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Effect of endosaccular flow disruption devices on procedural radiation dose and fluoroscopy time in endovascular treatment of intracranial aneurysms

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To my wife Ayse Naz and my daughters Leyla and Parla

Affidavit

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München, 12.08.2021

Yigit Özpeynirci

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Abbreviations

BA	Basilar artery
BAC	Balloon-assisted coiling
BSS	Basic Safety Standards
BTA	Basilar tip aneurysm
CE	Communauté Européenne
CNS	Central nervous system
CT	Computer tomography
DAP	Dose-area product
DRL	Diagnostic reference levels
DSA	Digital subtraction angiography
EFD	Endosaccular flow-disruptor
e. g.	example gratia = for example
et al.	et alii / aliae
EURATOM	European Atomic Energy Community
FD	Flow-diverter
ICRP	International Commission on Radiological Protection
NEP	Neuroendovascular procedure
PACS	Picture archiving and communication system
PCA	Posterior cerebral artery
UIA	Unruptured intracranial aneurysms
SAC	Stent-assisted coiling
SAH	Subarachnoid haemorrhage
SCA	Superior cerebellar artery
WEB	Woven EndoBridge

Publications

1. Forbrig R, **Ozpeynirci Y**, Grasser M, Dorn F, Liebig T, Trumm CG. Radiation dose and fluoroscopy time of modern endovascular treatment techniques in patients with saccular unruptured intracranial aneurysms. Eur Radiol 2020;30:4504–4513.

2. Ozpeynirci Y, Hutschenreuter B, Forbrig R, Brückmann H, Liebig T, Dorn F. Endovascular treatment of basilar tip aneurysms in the era of endosaccular flow disruption: a comparative study. Neuroradiology 2021;63:619–626.

1. Contributions

1.1 Paper I

I, Yigit Özpeynirci, was a co-author of the first publication. I participated in data acquisition, analysis and interpretation, critically reviewed the article, provided final approval and assisted in submission and revision process.

1.2 Paper II

I was the first author of the second publication and was responsible for the concept and design of the study, data collection, analysis and interpretation, preparation of the tables, literature search, writing, final editing, submission and revision. Co-authors were partly involved in data collection, analysis and interpretation and critical revision of the manuscript.

2. Introduction

2.1 Background

Saccular, unruptured intracranial aneurysms (UIAs) are dilations or outpouchings of brain arteries, typically located at bifurcations and representing focal weaknesses in the arterial wall. They have a prevalence of ≈3% in the middle-aged population [1, 2]. Most UIAs are incidentally found on cross-sectional imaging studies performed for nonspecific symptoms, such as headache or vertigo. Rupture of an intracranial aneurysm results in subarachnoid hemorrhage (SAH), which is associated with high morbidity and mortality, often affecting patients at a relatively young age. The annual rupture rate of all UIAs is estimated at ≈0.3% [1, 2]. Aneurysm repair eliminates the risk of rupture. Two methods are available: surgical clipping and endovascular treatment. Clipping involves the placement of a titanium clip on the aneurysm sac to exclude it from the bloodstream and mandates surgical opening of the skull (Figure 1). Endovascular treatment can be performed without craniotomy and is therefore minimally invasive. It is performed in a dedicated neuroangiography suite utilizing fluoroscopic guidance to visualize the vessels, catheters, wires, and implants.

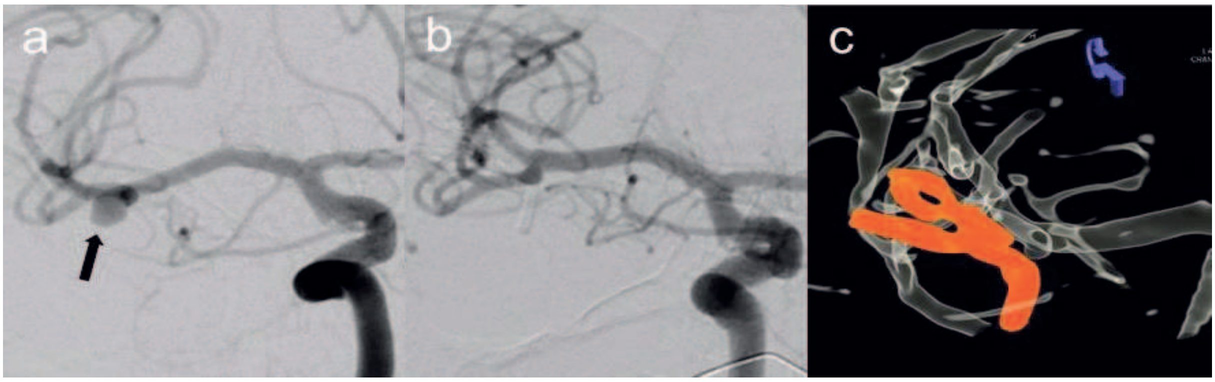


Figure 1 *Angiographic image of a right middle cerebral artery aneurysm (a, black arrow). Angiogram after clipping (b) demonstrates total occlusion of the aneurysm. 3D reconstruction shows the clips in red (c).*

Both techniques bear comparable success and complication rates, albeit with procedure-specific complications. A combined treatment-related fatality and morbidity of up to 5% are assumed [3-10]. Since not all UIAs have the same rupture risk, careful patient selection is required. Due to recent advances in angiographic technology and the neuroendovascular implant armamentarium, an increasing number of aneurysms are now occluded by endovascular means instead of conventional microsurgical clipping.

Endovascular treatment typically involves the insertion of platinum coils into the aneurysm through a microcatheter that is placed inside the aneurysm sac with or without the assistance of additional devices, such as balloons or stents (Figure 2). Newer technologies, such as flow-diverting stents or endosaccular flow-disruptors (EFD), are increasingly being used. Flow-diverters (FD) are high-mesh density stents placed in the parent artery (= the vessel that carries the aneurysm) across the aneurysm neck to divert the bloodstream away from the aneurysm dome (Figure 3). EFDs are devices usually comprising a tightly braided wire mesh implanted in the aneurysm sac to disrupt blood flow and prevent it from entering the aneurysm to promote intra-aneurysmal clot formation or shrinkage. WEB (Woven EndoBridge; Microvention, Aliso Viejo, California, USA) is by far the most widely used EFD to date (Figure 4).

Figure 2 *Angiographic image of a posterior communicating artery aneurysm in lateral projection (a). Embolization with platinum coils through the microcatheter (b). Insertion of the last coil (c). Final angiogram demonstrating near-total occlusion (d).*

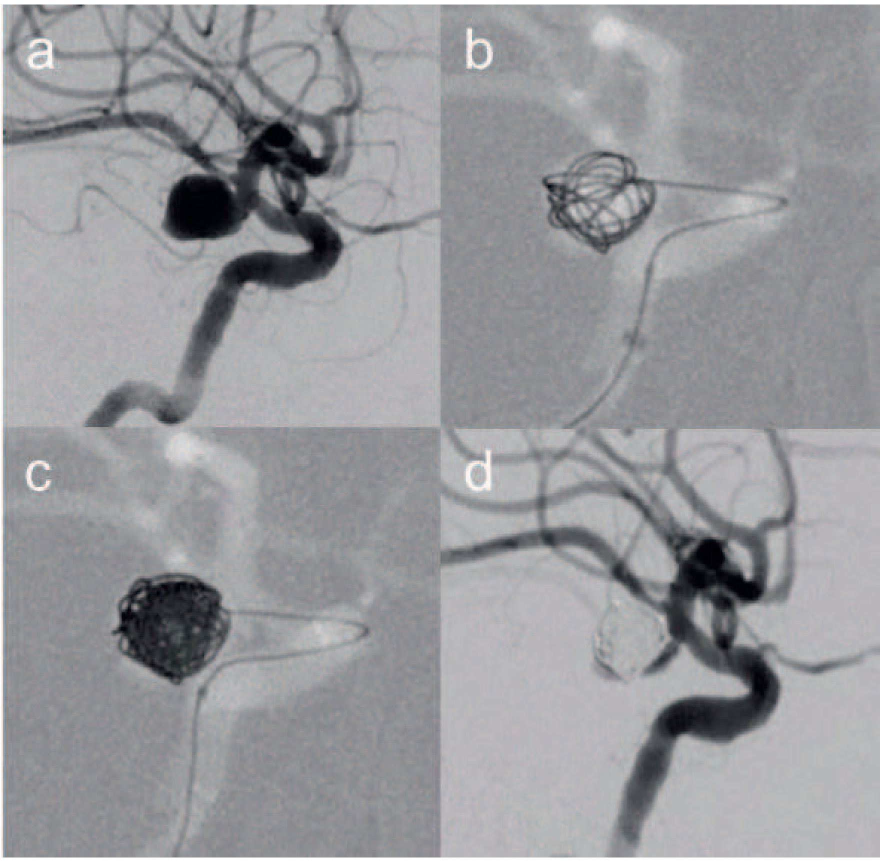
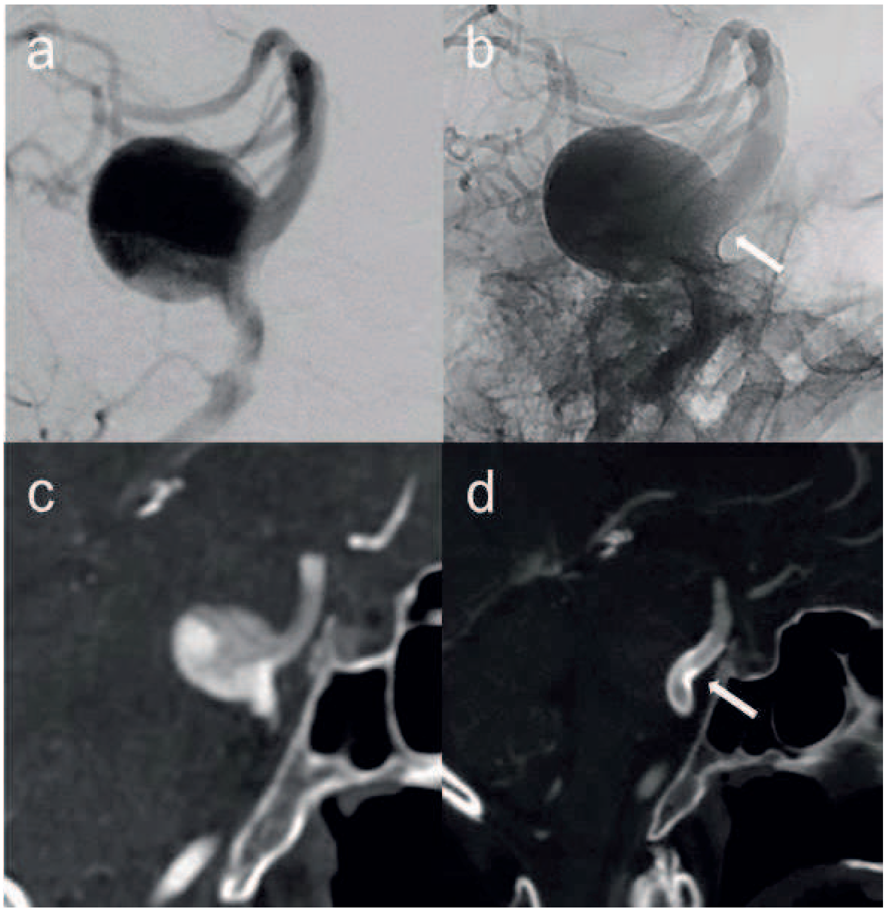


Figure 3 *Angiogram of a large basilar artery aneurysm in lateral projection (a). Contrast material stasis in the sac following implantation of a flow-diverting stent in the basilar artery (b, white arrow). Computer tomographic angiography before (c) and 14 days after the intervention (d). Total occlusion of the aneurysm with the flow-diverting stent (d, white arrow).*



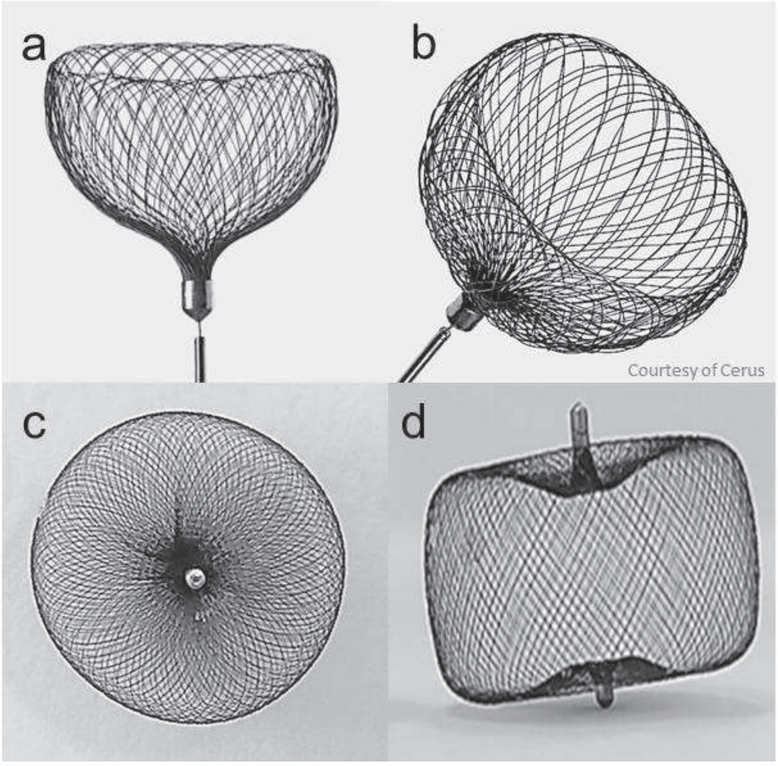


Figure 4 *Contour device in side (a) and oblique view (b). WEB device in top (c) and side (d) view.*

Neuroendovascular procedures (NEP) necessitate the acquisition of high-resolution digital subtraction angiography (DSA) images and, depending on the procedure, intensive use of live-fluoroscopy. This may cause considerable amounts of exposure of patients to radiation [11-16]. According to the guidelines from the American Heart Association and American Stroke Association regarding the management of UIAs, "endovascular treatment is recommended", but with a caution that "the procedural risk of radiation exposure should be explicitly reviewed in the consent process for NEPs" [3].

The side effects of high X-ray dosage include deterministic effects such as skin damage and focal hair loss or the risk of future cataract development but also stochastic risks like central nervous system (CNS) carcinogenesis [11-16]. As intracranial aneurysms are most prevalent in people aged 35 to 60, and general life expectancy has increased, radiation safety is an important issue to consider.

Studies show that proposed thresholds for skin damage and hair loss are frequently crossed during the NEPs, especially in the more complex cases. In their cohort, consisting of 702 NEPs, Peterson et al. found that roughly 40% of patients, in whose treatments the thresholds were exceeded, experienced skin or hair changes, with 30% of these alterations being irreversible. Permanent hair loss was strongly related to increasing skin dose [11].

NEPs for intracranial aneurysm treatment, according to Cheng et al., substantially enhance cataract incidence in exposed patients as compared to non-exposed or propensity score-matched controls [17].

Currently, there is no established method for estimating the risk of future CNS carcinogenesis from the radiation exposure during a single NEP. In the pediatric cohort, however, Thierry-Chef et al. found that the lifetime risk of brain tumor diagnosis was raised by 3 to 40% over the average background rates (57 instances per 10,000) depending on the dose received, age of exposure, and gender [18].

As a preventive measure and for standardization, diagnostic reference levels (DRL) were first introduced in 1996 by the International Commission on Radiological Protection (ICRP) to optimize patients' exposure. DRLs are proposed levels of radiation exposure for a patient for each diagnostic or therapeutic procedure using X-ray [19]. It is set to the 75th percentile of measured patient or phantom data, not to be expected to be exceeded for standard procedures, and indicates proposed action levels above which a facility should re-evaluate its technique and decide whether acceptable image quality can be obtained at lower doses.

The EURATOM (European Atomic Energy Community) Directive 2013/59 on medical exposure also states the need to establish DRLs [20].

Direct calculation of the surface skin dose, lens dose, or radiation dose absorbed by the intracranial structures is not practical. Therefore alternative markers such as dose-area product (DAP) meter (Gycm2) and air kerma (Gy) are usually used [11-15]. These are adequate substitutes for indirect estimation of the radiation dose, which are available in modern angiographic systems.

In 2018, the German Federal Office of Radiation Protection defined the national DRL for endovascular coil embolization of intracranial aneurysms as 250 Gycm2 without further differentiating between the embolization techniques or rupture status of the aneurysm [21].

The first paper examines the radiation dose and fluoroscopy time in a homogeneous group of patients with an incidental saccular UIA, who were treated endovascularly at Klinikum Großhadern using the following techniques: coiling, flow-diversion, endosaccular flow-disruption and combined techniques, e.g. coiling with an assisting device such as a stent or a balloon.

2.2 Publication I

2.2.1 Methods

We evaluated patients who had a saccular UIA and were treated endovascularly between January 2015 and May 2019 at Klinikum Großhadern. The following parameters were retrieved from patients' charts and the picture archiving and communication system (PACS) (syngo.via, Siemens Healthineers): patient age, aneurysm size, aneurysm location, endovascular technique, fluoroscopy time, total procedural DAP, and DSA protocol.

Two parameters, fluoroscopy time and DAP, were compared among subgroups defined according to following variables: endovascular technique, aneurysm location, and DSA protocol. Two protocols for DSA acquisition were pre-programmed by the manufacturer: One using normal dose parameters (=ND) and the other using a lower radiation dose to generate lower quality images without significantly compromising diagnostic accuracy (=LD).

The effect of aneurysm size and patient age on radiation dose and fluoroscopy time was investigated using correlation analysis. A p value <0.05 was considered statistically significant.

2.2.2 Results

We identified 87 patients with a saccular UIA who received endovascular treatment at our institution between January 2015 and May 2019. These 87 patients represented the study population.

Regarding the endovascular technique, 26/87 (29.9%) patients were treated by coiling, 24/87 (27.6%) with flow-diverting stents, 21/87 (24.1%) with EFDs, and 16/87 (18.4%) using a combined technique. Overall, the average DAP of 87 patients was 130 Gycm2. Average DAP (Gycm2) was 119 for coiling, 128 for FD, 128 for EFD, and 165 for combined techniques. Median fluoroscopy time was 49 min for coiling, 34 min for FD, 26 min for EFD, and 94 min for combined techniques.

Paired comparison of average DAPs between groups treated with different methods and different aneurysm locations did not reach statistical significance ($p>0.05$, each). Basilar tip aneurysms had the highest fluoroscopy times compared with aneurysms at other locations, but without statistical significance. Median fluoroscopy time of the interventions performed using combined techniques was significantly higher when compared with other groups ($p<0.003$, each) with the biggest increment in comparison with the EFD group (p<0.001), possibly reflecting the higher complexity in these cases. In contrast, the pair-wise comparison of median fluoroscopy time between the coiling, FD, and EFD groups was not significantly different (p>0.05). A 43% reduction of DAP could be achieved using a low-dose protocol (p<0.001). Significantly positive correlations were found between DAP and both aneurysm size and patient age, according to the Pearson correlation analysis.

2.3 Basilar Tip Aneurysms and Endosaccular Flow-Disruption

Aneurysms arising from the tip of the basilar artery (BA) form a special subset of intracranial aneurysms. They account for around half of all posterior circulation aneurysms and 5% of all intracranial aneurysms [22]. Currently, surgery is seldom used to treat these aneurysms due to a higher morbidity and mortality rate because of the deep location in the interpeduncular fossa, and close relation to the diencephalon and numerous surrounding perforating arteries supplying the brainstem and thalamus [22-27]. On the contrary, the almost straightforward anatomy of the BA makes these aneurysms ideal for endovascular therapy. As a result, endovascular methods have become standard for treating these aneurysms. However, the anatomy of the basilar tip, incorporating four arterial branches (one posterior cerebral artery (PCA) and superior cerebellar artery (SCA) on each side) and the often broad-based configuration of basilar tip aneurysms (BTA) may make endovascular treatment challenging (Figure 5). Complex treatment strategies may be needed which are usually associated with higher complication rates but not always resulting in higher occlusion rates [27-29]. Indeed, aneurysm recurrence at the basilar artery tip is more frequently reported than at other locations [30, 31].

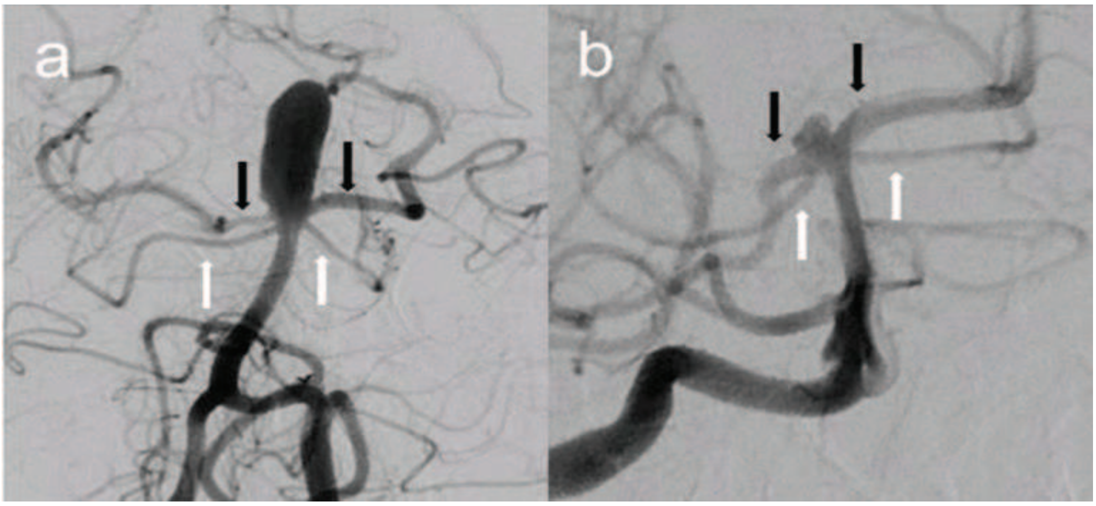


Figure 5 *Angiograms in frontal view showing two basilar tip aneurysms in two patients. Posterior cerebral (black arrow) and superior cerebellar arteries (white arrow) arising from the basilar tip (a, b). Note the incorporation of the right posterior cerebral artery origin by the aneurysm on b.*

Since up to 60% of basilar apex aneurysms are wide-necked [26, 27], length of attachment side of the aneurysm sack to the vessel measuring greater than 4 mm, assisting devices such as stents are usually used to avoid coil protrusion into the BA lumen or occlusion of the PCAs. However, stent-assisted techniques may increase the risk of procedural complications, especially thromboembolic events. Patients have to take double antiplatelet agents for 3 to 6 months, followed by single antiplatelet medication lifelong [32-34]. This is not favorable in the setting of an aneurysmal subarachnoid hemorrhage. The need for aggressive medical therapy and possible surgical procedures, such as external ventricular drainage placement or hemicraniectomy, is associated with an increased risk for hemorrhage in these patients as long as dual antiplatelet therapy is applied [35].

New generation implants have been designed to disrupt the blood flow inside the aneurysm sac and to promote stable clot formation and aneurysm occlusion, hence the name “endosaccular flow-disruptors” [36]. Of these devices, the WEB and the Contour Neurovascular System (Cerus Endovascular, Fremont, California, USA) are the most widely used. The technical success and safety of the WEB were supported by several prospective and retrospective multi-centered studies, including both ruptured and unruptured aneurysms [37-40]. Although the Contour device has only been introduced recently and received its CE Mark approval in 2020, there are already studies in the literature showing promising results and multi-center studies are underway [41, 42].

These devices are made up of a pre-shaped tightly woven wire mesh with shape memory characteristics (Figure 4). They are implanted fully within the aneurysm sac through a microcatheter. The implant restricts blood flow into and out of the aneurysm sac, causing stagnation and thrombosis. The mesh covering the aneurysm neck promotes neo-endothelial growth resulting in a permanent aneurysm occlusion (Figure 6 and 7) [43]. Because the whole implant is intra-aneurysmal, no long-term treatment with antiplatelets is necessary, making them an appealing treatment option for ruptured aneurysms [39].

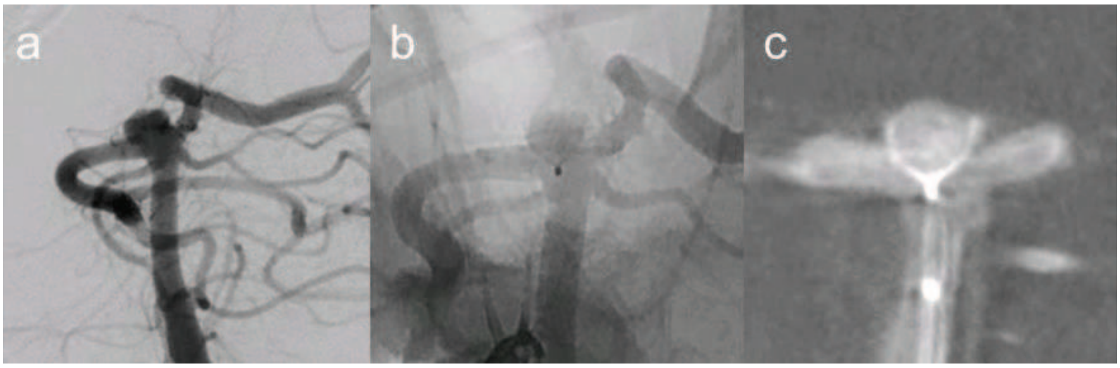
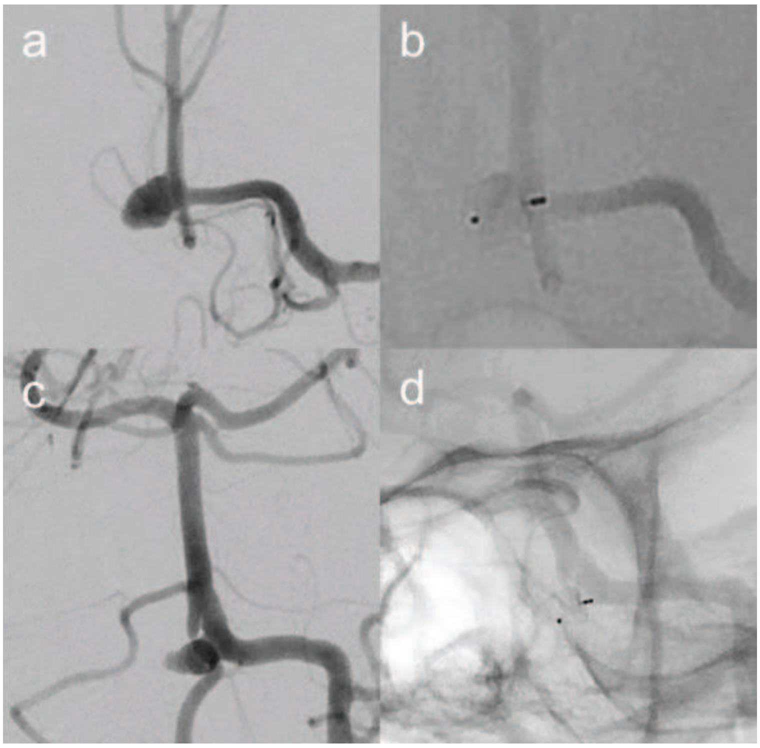


Figure 6 *Embolization of a basilar tip aneurysm with the Contour device. Angiogram in oblique projection before treatment (a). Unsubtracted image demonstrating decreased filling of the aneurysm after device detachment (b). Flat-panel CT showing optimal wall apposition and neck coverage (c).*

Figure 7 *Embolization of two aneurysms with the WEB device. Aneurysms of the anterior cerebral artery (a) and the vertebrobasilar junction (c). Unsubtracted images after device deployment demonstrate decreased contrast filling and optimal neck coverage (b, d).*



The most important factor for achieving shorter intervention times, fewer complication rates and less radiation exposure is the technical simplicity of the selected treatment method. Stent-assisted coiling (SAC), for instance, a technique commonly used to treat wide-necked BTAs, is a multi-step procedure that includes catheterization of the distal parent artery, deployment of the stent, catheterization of the aneurysm sac through the stent struts, and filling it with several coils [32-34]. Typically, numerous control injections are needed. Instead, with EFDs, precise measurement of the aneurysm size is essential for the selection of the proper implant. Following aneurysm catheterization, the intervention consists solely of device deployment.

Therefore, we believe BTAs represent a special subset of intracranial aneurysms, which would most benefit from endovascular treatment with EFDs in terms of procedural complication rates and radiation exposure. Only a few studies have compared stand-alone coiling and WEB, as well as SAC and WEB [44, 45]. However, in those series, aneurysms at all anatomical locations were evaluated. Higher complication rates in the SAC group compared with the WEB group and higher complete occlusion rates in aneurysms treated with WEB compared to those treated by coiling and similar rates to aneurysms treated by SAC have been reported, but, other potential benefits of the EFDs, such as reduced procedural fluoroscopy time and radiation exposure have not been discussed.

In the second study, we evaluated the clinical and radiation safety and efficacy of endosaccular flow disruption and conventional methods in the treatment of BTAs.

2.4 Publication II

2.4.1 Methods

A retrospective review of patients who were treated endovascularly for BTA between January 2013 and December 2019 at Klinikum Großhadern was performed. Recurring aneurysms were excluded. Patients treated with an EFD formed the “EFD group”, and patients treated with stand-alone coiling or coiling using any assisting device formed the “coiling group”.

Patient demographics, aneurysm characteristics, procedural data including fluoroscopy time and radiation exposure, complications, and clinical and angiographic outcomes of the two groups were compared. A p-value <0.05 was considered being statistically significant.

2.4.2 Results

Forty-one patients were included. Twenty-three (56%) patients were treated with an EFD and eighteen (44%) patients were treated with coiling. Average fluoroscopy time, treatment DAP and air kerma were significantly higher in the coiling group compared to the EFD group (33 min, 76 Gycm2, and 1.7 Gy vs. 81 min, 152 Gycm2, and 3.8 Gy, respectively (p<0.001)). There was no significant difference between the treatment groups regarding the thromboembolic complication rate (p=0.5), as well as the clinical (p=0.7) and final angiographic outcome (p=1). In the EFD group, six patients (26%) had long-term antiplatelet treatment, compared to eleven patients (61%) in the coiling group (p=0.02).

2.5 Discussion

This cumulative dissertation had the aim to investigate the effect of EFDs on procedural radiation dose and fluoroscopy time in endovascular treatment of intracranial aneurysms. In the first publication, we presented thorough data on radiation dose and fluoroscopy time for current endovascular treatment techniques for UIAs and introduced local DRLs. In the second publication, we evaluated clinical and radiation safety and efficacy of endosaccular flow disruption and standard methods (stand-alone coiling and combined techniques, such as balloon-assisted coiling (BAC), and SAC) in the treatment of BTAs.

Regarding aneurysms at all locations, there was no difference between patients treated with EFD and other devices in terms of radiation exposure. Treatment with EFD was significantly faster than treatment with combined methods, but the difference was not significant when compared with other groups, e.g. FD and coiling. Among all aneurysms, BTAs had the highest procedural fluoroscopy times.

Considering only BTAs, we found no significant difference between the therapy groups (coiling vs. EFD) in terms of thromboembolic complication rate, and clinical and final angiographic outcome. Patients who were treated with EFDs had significantly less procedural radiation exposure and fluoroscopy time.

Regarding the EURATOM Directive 2013/59 [20], we think that the presented data could be important for establishing up-to-date DRLs for new techniques such as EFDs, as the current national guidelines focus only on coiling [21]. Furthermore, the rupture status of the target aneurysm is not addressed in these guidelines. Through the creation of a homogenous population comprising patients treated only for one unruptured intracranial aneurysm per session without additional catheterization of other vessels for diagnostic purposes, we could present more reliable data.

Our DRLs ranged well below the recommendations in the national guidelines and were within the bounds of data previously reported. Contrary to the conclusions of Acton et al. [46], neither radiation dose nor fluoroscopy time was correlated with aneurysm location. But we could show a positive correlation with (1) aneurysm size (in accordance to D’Ercole et al.) [47], one of the important factors determining the endovascular technique and thus complexity of treatment, and (2) patient age, with which the vessel tortuosity increases and catheterization of the aneurysm becomes more challenging.

Our procedural fluoroscopy times were within the limits of data reported in the literature [47-49]. We demonstrated that the use of combined treatment techniques led to longer fluoroscopy times as compared to other techniques, with the biggest difference in comparison to EFD cases.

According to our literature search, there are only two studies that compare stand-alone coiling and EFD, and SAC and EFD [44, 45]. However, in these studies, different methods were not compared with each other regarding radiation safety. A prospective multi-center study with 150 aneurysms [40] and a retrospective multi-center study with 108 aneurysms [50] provide data on radiation exposure in the treatment of cerebral aneurysms using the WEB device. Arthur et al. [40] and Goertz et al. [50] reported average procedural fluoroscopy times of 30 min and 27 min, respectively. The average DAP was 113 Gycm2 in the series of Goertz et al.. Our findings in the EFD group (26 min and 128 Gycm2 in the first and 33 min and 76 Gycm2 in the second study) were comparable with those figures.

BTAs are unique among intracranial aneurysms in several ways: microneurosurgery is usually not an alternative, and because of the high frequency of broad-necked configuration (≈60%), coiling alone is in many instances not possible, and recurrence rates are typically high [22-31]. Therefore, SAC is the preferred technique by most interventionists but bears higher complication rates and demands more interventional experience [32-34]. In our second study, we showed no significant difference between endovascular treatment methods regarding morbidity, mortality, and angiographic outcome. But because of the technical simplicity of deployment of an EFD in an aneurysm compared to other methods, procedure times and radiation exposure were significantly less.

The major drawbacks of our studies were their retrospective, single-centered and non-randomized nature. Dosimetry data was gathered from only one angiography system (Artis zee, Siemens, Erlangen, Germany). In each case, the neurointerventionalists were free to choose the treatment technique. So, we cannot rule out a selection bias. In our first study, data on endovascular treatment of middle cerebral artery aneurysms are absent, since they are primarily treated by microneurosurgery at our institution.

3. Abstract

In my dissertation, I investigated the effect of endosaccular flow-disruptors on procedural radiation dose and fluoroscopy time in endovascular therapy of cerebral aneurysms.

Due to recent advances in angiography systems and neuroendovascular armamentarium, an increasing number of intracranial aneurysms can be treated by endovascular means instead of conventional microsurgical clipping. However, patient radiation exposure during neurointerventional procedures may cause skin damage, hair loss, cataract, or even central nervous system neoplasm formation. In the first study, we published procedural dosimetry data, including patient radiation exposure and fluoroscopy time for certain endovascular treatment techniques in patients with unruptured intracranial aneurysms treated at Klinikum Großhadern and made a comparison between each technique.

The amount of radiation exposure did not differ between groups treated with different methods. The average fluoroscopy time of the interventions performed using combined techniques was significantly longer as compared with other techniques, the biggest difference resulting from comparison with the endosaccular flow-disruptor group. Aneurysms originating from the tip of the basilar artery had longer fluoroscopy times compared with aneurysms at other locations. We believe this data will be useful for future updates of national patient radiation safety recommendations, especially regarding the novel treatment techniques.

Basilar tip aneurysms are mainly treated by endovascular means. They are usually wide-necked, often require complex treatment strategies, and recur more often than aneurysms at other locations. As already stated in the first paper, the treatment may involve longer fluoroscopy times and eventually a higher amount of patient radiation exposure. Therefore, they might most benefit from endosaccular flow-disruptors, single devices, implanted only in the aneurysm sac requiring no assisting devices, to disrupt the blood flow in the aneurysm sac and promote stable clot formation and aneurysm occlusion.

In the second study, we evaluated clinical and radiation safety and efficacy of endosaccular flow disruption and conventional methods in the treatment of basilar tip aneurysms and found no significant difference between treatment groups regarding the clinical and angiographic outcome. However, the use of endosaccular flow-disruptors significantly reduced the fluoroscopy times and radiation exposure in the treatment of basilar tip aneurysms.

According to our findings from the two studies, we claim that the tip of the basilar artery represents the location where intracranial aneurysms would most benefit from treatment with endosaccular flow-disruptors in terms of radiation safety without compromising the clinical outcome.

4. Zusammenfassung

Im Rahmen meiner Dissertation habe ich die Auswirkung von endosakkulären Flussteilern auf die prozedurale Strahlendosis und die Durchleuchtungszeit bei der endovaskulären Behandlung von intrakraniellen Aneurysmen untersucht.

Aufgrund technischer Fortschritte bei den Angiographiesystemen und den neuroendovaskulären Implantaten wird mittlerweile eine zunehmende Anzahl von intrakraniellen Aneurysmen mit endovaskulären Methoden anstelle eines mikroneurochirurgischen Clippings behandelt. Die Strahlendosen, denen die Patienten während der neurointerventionellen Verfahren ausgesetzt sind, können jedoch Hautschäden, Haarausfall, Katarakt oder sogar Neoplasien des zentralen Nervensystems verursachen.

In der ersten Studie haben wir prozedurale Dosimetriedaten, einschließlich der Strahlenexposition des Patienten und der Durchleuchtungszeit, für bestimmte endovaskuläre Behandlungstechniken bei Patienten mit nicht rupturierten intrakraniellen Aneurysmen, die im Klinikum Großhadern behandelt wurden, veröffentlicht und einen Vergleich zwischen den einzelnen Techniken durchgeführt.

Die durchschnittliche Höhe der Strahlenbelastung unterschied sich nicht zwischen den verschiedenen Behandlungsmethoden. Die durchschnittliche Durchleuchtungszeit war bei Anwendung kombinierter Techniken im Vergleich zu den anderen Gruppen signifikant höher. Der größte Zuwachs an Exposition fand sich im Vergleich zur Behandlung mit endosakkulären Flussteilern. Aneurysmen an der Spitze der Arteria basilaris, wiesen im Vergleich zu anderen Lokalisationen die höchsten Durchleuchtungszeiten auf. Diese Daten können für zukünftige Aktualisierungen der nationalen Empfehlungen zum Strahlenschutz von Patienten nützlich sein, insbesondere im Hinblick auf die neuen Behandlungstechniken.

Basilarisspitzenaneurysmen werden hauptsächlich endovaskulär behandelt. Sie sind meist breitbasig, erfordern oft komplexe Behandlungsstrategien und neigen häufiger zum Rezidiv als Aneurysmen anderer Lokalisation. Wie bereits in der ersten Arbeit erwähnt, kann die Behandlung mit längeren Durchleuchtungszeiten und eventuell höherer Strahlenbelastung des Patienten verbunden sein. Daher würden diese am deutlichsten vom Einsatz endosakkulärer Flussteilern profitieren, wobei es sich um Einzelimplantate handelt, die nur im Aneurysmasack freigesetzt werden und keine Hilfsmittel, wie einen Stent oder Ballon, benötigen um eine stabile Thrombusbildung und einen Verschluss des Aneurysmas zu fördern.

In der zweiten Studie haben wir endosakkuläre Flussteiler mit konventionellen Methoden zur endovaskulären Behandlung von ausschließlich Basilarisspitzenaneurysmen in Bezug auf die klinische und radiologische Sicherheit und Wirksamkeit verglichen und fanden keinen signifikanten Unterschied zwischen den Behandlungsgruppen hinsichtlich des klinischen und angiographischen Ergebnisses. Darüber hinaus ging die Verwendung von endosakkulären Flussteilern mit einer signifikanten Reduktion der Durchleuchtungszeit und der gesamten Strahlenexposition einher.

Nach den Erkenntnissen aus zwei Studien liegt es nahe, dass Patienten mit anatomischer Lokalisation intrakranieller Aneurysmen an der Spitze der A. basilaris in Bezug auf die Strahlenhygiene am deutlichsten von einer Behandlung unter Verwendung von endosakkulären Flussteilern profitieren würden, ohne das klinische Ergebnis zu beeinträchtigen.

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INTERVENTIONAL

Radiation dose and fluoroscopy time of modern endovascular treatment techniques in patients with saccular unruptured intracranial aneurysms

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Abstract

Objectives Modern endovascular treatment of unruptured intracranial aneurysms (UIAs) demands for observance of diagnostic reference levels (DRLs). The national DRL (250 Gy cm^2) is only defined for coiling. We provide dosimetric data for the following procedures: coiling, flow diverter (FD), Woven EndoBridge (WEB), combined techniques.

Methods A retrospective single-centre study of saccular UIAs treated between 2015 and 2019. Regarding dosimetric analysis, the parameters dose area product (DAP) and fluoroscopy time were investigated for the following variables: endovascular technique, aneurysm location, DSA protocol, aneurysm size, and patient age.

Results Eighty-seven patients (59 females, mean age 54 years) were included. Total mean and median DAP (Gy cm^2) were 119 ± 73 (89–149) and 94 (73; 130) for coiling, 128 ± 53 (106–151) and 134 (80; 176) for FD, 128 ± 56 (102–153) and 118 (90; 176) for WEB, and 165 ± 102 (110–219) and 131 (98; 209) for combined techniques ($p > .05$). Regarding the aneurysm location, neither DAP nor fluoroscopy time was significantly different ($p > .05$). The lowest and highest fluoroscopy times were recorded for WEB and combined techniques, respectively (median 26 and 94 min; $p < .001$). A low-dose protocol yielded a 43% reduction of DAP ($p < .001$). Significantly positive correlations were found between DAP and both aneurysm size ($r = .320$, $p = .003$) and patient age ($r = .214$, $p = .046$).

Conclusions This UIA study establishes novel local DRLs for modern endovascular techniques such as FD and WEB. A low-dose protocol yielded a significant reduction of radiation dose.

Key Points

- *This paper establishes local diagnostic reference levels for modern endovascular treatment techniques of unruptured intracranial aneurysms, including flow diverter stenting and Woven EndoBridge device.*
- *Dose area product was not significantly different between endovascular techniques and aneurysm locations, but associated with aneurysm size and patient age.*
- *A low-dose protocol yielded a significant reduction of dose area product and is particularly useful when applying materials with a high radiopacity (e.g. platinum coils).*

Keywords Cerebral angiography · Endovascular procedures · Intracranial aneurysm · Radiation exposure

Abbreviations

ACOM	Anterior communicating artery
BA	Basilar artery
BSS	Euratom Basic Safety Standards
DAP	Dose area product
DRL	Diagnostic reference level
DSA	Digital subtraction angiography
FD	Flow diverter
FOV	Field of view
ICA	Internal carotid artery
LD	Low dose
MD	Mixed dose
ND	Normal dose
SD	Standard deviation

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UIA Unruptured intracranial aneurysm
WEB Woven EndoBridge device

Introduction

Endovascular treatment of intracranial aneurysms has become a standard procedure since the International Subarachnoid Aneurysm Trial (ISAT) results confirmed at least equal clinical outcome when compared with neurosurgical approaches [1, 2]. As the guidelines for radiation protection have been updated recently [3], observance of diagnostic reference levels (DRLs) in endovascular treatment of intracranial aneurysms has increased in significance. The national DRL of the dose descriptor dose area product (DAP) defined by the Federal Office of Radiation Protection (250 Gy cm^2) only refers to coil embolisation of intracranial aneurysms [4]; alternative modern endovascular treatment techniques such as extra-aneurysmal flow diverter (FD) stenting [5–7] or intraaneurysmal flow disruption (Woven EndoBridge (WEB) device) [8–10], that nowadays are routinely used, e.g. in broad-neck aneurysms, are not yet considered in the guidelines cited above.

As a consequence, published data on radiation dose often only take into account coil embolisation [11–15]. Furthermore, these studies mainly contain interventional data of unselected patients, i.e. patients with both elective and emergency aneurysm treatment (in case of a ruptured and/or symptomatic aneurysm).

Regarding endovascular treatment, a risk-benefit assessment is particularly essential in patients with an incidental, unruptured intracranial aneurysm (UIA). Recommendations on elective endovascular treatment of UIAs are (i) a high technical success and low peri-procedural complication rate, (ii) a reasonable radiation dose particularly in young patients according to the ALARA (as low as reasonably achievable) principle, and (iii) a limited intervention duration, as a prolonged fluoroscopy time is associated with an increased peri-procedural complication rate [16].

The aim of this retrospective single-centre study is the evaluation of radiation dose and fluoroscopy time in patients with an incidental saccular UIA, who underwent an elective aneurysm treatment using the following endovascular procedures: Coiling, FD, WEB, combined techniques. The provided data may be useful for the establishment of novel DRLs in the field of modern endovascular treatment of intracranial aneurysms.

Material and methods

This retrospective single-centre study was approved by the responsible Institutional Review Board (project number 19-813) of the Ludwig-Maximilians-University Munich, Germany. The study was performed in accordance with the Declaration of Helsinki.

We analysed patients with a saccular UIA who were endovascularly treated between January 2015 and May 2019. To increase the dosimetric homogeneity of the data pool and to reduce treatment bias, the following inclusion and exclusion criteria were defined (see flowchart in Fig. 1):

Inclusion criteria:

- Age $\geq$ 18 years
- Location: anterior communicating artery (ACOM); intradural segments of the internal carotid artery (ICA), including posterior communicating artery and carotid T; tip of the basilar artery (BA)
- Endovascular treatment: coiling, FD, WEB, combined techniques

Exclusion criteria:

- Ruptured and/or symptomatic aneurysms
- Non-saccular (e.g. fusiform, dissecting, mycotic) aneurysms
- Multiple aneurysms
- Other intracranial aneurysm locations
- Additional diagnostic pan- (four-vessel) angiography during the same intervention
- No 3D angiography
- Exclusively monoplanar digital subtraction angiography (DSA) acquisitions due to difficult working projection

Endovascular procedures were performed by five consultant neuroradiologists with six to more than 20 years of experience in interventional neuroradiology. The applied angiographic system was a biplane angiographic unit (Axiom Artis dBA, Siemens Healthineers). A transfemoral approach was used in each patient. Regarding the vessel visualisation, a non-ionic iodinated contrast agent was applied (iomeprol 300 mg iodine/ml; Imeron, Bracco Imaging). The angiographic workflow routinely comprised initial and final DSA acquisitions including arterial and venous phases on standard anteroposterior and lateral projections with a preferred field of view (FOV) of 32 cm, a 3D DSA with a FOV of 48 cm (or minimum of 42 cm) preset by the manufacturer, peri-procedural DSA acquisitions in arterial phase on working projections using a targeted FOV of 11 cm or 16 cm, and a pulsed fluoroscopy with a frame rate of 7.5 f/s. Regarding the DSA acquisition type, two protocols were preset by the manufacturer:

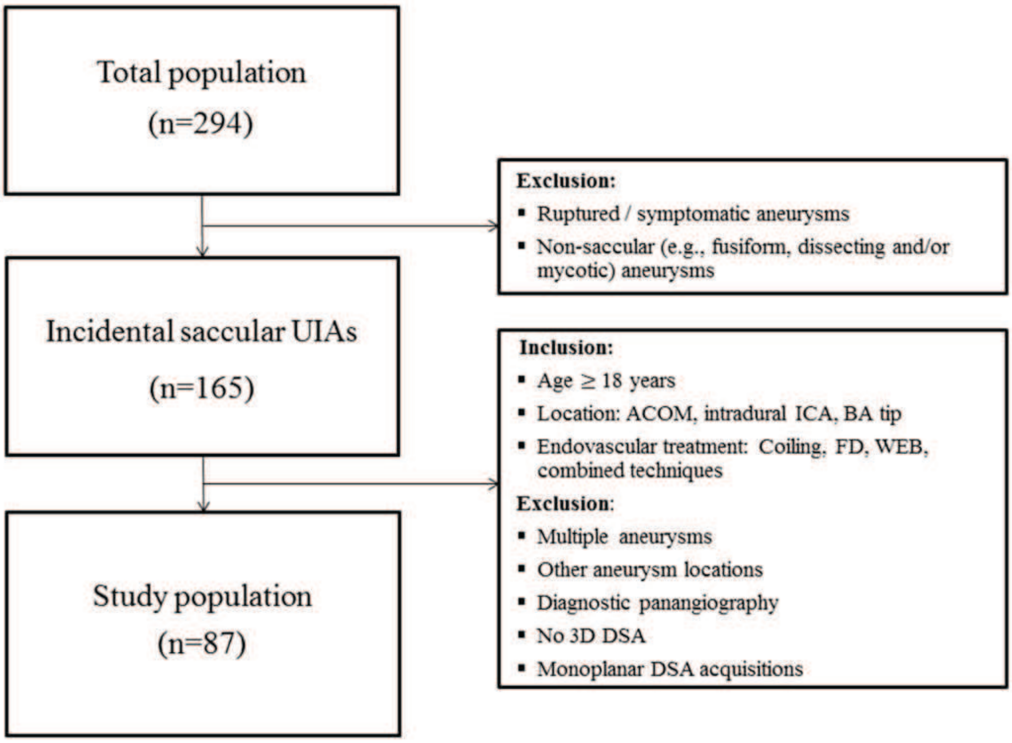

Fig. 1 Flow chart of the inclusion and exclusion criteria. ACOM, anterior communicating artery; BA, basilar artery; DSA, digital subtraction angiography; FD, flow diverter; ICA, internal carotid artery; *n*, number; UIA, unruptured intracranial aneurysm; WEB, Woven EndoBridge device

- Low dose (LD): 2 or 4 f/s (arterial phase), 1 f/s (venous phase), kV 73, pulse width 50 ms, dose 1820 μGy/p
- Normal dose (ND): 2 or 4 f/s (arterial phase), 1 f/s (venous phase), kV 73, pulse width 100 ms, dose 3000 μGy/p

Radiation metrics

In each patient, all imaging data and dose reports retrieved from a dedicated picture archiving and communication system (syngo.via, Siemens Healthineers) were reviewed by two experienced neuroradiologists with 9 (R.F.) and 10 (C.G.T.) years of experience in diagnostic and interventional neuroradiology. In detail, the following parameters were documented: aneurysm size, aneurysm location, endovascular technique, DSA acquisition count, DSA protocol, fluoroscopy time and DAP (representing a surrogate measure of energy delivered to patients [15]), and DSA DAP. The individual total DAP was calculated by summing fluoroscopy and DSA DAP. Data of DSA acquisition count, fluoroscopy time, and DAP were documented by summing respective values of both X-ray tubes (biplane mode).

Furthermore, the impact of different DSA protocols on DAP was investigated. In detail, (1) the total DAP was compared between the LD, ND, and mixed-dose (MD; both LD and ND DSA acquisitions) groups, and (2) the individual dose index was calculated for each patient in the three groups, by using the following formula:

$$\text{Dose index} = \text{DSA DAP}/\text{DSA acquisition count}$$

Statistics

Continuous data are provided as mean ± standard deviation (95% confidence interval) and/or median (25%; 75% interquartile range), and categorical data as counts and percent. Regarding the two outcome parameters DAP and fluoroscopy time, data were initially assessed for normality applying the Kolmogorov-Smirnov test considering the endovascular technique, aneurysm location, and DSA protocol. Variables were then compared according to the *t* test if data were normally distributed. The Mann-Whitney *U* test was used if data were not normally distributed. When statistically significant differences occurred, single posttest comparisons were performed by using the Mann-Whitney *U* test and *t* test with Bonferroni's correction for multiple comparisons. To note, though DAP values were normally distributed, we also calculated and compared the respective median DAP for different endovascular techniques and aneurysm locations, enabling adjustment to the local DRL defined by the 75% percentile [17]. The Pearson correlation analysis was applied to investigate the impact of the two variables aneurysm size and patient age on radiation dose and fluoroscopy time, respectively. Data analysis was performed using IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp.). A level of significance of $\alpha = 0.05$ was used throughout the study.

Results

Patient characteristics

Patient characteristics are summarised in Table 1 and Fig. 1. We identified a total of 294 patients with either an UIA or ruptured/symptomatic intracranial aneurysm who have been treated endovascularly at our institution between January 2015 and May 2019. Eighty-seven out of 294 patients (29.6%; 59 females, mean age 54 years) had a saccular UIA and met further inclusion and exclusion criteria as described above. These 87 patients represent the study population.

The median aneurysm size was 6.7 mm, with a minimum diameter of 2 mm ($n = 3$) and a maximum diameter of 30 mm ($n = 1$). To note, the three patients with the smallest UIA diameter were treated, as they had a history of subarachnoid haemorrhage due to rupture of another intracranial aneurysm, consequently harbouring a statistically increased risk of re-bleeding. Thirty out of 87 (34.5%) aneurysms were located at the ACOM, 40/87 (46%) at the intradural ICA, and 17/87 (19.5%) at the BA tip. Regarding the endovascular technique, 26/87 (29.9%) patients were treated by coiling (median 5 coils; range 1–21 coils), 24/87 (27.6%) by FD (1 device in 22/24 patients; 2 devices in 2/24 patients), 21/87 (24.1%) by WEB (1 device in 21/21 patients), and 16/87 (18.4%) by a combined technique (coiling + stent, $n = 7$; coiling + balloon remodeling, $n = 2$; coiling + FD, $n = 5$; WEB + stent, $n = 1$; FD + stent, $n = 1$). In detail, 15/30 (50%) ACOM aneurysms were treated by coiling, 1/30 (3.3%) by FD, 11/30 (36/7%) by WEB, and 3/30 (10%) by a combined technique (coiling + stent, $n = 2$; WEB + stent, $n = 1$). Intradural ICA aneurysms were treated by coiling in 8/40 (20%), using a FD in 23/40 (57.5%), and a combined technique in 9/40 patients (22.5%; coiling + stent, $n = 2$; coiling + balloon remodeling, $n = 2$; coiling + FD, $n = 4$; FD + stent, $n = 1$). BA tip aneurysms were treated by coiling in 3/17 (17.7%), using a WEB in 10/17 (58.8%), and a combined technique in 4/17 patients (23.5%; coiling + stent, $n = 3$; coiling + FD, $n = 1$).

Radiation dose and fluoroscopy time

Results of radiation dose and fluoroscopy time are illustrated in Table 2 and Figs. 2 and 3.

Overall, the total mean and median DAP (Gy cm^2) of 87 patients were 130 ± 65 (116–144) and 116 (78; 165), respectively. In detail, total mean and median DAP (Gy cm^2) were 119 ± 73 (89–149) and 94 (73; 130) for coiling, 128 ± 53 (106–151) and 134 (80; 176) for FD, 128 ± 56 (102–153) and 118 (90; 176) for WEB, and 165 ± 102 (110–219) and 131 (98; 209) for combined techniques. We calculated the lowest mean and median DAP for the coiling group, and the highest mean DAP for the combined-technique group; however, pairwise comparison of total mean and median DAP between groups did not reach statistical significance ($p > .05$, each; Table 2). Concerning the aneurysm location, total mean and median DAP (Gy cm^2) were 134 ± 68 (109–159) and 116 (75; 178) for ACOM aneurysms, 130 ± 69 (108–152) and 120 (80; 162) for intradural ICA aneurysms, and 133 ± 87 (89–178) and 110 (66; 172) for BA tip aneurysms ($p > .05$, each; Table 2).

Median fluoroscopy time was 49 min (32; 68) for coiling, 34 min (27; 44) for FD, 26 min (18; 65) for WEB, and 94 min (59; 133) for combined techniques. Median fluoroscopy time of the latter group was significantly higher when compared with the three other groups ($p < .003$, each; Table 2), with the biggest increment in comparison with the WEB group ($p < .001$). In contrast, pairwise comparison of median fluoroscopy time between the coiling, FD, and WEB groups was not significantly different ($p > .05$, each; Table 2). Regarding the aneurysm location, median fluoroscopy time was 51 min (25; 80) for ACOM aneurysms, 41 min (31; 82) for intradural ICA aneurysms, and 58 min (19; 90) for BA tip aneurysms ($p > .05$, each; Table 2).

A LD protocol was applied in 25/87 (28.7%), a ND protocol in 37/87 (42.5%), and a MD protocol in 25/87 patients (28.7%). Mean DSA acquisition count (biplane) did not

Table 1 Characteristics of 87 patients with a saccular UIA undergoing endovascular treatment

Age, mean (range)	54 years (18–74)		
Sex	59 females (67.8%), 28 males (32.2%)		
Aneurysm size, median (range)	6.7 mm (2–30 mm)		
	ACOM ($n = 30$)	Intradural ICA ($n = 40$)	BA tip ($n = 17$)
Coiling ($n = 26$)	15/26 (57.7%)	8/26 (30.8%)	3/26 (11.5%)
FD ($n = 24$)	1/24 (4.2%)	23/24 (95.8%)	0/24 (0%)
WEB ($n = 21$)	11/21 (52.4%)	0/21 (0%)	10/21 (47.6%)
Combined ($n = 16$)	3/16 (18.75%)	9/16 (56.25%)	4/16 (25%)

ACOM, anterior communicating artery; *BA*, basilar artery; *FD*, flow diverter; *ICA*, internal carotid artery; *n*, number; *UIA*, unruptured intracranial aneurysm; *WEB*, Woven EndoBridge device

Table 2 DAP and fluoroscopy time regarding different endovascular techniques, aneurysm locations, and DSA protocols

Total DAP ($n = 87$) (Gy cm^2)	130 ± 65 (116–144) (mean)	116 (78; 165) (median)			
Endovascular technique	Coiling ($n = 26$)	FD ($n = 24$)	WEB ($n = 21$)	Combined ($n = 16$)	p value
Mean DAP* (Gy cm^2)	119 ± 73 (89–149)	128 ± 53 (106–151)	128 ± 56 (102–153)	165 ± 102 (110–219)	Coiling vs. FD: $p = .550$ Coiling vs. WEB: $p = .591$ Coiling vs. combined: $p = .199$ FD vs. WEB: $p = .998$ FD vs. combined: $p = .277$ WEB vs. Combined: $p = .335$
Median DAP# (Gy cm^2)	94 (73; 130)	134 (80; 176)	118 (90; 176)	131 (98; 209)	Coiling vs. FD: $p = .085$ Coiling vs. WEB: $p = .203$ Coiling vs. combined: $p = .060$ FD vs. WEB: $p = .991$ FD vs. combined: $p = .547$ WEB vs. combined: $p = .542$
FL time# (min)	49 (32; 68)	34 (27; 44)	26 (18; 65)	94 (59; 133)	Coiling vs. FD: $p = .267$ Coiling vs. WEB: $p = .061$ Coiling vs. combined: *$p = .002$* FD vs. WEB: $p = .087$ FD vs. combined: *$p = .001$* WEB vs. combined: *$p < .001$*
Aneurysm location	ACOM ($n = 30$)	Intradural ICA ($n = 40$)	BA tip ($n = 17$)		
Mean DAP* (Gy cm^2)	134 ± 68 (109–159)	130 ± 69 (108–152)	133 ± 87 (89–178)		ACOM vs. intradural ICA: $p = .303$ ACOM vs. BA tip: $p = .173$ Intradural ICA vs. BA tip: $p = .505$
Median DAP# (Gy cm^2)	116 (75; 178)	120 (80; 162)	110 (66; 172)		ACOM vs. intradural ICA: $p = .410$ ACOM vs. BA tip: $p = .255$ Intradural ICA vs. BA tip: $p = .579$
FL time# (min)	51 (25; 80)	41 (31; 82)	58 (19; 90)		ACOM vs. intradural ICA: $p = .491$ ACOM vs. BA tip: $p = .812$ Intradural ICA vs. BA tip: $p = .382$
DSA protocol	LD ($n = 25$)	ND ($n = 37$)	MD ($n = 25$)		
Acquisition count* (n)	27 ± 13 (19–35)	28 ± 17 (19–37)	25 ± 13 (18–32)		LD vs. ND: $p = .887$ LD vs. MD: $p = .637$ ND vs. MD: $p = .552$
Mean DAP* (Gy cm^2)	102 ± 45 (83–121)	144 ± 78 (118–170)	144 ± 77 (113–176)		LD vs. ND: *$p = .018$* LD vs. MD: *$p = .022$* ND vs. MD: $p = .904$
Mean dose index* (Gy cm^2)	4.49 ± 1.76 (3.77–5.22)	7.89 ± 2.97 (6.90–8.88)	6.78 ± 3.06 (5.52–8.04)		LD vs. ND/MD: *$p < .001$, each* ND vs. MD: $p = .159$

Values of radiation dose, FL time, and acquisition count are summed for both X-ray tubes (biplane mode). Significant values with post hoc comparisons are indicated in italics

ACOM, anterior communicating artery; *BA*, basilar artery; *DAP*, dose area product; *DSA*, digital subtraction angiography; *FD*, flow diverter; *FL*, fluoroscopy; *ICA*, internal carotid artery; *LD*, low dose; *MD*, mixed dose; *min*, minutes; *n*, number; *ND*, normal dose; *ns*, not significant; *WEB*, Woven EndoBridge device

*Mean values were calculated using the t test and are shown as mean ± standard deviation (95% confidence interval)

Median values were calculated using the Mann-Whitney U test and are shown as median (25%; 75% percentile)

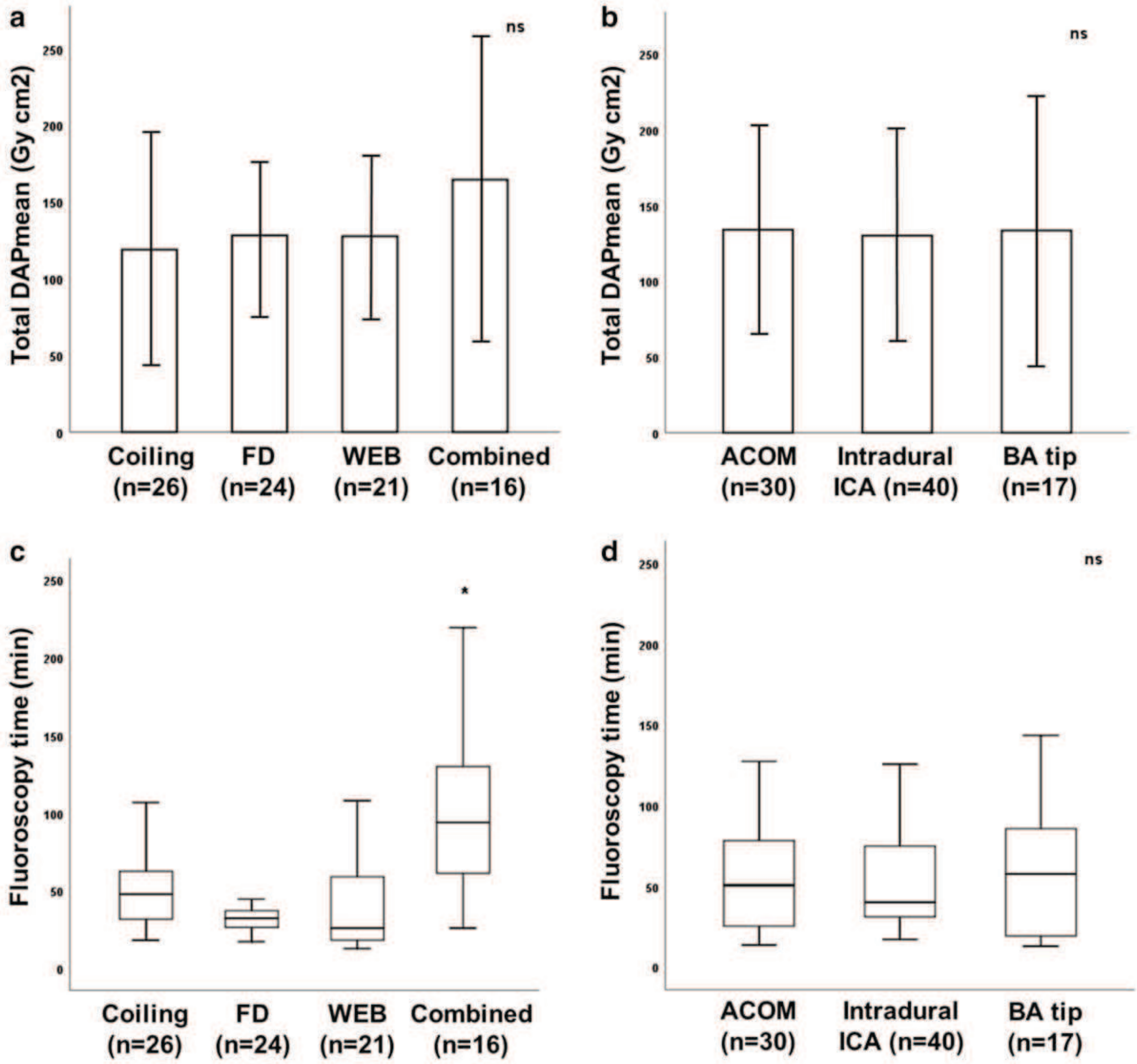

Fig. 2 Total DAP and fluoroscopy time with regard to different endovascular techniques and aneurysm locations. Values are shown as mean ± standard deviation and median (25%; 75% percentile). Difference of mean total DAP did reach statistical significance when comparing neither the endovascular technique (**a**) nor the aneurysm location (**b**) ($p > .05$, each). Utilisation of a combined endovascular technique yielded a significant higher median fluoroscopy time in pairwise comparison to the three other groups (asterisk in **c**; $p < .003$, each), whereas median fluoroscopy time was not significantly different when comparing the aneurysm location (**d**; $p > .05$, each). DAP, dose area product; ACOM, anterior communication artery; BA, basilar artery; FD, flow diverter; ICA, internal carotid artery; min, minutes; *n*, number; ns, not significant; WEB, Woven EndoBridge device

significantly differ between groups (LD 27 ± 13 (19–35), ND 28 ± 17 (19–37), MD 25 ± 13 (18–32); $p > .05$, each; Table 2). Mean total DAP (Gy cm^2) was 102 ± 45 (83–121) for the LD group, 144 ± 78 (118–170) for the ND group, and 144 ± 77 (113–176) for the MD group. The mean dose index (Gy cm^2; mean DSA DAP/mean DSA acquisition count) was 4.49 ± 1.76 (3.77–5.22) for the LD, 7.89 ± 2.97 (6.90–8.88) for the ND, and 6.78 ± 3.06 (5.52–8.04) for the MD groups. Values were significantly lower in the LD group when compared with those in the ND and MD groups (mean total DAP: $p = .018$ and .022, respectively; mean dose index: $p < .001$, each), whereas difference of values between the ND and MD groups did not reach statistical significance ($p = .159$). According to the mean dose index, a LD protocol yielded a 43% reduction of DAP per DSA acquisition when compared with a ND protocol. A LD protocol was most commonly applied in patients undergoing coil embolisation ($n = 10/25$, 40%), whereas a ND protocol was preferentially chosen in FD (15/37, 40.5%) and WEB cases (10/37, 27%).

Impact of aneurysm size and patient age on radiation dose and fluoroscopy time

Considering the entire study population ($n = 87$), we found a significantly positive correlation between the aneurysm size and both total DAP ($r = .320$, $p = .003$) and fluoroscopy time ($r = .284$, $p = .008$). Moreover, a significantly positive correlation was found between patient age and total DAP ($r = .214$,

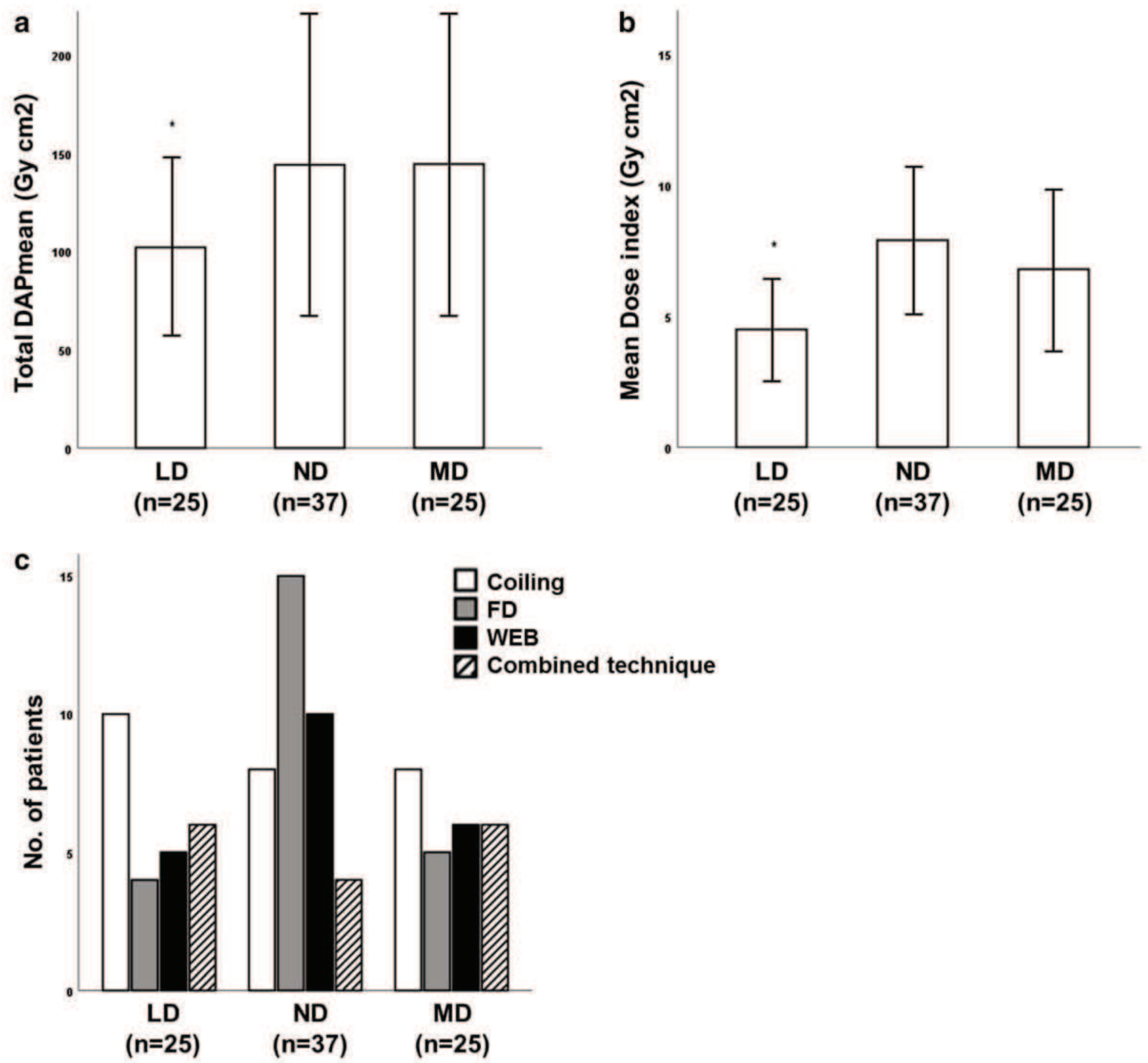

Fig. 3 Total DAP and dose index with regard to different DSA protocols. Values are shown as mean ± standard deviation. Both mean total DAP and dose index were significantly lower in the LD group when compared with those in the ND and MD groups, respectively (asterisk in **a**, $p < .023$, each; and **b**, $p < .001$, each). A LD protocol was preferentially chosen in patients undergoing coil embolisation, whereas a ND protocol was most commonly applied in (**c**) FD and WEB cases. DAP, dose area product; DSA, digital subtraction angiography; LD, low dose; MD, mixed dose; *n*, number; ND, normal dose

$p = .046$), whereas correlation between patient age and fluoroscopy time did not reach statistical significance ($r = .122$, $p = .261$).

Discussion

In the present study, we provide detailed data of radiation dose and fluoroscopy time for modern endovascular treatment techniques in patients with saccular UIAs. With regard to the Euratom Basic Safety Standards (BSS) directive [18], we believe that our observed data may be substantial for the establishment of novel DRLs for modern techniques such as FD and WEB, as the existing national guidelines only provide DRLs for coiling (DAP 250 Gy cm^2) [4]. Moreover, the indication for aneurysm treatment (elective or emergency) is not mentioned in these guidelines. In order to report dosimetric data of a standardised elective UIA treatment, data collection comprised the following angiographic algorithm: (1) catheterisation of the target vessel only, (2) initial biplane DSA run on standard anteroposterior and lateral projections, (3) 3D rotational angiography, (4) aneurysm treatment using the working projection and peri-procedural biplane control DSA runs, and (5) final biplane DSA run. We explicitly excluded patients with ruptured and/or symptomatic aneurysms, as an additional diagnostic cerebral four-vessel angiography during the same intervention is usually required in these cases (to detect/rule out further aneurysms), itself yielding a distinct amount of DAP [12–14, 19] and thus escalation of overall radiation dose. For example, Acton and colleagues [19] reported a median DAP of 74 Gy cm^2 for a cerebral four-vessel angiogram. According to the Federal Office of Radiation Protection [4], we thus intended to report dosimetric data of the aneurysm treatment only.

According to the ICRP 135 publication [17], application of several radiation dose metrics (e.g. DAP and fluoroscopy time) is recommended for DRL establishment of fluoroscopically guided interventions. In this context, the DRL value is defined as the 75th percentile of the distribution of the DRL quantity [17], representing a commonly calculated radiation dose metric in neurointerventional procedures [11–15, 19–22]. In the present study, we observed a total mean and median DAP of 130 ± 65 (116–144) Gy cm^2 and 116 (78; 165) Gy cm^2, respectively. In detail, the calculated 75th percentile was 130 Gy cm^2 for coiling, 176 Gy cm^2 for each FD and WEB, and 209 Gy cm^2 for combined techniques. The measured difference in radiation dose between the treatment groups clearly reflects the grade of aneurysm complexity, with a comparably lower DAP in simple coiling and a higher DAP in aneurysms treated by combined techniques; however, this difference did not reach statistical significance. To note, as the data pool was homogenised in order to reduce inter-individual dosimetric variations as described above, we indeed noted normally distributed DAP values, additionally enabling reliable report of the statistical mean considering the different endovascular techniques, aneurysm locations, and applied DSA protocols.

With regard to the literature, the median DAP for coiling was within the range of previously published data by other authors, e.g. Hassan et al 78.7 (59.5; 111.9) Gy cm^2 [11] and Acton et al 100 (74; 123) Gy cm^2 [19]. Furthermore, the slightly higher DAP values (when compared with coiling) in patients treated by FD, WEB, or a combined technique were still clearly below the values provided by recent dosimetric studies dealing with aneurysm embolisation [14, 20, 23, 24]. Moreover, as illustrated by other authors [13, 19, 20, 22], radiation dose metrics of fluoroscopically guided procedures are influenced by several confounders particularly in the field of interventional neuroradiology (e.g. complexity of procedures, tube settings and position, implementation of radiation reduction technologies, and experience of the medical staff); thus, DRLs should be defined locally for each centre.

Considering the aneurysm location, neither the DAP nor fluoroscopy time was significantly different when comparing the three most common anatomic sites treated in our institution (ACOM, intradural ICA, BA tip). We therefore assume that neither radiation dose nor fluoroscopy time is necessarily dependent on the aneurysm location as reported by Acton and colleagues [19], but rather on (1) the aneurysm size (as suggested by D'Ercole et al [13]) which itself more properly defines the choice of the dedicated endovascular technique and thus complexity of treatment, and (2) the anatomic approach which is often more sophisticated in elderly patients due to a commonly increased vessel tortuosity. In this context, we indeed found a significantly positive correlation between DAP and both aneurysm size ($r = .320$, $p = .003$) and patient age ($r = .214$, $p = .046$).

We observed a median fluoroscopy time of 49 min for coiling, 34 min for FD stenting, and 26 min for implantation of a WEB. These values are clearly in the range of published data on endovascular aneurysm embolisation [11–13]. In contrast, application of combined techniques in more complex aneurysms yielded a significantly higher fluoroscopy time (median 94 min) when compared with the solitary techniques, with the largest gap in comparison with WEB cases ($p < .001$).

With regard to the DSA acquisition mode, application of a LD protocol yielded a significantly lower DAP when compared with a ND protocol (mean DAP 102 versus 144 Gy cm^2, $p = .018$). The impact of a LD protocol on radiation dose reduction was more objectively illustrated by calculating the dose index, which reflects the DAP per single DSA acquisition (mean dose index LD 4.49 Gy cm^2 versus ND 7.89 Gy cm^2, DAP reduction 43%; $p < .001$). A LD protocol was most commonly applied in aneurysms treated by coiling. Contrarily, a ND protocol was preferentially chosen in FD and WEB cases. This distribution in turn explains the slightly increased radiation dose in the FD and WEB groups when compared with the coiling group as illustrated above. However, the provided DRLs are still clearly below the official local DRL for coil embolisation [4]. Even though the choice of both the dedicated endovascular technique and DSA acquisition protocol is at the discretion of the interventional neuroradiologist, we believe that the following DSA protocol algorithm can be derived from our data, probably yielding—in addition to other techniques such as image noise reduction [22, 25]—further radiation dose optimisation in the field of endovascular UIA treatment:

1. The standard initial and final DSA runs of the relevant vascular territory (FOV 32 cm) should preferentially be conducted in LD mode, as this protocol is both appropriate for aneurysm visualisation and robust enough to detect/rule out catheter-associated complications such as thromboembolism, vasospasm, and arterial dissection.
2. Regarding peri-procedural targeted DSA runs in working projections (FOV 11–16 cm), application of a LD protocol is particularly useful in endovascular aneurysm treatment using materials with a high X-ray opacity (e.g. platinum coils). Contrarily, a ND protocol is reasonable when applying materials with a comparably lower fluoroscopic visibility (e.g. nitinol FD or WEB), allowing for a more detailed visualisation of the implanted device with respect to the aneurysmal sac and parent vessel.

As data reported in this study were retrospectively collected from only one neurovascular centre, our results have to be evaluated in light of several study limitations. First, neurointerventions were performed by usage of only one specific angiographic system from a single vendor (Siemens Healthineers). Second, the following parameters were not documented: peri-procedural change of strategy, size of the aneurysm neck, type of aortic arch. Third, several aneurysm locations were excluded due to procedural in-house management in our neurovascular centre (e.g. aneurysms of the middle cerebral artery are primarily treated by open neurosurgery) and/or rare occurrence (e.g. superior cerebellar artery, posterior cerebral artery); thus, dosimetric data observed in the present study cannot be generalised for all endovascular procedures. However, we believe that our selected study population may serve as a representative cohort of patients harbouring saccular UIAs at common anatomic sites accessible for endovascular treatment, as comparable data—particularly with regard to FD and WEB—are missing.

In conclusion, the present study introduces novel DRLs in the field of modern endovascular treatment of UIAs, including FD and WEB. Radiation dose was not significantly different between the endovascular procedures. However, radiation dose was comparably low in simple coiling and higher when using combined techniques, which are particularly applied in patients characterised by complex aneurysms. Aneurysm location did significantly alter neither radiation dose nor fluoroscopy time, whereas both aneurysm size and patient age were associated with radiation dose. Fluoroscopy time was the lowest for WEB and highest for combined techniques. A low-dose DSA protocol yielded a significant reduction of radiation dose and is particularly useful when applying high-opacity materials (e.g. platinum coils). With regard to the next Euratom version, we recommend a prospective collection of dosimetric data derived from multiple centres for definition of DRLs, considering different manufacturers and dose reduction techniques.

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Compliance with ethical standards

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Methodology
• Retrospective
• Observational
• Performed at one institution

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INTERVENTIONAL NEURORADIOLOGY

Endovascular treatment of basilar tip aneurysms in the era of endosaccular flow disruption: a comparative study

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Abstract

Purpose This study aims to compare endosaccular flow disruptor (EFD) for treatment of basilar tip aneurysm (BTA) with coiling in terms of safety and efficacy.

Methods We retrospectively reviewed patients treated with an EFD for BTAs at our institution between 2013 and 2019 to standard coiling from the same period (control group). Patient demographics, aneurysm characteristics, procedural data, complications and clinical and angiographic outcome were compared between groups.

Results Twenty-three (56%) patients were treated with an EFD and eighteen (44%) patients were treated with coiling. Average aneurysm size was 8 mm in the EFD group and 6.9 mm in the coiling group, respectively ($P = 0.2$). Average fluoroscopy time, treatment DAP and air kerma were 33 min, 76 Gycm^2 and 1.7 Gy in the EFD group and 81 min, 152 Gycm^2 and 3.8 Gy in the coiling group, respectively ($P < 0.001$). In the EFD group, clinically relevant thromboembolic complications occurred in one patient (4%) vs. in 5 patients (28%) in the coiling group ($P = 0.07$). In each group, 4 patients had an unfavourable outcome at discharge ($P = 0.7$). Adequate occlusion rates were 96% in the EFD group and 100% and coiling group. Six (26%) patients were prescribed long-term antiplatelet therapy in the EFD group vs. eleven (61%) patients in the coiling group ($P = 0.02$).

Conclusion Both treatment concepts provided similar technical success and safety. However, procedure time, radiation exposure and a need for long-term antiaggregation were lower with EFD.

Keywords Aneurysm · Endovascular · Endosaccular · Web · Coils

Introduction

Endovascular occlusion is the treatment of choice for basilar tip aneurysm (BTA). However, the anatomy of the basilar apex and the often broad-based configuration of BTAs may make treatment challenging.

A variety of different techniques has been developed to enable safe and successful endovascular treatment of bifurcation aneurysms including balloon and stent assistance in various configurations and recently developed neck-bridging devices [1, 2]. However, all these techniques require several steps, making the procedure complex and prone to device- and procedure-related complications.

The Woven EndoBridge (WEB; Microvention/Terumo, Aliso Viejo, CA, USA) is deployed completely endosaccular in order to reduce the inflow into the aneurysm at the level of the neck, thus leading to thrombus formation and potentially shrinkage of the aneurysm sac. The technical success and safety of WEB was supported by several studies resulting in widespread use for both ruptured and unruptured aneurysms [3–7].

Recently, the Contour device (Cerus Endovascular, Fremont, CA, USA) was introduced; similar to WEB, it is designed to disrupt the inflow into the aneurysm sac at the level of the neck of the aneurysm. The device is composed of nitinol wires forming a dual-layer mesh and has a flat, disc-like configuration when unconstrained. Once optimally deployed at the aneurysm neck, it adopts a conical shape, covering the lower part of the aneurysm and the neck [8, 9].

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Several studies compared different techniques for the treatment of intracranial aneurysms [10, 11]. However, to the best of our knowledge no studies are available comparing the safety and efficacy of different endovascular techniques specifically in BTAs.

In the current study, we compared endosaccular flow disruption to conventional methods for treatment of BTAs in terms of safety and efficacy.

Material and methods

We retrospectively reviewed consecutive patients who underwent endovascular treatment for saccular BTA at our institution between January 2013 and December 2019. Local ethics committee approved this study and requirement of patient consent was waived because of the retrospective nature of the study.

The inclusion criteria were defined as (1) successful endovascular treatment of a BTA using an endosaccular flow disruptor and (2) successful endovascular treatment of a BTA by stand-alone coiling, balloon-assisted coiling (BAC) or stent-assisted coiling (SAC).

Cases fulfilling the first inclusion criterion formed the “endosaccular flow disruptor (EFD) group” and the rest formed the “coiling group”.

Exclusion criteria were (1) recurring aneurysms and (2) aneurysms treated with an endosaccular flow disruptor using stent assistance.

Procedure

The technique chosen for aneurysm occlusion was left to the discretion of the neurointerventionalist. Generally, stand-alone coiling or WEB was used as standard approach. In wide-necked aneurysms, anatomical features requiring stent or balloon assistance or the Contour were as follows: irregular shape, daughter sacs, low aspect ratio (≤ 1.3) or very small or large aneurysm size (i.e. not covered by the available sizes of WEB). Configuration and size of the posterior cerebral arteries was also a factor when choosing between BAC and SAC or EFD.

All procedures were performed on a biplane angiosuite (Siemens, Erlangen, Germany) under general anaesthesia. A bolus of intravenous heparin (5000 IU) was administered after groin puncture, followed by smaller doses to maintain an activated clotting time (ACT) of 2 to 3 times of the baseline. After navigating a guiding catheter into the larger vertebral artery, the aneurysm was catheterized with a dedicated microcatheter over a 0.014-in. microguidewire.

EFD group

Endosaccular flow disruptors that have been used were WEB single layer (SL), WEB single-layer sphere (SLS) and the Contour device.

WEB was delivered through a VIA microcatheter (Microvention/Terumo, Aliso Viejo, CA, USA). The appropriate WEB size was selected to slightly exceed the aneurysm width as recommended by the manufacturer. Contour was delivered through a Headway 27 microcatheter (Microvention/Terumo, Aliso Viejo, CA, USA).

Coiling group

Coiling was performed through a 0.017-in. SL-10 microcatheter (Stryker, Kalamazoo, MI, USA). In all BAC procedures, Sceptre balloons (Microvention/Terumo, Aliso Viejo, CA, USA) were used.

For SAC, single-stenting or Y- and T-stenting techniques were used. Stent types implanted were Solitaire AB (Covidien, Irvine, CA, USA), Neuroform EZ and Atlas (Stryker, Kalamazoo, MI, USA), LEO Baby (Balt, Montmorency, France) or LVIS Jr. (Microvention/Terumo, Aliso Viejo, CA, USA).

In one case, the eCLIPs (Endovascular Clip System; Evasc Medical Systems Corp., Vancouver, BC, Canada) device was used to reconstruct the neck.

Antiaggregation therapy

Unruptured aneurysms

Patients scheduled for elective treatment with an EFD or a stent were premedicated with acetylsalicylic acid (ASA) 100 mg and clopidogrel 75 mg daily, started 5 to 7 days before treatment. In cases treated with EFD, ASA monotherapy was continued for a minimum of 4 weeks. If a stent was used, a dual antiplatelet regimen (ASA 100 mg and clopidogrel 75 mg daily) was required for 4–6 months after the procedure, followed by life-long ASA 100 mg/day.

In cases treated with stand-alone or balloon-assisted coiling, depending on the size of the neck and the protrusion of coil mass into the parent artery, ASA monotherapy was continued for a minimum of 3 months.

Ruptured aneurysms

In patients with ruptured aneurysms treated with SAC, tirofiban (Aggrastat; Merck, New York, USA) was administered during the procedure and usually continued for 12 h after the procedure, followed by a loading dose of ASA (500 mg) and clopidogrel (300 mg). Antiplatelet therapy was continued as described above for unruptured aneurysms.

In EFD or stand-alone coiling cases with wide neck and device protrusion into the parent vessel, short-term monotherapy with ASA was considered after securing the rupture point.

If acute thrombosis occurred during the procedure, intravenous tirofiban was started irrespective of the rupture status, usually continued for 12 h after the procedure and followed by a double antiplatelet therapy as described above.

Antiplatelet therapy ending within the first 6 months after the procedure is considered short term and therapy continuing more than 6 months is considered long-term therapy.

Drug response was tested in all patients (Multiplate® Analyser; Roche, Basel, Switzerland). An insufficient response to either drug was managed either by dose escalation or substitution with an agent such as prasugrel.

Data collection

Patient demographics, aneurysm characteristics, procedural data, procedure-related complications and clinical and angiographic outcome at follow-up were retrospectively obtained from the medical charts. Procedural radiation exposure was measured as fluoroscopy time, air kerma (Gy) and dose area product (DAP, Gycm^2). The Fisher scale (1: no subarachnoid (SAH) or intraventricular haemorrhage (IVH); 2: diffuse thin SAH without IVH; 3: thick SAH without IVH; 4: IVH or intracerebral haemorrhage with or without SAH) was used to evaluate the extent of SAH on CT and the WFNS (World Federation of Neurosurgical Societies) grading system (1: GCS (Glasgow Coma Scale) 15 without deficit; 2: GCS 13–14 without deficit; 3: GCS 13–14 with focal neurological deficit; 4: GCS 7–12 with or without deficit; 5: GCS < 7 with or without deficit) was used to evaluate the clinical status. Wide neck was defined either as a neck >4 mm or an aspect ratio < 1.6. Clinical outcome was evaluated by the modified Rankin Scale (mRS) before treatment and at discharge. Unfavourable outcome was defined as mRS > 2.

Angiographic control and retreatment

Our follow-up protocol consists of angiographic controls at 6 and 24 months after the procedure using DSA (digital subtraction angiography) in the majority of cases and magnetic resonance angiography (MRA) or computed tomography angiography (CTA) in other cases. The Raymond-Roy occlusion classification was used to assess aneurysm occlusion at follow-up (grade I: complete occlusion; grade II: neck remnant; grade III: aneurysm remnant). Complete occlusion and neck remnants were defined as adequate occlusion.

Statistical analysis

Continuous variables were presented as means, percentages and ranges. They were tested for normality using the Shapiro-Wilk test and compared between the EFD group and coiling group using the 2-sided unpaired Student *t* test (for normally distributed data) and the Mann-Whitney *U* test (for non-normally distributed data).

Categorical variables were expressed as names or numbers with percentages and compared between the groups using the χ^2 and the Fisher exact test, when appropriate.

Univariate logistic regression analysis was performed to test the predictive power of treatment type on short- and long-term antiplatelet use and angiographic and clinical outcome. A linear regression analysis was made to analyse the relationship between aneurysm size, height, neck width or aspect ratio and the amount of fluoroscopy time or radiation exposure. All calculations were performed using SPSS software Version 25.0 (IBM, Armonk, New York, USA). A *P* value <0.05 was considered statistically significant.

Results

Patient and aneurysm characteristics

Forty-one patients who underwent endovascular treatment for a saccular BTA between 2013 and 2019 were included. Twenty-three (56%) patients were treated with an EFD and eighteen (44%) patients were treated with other techniques. The characteristics of patients and aneurysms from each group are shown in Table 1. All SAHs were grade 4 according to the Fisher scale. The median WFNS score of SAH patients was 4.

Aneurysm treatment and procedural radiation exposure

All but two cases were performed via transfemoral approach. In two cases (one in each group), transbrachial approach was selected because of chronic bilateral iliac artery occlusions. Endovascular treatment techniques are presented in Table 2.

In three SAH patients (17%) from the coiling group, endovascular treatment of an aneurysm at another location (two anterior communicating artery and one superior cerebellar artery (SCA) aneurysms) was necessary during the same session as the BTA. All of them were treated with coils. In one SAH patient, BTA and the additional SCA aneurysm were covered with the same stent and occluded with coils.

Procedural radiation doses and procedure times are reported in Table 1. In the coiling group, after exclusion of the patients with other aneurysms treated during the same session, the average fluoroscopy time, DAP and air kerma dropped to 76 min, 145 Gycm^2 and 3.7 Gy, respectively, maintaining the significant difference from the EFD group.

According to linear regression analysis, there was no significant relationship between aneurysm size, height, neck width or aspect ratio and the amount of fluoroscopy time or radiation exposure.

Table 1 Characteristics of patients, aneurysms and procedures and list of complications and follow-up

	EFD (*n* = 23)	Coiling (*n* = 18)	*P* values
Mean age (range)	61 (35–81)	58 (40–76)	0.5
Male sex	8 (35%)	6 (33%)	0.9
Ruptured aneurysms	4 (17%)	9 (50%)	0.02
Mean size in mm (range)	8 (3.1–16)	6.9 (3.1–12)	0.2
Mean neck size in mm (range)	4.4 (2.3–6.8)	3.9 (2.1–6.7)	0.1
Wide-necked aneurysms	20 (87%)	12 (67%)	0.1
Mean aspect ratio (range)	1.4 (0.9–2.8)	1.5 (0.7–2.8)	0.7
Mean fluoroscopy time in min (range)	33 (8–108)	81 (30–143)	< 0.001
Mean dose area product in $Gycm^2$ (range)	76 (11–199)	152 (58–298)	< 0.001
Mean air kerma in Gy (range)	1.7 (0.3–5)	3.8 (1.5–7.8)	< 0.001
Thromboembolic complications	5 (21%)	6 (33%)	0.5
Clinically relevant thromboembolic complications	1 (4%)	3 (17%)	0.3
Unfavourable clinical outcome	4 (17%)	4 (22%)	0.7
Adequate aneurysm occlusion	22 (96%)	18 (100%)	1
Retreatment	1 (4%)	0 (0%)	1
Short-term antiplatelet medication	16 (70%)	12 (67%)	0.8
Long-term antiplatelet medication	6 (26%)	11 (61%)	0.02

Complications

In the EFD group, adverse events occurred in five WEB patients (21%). All of them were thromboembolic events and happened in elective cases. However, only one of the patients had a transient neurologic deficit and the MR Imaging showed multiple embolic lesions in multiple vascular territories. Others were clinically silent.

In the coiling group, complications occurred in seven patients (39%). Six (33%) of them were thromboembolic events (5 in SAH patients). In only 3 (17%) patients thromboembolic complications were clinically relevant. One of them presented itself 4 months after the intervention after cessation of clopidogrel. All others occurred were periprocedural. In one elective case, a LEO Baby 3/25 stent was positioned at the level of the aneurysm neck initially but dislocated during deployment. It was then safely placed in the distal cervical segment of the vertebral artery. The aneurysm was subsequently coiled with stent assistance using two LVIS Jr. stents in T-configuration. The patient showed no postoperative neurological deficit.

There was no statistical significance between two groups regarding the thromboembolic complication rates ($P = 0.5$).

Including only clinically relevant thromboembolic complications, the rates dropped down to 4% (1/23) and 17% (3/18) in the EFD group and coiling group, respectively. The difference was still not statistically significant ($P = 0.3$).

No haemorrhagic event was recorded.

Clinical outcome

In each group, 4 patients (17% in the EFD group and 22% in the coiling group) had an unfavourable outcome at discharge ($P = 0.7$). From the four patients, two had SAH in the EFD group and all had SAH in the coiling group.

In the EFD group, two of the SAH patients (9%) died; one due to multiple cerebral infarctions because of intractable cerebral vasospasm and the other one due to multi-organ failure. Remaining cases with unfavourable outcome had already high mRS scores because of pre-existing comorbidities.

In the coiling group, one patient (5%) presented with SAH and treated with SAC died because of haemorrhagic transformation of a large posterior cerebral artery infarction due to stent occlusion. Other patients had unfavourable scores because of SAH-related incidences.

Table 2 Endovascular treatment techniques

Treatment group	Treatment method	Number of patients
EFD	WEB	18 (78%)
	Contour	4 (17%)
	WEB + coils	1 (5%)
Coiling	Coiling	7 (39%)
	BAC	4 (22%)
	SAC	6 (33%)
	Neck-bridging device	1 (6%)

Angiographic outcome

Median follow-up was 8 months (min 1, max 60). Eight patients (5 in the EFD group and 3 in the coiling group) were lost to follow-up. Sixteen patients had no DSA, but MR or CT angiography at follow-up. In the EFD group, adequate occlusion rate was 96% (19 complete occlusions, 3 neck remnants and 1 aneurysm remnant). Only one patient (4%) who was initially treated with a WEB device showed recurrence after 11 months and was retreated with BAC. In the coiling group, adequate occlusion was obtained in 100% of the patients (16 complete occlusions and 2 neck remnants). Adequate occlusion rates were not significantly different between the two groups ($P = 1$).

According to univariate logistic regression analysis, treatment type was not predictive of angiographic and clinical outcome.

Antiplatelet medication

Antiaggregation status of patients at baseline, < 6 months and > 6 months after the procedure is presented in Table 3. In short term, 16 (70%) patients in the EFD group took single or double antiplatelets vs. 12 (67%) patients in the coiling group ($P = 0.8$). Six (26%) patients were prescribed long-term antiplatelet therapy in the EFD group vs. eleven (61%) patients in the coiling group ($P = 0.02$). Two patients in the EFD group took double antiplatelet medication for 6 months after the procedure (9%) vs. eight (44%) patients in the coiling group ($P = 0.01$). However, treatment type was not a predictor of short- or long-term antiplatelet therapy.

Discussion

In the current study, we compared endosaccular flow disruption with conventional methods (stand-alone coiling, BAC and SAC) for treatment of BTAs in terms of safety and efficacy. We did not find a significant difference between the treatment groups regarding the thromboembolic complication rate, as well as the clinical and final angiographic outcome. However, procedural fluoroscopy time and radiation exposure were significantly lower in patients who were treated with endosaccular flow disruptor devices. In addition, they were significantly less likely to have an indication to take antiplatelets in long term.

BTAs are special among cerebral aneurysms in several respects: surgical treatment is usually not an option, but due to the often broad-necked configuration (up to 60% according to Lozier et al.), pure coiling is also in many cases not possible [12–16].

Rates of recurrence after stand-alone coiling have been reported to be as high as 25 to 30% in large and wide-necked aneurysms [17, 18]. While additional devices such as balloons, self-expanding stents or neck-bridging devices may improve the coil packing density and thereby the efficacy of endovascular coil embolization on one hand, they increase the complexity of the procedure on the other hand, which in turn may increase the risk for complications [19–21]. Furthermore, antiplatelet medication is mandatory for all patients after any stent treatment, which may complicate subsequent surgical procedures, especially for patients after SAH [21, 22].

The WEB and Contour devices represent a completely different concept: different from stents and intraluminal flow diverter stents, these dense-meshed devices are placed completely in the aneurysm sac and aim to disrupt the blood flow entering and exiting the sac at the level of the neck in order to promote stagnation and thrombus formation. The WEB device proved efficacy and safety in multiple prospective and retrospective multi-centred studies, especially in the treatment of ruptured and wide-necked aneurysms [3–7].

Currently, there are two studies that compare stand-alone coiling and WEB treatment, as well as SAC and WEB [10, 11]. Kabbasch et al. included aneurysms at all anatomical locations in the evaluation. They reported a significantly higher complication rate in the SAC group (14/66 aneurysms, 21%) compared with the WEB group (8/66 aneurysms, 12%). The complete occlusion rate was higher in aneurysms treated with the WEB device (41/47, 87%) compared with aneurysms treated by coiling (31/51, 61%) and similar to those treated by SAC (55/66, 84% vs. 56/66, 85%). Retreatment rates were significantly higher in the coiling group (9/51, 18% vs. 2/47, 4%) and similar between the WEB (7/66, 11%) and the SAC (8/66, 12%) group.

Table 3 Antiplatelet regimen at baseline, < 6 months and > 6 months after the procedure

Number of antiplatelets	EFD group			Coiling group		
		Treatment duration			Treatment duration	
	Baseline	< 6 months	> 6 months	Baseline	< 6 months	> 6 months
0	19 (83%)	7 (30%)	17 (74%)	18 (100%)	6 (33%)	7 (39%)
1	4 (17%)	14 (61%)	6 (26%)	0 (0%)	4 (22%)	10 (55%)
2	0 (0%)	2 (9%)	0 (0%)	0 (0%)	8 (45%)	1 (6%)

Other potential advantages of the EFDs, such as potential reduction of procedural fluoroscopy time and radiation dose have, however, not been addressed yet.

Complications

The rate of clinically relevant thromboembolic events was higher in the coiling group (17%) than in the EFD group (4%), however without statistical significance ($P = 0.3$). The thromboembolic complication rate in the EFD group was in compliance with the literature [3–7].

The coiling group showed a higher rate than previously reported. In large coiling series including only BTAs, thromboembolic complication rates varied from 6 to 12% [12–14, 16, 17]. Explanations might be small size of our study group and significantly higher numbers of ruptured cases in the coiling group.

Radiation exposure

Radiation exposure in endovascular aneurysm therapy has so far received little attention. Differences in individual aneurysm geometry and vessel anatomy, as well as in experience levels and treatment preferences of neurointerventionalists, make a comparison of radiation exposure and a definition of acceptable thresholds difficult.

Direct measurement of the absolute entrance skin doses is not practicable and therefore surrogate markers such as DAP (Gycm^2) and air kerma (Gy) are usually used [23–27].

The threshold for deterministic skin damage such as erythema or hair loss is considered to be at 2 to 3 Gy [27, 28]. Struelens et al. proposed a DAP trigger level of 220–330 Gycm^2 as a threshold for skin effects in cerebral embolization procedures [26].

In a study of Peterson et al. [23] including 702 neurointerventional procedures, skin entrance doses exceeding 2 Gy occurred in 73% of procedures. After almost 40% of them, patients reported changes of their skin or hair and 30% of the changes were permanent. Increasing skin dose was significantly associated with permanent hair loss.

Ihn et al. evaluated 371 aneurysm treatments nationwide in 2015 [25]. Total mean DAP, air kerma and fluoroscopy time were 219 Gycm^2, 3.3 Gy and 51 min, respectively. The reported radiation exposure exceeded the cited threshold values but the patients were not specifically followed up for radiation-induced skin or hair changes.

Data regarding the radiation exposure in treatment of intracranial aneurysms with the WEB device is available from a prospective multi-centre study including 150 aneurysms. Arthur et al. reported an average procedural fluoroscopy time of 30 min and an average air kerma of 2.7 Gy [7]. Our findings in the EFD group (33 min, 76 Gycm^2, 1.7 Gy) were comparable with those figures. Both the procedural time and the radiation dose were higher in the coiling group (81 min, 152 Gycm^2, 3.8 Gy); however, these numbers are still in compliance with the literature [24, 25].

Technical simplicity is certainly the major reason for faster procedure times and low radiation exposure in treatments with EFD. SAC, for example, requires multiple steps including catheterization of the distal parent vessel, stent deployment, catheterization of the aneurysm sac and filling it with multiple coils. Usually several control injections are needed. In EFDs, in particular for WEB, exact measurements and device selection prior to the procedure are necessary, but the procedure itself after catheterization consists only of device deployment.

Angiographic outcome

In our study group, both treatment groups had similar rates of adequate occlusion (22/23, 96% in the EFD group vs. 18/18, 100% in the coiling group). Retreatment was necessary only in one patient after WEB and in none of the aneurysms treated with other techniques.

In general, complete occlusion seems to be less frequently achieved in BTAs and retreatment is more often necessary when compared with other aneurysm localizations [14, 17, 29, 30]. In a systematic review including 226 coiled BTAs, Lozier et al. [16] reported an initial complete or near-complete aneurysm occlusion in 88% of the patients; however, the recanalization rate was 26% with a 0.7% annual risk for recurrent haemorrhage. In another study by Henkes et al. [12] including coil embolization of 316 BTAs, recurrence, retreatment and recurrent haemorrhage rates were found to be as high as 35%, 15% and 5%, respectively. After the initial embolization procedure, a 90 to 100% occlusion rate was achieved in 86% of the aneurysms.

In the cumulative population of three prospective WEB studies, Pierot et al. observed an adequate occlusion rate of 81% and retreatment rate of 9% at 2-year follow-up [4]. Just as in our study, Kabbasch et al. found equal adequate occlusion rates between WEB and SAC (94%) in their series including 66 wide-necked bifurcation aneurysms from each group [11].

Antiplatelet medication

So far, there has been no standard regarding the use of antiplatelet medication after endovascular aneurysm treatment. This applies to stand-alone coiling, as well as to SAC and EFD. The peri- and postprocedural antiplatelet regimen is usually left to the neurointerventionalists' discretion. In cases treated without stent assistance, usually a short-term single or double antiplatelet therapy is given, especially in wide-necked aneurysms or when the parent artery or incorporated vessels are compromised by the implant. In patients treated by stent-assisted coiling, a short-term double antiplatelet therapy is required.

In the multi-centred prospective WEB studies, antiplatelet therapy was not mandatory. However, the majority of the patients received double antiplatelet medication prior and during the procedure (69% in the WEB-IT study and 45% in the WEBCAST and French Observatory group) [4, 7].

In the WEB-IT study, 74% of patients had short-term antiplatelet therapy in keeping with our results (70%) from the EFD group. In the coiling group, the overall rate was similar (67%), but the percentage of patients using double antiplatelets was higher (67% in the coiling vs. 12% in the EFD group) [7].

In long term, patients in the coiling group (61%) were significantly more often prescribed antiplatelets than in the EFD group (26%). As a comparison, that rate was 48% in the WEB-IT study group [7]. Unfortunately, we could not find any comparable study reporting antiaggregation use in coiled aneurysms.

Limitations

Major drawbacks of this study are mainly its retrospective, single-centred and non-randomized nature and the relatively small number of included cases. The method chosen to occlude the aneurysms was based on the discretion of the neurointerventionalist and various factors such as the surgeon's experience, rupture status or patients' comorbidities may have influenced these decisions. Thus, we cannot exclude a potential selection bias, because some of the aneurysm in the coiling group may have had an unfavourable configuration for EFD. Furthermore, heterogeneity of the occlusion techniques used (stand-alone, balloon- or stent-assisted coiling) and larger proportion of ruptured aneurysms among the coiling group might confound a meaningful comparison between two main treatment strategies.

Only one patient was included who was treated with a dedicated bifurcation stent (eCLIPs) and our data thus does not allow any conclusion about treatment with these devices.

Conclusion

Our data provides the first comparative analysis of endosaccular flow disruption with other treatment methods for endovascular management of basilar tip aneurysms.

Both treatment concepts provided similar technical success and safety. However, procedural time, radiation exposure and the indication for long-term antiaggregation were significantly in favour of EFD. It may thus be argued, that with both strategies deemed suitable, EFD should be preferred.

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Compliance with ethical standards

Conflict of interest TL consults and proctors for Microvention (previously Sequent), CERUS medical, Stryker, and phenox, and has received service related fees by Medtronic, Pfizer, and Acandis in the past. FD is a consultant for Balt, phenox and received speaker honorary by Acandis und Cerenovus. Other authors declare that they have no competing interests.

Ethical approval All procedures performed in the studies involving human participants were in accordance with the ethical standards of the Ethics Committee of Ludwig Maximilian University (Date:07.03.2019/ No.:19-092) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Requirement of patient consent was waived because of the retrospective nature of the study.

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