared to 30 of 248 patients (12.1%) in the last 4.5 years of this study. In the first group we found 3 aneurysms during repeat angiography, and in the second group we found 1. No significance was reached (p = 0.29) but there was a tendency towards higher diagnostic security using 3D DSA.

Conclusion: Using 3D rotational DSA in initial imaging workup might help to reduce false-negative results concerning the bleeding source of acute SAH. At least because of this fact, 3D rotational DSA should be part of the diagnostic workup after acute SAH.

Key Points:
- In 15% of SAH patients no causative vascular lesion can be found using conventional DSA compared to 12% using 3D DSA.
- Patients with perimesencephalic SAH and CT-negative SAH do not require repeat DSA.
- 3D DSA might help to avoid repeat DSA in SAH patients.

Citation Format:
Introduction

Despite the combination of computed tomography angiography (CTA) and digital subtraction angiography (DSA), initial imaging does not show the bleeding source in 15–20% of patients with an acute non-traumatic SAH [1]. This results in a large number of invasive repeat angiography procedures even if the indication for repeat angiography in the case of non-traumatic SAH and a failure to detect the bleeding source has been questioned, for example in a publication by du Mesnil de Rochemont [2]. This group of SAH patients without detection of an aneurysm in the initial DSA examination includes more patients than to be expected in the total collective with perimesencephalic SAH or CT-negative bleeding that can only be verified by cerebrospinal fluid puncture and in total more frequently includes patients in an initially good clinical condition (Hunt and Hess grade 1 or 2) [3, 4].

In general, occult aneurysms are to be expected as the bleeding source. However, other causes of non-traumatic basal SAH such as vessel dissections, arteriovenous malformations, or venous pathologies must also be anticipated. For a long time diagnostic angiography was performed using the conventional 4-plane technique. This technique was supplemented over 10 years ago by the option of performing rotational angiography (3D DSA). These datasets can be reconstructed in any projection so that all vascular segments can be viewed 3-dimensionally. Since its introduction, 3D DSA has been touted as an improvement particularly of the aneurysm detection rate [5, 6]. However, a small study suggests a benefit of 3D DSA over 2D DSA in SAH patients without initial detection of the source of bleeding [7]. According to Van Rooij et al., a small ruptured aneurysm was first diagnosed in the 3D reconstructions in 78% of these patients. In our study we examined whether 3D DSA increases diagnostic reliability in the acute phase compared to 2D DSA thus helping to avoid repeat angiography, initiate early treatment, and prevent rebleeding.

Materials and Methods:

649 consecutive patients with an acute non-traumatic SAH who underwent angiography between January 2004 and December 2012 were retrospectively evaluated. Patients in whom a bleeding source was found, i.e., patients with aneurysms, dural fistulas, venous thromboses, angiomata, spinal bleeding sources, or patients in whom the SAH proved to be traumatic were not included in the study. The bleeding source could not be detected during acute diagnosis in a total of 90 patients (91/649 = 14%) who consequently underwent repeat angiography. This included 50 women and 41 men with an average age of 57.7 (22 – 91 years). During the first 4.5 years of the examination period, a total of 401 patients with an acute non-traumatic SAH were examined and 61 patients had to undergo repeat angiography.

Since the introduction of the routine use of 3D DSA, 30 of 248 SAH patients had to undergo repeat angiography in another 4.5-year period. The Fisher’s exact test was used to check whether this was a significant decrease in the number of necessary repeat angiography procedures. During admission, 74 of the patients who underwent repeat angiography were classified as Hunt and Hess grade 1 or 2, 11 patients as Hunt and Hess grade 3 and 6 patients as Hunt and Hess grade 4 or 5. As a rule, repeat angiography was performed at the earliest 10 days after acute hemorrhage. 20 of 91 patients showed isolated perimesencephalic blood distribution (11 perimesencephalic SAHs during the first 4.5 years, 9 during the second period of the study) in the initial examination. The SAH could only be verified in the acute phase via cerebrospinal fluid puncture in 9 patients. One patient suffered rebleeding after a second normal DSA examination.

All patients with an acute SAH initially underwent 4-vessel DSA in the acute phase. If no bleeding source was found here, angiographic series of the external carotid artery and the cervical segments of the vertebral artery were generally added. If the anterior communicating branch did not show spontaneous contrast enhancement in any of the series, a series of an ACI with compression of the contralateral side was added. The repeat angiography was performed in the same manner as the first DSA.

From 2004 to July 2008, DSA of the intracranial vascular territories was performed on 4 planes (Toshiba Infinix, Toshiba Medical, Nasu, Japan). The angiograms achieved a matrix of 1024 x 1024 with an FOV of 21 cm. The series were performed using a biplanar technique with 6 – 8 ml of manually injected contrast agent and a total of 4 projections were acquired. After the standardized introduction of 3D DSA (Philips Allura, Philips Healthcare, Best, The Netherlands), the previously performed “oblique” 2-plane projections of the posterior circulatory system and both ACI circulation areas were typically replaced by one rotational series resulting in a reduction of the radiation exposure for patients and examiners [8]. The 3D DSA scans were acquired over a period of 4.1 seconds with a C-arm rotation of 240°. The injection of 18 ml of contrast agent with a flow rate of 3 ml/s into the ACI and 15 ml of contrast agent with a flow rate of 2 ml/s in the posterior circulatory system was performed automatically with the help of an injector (MedRad, Mark V ProVis®, MEDRAD Medizinische Systeme GmbH, Volkach, Germany). During the rotation, 122 images were acquired and used to 
create 3-dimensional reconstructions. Reconstructions can be created and evaluated easily and quickly with currently available software. The “fluoroscopy images” of the rotational series were loaded in a reconstruction program. A 3D reconstruction of the examined vascular tree was created via a virtual rendering step and can then be interpreted and postprocessed by the user. Individual exposures or single images combined as a “film” from these reconstructions are stored. The fluoroscopy images of the rotational series are additionally archived in the PACS and are available at any time for a new reconstruction. If an aneurysm was able to be detected during 3D DSA, an optimal projection was selected with the help of the reconstructions and a spotfilm of the aneurysm on one plane and with maximum magnification was generated.

Both the first DSA scans and those generated over time were retrospectively reevaluated independently by two neuroradiologists. Both examiners were not blinded for the follow-up examinations to ensure that the first examinations would be interpreted as negative even with knowledge of the second DSA scan.

**Results**

During the first 4.5 years of the examination period, a total of 401 patients with an acute non-traumatic SAH were examined and 61 of these patients (61/401, 15.2%) had to undergo repeat angiography because no bleeding source was found. 3 initially occult aneurysms (3/61, 4.9%) were found during repeat angiography. Since standardized introduction of 3D DSA in the routine workup, only 30 of 248 SAH patients (30/248, 12.1%) had to undergo repeat angiography in 4.5 years. These included only one additional aneurysm during repeat angiography (1/30; 3.3%) (Fig. 1).

Using Fisher’s exact test, this is not a significant decrease in the number of necessary repeat angiography procedures and only represents a tendency (p = 0.29). Even considering the detection rate of initially occult aneurysms during repeat angiography, the number of aneurysms detected during repeat angiography since the introduction of routine 3D DSA has not significantly increased or decreased (4.9% vs. 3.3%; p = 0.35). Finally there are 4 aneurysms in our collective (middle cerebral artery, vertebral artery, anterior communicating artery, ACI rear wall) with a maximum size

![Fig. 1](initial 3D rotational DSA A and the correlated biplane images C showing no aneurysm. Perhaps a discreet irregularity of the wall of the ICA can be seen. Repeat angiography scan 2 weeks after symptom onset showing the aneurysm in the 3D reconstruction B and biplane series D, especially in the targeted upscaled image E made with the aid of 3D DSA.)
of 4 mm in repeat angiography (4/91, 4.4%). Three of the aneurysms were treated with clipping and one aneurysm via coiling. The aneurysm in one patient who suffered from rebleeding after the second normal DSA scan was first diagnosed during a third DSA examination performed under these circumstances. A bleeding source could not be found in any of the patients with a perimesencephalic SAH (20/91) and in any of the patients with subarachnoidal blood (9/91) only detectable in the cerebrospinal fluid puncture. The distribution of 11 perimesencephalic SAHs during the first 4.5 years (11/61 = 18%) and 9 patients with this type of bleeding in the second time period (9/30 = 30%) of the study did not result in a bias. The use of the chi-square test also did not result in a (two-sided) significance (two-sided significance 0.195).

**Discussion**

Since the standardized introduction of 3D DSA in acute diagnosis at our institute, 12.1% of bleeding sources have remained occult over a period of 4.5 years compared to 15.2% in the previous 4.5 years. These numbers must be considered in a differentiated manner because our collective includes 31.9% (29/91) perimesencephalic and CT-negative cases of bleeding. Moreover, it was noteworthy that the patients undergoing repeat angiography (74/91, 81.3%) were frequently classified as Hunt and Hess grade 1 or 2. Firstly, the rate of repeat angiography is presumably particularly high in these subgroups because a bleeding source is able to be initially detected less frequently in the case of perimesencephalic and CT-negative subarachnoidal bleeding in particular. Secondly, it can generally be expected that fewer initially occult bleeding sources are detected in repeat angiography so that the success rate must also be lower than in the case of repeat angiography of patients with a subarachnoidal bleeding pattern typical of an aneurysm [9]. To guarantee that the initial imaging does not show a bleeding source retrospectively, all images from the initial diagnosis were independently reevaluated by two neuroradiologists in our study. In addition, the readers were not blinded with respect to the follow-up imaging so that the acute diagnosis could also be retrospectively evaluated as negative. Moreover, the indication for repeat angiography was checked in all patients under consideration of anamnestic and clinical parameters. All initially occult findings that were then subsequently verified in repeat angiography had a therapeutic consequence. The three aneurysms treated via clipping could all be intraoperatively identified as a bleeding source. A connection between false-negative acute diagnosis and aneurysm location could not be established in this study. Statistically speaking, the number of repeat angiography procedures did not decrease significantly nor were the repeat angiography examinations less frequently negative in this collective after standardized introduction of 3D DSA which would be an indication of a higher degree of reliability of the initial diagnosis. There is only a tendency to avoid repeat angiography by using 3D DSA. In total, the rate of repeat angiography procedures was able to be lowered by 3%. Of course, every aneurysm detected in a 3D reconstruction could potentially also be detected on 2D images if the correct projection is prospectively selected, particularly because the spatial resolution of 2D images is higher than that of rotational angiography. Aneurysms could also be visualized or obscured due to incorrect windowing of VRT images so that there is a certain degree of user dependence. Smaller aneurysms and/or infundibular vessel branches could then be missed in the diagnosis. However, since it is not possible to prospectively test all conceivable two-dimensional projections and thus to rule out an aneurysm with reasonable radiation exposure and appropriate contrast agent use, 3D DSA is a useful method, particularly because 3D rotational angiography requires a fraction of the radiation dose of a conventional series [8]. Moreover, 3D rotation is also useful when a projection that is not possible due to contact with the patient and a tilted tube position would have to be selected for the two-dimensional visualization of an aneurysm. Therefore, it is useful to analyze the 3D reconstructions already during the examination, to view them with different window settings, and to perform a 1-plane target projection in the case of a detected aneurysm.

Although only a few repeat angiography scans are necessary in individual cases as mentioned above and a significance level is not reached, we feel that there is still a benefit of 3D DSA over biplanar DSA with respect to the sensitivity of acute diagnosis so that false-negative findings occur less frequently and repeat angiography can thus be avoided. In an article published in 2007 by Ishihara et al., this was studied and confirmed in a small collective of 15 patients [10]. Other studies evaluate different advantages of 3D DSA, e.g. the number of detected aneurysms [11], and the advantages of 3D DSA for treatment planning [12] and for treatment success monitoring [13]. We also use 3D DSA for diagnostic verification of bleeding source as well as for intervention/operation planning. Due to the freely selectable and reproducible projections, repeat angiography for treatment planning is no longer necessary [14]. Some articles call for the limiting of 3D DSA to individual circulation areas mainly because of the additional radiation exposure but this was able to be refuted in 2007 [8]. The prevention of repeat angiography is also relevant with respect to medicolegal aspects: Both with regard to the lack of detection of a source of bleeding and to possible complications.

**Summary**

In individual cases 3D DSA can detect aneurysms during initial diagnosis that would have been missed on conventional 4-plane exposures. It is not capable of significantly reducing the number of necessary repeat angiography procedures. However, 3D DSA is a useful diagnostic tool for reasons of radiation hygiene and for treatment planning and can replace “oblique” projections, for example. An additional independent secondary evaluation of the initial images and possibly an interdisciplinary discussion of problematic cases can also be useful.
Clinical relevance of the study

▶ 3D DSA can have a tendency to avoid repeat angiography in the case of an initial lack of bleeding source detection but a significance level is not reached.

▶ The number of aneurysms found with 3D DSA in repeat angiography is not significantly higher than with the conventional technique but individual aneurysms are initially only able to be detected in 3D reconstructions if the correct angulation of the biplanar series was not randomly selected.

▶ It is useful to perform 3D DSA for bleeding source detection in acute non-traumatic SAH under consideration of medicolegal aspects because 3D angiography helps to increase the bleeding source detection rate even during initial diagnosis.

References