A COMPARATIVE STUDY OF DETACHABLE TIP MICROCATHETERS VERSUS CONVENTIONAL MICROCATHETERS IN LIQUID EMBOLIZATION OF BRAIN AVMS.

THESIS

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CERTIFICATE

This is to certify that the work incorporated in this thesis titled

"A Comparative Study of Detachable Tip Microcatheters Versus Conventional Microcatheters In Liquid Embolization of Brain AVMs"'

for the degree of

DM NEUROIMAGING AND INTERVENTIONAL NEURORADIOLOGY

has been carried out by ***Dr. Chinmay P. Nagesh*** *under my supervision and guidance. The work done in connection with this thesis has been carried out by the candidate himself and is genuine.*

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DECLARATION

I hereby declare that this thesis titled **"A Comparative Study of Detachable Tip Microcatheters Versus Conventional Microcatheters In Liquid Embolization of Brain AVMs"** has been prepared by me under the supervision and guidance of Dr. Santhosh Kumar Kannath (Associate Professor), Dr Jayadevan ER (Associate Professor), and Dr. TR Kapilamoorthy (Professor & Head), Department of Imaging Sciences and Interventional Radiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram.

Date: 5/10/2017 Dr Chinmay P. Nagesh

Place: Thiruvananthapuram

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CONTENTS

INTRODUCTION

INTRODUCTION

Arteriovenous malformations of the brain (bAVMs) are characterized by a direct communication between arterial feeders and draining veins via a network of abnormal vascular channels that lack a normal intervening capillary network[1]. Although rare, their tendency to bleed may result in significant long-term morbidity and mortality underscoring the need for careful consideration of lesion characterization and appropriate tailored management of these lesions.

When indicated, treatment may be multimodal with the availability of endovascular, microsurgical and radiotherapeutic techniques used alone or in combination. The primary aim of treatment is to reduce the risk of hemorrhage associated with these lesions. Treatment strategies are variable between different centres and balance the risk of treatment with the potential benefit to the patient. Endovascular embolization of AVMs has predominantly been used as an adjunctive treatment with the goal of devascularizing the nidus prior to definitive treatment in the form of surgery or radiotherapy. However, embolization with a curative intent has been made recently possible in a subset of lesions with advances in embolization agents and delivery hardware.

Ethyl vinyl alcohol (EVOH) based embolic agents are a more recent development whose physical characteristics make it more optimal than cyanoacrylate glues for the embolization of brain AVMs. However, their use entails a number of precautions and specialized hardware such as compatible microcatheters. The risk of catheter entrapment and resultant rupture during retrieval has spurred the development of microcatheters

with detachable tips. These microcatheters offer a theoretical advantage of reduced risk of catheter entrapment allowing for more prolonged injection of the embolic agent. However, there is a relative paucity of literature that examines whether this translates into better outcomes. The aim of this study is to therefore compare the efficacy of embolization using the older conventional microcatheters with the newer detachable tip microcatheters.

AIMS

&

OBJECTIVES

AIMS & OBJECTIVES

1. To compare the effectiveness of liquid embolization of brain AVMs using Detachable Tip or Conventional microcatheters in terms of rate of angiographic obliteration of brain AVMs.

2. Assess the safety profile of detachable tip microcatheters in comparison to conventional microcatheters.

REVIEW

OF

LITERATURE

REVIEW OF LITERATURE

Arteriovenous malformations of the brain (BAVMs) are characterized by a congenital direct communication between pial arterial feeders and draining veins via an intervening nidus of abnormal vascular communicating channels that lack a true capillary bed. [2] Despite being relatively rare (incidence varying between 0.001-0.5%[3]), their propensity to rupture makes them the leading cause of young hemorrhagic stroke with significant resultant morbidity and mortality elevating their importance to much above what epidemiology alone justifies [4,5]. Anywhere between 40-72% of BAVMs become clinically apparent after a hemorrhagic event, while the rest may present with seizures, symptoms secondary to mass effect or ischemic steal or just as headaches, typically migraines. With the advent of non-invasive imaging, an increasing proportion are also being discovered incidentally [6].

The importance of risk stratification when considering treatment lies in the fact that brain AVMs have a varied natural history. The overall annual rate of hemorrhage of untreated AVMs is approximately 2.3% [7]. However, a hemorrhagic presentation itself confers a higher risk of re-hemorrhage of 4.5 to as high as 34%, as compared to previously unruptured AVMs which may have a lower risk of 0.9-8%. This is dependent on the presence of risk factors such as a advancing age, a deep location, the presence of any or exclusive deep venous drainage or associated aneurysms[8]. In unruptured AVMs with the lack of clarity on long term natural history, treatment remains varied and controversial[9]. In light of the results of the ARUBA (A Randomized trial of UnRuptured Brain AVMs)[10] and Scottish Intracranial Vascular Malformation Study[11] trials, when this subset of patients are placed on conservative management, the understanding is that the patient remains

exposed to the variable but ever present risk of a hemorrhagic event lifelong[7]. When considered for treatment, this risk must be weighed against the risks and potential benefit of treatment in each patient. The goal of treatment in both ruptured and unruptured AVMs therefore, is to reduce the risk of intracerebral hemorrhage and the attendant morbidity and mortality thereof[9]. Three main modalities exist for the treatment of AVMs: Microsurgical resection, endovascular embolization and stereotactic radiosurgery (SRS). These may be used individually or in combination with the therapeutic goal of complete nidus obliteration since subtotal treatment does not protect against future hemorrhage and may indeed worsen natural history[9].

Endovascular embolization of an AVM was first described by Luessenhop and Spence in 1960 when they reported treating a large left-frontal AVM with 4 methyl methacrylate pellets[12]. Endovascular techniques have since shown rapid evolution with the development of newer embolic agents and better hardware to deliver them. Today, 4 main embolic agents are in use: n-butyl cyanoacrylate(NBCA), and the ethyl vinyl alcohol based agents, Onyx and Squid and the iodine based agent PHIL (Precipitating Hydrophilic Injectable Liquid). Coiling, particulate and balloon embolization play an increasingly less of an adjunctive role[13]. The intent of embolization varies with the presentation and individual architecture of AVMs as well as the experience of the treating team and can be categorized into 5 main indications: 1) preoperative flow reduction; 2) preradiosurgical volume reduction; 3) targeting of specific high risk angioarchitectural features; 4) palliative flow reduction; and 5) complete curative occlusion[14,15].

The most common intent of embolization is primarily adjunctive achieving partial obliteration of the nidus prior to microsurgery or radiotherapy[16]. However, many series have reported complete obliteration using embolization alone, albeit with significant

variation ranging from 5% to 94%, likely due to heterogeneity in the goal of embolization, selection biases and characteristics of AVMs treated [13].

Many factors of the AVM itself influence the curative ability of embolization. A smaller size of the AVM either in terms of maximal diameter (<3cms)[17], or volume (<6ml)[18] supplied by fewer (≤ 3 feeders)[19], larger (atleast twice normal diameters)[20] and superficial origin of terminal feeders (as opposed to en-passage or perforator feeders)[20,21] have a positive correlation with higher cure rates. A superficial[22] non-eloquent[20] location and consequently a lower Spetzler-Martin grade[23] also allow a more aggressive embolization resulting in higher cure rates, as also a previously ruptured status[17]. Single compartment niduses or a predominantly fistulous (as opposed to purely fistulous) angioarchitecture were also associated with higher occlusion rates[24].

The technique and hardware used for embolization also influence outcomes. Liquid embolic agents have in large part contributed to the success of modern endovascular treatments. The cyanoacrylates (commonly called glue), isobutyl cyanoacrylate (IBCA) and n-butyl cyanoacrylate (NBCA) cause occlusion by polymerizing to form a solid cast on exposure to ionic solutions such as blood or saline with secondary inflammatory vasculitic reaction[25]. However, there are several disadvantages to the use of glue agents. Despite ability to modify the rates of polymerization by mixing it in varying proportions with non-ionic liquids such as Lipiodol (Guerbert GmbH, France) the use of NBCA remains often unpredictable, even in experienced hands[26]. Proximal occlusions and inadequate penetrations are more common, requiring a considerable time spent in reaccessing the nidus with multiple cannulations, each time with a new microcatheter in order to achieve a higher rate of complete occlusion, with an increase in the cumulative attendant procedural risks[27,28]. Further, the risks associated with retrieval or retention of unexpected

microcatheter tip gluing to the cast are also present[29]. As a result, most series that used NBCA with a curative intent achieved complete occlusion rates of ≈10%[30-33].

The development of ethylene vinyl alcohol (EVOH) based copolymers provided the needed impetus in the curative embolization of AVMs. These are non-adhesive agents that are dissolved in dimethyl sulfoxide (DMSO), an organic solvent with well-studied biologic properties[34]. Once in the blood stream, the DMSO dissolves and gets washed out resulting in precipitation of the copolymer within the vessel[35]. This precipitation occurs in an inside-out fashion and has been likened to the flow of lava from volcanoes[36]. Thus, unlike the adhesive and inflammatory occlusion of NBCA, EVOH based agents cause more of a mechanical occlusion of the nidus, underlining the need to overfill the nidus during embolization for a durable cure[37]. EVOH based agents take a longer time to form a cast (up to 5 minutes) than NBCA and therefore due to their non-adhesive nature, allow a more prolonged and controlled injection with the option of serial check angiograms. Further, redirection of percolation may be achieved by temporarily interrupting injection for up to 2 minutes at a time, so as to allow solidification of the cast and create new channels of low resistance in alternate pathways, a technique referred to as "road-blocking"[38]. The formation of a proximal plug of up to a cm in length, around the tip of the microcatheter facilitates antegrade flow of the copolymer – the so called "plug-and-push technique"[39]. Injection is facilitated further by the viscosity of the agents, which is conferred to by a significant extent by the opacifying agent of micronized tantalum. Two formulations are currently available in the market: Onyx (eV3, USA) and Squid (Emboflu, Switzerland) that differ with regards to the extent of micronization of tantalum, being finer in Squid and theoretically conferring better homogeneity, longer injection times and more control.

Onyx has FDA approval and is CE marked, while the newer Squid is CE marked alone and is hence marketed outside of the USA.

Series that have utilized EVOH based embolic agents in the embolization of AVMs have described better control of injections as compared to NBCA as well as better surgical handling properties, with onyx forming a soft spongy cast as opposed to the more brittle and hard cast of NBCA[34,36]. Further higher rates of curative embolization have been reported with the use of Onyx ranging 8.3% to as high as 53.9% in large case series (table 1).

Since DMSO is a highly potent solvent which is known to have damaged older catheters, newer DMSO compatible microcatheters were designed for injection[35]. The conventional DMSO compatible microcatheters are Marathon (ev3/Medtronic, USA), Echelon (ev3/Medtronic, USA). The newer intracranial balloon microcatheters such as the Sceptre C and XC, (Microvention Terumo, USA) have also been used in the embolization of AVMs with particularly high flow fistulae. These have DMSO compatible lumens, but not balloon per say is not DMSO compatible. Most studies on Onyx embolization in AVMs utilized conventional microcatheters. However, since Onyx embolization demands that a proximal plug be formed at the microcatheter tip, almost all studies reported an incidences of catheter gluing into the cast (table 1). Catheter entrapment in turn led to 2 types of risks. Attempts at retrieval led to the risk of rupture of the pial artery and secondary intracranial hemorrhage. Leaving the microcatheter in situ required additional antiplatelet therapy and exposed the patient to a lifelong risk of thromboembolic phenomena. After more than a 100 cases of catheter entrapment and 9 related deaths were reported, the United States Food and Drug Administration (US FDA) issued a Safety Communication with regards to the risks of catheter entrapment with the use of Onyx[40].

To offset the risks of catheter entrapment, microcatheters with a detachable tip were designed. The first reported case of their use was in 2008 when Ozturk et al reported embolization of a multicompartmental AVM using NBCA glue using a Sonic microcatheter (Balt, Montmorency, France) achieving obliteration similar to that encountered with Onyx owing to an increased operator confidence. While the tip did not detach as expected they hypothesized that the NBCA cast itself seemed to have less of adhesiveness to the catheter as it smoothly came out[41]. The Sonic microcatheter comes in 7 forms: with a distal outer diameter of 1.2F or 1.5F and lengths of distal detachable segment of 15, 25 and 35mm and one variant with 190cm total length while the rest with 165cms. The detachable segment is bound to the proximal part of the microcatheter by a DMSO incompatible glue. This glue degrades as it comes in contact with the DMSO both within the lumen as well as on the outside of the microcatheter during reflux thereby allowing for detachment. The Sonic microcatheter has 3 markers: one at the distal tip, the second at the detachment tip and the third 5mm proximal to the detachment zone to serve as a marker for maximal allowed reflux. The Sonic comes with its own 0.07" or 0.08" Hybrid microwire.

The other more recently introduced microcatheter is the Apollo microcatheter (Medtronic, USA) based on the Marathon platform. The Apollo uses a heat shrinkable thermoplastic LDPE (Low Density PolyEthylene) sleeve to form a friction based bond proximal catheter and the distal detachable tip.[42] This requires sole mechanical traction for retrieval with detachment. Its use was first reported in an oral abstract by Turk et al in 2012 who embolized an AVM resulting with near complete obliteration and detachment of the tip[43]. The first published report was by Herial et al in 2014 who embolized an SM grade 3 lesion with near complete (80%) obliteration[44]. Both these case reports described the use of the Apollo microcatheter with improved operator confidence and without

complications. The Apollo comes in 3 forms, all with a distal OD of 1.5F and detachable tip lengths of 15, 30 and 50mm. It has 2 markers, the first 0.5mm proximal to the tip and the second 1.25mm proximal to the separation point. The microcatheter is compatible with 0.08" or 0.10" microwires.

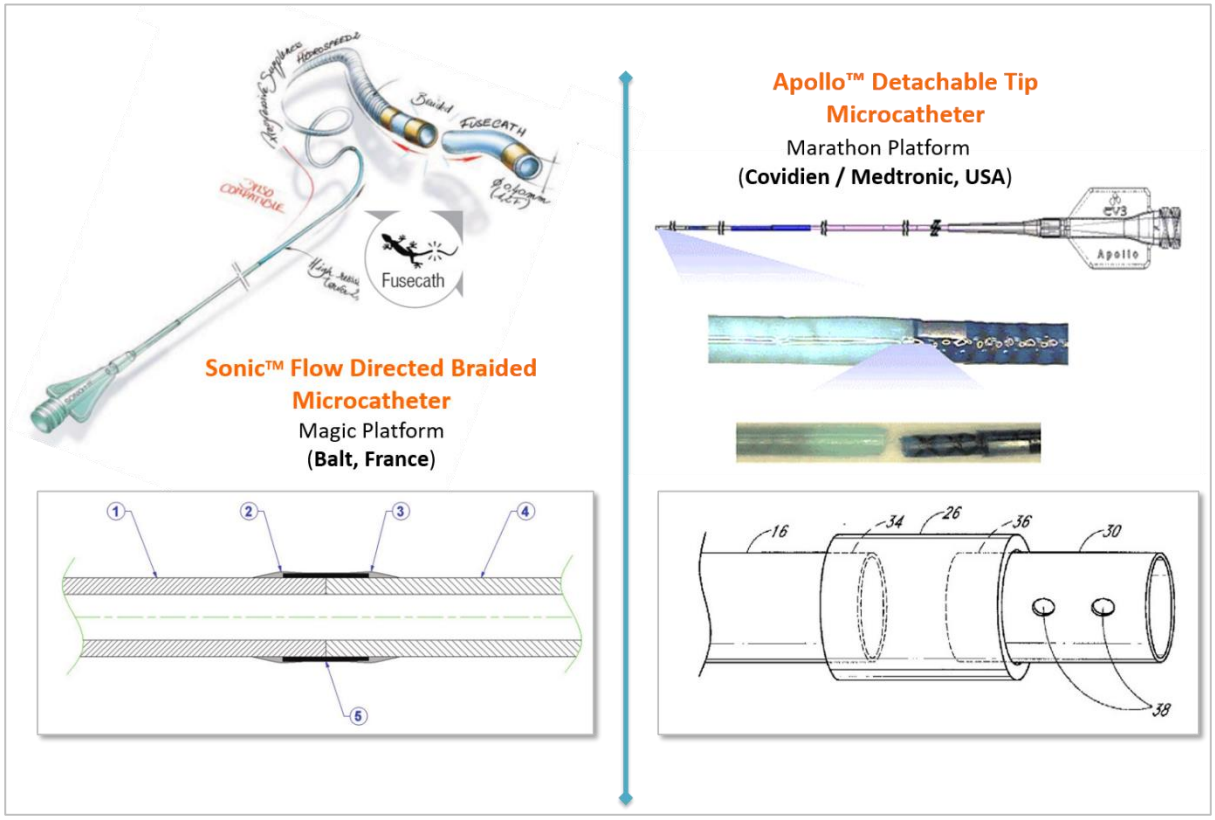


Figure 1: The 2 types of detachable tip microcatheters – Sonic and Apollo.

A common disadvantage to the present generation of conventional microcatheters is that they are not truly flow guided and require to be navigated over the wire (OTW), unlike the truly flow guided microcatheters such as Magic (Balt, France) and Ultraflow (ev3/Medtronic, USA). A risk of wire perforation during navigation thus exists. This disadvantage is theoretically mitigated to some extent with the use of detachable microcatheters whose detachable tips are less stiff and are hence are partially flow guided.[37]

One of the largest series regarding the use of detachable tip microcatheters, specifically Sonic, was by Maimon et al in 2010. They reported 124 injections in 43 patients, with 75% of feeders (93) embolized using Sonic while the rest 25% feeders (31) were embolized using Marathon. While they did not compare the obliteration rates achieved between the 2 different types of microcatheters, they did find a statistically significant difference between the volumes of onyx injected via the detachable versus the conventional microcatheters (2.5±2.2ml and 1.7±1.3ml respectively, $p<0.05$, t test). They achieved complete occlusion in 16/43 (37%) of patients by embolization alone. Amongst SM Grade 1-3 AVMs, they achieved a complete embolization rate in of 73% of AVMs, while they in high grade AVMs (SM grade 4 and 5), which were previously considered untreatable, they achieved complete embolization in 36%. Commensurate with this aggressive approach however, they reported a relatively high incidence of periprocedural bleeding in 6 patients (13.9% of patients, 7.8% per procedure) with clinical consequences in 2 of 6 patients, who both required emergent craniotomy and evacuation. None of these were in SM grade 1 and 2 lesions. In the single case in which the hemorrhage was related to the technique, the cause was due to vessel damage while retrieving the Marathon catheter. Additionally, another patient had extravasation of contrast due to wire perforation during navigation, which resolved spontaneously with no additional treatment. Thus their total rate of complications was 16.2% of patients (7/43 patients, 9.2% per procedure). They encountered 6 technical complications (7.8% per procedure) with clinical consequences in 1 case. Three of these were related to the Sonic microcatheter during the initial 4 months of use and were thus attributed to a learning curve phase. In 2 cases, there was perforation of the soft detachable segment of the Sonic when a wire was

reinserted in a acutely curved vessel. The third case was an unintended detachment while reinserting a microwire in a tortuous vessel[37].

The largest series to date reporting the use of Sonic was published by the same group again in 2013 with 92 patients, of whom treatment was completed in 68[20]. The main objective of this study was to critically evaluate their ongoing results in comparison to their prior experience and hence included the original 43 patients published 2 years prior.[37] In this combined cohort, they achieved complete obliteration of the nidus by embolization alone in 25 patients (37% of the 68patients who completed treatment, 27% of entire population). They achieved near complete obliteration in 32 patients (47% of patients who completed treatment, 35% of entire population). Of these, 28 underwent SRS. Similar to their prior experience, they were able to completely obliterate an impressive number of high grade AVMs (SM grade IV and V) with this combined approach of embolization and SRS – a total of 42 AVMs or 45.6% of the entire population. They reported a progressive improvement in their technique, for eg., they injected higher amounts of Onyx in the latter part of their experience, than in the first 2 years (2.5±2.2ml vs. 1.5±1.3ml, $p<0.01$) and found a progressive reduction of complications with more experience. They continued to experience a relatively high rate complications with 15 symptomatic perioperative bleedings (8.4% per procedure, 16.3% of patients), being mild in 7 patients (mRS<1) and severe in the rest. They identified 3 main causative factors for these bleeds: during retrieval of microcatheter (in 1 case, a Sonic with excess reflux), venous outflow disturbance and microwire perforation (5 additional asymptomatic hemorrhages).

van Rooij et al also utilized Sonic microcatheters but did not describe their use in any detail since the main aim of their study was to study the techniques of and patient selection for onyx embolization[45].

Unlike the Sonic microcatheter, the Apollo microcatheter has been relatively less extensively studied. Apart from Herial et al's[44] case report, who reported that a detachable-tip design allowed prolonged Onyx injection times with safe micro catheter disengagement, with no limitation in accessing target arterial feeders, 2 other smaller case series have been reported. Paramasivam et al reported enhanced safety of these detachable tip microcatheters in their series of 16 adult patients. Atschul et. al. described their experience with the Apollo microcatheter in 11 paediatric patients with varied vascular malformations, only 4 of which were AVMs. They reported increased operator confidence resulting in a more relaxed injection to allow increased time for a complete embolization. They also found as expected a higher rate of detachment with NBCA (37.5%) rather than Onyx (9%) and reported an excellent safety profile with no periprocedural or post-procedural complications whatsoever[46]. A similar safety profile has also been reported by the same group with regards to the use of Apollo with NBCA in their series of 5 patients[47].

Detachable tip microcatheters also allow modifications of techniques to allow improved percolation. The pressure cooker technique is one such method in which a proximal plug is created around the detachable segment using a combination of coils and glue by means of second conventional microcatheter so as to create an immediate wedged flow effect and thereby improve antegrade percolation[48]. Modifications of this technique involve using concentrated glue (the modified pressure cooker technique)[49] or using a more viscous formulation of Onyx (such as Onyx-34)[50] to form the proximal plug by means of conventional or detachable tip microcatheters respectively.

Comparing the results of series using detachable tip microcatheters with those that use conventional microcatheter is fallacious since the techniques involved and

aggressiveness of embolization vary between different groups. For example Maimon et al.[37] and Strauss et al.[20] achieved a curative embolization rate of 37% using the Sonic microcatheter while authors such as Saatci et al[51] and Katsaridis et al[38] who used conventional microcatheters achieved a rates of 51-53.9%. Further, apart from the 2 large series on the Sonic, most of the other studies have primarily focused on the improved safety and increased operator confidence afforded by detachable tip microcatheters. However, the efficacy of these detachable tip microcatheters in comparison to conventional microcatheters in the embolization of brain AVMs is yet to be objectively demonstrated in a large case series and forms the basis and rationale for this study.

Sl. No.	Series	Year	No. of Patients completed treatment () = Full study pop.	Embolic Agent	Mean Sessions/ Feeders/ Patient	Complete Obliteration Rate by Embolization Alone	Rate of permanent morbidity/ Mortality	Rate of Microcatheter Retention	Remarks
1	**He et al[52]**	2005	22	Onyx	NR	13.6%	0	9%	Transient neurological abnormalities in 9% of patients.
2	Perez-Higueras et al[53]	2005	45	Onyx	2.5	22.2%	17.7%		
3	Song et al[54]	2005	50	Onyx	1.3	20%	10%		
4	**Mounayer et al[26]**	2007	53 (94)	Onyx	2.2	49%	11.7%	4.2%	
5	Weber et al[22]	2007	93	Onyx	NR	20.4%	9.7%	4%	
11	**van Rooij et al[55]**	2007	44	Onyx	1.3	15.9%	6.8%	4.5%	
6	**Katsardis et al[38]**	2008	52 (101)	Onyx	2.2	53.9%	10.9%	0.9%	Near-total occlusion (>80%) in 34.6%
7	**Panagiotopoulos et al[56]**	2009	82	Onyx	1.5	24.4%	11.3%	1.2%	
8	**Pierot et al[57]**	2009	50	Onyx+Glue	2.9	8.3%	11%	8%	Near total occlusion in 56.3%
9	Xu et al[58]	2011	86	Onyx	1.4	18.6%	4.7%		
10	Abud et al[59]	2011	17	Onyx	1.4	94.1%	5.9%		Used a double arterial catheterization technique.
11	Saatci et al[51]	2011	350	Onyx+Glue	1.7	51%	8.5%	8%,	
12	Pierot et al[17]	2013	117	Onyx	2	23.5%	12.5%	NR	
13	Strauss et al[20]	2013	68 (92)		2 (Median)	37%	8.7%	4.5%	3 symptomatic ICHs related to retrieval
14	Present Study		116	Onyx, Squid, Adjunctive NBCA					

Table 1: Major studies reporting the use of Onyx embolization for Brain AVMs.

Sl. No.	Series	Year	No. of P/S/F*	Microcatheter	Embolic Agent	Obliteration Rate by Embolization Alone	Remarks
1	**Ozturk et al[41]**	2008	1/1/1	Sonic	NBCA	50% obliteration	• AVM size of 6x5x3cms, No SM Grade • 16 min long injection, no detachment of tip at retrieval
2	**Maimon et al[37]**	2010	43/76/124	Sonic – 93 Marathon – 31	Onyx + 3 pts adjunctive NBCA	Compete Obliteration 16/43 (37%) SM I-III – 11/15 = 73% SM IV-V – 5/14 = 36%	• Curative intent, did not share cases with other modalities. • Did not compare obliteration rates between Sonic & Marathon • Statistical significance between volumes injected between Sonic & Marathon: (2.5±2.2 vs. 1.7±1.3ml), p<0.05, t test. • Did not mention detachment rates. • 6 technical complications (7.8% per procedure) • 7 clinical complications (9.2% per procedure, 16.2% of patients)
3	**Turk AS et al[43]**	2012	1/1/2	Apollo	Onyx	Near complete obliteration	• Oral Poster Abstract: Single patient, No SM grade given. • Single session, 2 feeders embolized with Apollo microcatheters, both detached. • No complications.
4	**Strauss et al[20]**	2013	68/	Sonic – 233 Marathon - 43	Onyx	Complete obliteration in 37% Near complete obliteration in	• Same group as 2 (Maimon et al). • Did not compare efficacy of detachable tip versus conventional microcatheters, but evaluated ongoing experience with Sonic and Onyx.
4	**Herial et al[44]**	2014	1/2/3	Apollo	Onyx	Achieved 80% final obliteration	• SM grade 3 lesion, • Session 1: Headway Duo Session 2: 2 feeders with 2 Apollo microcatheters, 1 detached, 2nd did not., No complications.
5	**Altschul et al[46]**	2014	11/14/27	Apollo	Onyx	No obliteration rates given for the 4 AVMs	• Paediatric (age 3months – 8 years) • Variety of vascular malformations: 4 AVMs, 5 VOGMs, 2 Pial AVFs. • Tip detachment in 7/27 (25.9%), none in AVMs.
6	**Paramasivam et al[47]**	2015	5/-/9	Apollo	NBCA	No report of degree of obliteration.	• 45% cases detached safely – detachment did not correlate with length of reflux • No complications

Table 2: Series and case reports of AVM embolization using detachable tip microcatheters. (P=Patients, S=Sessions, F=Feeders).*

MATERIALS & METHODS

MATERIALS & METHODS

Study Design

This is a retrospective study (approved by the Institutional Ethics Committee SCT/IEC/806/AUGUST-2015) between 1st of January, 2010, and 31st July, 2017, at Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Trivandrum, Kerala, a tertiary care hospital in India. Consent for retrospective review was exempted.

Study Population

Medical records of all patients who underwent embolization in the department of Imaging Sciences and Interventional Radiology between 1st of January, 2010, and 31st July, 2017 were reviewed.

Only patients with plexiform or mixed plexiform-fistulous AVM nidus angioarchitecture as determined on angiography were included in the study. The study population was categorized into 2 groups:

- **Group 1** – AVMs for which **Detachable tip microcatheters** were used.
    - **Group 1a:** A subcategory in which only detachable tip microcatheters were used for embolization using ethyl vinyl alcohol (EVoH) based agents such as Squid or Onyx only.
    - **Group 1b:** A subcategory in which both detachable tip and conventional microcatheters were used, but in which more volume of EVoH embolic agent was injected via the detachable tip microcatheter.
    - **Group 1c:** Another subcategory in which ancillary targeted glue embolization was done for fistulous components or intranidal aneurysms

resulting in only minimal nidus obliteration while the rest of AVM was embolized with EVoH based agents using detachable tip microcatheters.

- **Group 2** – AVMs for which **Conventional microcatheters** were used.
    - **Group 2a:** A subcategory in which only conventional microcatheters were used for embolization using ethyl vinyl alcohol (EVoH) based agents such as Squid or Onyx only.
    - **Group 2b:** A subcategory in which both conventional and detachable tip microcatheters were used, but in which more volume of EVoH based embolic agent was injected via the conventional tip microcatheter.
    - **Group 2c:** Another subcategory in which ancillary targeted glue embolization was done for fistulous components or intranidal aneurysms resulting in only minimal nidus obliteration while the rest of AVM was embolized with EVoH based agents using conventional microcatheters.

Exclusion Criteria

1. Patients with pial arteriovenous fistulae (AVF) for whom only glue embolization with or without adjunctive use of coils was done.
2. Patients for whom only Glue was used for targeted embolization.
3. Patients for whom embolization was attempted, but en-passage feeders were found at superselective angiography.

Data Recording

A. Population characteristics

Age and sex of patients, their clinical presentation were recorded.

B. AVM Classification

AVMs were classified as per the Spetzler Martin (SM) grading. AVMs were classified as Small (0-3cms), Medium (3-6cms) or Large (>6cms) based on their largest dimension as per the SM grade. Since many AVMs tend to be oblong, an idealized size based classification was used to avoid miscategorization of size. All 3 dimensions were measured (a, b, c) and a volume (V) in cc was calculated based on the abc/2 equation[60]. From this volume the diameter (d) of an idealized spherical AVM was calculated using the formula $V=4/3\prod(d/2)^3$.[61] These idealized spherical diameters were classified as small (<2cms), medium (2-4cms) and large (>4cms)[26].

Embolization Methodology

C. Embolization Materials

Two ethyl vinyl alcohol based liquid embolic agents were used for embolization: Squid and Onyx. Both these consist of an ethyl vinyl alcohol copolymer dissolved in a solvent, dimethyl sulfoxide (DMSO) with micronized tantalum as a radio-opacifier. Onyx (ev3, now Medtronic, USA) is supplied in ready to use vials in 3 concentrations of 6%, 6.5% and 8% corresponding to a viscosity of 18, 20 and 34cp. Squid (Emboflu, Switzerland) is an agent with a formulation similar to Onyx but has higher micronization of tantalum with purported advantages of higher homogeneity and slower precipitation. Squid is provided in 4 formulations: standard viscosity - Squid 18, Squid 18LD and low viscosity- Squid 12 and Squid 12LD. We used primarily Onyx 18, Squid 12 and Squid 18 in our case series.

Histoacryl (Braun Surgicals, Spain) is an adhesive glue consisting of NBCA (n-butyl cyanoacrylate). It is mixed with Lipiodol (Guerbet LLC, Villepinte, France) an ethiodized oil formulation that provides both radio-opacity and allows modulation of the polymerization times of the glue based on dilution. We used between 21% to 80% dilutions of NBCA depending on the shunting velocity encountered at superselective angiography. NBCA

was used for only targeted embolization of fistulous components or intranidal aneurysms prior to adjunctive embolization with EVoH based agents.

D. Microcatheters

All microcatheters that were used were DMSO compatible with distal outer diameters (OD) most commonly of 1.5F.

The conventional microcatheters consisted of Marathon (ev3/Medtronic, California), Ultraflow HPC (ev3/Medtronic, USA), and Scepter XC (Microvention Terumo, USA), an extracompliant balloon catheter.

Detachable tip microcatheters that were used were Apollo (ev3/Medtronic, USA) with a detachable tip of 3cms length and Sonic (Balt, Montmorency, France) with a distal OD of 1.2F and 1.5F and detachable tip lengths of 1.5 and 2.5cms). We used both 1.2F and 1.5F calibre Sonic microcatheters with a detachable tip length of 1.5 and 2.5cms.

All microcatheters, except Sonic were navigated using 0.08" Mirage microwires (ev3/Medtronic, USA). We used Sonic's own pre-packaged 0.08" Hybrid microguidewire.

E. Procedure

The objective of embolization in our department is adjunctive with the primary aim being to reduce the size of the AVM nidus and obliterate intranidal aneurysms or fistulous components prior to definitive treatment with stereotactic radiotherapy (SRS) or microsurgical excision.

We use a GE Innova 3131 (GE Healthcare, USA) biplane system for intervention. Vascular access was obtained via transfemoral route. Treatment was always preceded by a diagnostic cerebral angiography and an analysis of nidal architecture with 3D rotational angiography. For intervention, we used either a 6F Neuron (Penumbra, Inc. USA) or 6F Envoy (Codman Neurovascular, USA) both with distal internal diameters (ID) of 0.07". We

used systemic anticoagulation with a bolus dose of 5000IU of Heparin followed up by hourly doses of 1000IU maintaining Activated Clotting Time (ACT) between 250-300 seconds.

The microcatheter-wire assembly was navigated under roadmap guidance commonly into the most accessible dominant feeder supplying the nidus. Once the arterionidal junction was reached, flow was assessed with superselective angiograms and the microcatheter position was further refined to achieve as close to a wedged position as possible. If wedging did not occur, we created a pseudowedged effect by creating a small plug of Onyx/Squid around the microcatheter tip to prevent reflux around the microcatheter tip and enhance antegrade percolation into the nidus (plug creating technique).

Embolization was continued as long as nidal percolation occurred without the embolic agent entering into a draining vein or refluxing around the microcatheter tip. When either of these occurred, flow was redirected by briefly pausing the injection for time periods always <2minutes and then resumed. The mode of injection was usually continuous with intermittent pulses to allow for flow redirection. Multiple feeders were accessed in the same or a consequent sitting if there was an unsatisfactory outcome with embolization from a single feeder.

Embolization was terminated if the angiographic endpoint of complete occlusion was reached or prior to that in the event of failure of further percolation, persistent flow of the embolic agent into a draining vein occurred, significant reflux occurred at the microcatheter tip or a further embolization of a large volume AVM was deemed to be of high risk in a single sitting. The microcatheter was retrieved using controlled traction. If retrieval was not possible despite repeated sustained attempts, the microcatheter was cut

at the groin and left in situ. The patient was started on a single antiplatelet (aspirin 150mg OD) and continued for varying periods depending on presence of clinical symptoms and the status of the feeding vessel at follow-up invasive angiography.

Any residue of the AVM was treated with SRS if it was deep or in an eloquent region while more superficial residue were treated by surgery.

Outcomes

Primary outcomes measured were:

- **Final angiographic obliteration rate:** This was visually graded by the 2 neurointerventionists and retrospectively corroborated into 4 grades of obliteration: Complete (100% obliteration), Near-complete (80-95%) obliteration, acceptable (50-80% obliteration) and unsatisfactory (<50% obliteration)[38]. These were dichotomized into good angiographic outcome (any obliteration between 80-100%) or poor angiographic outcome (<80%) obliteration. Rates of obliteration were classified based on Spetzler Martin grading of AVMs and a size classification by maximal diameter (A/B/C - <3cms, 3-6cms and >6cms) and idealized spherical diameter grade (a/b/c - <2cms, 2-4cms and >4cms).
- **Injection duration and volume of embolic agent** injected.
- **Number of feeders** through which embolization was done till embolization was terminated for any of the reasons outline above.

Secondary Outcomes measure were

- **Technical Safety:**
    - Rate of **detachment of the tips** of the newer detachable microcatheters. Incidence of unintended premature detachment.

  - Rates of **catheter entrapment** resulting in retention of the microcatheter in situ.
  - Other technical complications such as **microcatheter rupture** resulting Onyx/Squid extravasation.

- **Clinical outcomes**
  - **Rates of hemorrhage or non-hemorrhagic ischemic neurological deficits** related to embolization.

Statistical Analysis:

IBM SPSS software v22 was used for statistical analysis.

- Distribution of SM grades across group 1 and 2 were tested for using independent sample Kruskal Wallis test.
- Statistical significance of rates of obliteration (categorical variables) between 2 groups were tested for using 2-tailed Fisher exact test.
- Statistical significance of rates of volume and durations of injections (continuous variables) were tested for using ANOVA (Analysis of One way Variance).

RESULTS

RESULTS

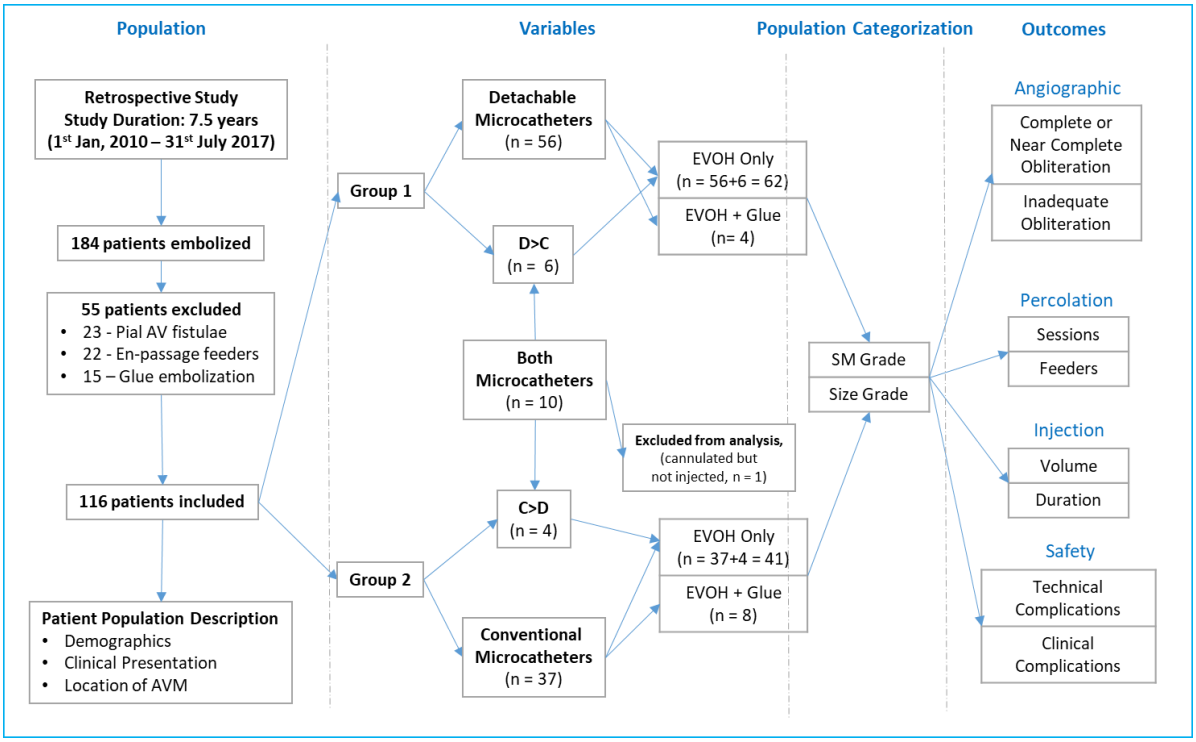


Figure 2: Study flow.AV=Arteriovenous Malformation, D=Detachable tip microcatheter, C=Conventional microcatheter, D>C or C>D = patients where both microcatheters were used, but one more predominantly over the other. EVOH=Ethyl vinyl alcohol based embolic agent, SM=Spetzler-Martin grade, n=number.

A. PATIENT POPULATION PARAMETERS

A total of 184 patients were taken up for embolization between 1st January, 2010 to 30th July, 2017. Of these **55** patients were excluded due to non-embolizable (en-passage) feeders at superselective angiography (**23 patients**), purely fistulous architecture (**12 patients**) or sole of use of glue for targeted embolization (**20 patients**). Hence a total of **116** patients were included in the final analysis.

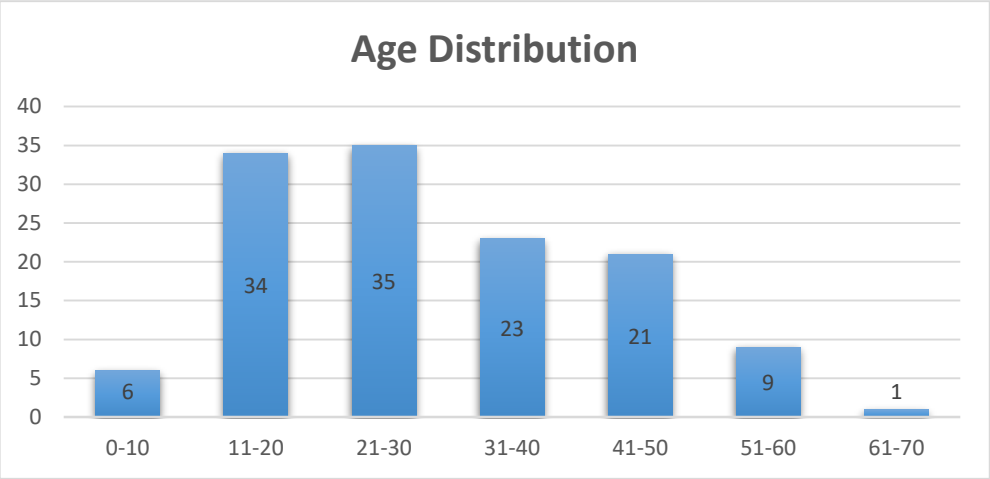
I. Demographic Profile:

Age Characteristics

Average Age: 29.35 years, **Range**: 5 to 65 years. Most patients were in the 3rd or 4th decade with only 6 patients being <10 years of age.

Age Group (Years)	0-10	11-20	21-30	31-40	41-50	51-60	61-70	Total
No. of Patients	4	30	33	20	20	8	1	116

Table 3: Age distribution of patient population.



Graph 1: Distribution of age by decadal groups within the study population.

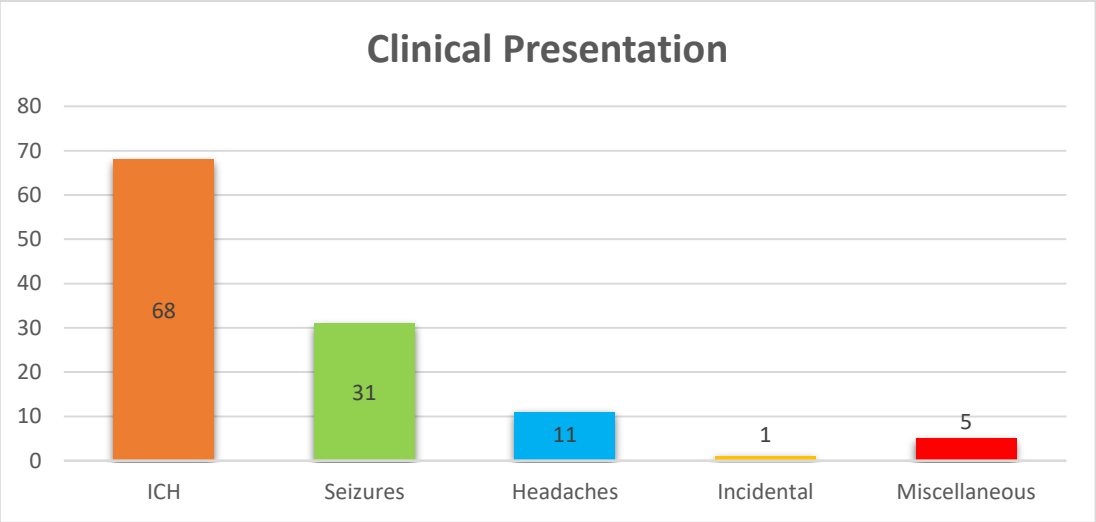
Sex Distribution: 68 (58.6%) of patients were male while 48 patients (41.3%) were female(check sum).

Clinical Presentation:

The most common presentation was that of acute intracranial hemorrhage, followed by epilepsy and chronic episodic headaches. Of patients with other miscellaneous presentations, 2 patients presented with insidious gradually progressive visual deterioration along with other features of **raised intracranial pressure.** 1 patient presented with features **mimicking carotid cavernous fistula** with proptosis and conjunctival chemosis; this patient had drainage of the AVM into the ophthalmic veins. 1 patient with an unbled cerebellar AVM presented with **ataxia**. Another patient with a cerebellar AVM presented with features of **trigeminal neuralgia** secondary to neurovascular conflict by a hypertrophied superior cerebellar artery.

Presentation	No. of Patients
Intracranial hemorrhage	68 (58.6%)
Seizures	31 (26.7%)
Headaches	11 (9.4%)
Incidental	1 (0.8%)
Other Presentations	5 (4.3%)
TOTAL	116

Table 4: Spectrum of presentations in study population.



Graph 2: Most common presentations of AVMs in the study population.

II. AVM Characteristics

Location

Location by Lobe/ Region	No. of Patients
Frontal	24
Parietal	26
Temporal	9
Occipital	15
Frontoparietal	4
Temporoparietal	5
Parieto-occipital	3
Temporo-occipital	7
Basal Ganglia, Thalamus, Corpus Callosum	4
Intraventricular (Choroidal)	10
Cerebellar	9
TOTAL	116

Table 5: Location and number of AVMs by region.

A. TREATMENT DATA

Treatment Sessions & Feeders Cannulated

A total of 175 feeders were cannulated in the 116 AVMs. Of these, feeders that were embolized with NBCA (12 with conventional microcatheters, 1 with Sonic) were not included in analysis. 2 feeders cannulated with Apollo and Marathon in a single patient were also excluded from analysis due to premature unintended tip detachment and catheter blockage respectively. **Thus a total of 115 AVMs were embolized via 160 feeders using EVOH** (table 6)**.**

Of these 115 AVMs, 66 (57.3%) AVMs were treated solely or predominantly with detachable microcatheters while 49 (42.6%) were treated solely or predominantly with conventional microcatheters(table 6).

No. of AVMs	No. of Patients	Group 1	Group 2
Total	115	66 (57.3%)	49 (42.6%)

Table 6: Total number of AVMs treated exclusively or predominantly by detachable tip microcatheters (group 1) and exclusively or predominantly by conventional microcatheters (group 2).

SM Grade	Group 1 (Detachable Tip)						Group 2 (Conventional)					
	EVOH Only				EVOH + Glue		EVOH Only				EVOH +Glue	
	1a Detachable		1b D>C		1c Detachable		2a Conventional		2b C>D		2c Conventional	
Sessions (S) & Feeders (F)	S	F	S	F	S	F	S	F	S	F	S	F
I	10	10	1	2	-	-	8	9	-	-	2	2
II	22	23	5	6	1	1	11	16	3	5	3	4
III	17	20	-	-	3	3	15	18	2	3	3	3
IV	11	11	5	7	4	4	7	9			2	2
V	-	-	-	-	-	-	1	2			-	-
Total	60	64	11	15	8	8	42	54	5	8	10	11
Avg. Sessions & Feeders/AVM	1.07	1.14	1.83	2.44	2.0	2.0	1.13	1.58	1.25	2	1.25	1.37
Total Avg. Sessions & Feeders	1.63/1.86						1.21/1.65					

Table 7: Number of Sessions (S) and Feeders (F) utilized for embolization averaged by treatment groups.

Microcatheters Utilized

Amongst the 162 feeders, an equal number were cannulated using the 2 types of microcatheters. The most common microcatheter amongst the detachable group was Apollo, used in 49/81 (60.4%) of feeders with the rest being Sonic (32/81, 39.6%). Amongst the conventional microcatheters, Marathon was used in nearly all cases, 76/81 (93.8%)(table 8).

Microcatheter	Number	Total
Sonic	32	**81 (50%)**
Apollo	49	
Marathon	76	**81 (50%)**
Ultraflow	4	
Scepter XC	1	
Total No. of feeders	**162**	

Table 8: Microcatheters used by number of cannulations of feeders

Embolic Agent Utilized

Onyx was more commonly used embolic agent. 62.6% of AVMs and 65% of feeders were embolized with Onyx while the rest 36.5% of AVMs and 35% of feeders were embolized with Squid. A single patient underwent embolization with both Squid and Onyx in 2 sessions (table 9 and 10).

Group	Subgroup	Squid 12/18	Both	Onyx 18
Group 1	**1a [Detachable (EVOH Only)]**	28	1	2
	1b [D>C (EVOH Only)]	2		4
	1c [Detachable (EVOH+Glue)]	1		3
Group 2	**2a [Conventional (EVOH Only)]**	9		28
	2b [C>D (EVOH Only)]	0		4
	2c [Conventional (EVOH+Glue)]	2		6
TOTAL (115 AVMs)		**42 (36.5%)**	**1 (0.8%)**	**72 (62.6%)**

Table 9: Embolic agent used by number of patients/AVMs.

Group	Subgroup	Squid 12/18	Onyx 18
Group 1	1a [Detachable (EVOH Only)]	36	28
	1b [D>C (EVOH Only)]	5	10
	1c [Detachable (EVOH+Glue)]	2	6
Group 2	2a [Conventional (EVOH Only)]	11	43
	2b [C>D (EVOH Only)]	0	8
	2c [Conventional (EVOH+Glue)]	2	9
TOTAL (160 Feeders)		**56 (35%)**	**104 (65%)**

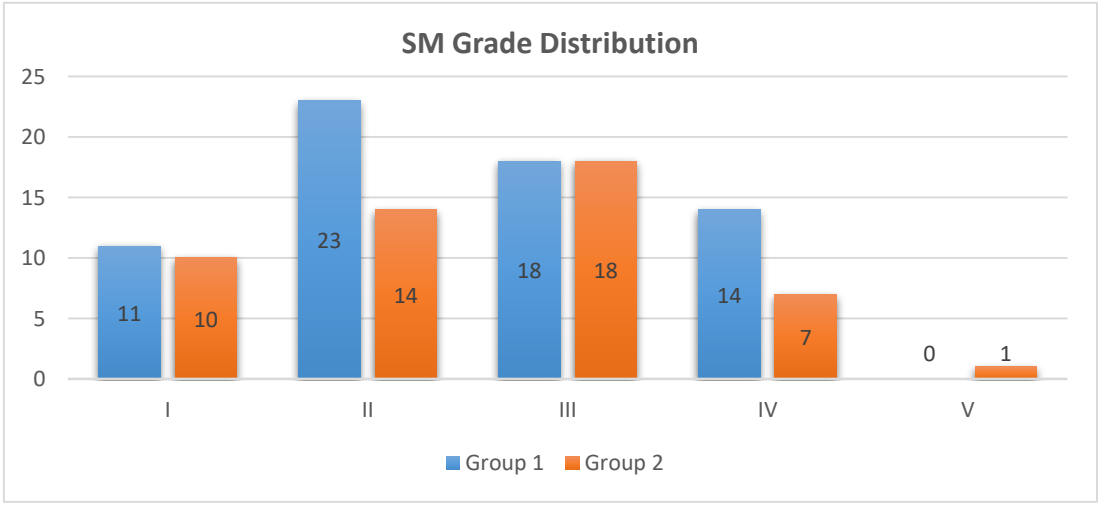
Table 10: Embolic agent used by number of feeders cannulated.

Spetzler Martin Grading

Majority of patients belonged to SM Grades II & III (63.4%). No significant difference in distribution of SM Grades was noted between Group 1 and Group 2 (p=0.406, Kruska Wallis test) (table 11 and 12; graph 3).

SM Grade	No. of Patients	Group 1	Group 2
I	22 (18.2%)	11 (16.7%)	10 (20.4%)
II	37 (31.3%)	23 (34.8%)	14 (28.5%)
III	36 (31.3%)	18 (27.2%)	18 (36.7%)
IV	21 (18.2%)	14 (21.2%)	7 (14.2%)
V	1 (0.8%)	0 (0%)	1 (2%)
Total	**115**	**66 (57.3%)**	**49 (42.6%)**

Table 11: Distribution of AVMs across SM grades in whole population and categorized by treatment groups.



Graph 3: Distribution of AVMs across SM grades in the treatment groups

SM Grade	Group 1 (Detachable Tip)			Group 2 (Conventional)		
	EVOH Only		EVOH + Glue	EVOH Only		EVOH +Glue
	1a Detachable	1b D>C	1c Detachable	2a Conventional	2b C>D	2c Conventional
I	10	1	0	8	0	2
II	20	2	1	10	2	2
III	17	0	1	13	2	3
IV	9	3	2	5	0	2
V	0	0	0	1	0	0
Total Pts.	**56**	**6**	**4**	**37**	**4**	**8**

Table 12: Distribution of AVMs across SM grades subcategorized by treatment groups

Size Grading

When considering the maximal dimension of the AVMs, when graded similar to the Spetzler Martin gradation, the majority of AVMs were <3cms in size (49.5%). There was no significant difference in distribution of SM size grade between Groups 1 and 2 (p=0.368, Kruska Wallis test)(table 13).

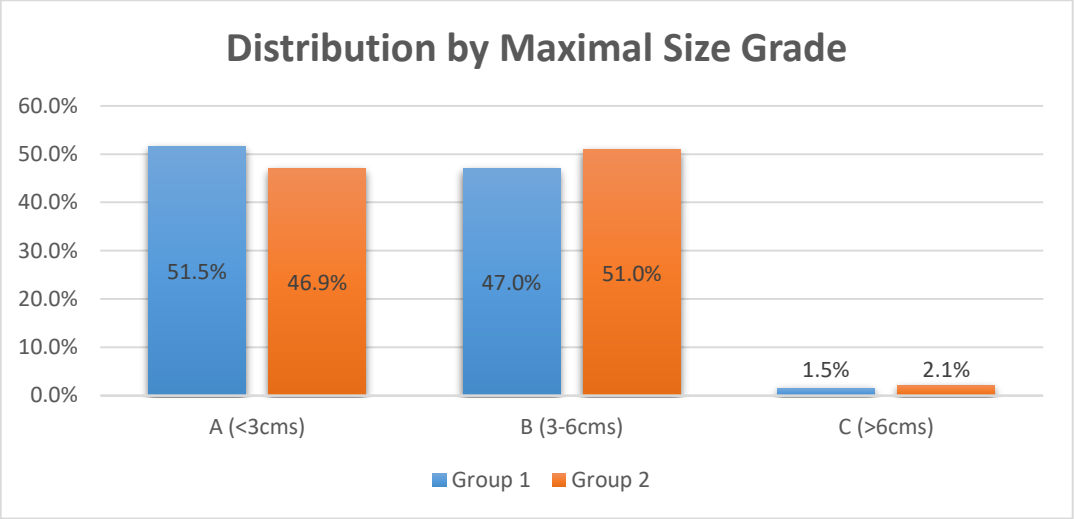
SM Size Grade	No. of Patients	Group 1	Group 2
A (<3cms)	57 (49.5%)	34 (51.5%)	23 (46.9%)
B (3-6cms)	56 (48.6%)	31 (47%)	25 (51.0%)
C (>6cms)	2 (1.7%)	1 (1.5%)	1 (2.1%)
Total	**115**	**66**	**49**

Table 13: Distribution of AVMs by maximal dimension across the whole study population and categorized by treatment groups.

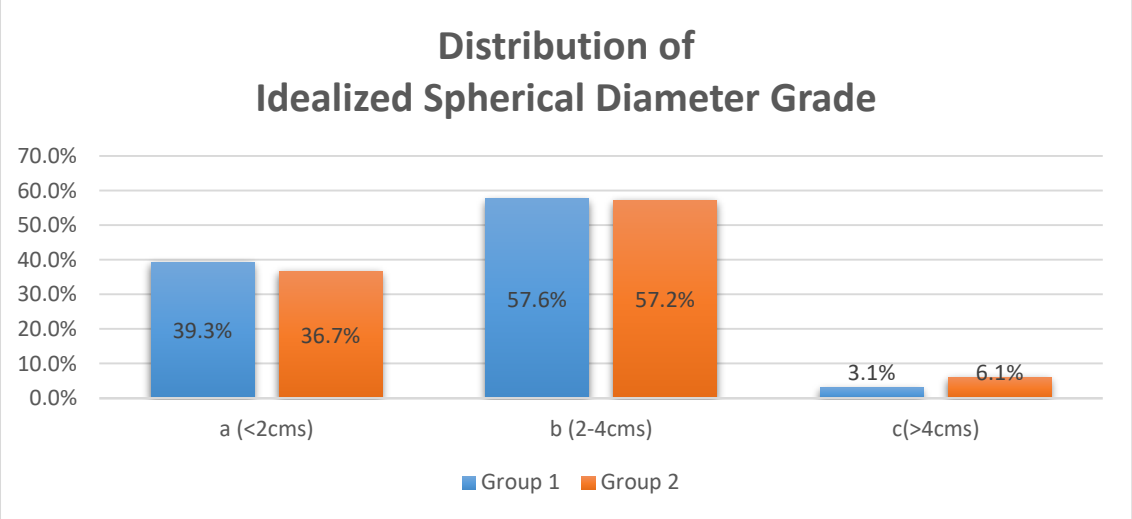
When considering the idealized spherical diameter of the AVMs, when graded similar to the Spetzler Martin gradation, the majority of AVMs were between 2-4cms in size (46.9%). There was no significant difference in distribution of SM size grade between Groups 1 and 2 (p=0.368, Kruska Wallis test).

Spherical Diameter Grade	No. of Patients	Group 1	Group 2
a (<2cms)	44 (38.2%)	26 (39.3%)	18 (36.7%)
b (2-4cms)	66 (57.3%)	38 (57.6%)	28 (57.2%)
c (>4cms)	5 (4.3%)	2 (3.1%)	3 (6.1%)
Total	**115**	**66**	**49**

Table 14: Distribution of AVMs by idealized spherical diameter across the whole study population and categorized by treatment groups.



Graph 4: Distribution by Maximal Dimension of AVMs between groups 1 and 2.



Graph 5: Distribution by Idealized Spherical Diameter of AVMs between groups 1 and 2.

B. TREATMENT OUTCOMES

Overall Rates of Complete or Near Complete Obliteration

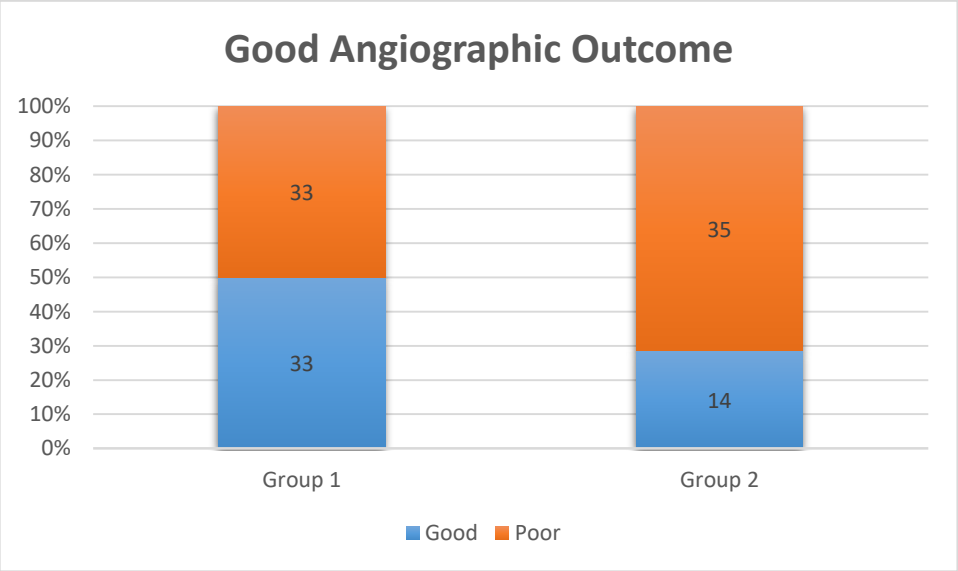
In the complete study population, a total of **11/115 (9.5%)** AVMs were completely obliterated by embolization alone, while **36/116 (31.1%)** of AVMs had near complete obliteration (80-95% obliteration) with embolization alone making a total number of **47/115 *(40.8%)*** patients having a good angiographic outcome.

Complete angiographic cure of 100% obliteration was reached in 9/66 (13.6%) in group 1 and in 2/40 (4.1%) in group 2. However, this was not statistically significant (p=0.2, Fisher test).

In group 1 embolized solely or predominantly by detachable tip microcatheters, a good angiographic outcome (both complete and near complete obliteration) was reached in 33/66 patients (50%) as compared to group 2 AVMs embolized solely or predominantly by conventional microcatheters, good angiographic outcome was reached in 14/49 patients (28.6%). Statistical significance for good angiographic outcome was significant (p=0.0229, Fisher test).

Group	Group 1 (D)		Group 2 (C)		Total	
Obliteration	N	%	N	%	N	%
Complete (100%)	8/66	12.1%	2/49	4.1%	10	8.6
Good (80-100%)	33	**50.0%**	14	**28.6%**	47	**40.8%**
Poor (<80%)	33	**50.0%**	35	**71.4%**	68	**59.1%**
Total	66	100.0%	49	100%	115	100%
p= 0.0229						

Table 15: Good angiographic outcomes (80-100% nidus obliteration) by categorized by treatment groups and of the the whole study population.



Graph 6: Number of patients with Good angiographic outcome in Group 1 and 2.

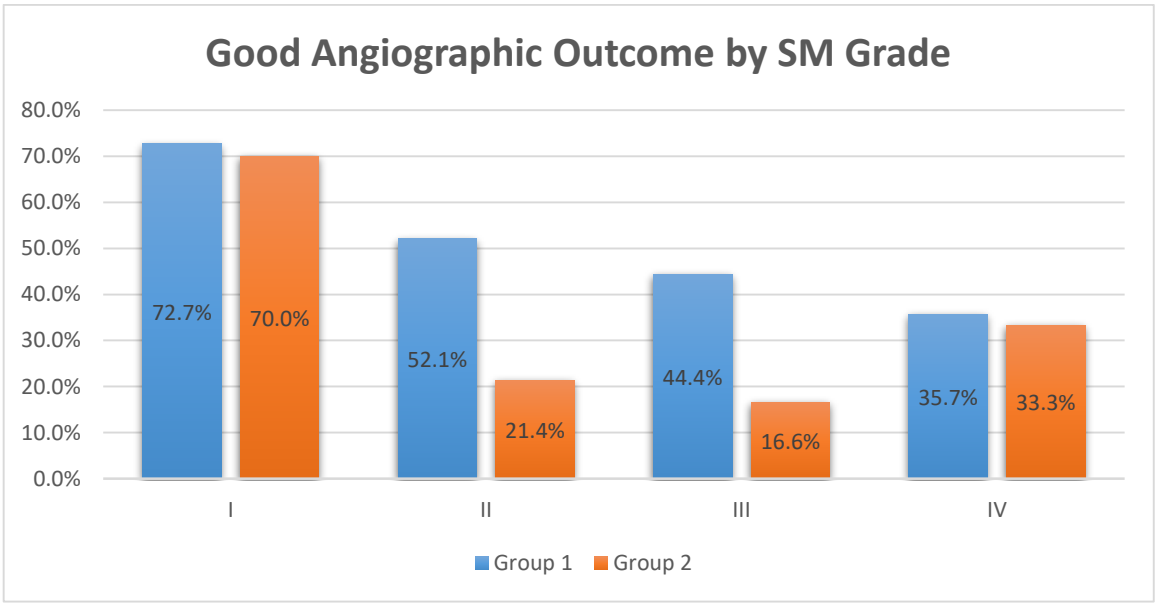
Obliteration Rates by SM Grade

For subgroup analysis by SM grade, the single SM Grade 5 lesion in group 2 was excluded from analysis since no comparable grade was embolized in group 1.

Although detachable microcatheters performed better reaching a good angiographic outcome in a numerically larger number of cases in every category of SM grade, this was a trend for only for SM Grade 2 (p=0.09) and 3 (p=0.07) lesions. Rates of complete obliteration at any grade of AVM were not statistically significant between the 2 groups.

	Group 1		Group 2		Total	
SM Grade	N	%	N	%	N	p Value
I	8/11	**72.7**	7/10	**70**	19	1.00
II	12/23	**52.1**	3/14	**21.4**	34	**0.09**
III	8/18	**44.4**	3/18	**16.6**	32	**0.07**
IV	5/14	**35.7**	2/6	**33.3**	17	1.00
Total	66	**50%**	48	**29.1**	114	100.0

Table 16: Rates of good angiographic outcome by SM Grade.



Graph 7: Rates of good angiographic outcomes between groups 1 and 2.

Obliteration Rates by Size Grade

When graded by their maximal size, group 1 embolized solely or predominantly by detachable tip microcatheters produced better rates of good angiographic outcome than group 2. This was statistically significant however, only for 3-6cms sized AVMs(table 17, 19; graph 8).

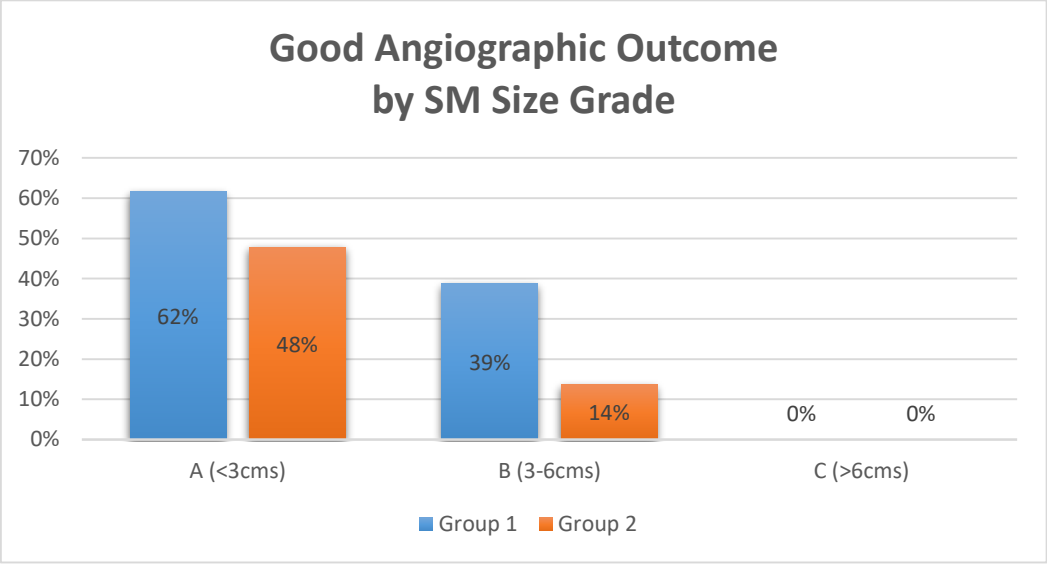
When graded by their idealized spherical diameter, Group 1 AVMs again had better angiographic outcomes at any diameter <4cms, but this was statistically significant only for AVMs whose diameters were between 2-4cms (table 19, graph 9).

SM Size Grade & Good Angiographic Outcome	Group 1		Group 2		Total	
	N	%	N	%	N	p Value
A (<3cms)	21/34	61.7	11/23	47.8	57	0.43
B (3-6cms)	12/31	38.7	3/22	13.6	53	**0.03**
C (>6cms)	0/1	0	0/1	0	2	1.00
Total	33/66	50	49	28.5	115	

Table 17: Good angiographic outcome by SM maximal size grades.

Group		Group 1															Group 2													
Subgroup		**1a Detachable**					**1b D>C**					**1c EVOH+ Glue**					**2a Conventional**					**2b C>D**					**2c EVOH + Glue**				
SM Grade		I	II	III	IV	V	I	II	III	IV	V	I	II	III	IV	V	I	II	III	IV	V	I	II	III	IV	V	I	II	III	IV	V
Overall Outcome	100%	3	3	2			1										2													
	80-95%	4	8	6	1					3			1		1		4	1	3	1			1				1	1			
	50-80%	3	6	5	3			2						1			2	3	3	1				2				1	1		
	<50%		3	4	5										1			6	7	3	1		1				1		2	1	
	Total	10	20	17	9		1	2		3			1	1	2		8	10	13	5	1		2	2			2	2	3	1	
Dichotomized Outcome	Good (>80%)	7	11	8	1		1	0		3			1	0	1		6	1	3	1	0		1	0			1	1	0	0	
	Poor (<80%)	3	9	9	8		0	2		0			0	1	1		2	9	10	4	1		1	2			1	1	3	1	
Total Subcategory	Good (>80%)	31										2					12										2				
	Poor (<80%)	31										2					29										5				
Total EVOH only & EVOH + Glue	Good (>80%)	**33**															**14**														
	Poor (<80%)	**33**															**35**														

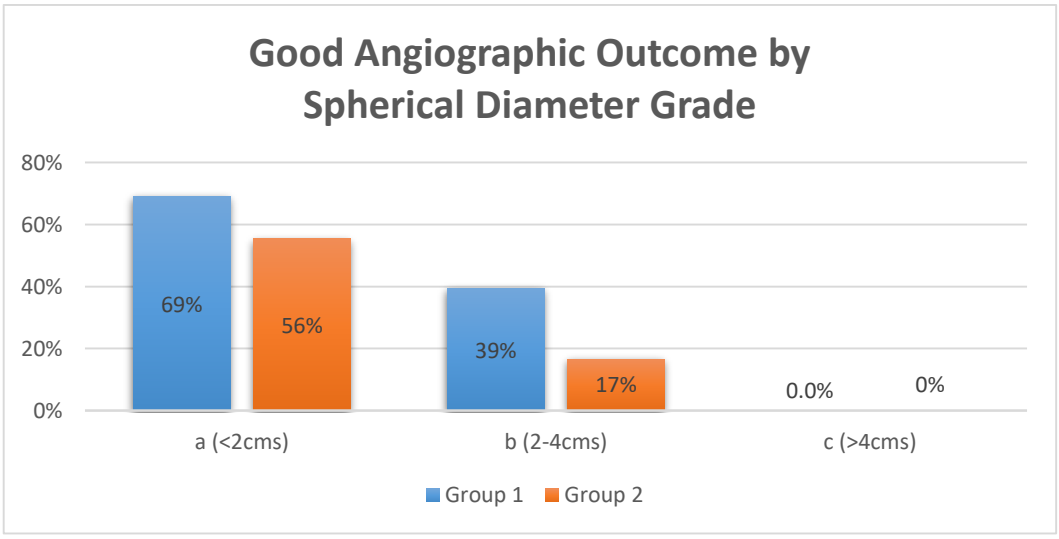
Table 18: Outcomes of embolization subcategorized by the treatment groups.



Graph 8: Good angiographic outcome by SM maximal size grades.

Spherical Diameter Grade & Good Angiographic Outcome	Group 1		Group 2		Total	
	N	%	N	%	N	p Value
a (<2cms)	18/26	69.2	10/18	55.5	46	0.52
b (2-4cms)	15/38	39.4	4/24	16.6	54	**0.03**
c (>4cms)	0/2	0	0/3	0	15	1.00
Total	33/66	50%	14/49	39.2	115	

Table 19: Good angiographic outcome by idealized spherical diameter grades.



Graph 9: Good angiographic outcome by idealized spherical diameter grades.

Volume of Embolic Agent Injected vs. Type of Microcatheter

Overall, 1.68±1.41cc of either Squid or Onyx was injected in 151 feeders. Disregarding groups, 69 feeders were cannulated using detachable tip microcatheters while 82 feeders were cannulated using conventional microcatheters. A significantly higher volume of embolic agent was injected using detachable tip microcatheters (p<0.001, independent samples t-test)(table 20).

	Detachable Tip Microcatheters	Conventional Microcatheter
Feeders	69	82
Volume	2.18cc, SD 1.26,	1.26, SD 1.41
Overall	1.68cc, SD 1.41	
p<0.001		

Table 20: Volumes of Squid or Onyx injected for each feeder cannulated between detachable tip and conventional microcatheters.

Duration of injection of Embolic Agent vs. Type of Microcatheter

Overall, embolization was carried out for 42.98 ± 29.84 minutes per feeder. A statistically significantly were higher with detachable tip microcatheters (54.05 ± 27.9mins) than conventional microcatheters (33.65 ± 28.34mins) (p<0.001, independent samples t-test)(table 21).

	Detachable Tip Microcatheters	Conventional Microcatheter
Feeders	69	82
Duration	54.05mins, SD 27.9mins,	33.65mins, SD 28.34mins
Overall	42.98 mins SD 29.84mins	
p<0.001		

Table 21: Durations of Squid or Onyx injection for each feeder cannulated between detachable tip and conventional microcatheters.

Detachment of Tip occurring in Detachable Tip Microcatheters

The Sonic microcatheter tended to detach less often (36.3%) than the Apollo microcatheter (59.1%). There were 2 cases of entrapment of the Sonic microcatheter that occurred, both due to reflux beyond the detachment zone. Both were cut at the groin and left in situ.

Patients were started on single antiplatelet therapy with no clinical consequences(table 22).

Microcatheter	No. of Feeders	% Detached	Failed detachment
Sonic	12/33	36.36%	2/33
Apollo	29/49	59.1%	0/49
Total Feeders	82		

Table 22: Detachment of tips of the Sonic and Apollo microcatheters.

C. SAFETY OUTCOMES

Technical Complications

Entrapment of the microcatheter occurred in 8 embolizations. Six of these were with conventional microcatheters (all Marathon) while 2 occurred with Sonic microcatheters due to excessive reflux beyond the detachment zone. 5 entrapments occurred in medium sized AVMs (maximal dimension grade B and spherical diameter grade b) while 3 occurred in small sized AVMs. The difference in grade or size of AVMs who had catheter entrapment was not statistically significant. All patients were started post-procedurally on single antiplatelets. None of these patients developed clinical deficits on follow-up (table 23).

AVM Grade	No. of Patients with Catheter Entrapment
Spetzler Martin Grade	
I	2
II	2
III	3
IV	1
Size Grade (Both maximal dimension or spherical diameter)	
A/a	3
B/b	5
C/c	1
TOTAL	8

Table 23: Number of entrapped microcatheters by AVM SM grade and Size/Diameter grades.

One case of catheter rupture occurred with a marathon microcatheter leading to intravasation of onyx within the vertebrobasilar arteries. This required to be retrieved using a Solitaire stentriever. One case of premature unintended detachment of the tip occurred with an Apollo microcatheter. The rates of technical complications, while higher with conventional microcatheters, did not reach statistical significance (p=0.228) (table 24).

Complications	Microcatheter	Number	Outcome
Retained microcatheter	Marathon Sonic	6 2	All started on single antiplatelets. No clinical complications
Premature Detachment	Apollo	1	Solitaire retrieval, no clinical sequelae
Blockage	Marathon	1	Same patient as prematurely detached Apollo, Procedure abandoned
Catheter Rupture	Marathon	1	Solitaire retrieval of onyx Non-target embolization - Cerebellar infarcts, Permanent mild clinical neurological deficits
Rate of complications per patient & per procedure (feeder)	**11/116 (9.4%)**		11/162 (6.7%)
Total Complication Rate per microcatheter • Detachable • Conventional		 3/69 (4.3%) 8/82 (9.7%)	 p= 0.228

Table 24: Complications encountered in study population.

Clinical Complications

Clinical complications occurred in 6 patients with the most common complication being Intraprocedural hemorrhage (3 patients). Intraprocedural hemorrhage occurred in an 11-year-old child with an SM grade 2 lesion towards the end of near complete Onyx

embolization which was unrelated to the use of the Apollo microcatheter and was likely due to rupture of an intranidal aneurysm. The patient was taken up for emergent craniotomy and developed mild contralateral hemiparesis subsequently. Two other patients had asymptomatic small intranidal hemorrhages that were managed conservatively with no clinical consequences. Post-procedural hemorrhage developed in a case of a 59 year old male with an SM grade 4 lesion who underwent embolization with 6ml of Onyx using a Sonic microcatheter resulting in near complete obliteration. The patient was asymptomatic in the immediate post-procedure period but developed depression of sensorium a few hours later with CT revealing a large intraparenchymal hematoma. He underwent emergent craniotomy and evacuation with residual neurological deficits. A third case of intraprocedural rupture occurred in an 18-year-old female with an SM grade 2 lesion that occurred during navigation of a second feeder after partial embolization in the same session with a Marathon microcatheter. The size of the hematoma was small however and she was conservatively managed with no clinical deficits. We had no incidences of hemorrhage related to catheter retrieval.

Complication with permanent neurological deficits	**Number of Patients**
Intraprocedural hemorrhage	3 (1 asymptomatic)
Post-procedural hemorrhage	1
Infarction	2
Total	**6/116 (5.2%)** **Morbidity rate 4.3%**
Complications without neurological deficits	**Number of Patients**
Feeder thrombosis	1
Draining vein secondary thrombosis	1
Seizures	1
Total	**3/115 (2.6%)**
Non-neurological Complications	**Number of Patients**
Common femoral artery thrombosis	1
Total	**1 (0.86%)**

Table 25: Spectrum of complicaitons encountered during treatment.

Infarction occurred in two patients. One was the patient previously described who had catheter rupture leading to intravasation of onyx into the vertebrobasilar system resulting in cerebellar infarcts and subsequently developed mild ataxia.

Post-procedural new-onset seizures unrelated to hemorrhage or infarction occurred in a 24-year-old male who underwent Squid embolization using an Apollo microcatheter resulting in complete obliteration in a single sitting of an SM grade 2 lesion. The patient was started on antiepileptic medications and was subsequently seizure free with no clinical deficits.

Adjuvant Treatment

Of the 11 patients with complete obliteration achieved by embolization alone, 10 patients had undergone follow-up angiographies at an average of 6.4months (range 1-14months) post-treatment. No recurrences were noted in this patient group.

Amongst both groups, a total of 36 patients had near complete obliteration of their AVMs achieved by embolization. The majority, 21 patients, underwent stereotactic radiosurgery (SRS), 3 underwent surgical resection and the rest were either awaiting adjunctive treatment or, in the case of unruptured AVMs or high grade AVMs, conservative management with clinical follow-up was planned. Amongst those who underwent surgery, one patient underwent emergent hematoma evacuation with combined AVM resection for development of Intraprocedural hemorrhage. Of the patients who underwent SRS, follow up DSA was available in 13 (61.9%) patients. Nine patients (69.2%) had no residue at a mean of 21.8 months (range 12-43 months) post SRS. Four patients had residues, albeit with a reduction of varying degrees at an average of 30 months (range 18-48 months) post SRS.

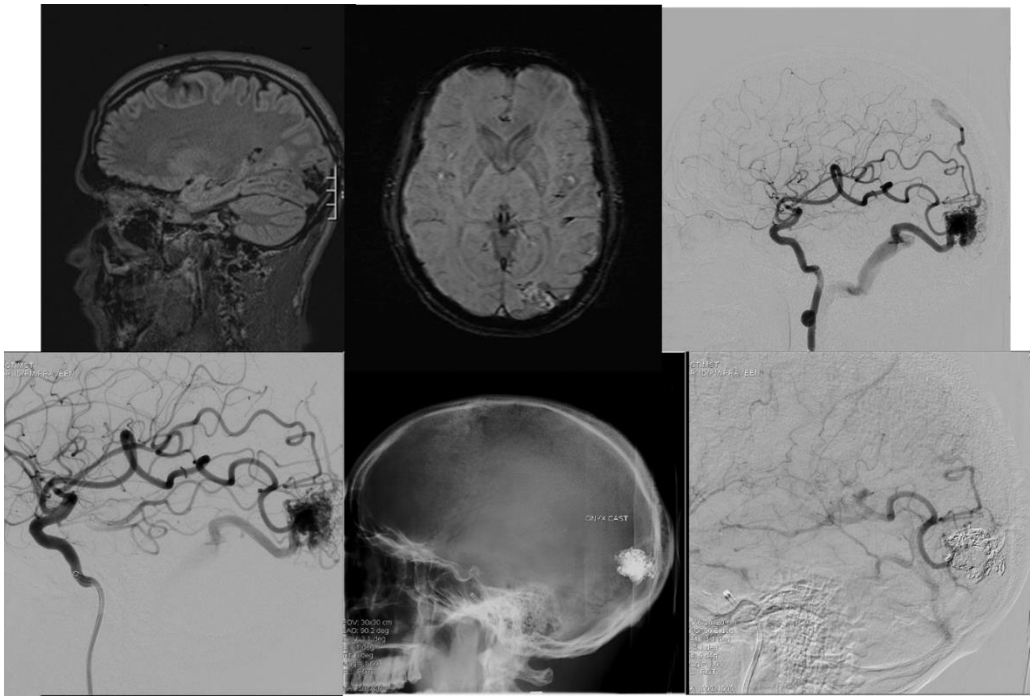
Of the patients with grade 2 (50-80% obliteration), 18 patients underwent SRS. One of these patients had bleeding during the latency period requiring surgery with development of clinical deficits. She later underwent surgical resection of the residual AVM as well.

Obliteration Grade	No.	SRS	Surgery	Awaiting Adjunctive Treatment / Conservative management
4 (100% obliteration)	10	0	0	10
3 (80-95% obliteration)	37	21	3	13
2 (50-80% obliteration)	33	18	1	14
1 (<50% obliteration)	36	20	0	16
Total	**116**	**59**	**4**	**53**

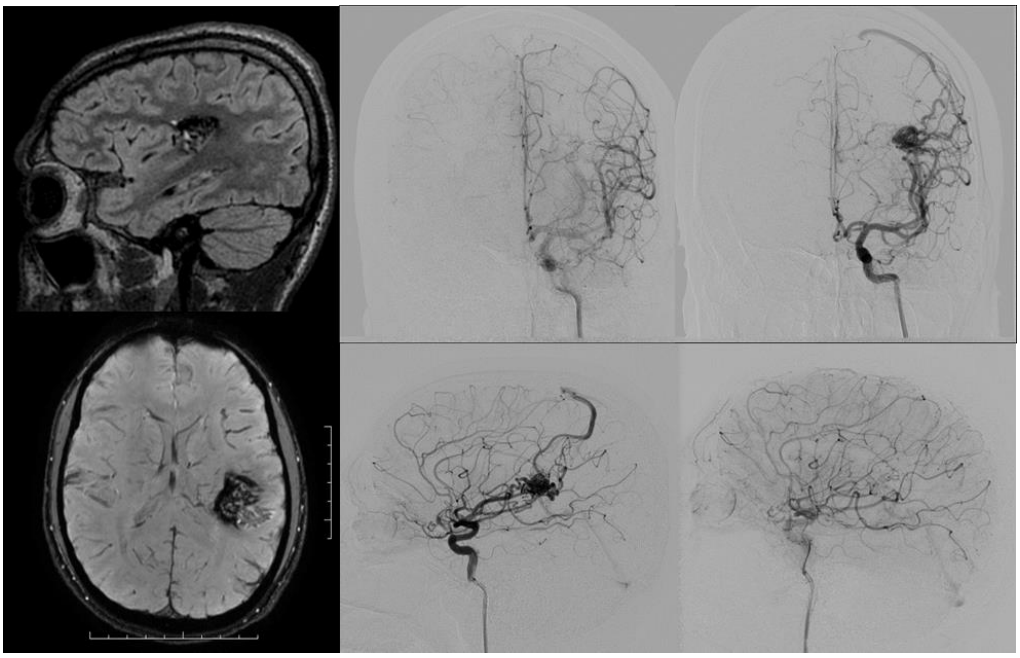
Table 26: Other modalities of treatment utilized in patient cohort.

REPRESENTATIVE CASES

REPRESENTATIVE CASES: Small Sized AVMs

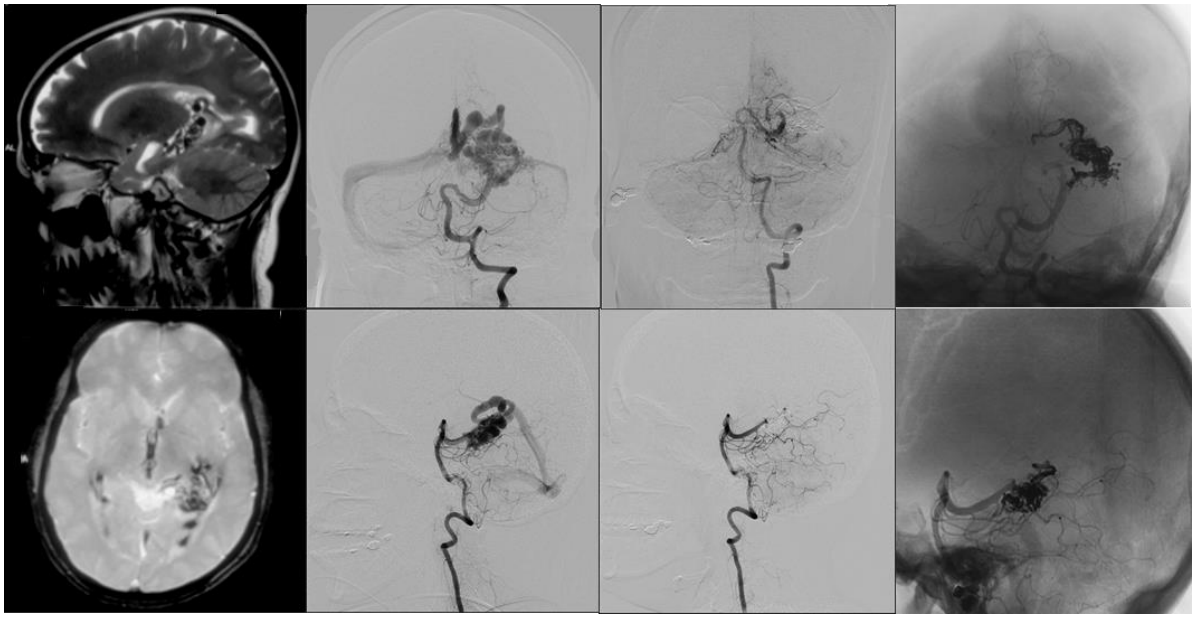


Case 1: This 22 year old male patient with seizures secondary to an SM grade 1 AVM (maximal dimension 2.7cms, idealized spherical diameter of 2.2cms) underwent embolization with 3.4ml of Onyx over 85 minutes through a single feeder cannulated using the Sonic microcatheter resulting in complete obliteration. No recurrence was noted at the 3 month check DSA.

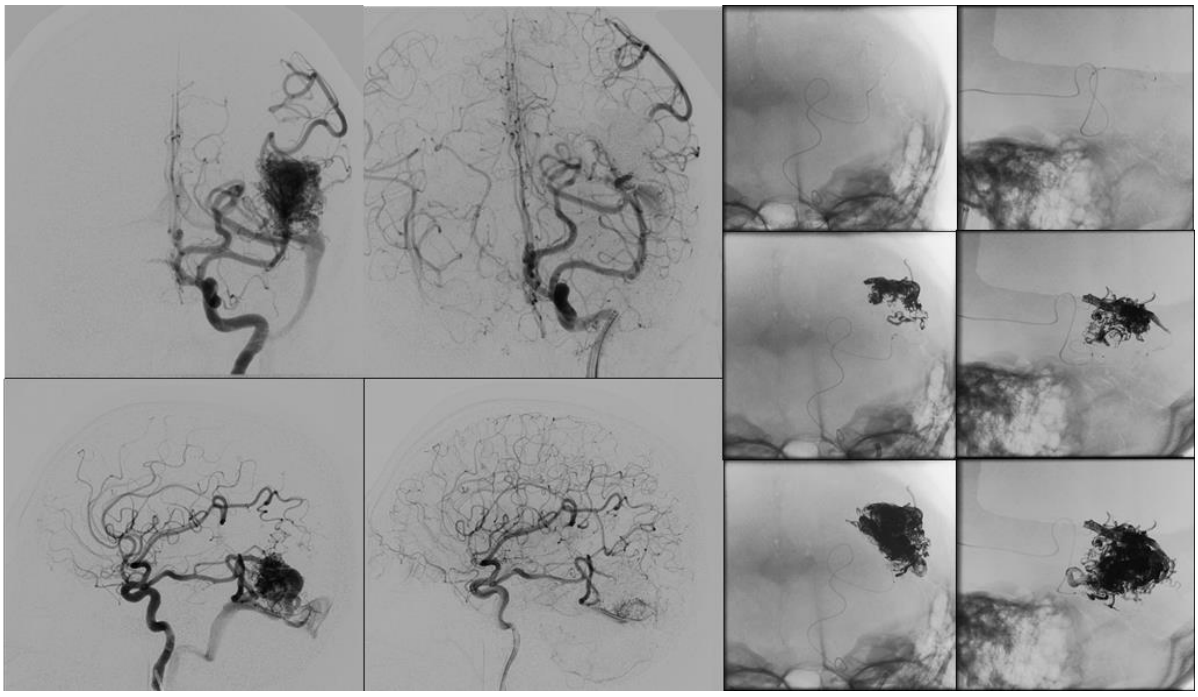


Case 2: This 22 year old male patient with lobar hemorrhage secondary to an SM grade 3 AVM (maximal dimension 2.2cms, idealized spherical diameter of 2.1cms) underwent embolization with 1ml of Squid over 45 minutes through a single feeder cannulated using the Apollo microcatheter resulting in near-complete obliteration with minimal deep residue. The patient underwent SRS and is awaiting a check angiography.

REPRESENTATIVE CASES: Medium Sized AVMs

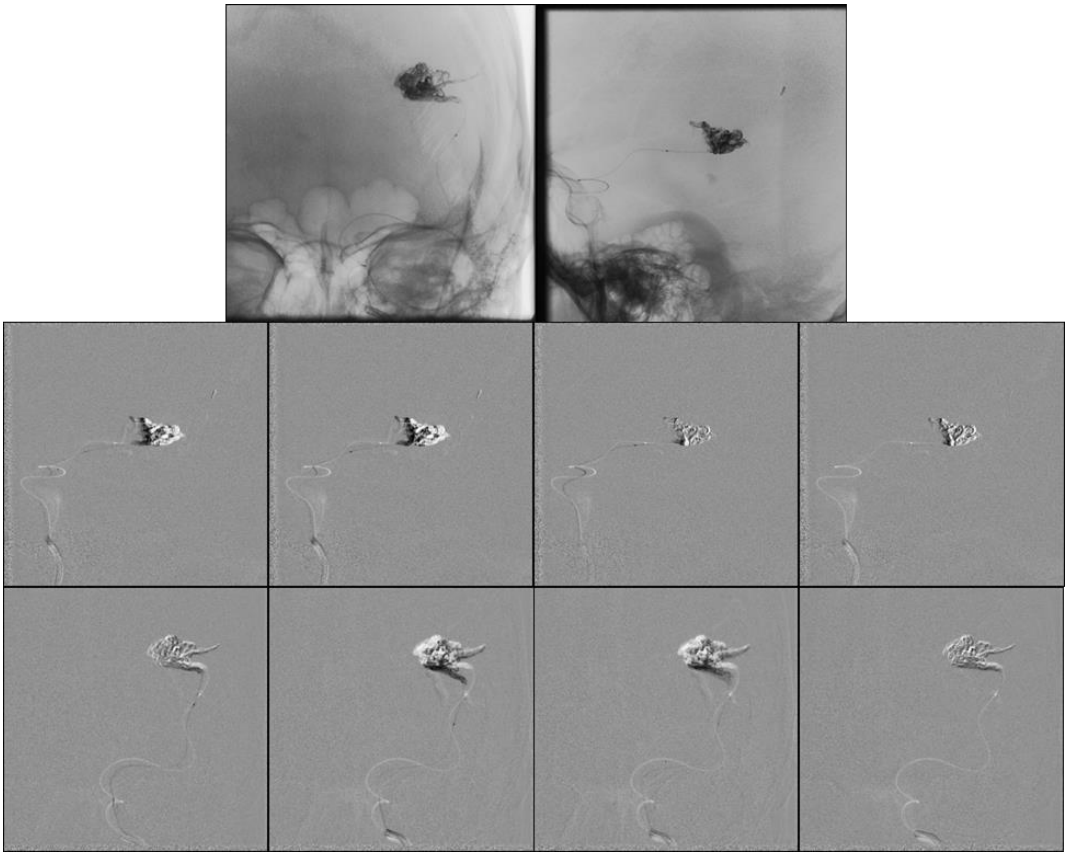


Case 3: This 50 year old female patient with intraventricular hemorrhage secondary to an SM grade 3 choroidal AVM (maximal dimension 3.1cms, idealized spherical diameter of 2.2cms) underwent embolization with 2.3ml of Onyx over 70 minutes through a single feeder cannulated using the Apollo microcatheter resulting in complete obliteration. No recurrence was noted at the 11 month check DSA.



Case 4: This 28 year old male patient with intracranial hemorrhage secondary to an SM grade 2 AVM (maximal dimension 3.1cms, idealized spherical diameter of 2.7cms) underwent embolization with 9.1ml of Onyx via 2 feeders over a total of 175 (75+100) minutes using the Sonic microcatheters resulting in near-complete obliteration. She is planned for SRS.

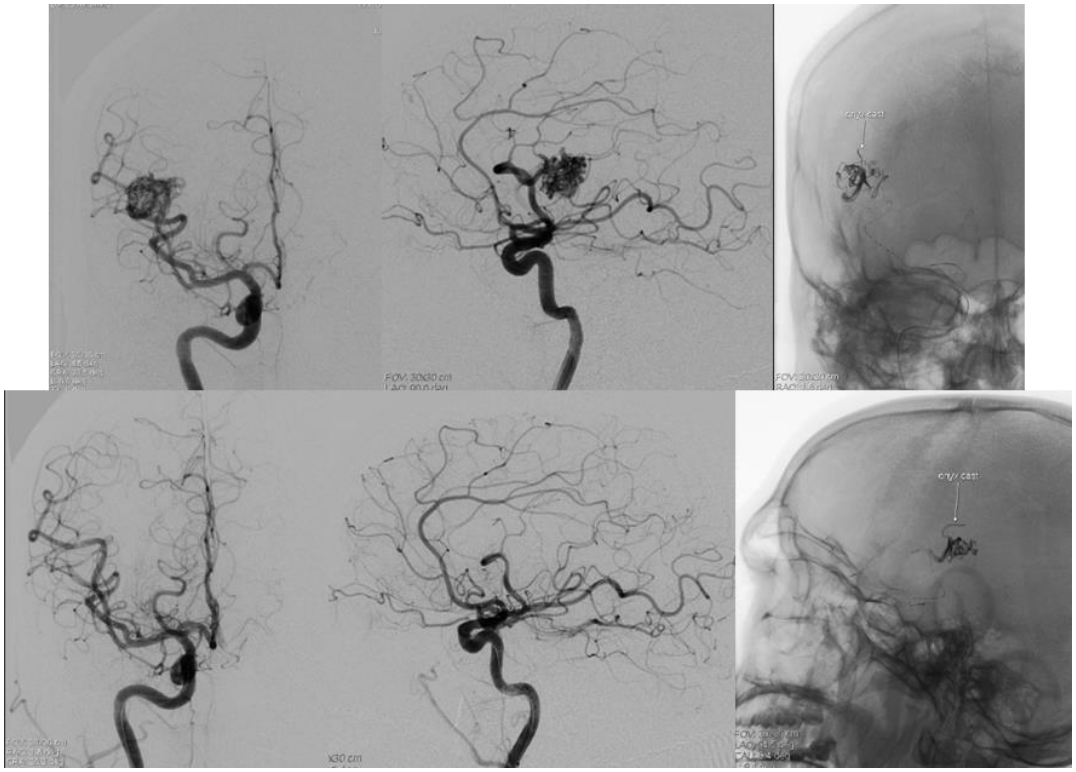
REPRESENTATIVE CASES: Microcatheter Retrieval with Tip Detachment



Case 5: This is the video frame capture of an Apollo microcatheter being retrieved with sustained traction over 1 minute resulting in a nidal movement of 4mm with detachment of the tip after embolization for 85 minutes. Retieval was uneventful with no clinical complications.

REPRESENTATIVE CASES: Complications

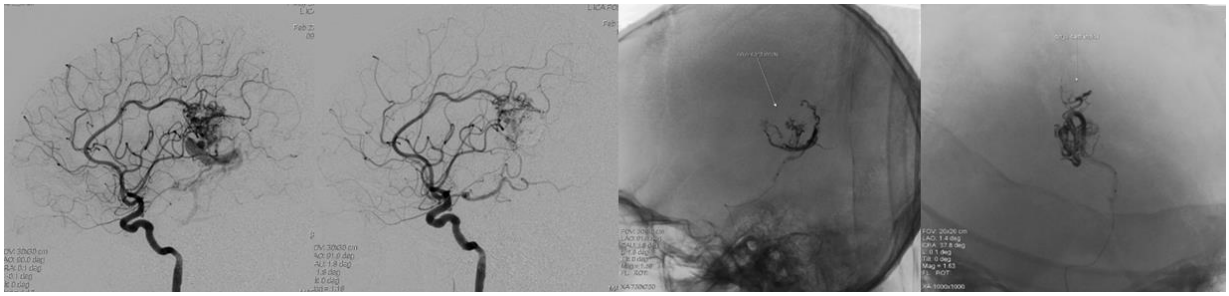
Conventional Microcatheter Entrapment



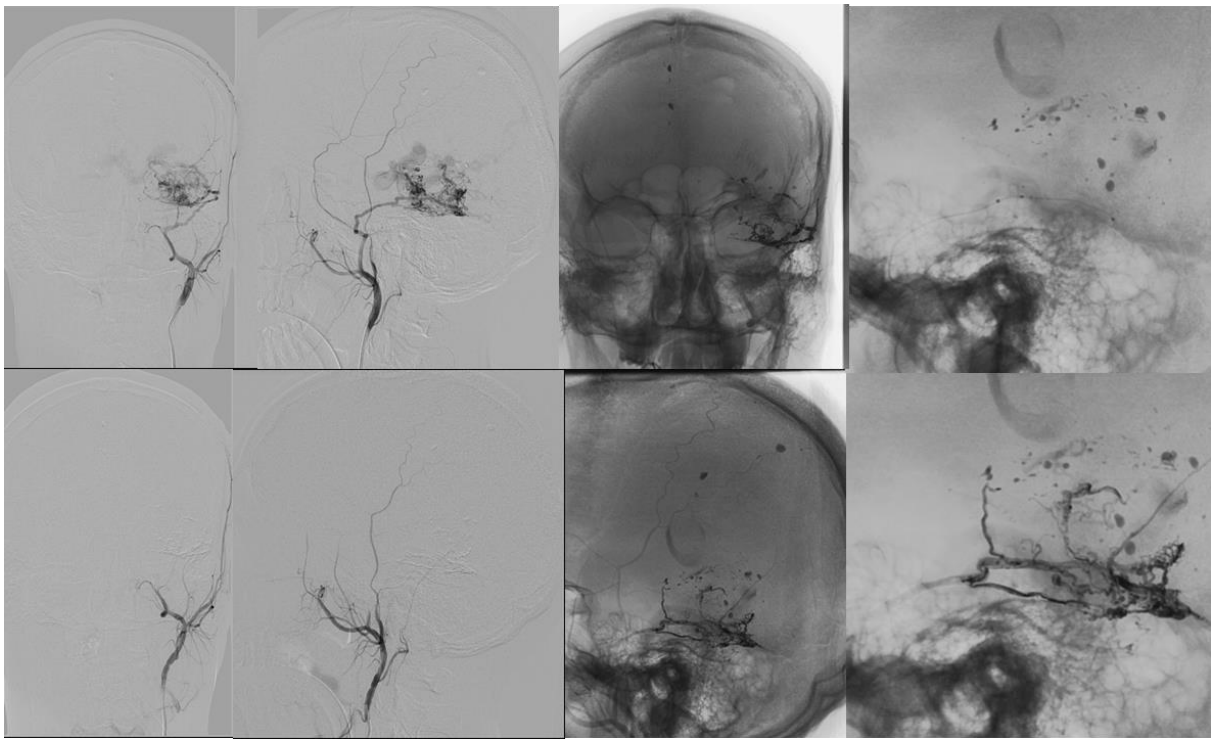
Case 6: This patient underwent embolization using a Marathon microcatheter with 2.5ml of Onyx injected over 55 minutes. Catheter entrapment occurred with the catheter cut at the groin. No clinical complications.

REPRESENTATIVE CASES: Complications

Detachable Tip Microcatheter Entrapment



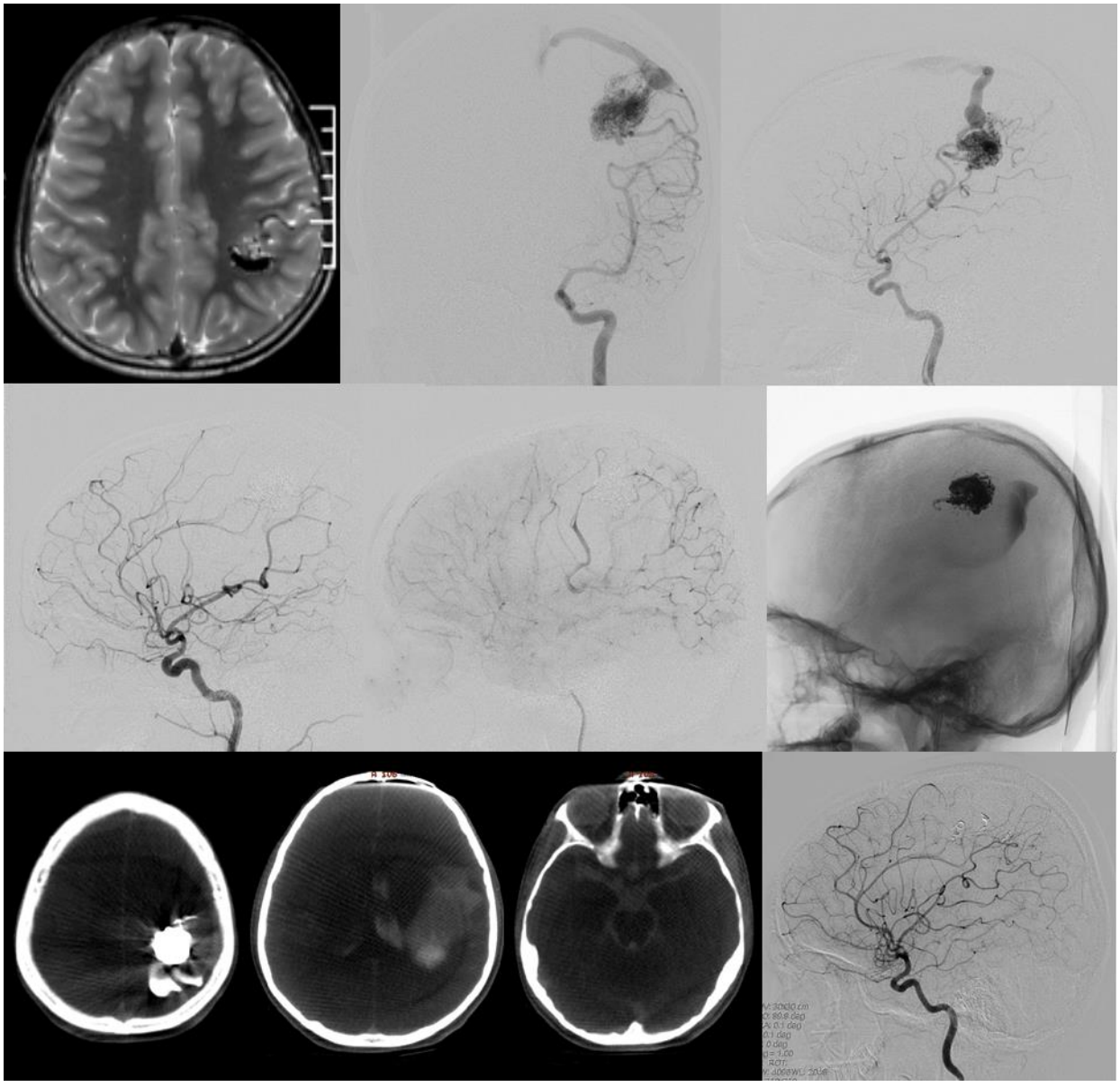
Case 7: This SM grade 1 lesion was embolized with 1.5ml of Onyx over 50 minutes. Note reflux of onyx beyond the detachment zone of this Sonic microcatheter.



Case 8: Another case of Sonic entrapment occurring due to reflux beyond the detachment zone during Squid embolization of a dural feeder of an SM grade 2 AVM. Glue cast from prior targeted embolization is visible within the rest of the nidus and draining veins.

REPRESENTATIVE CASES: Complications

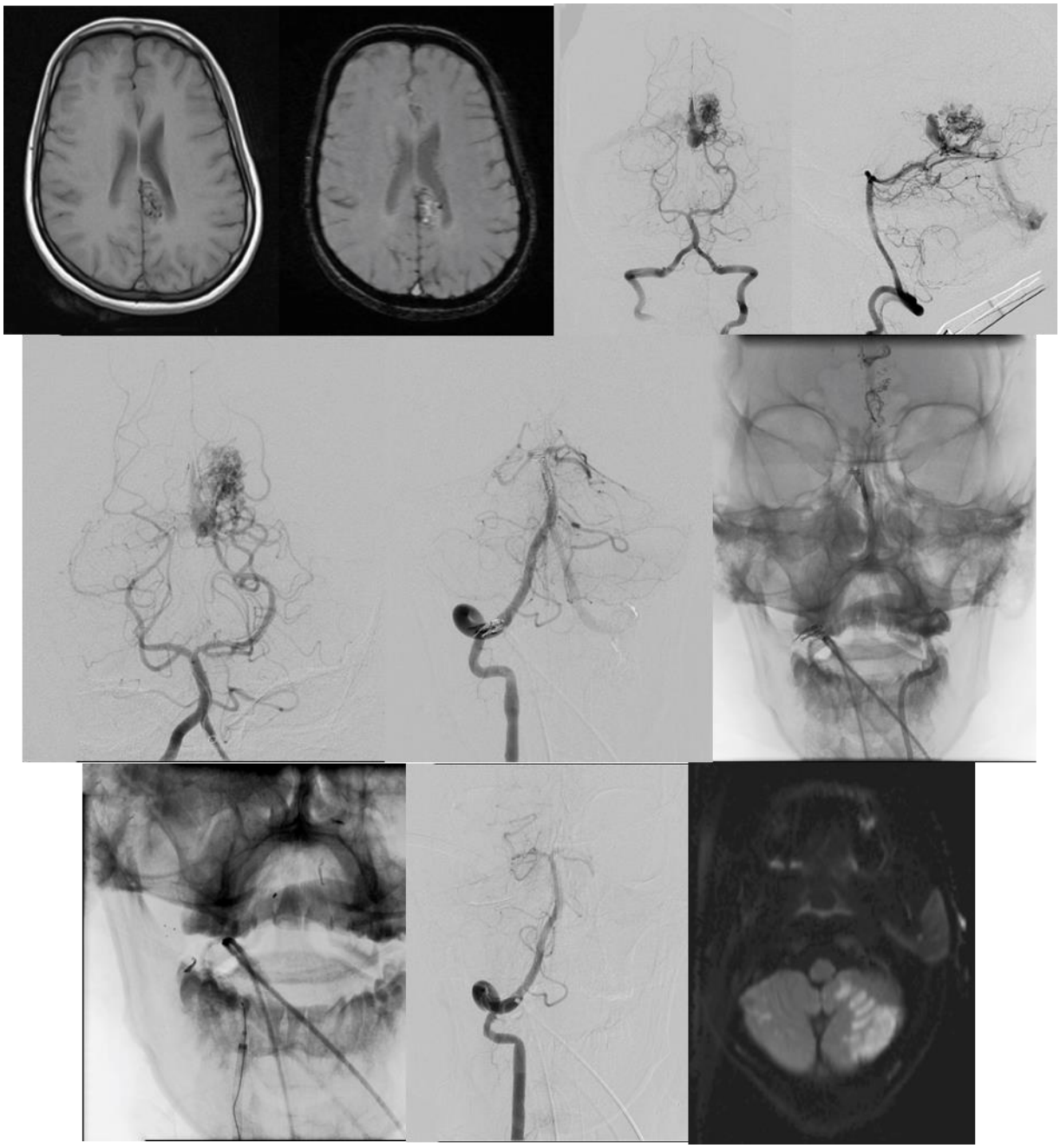
Intraprocedural Hemorrhage



Case 9: This 11 year old boy with seizures developed an intraparenchymal hematoma towards the end of near complete embolization of his SM grade 2 lesion. He underwent emergent craniotomy with evacuation of hematoma and resection of nidal remnants. Check DSA 3 months later shows no residual AVM.

REPRESENTATIVE CASES: Complications

Marathon Rupture with Onyx Intravasation



Case 10: This 25 year old female with an SM grade 2 cingulate AVM underwent embolization with a Marathon microcatheter. After obliteration of a significant portion of the nidus, sudden intravasation of the onyx occurred into the basilar top and right V4 vertebral artery. This was removed using the Solitaire stentriever successfully. However, the patient developed mild cerebellar signs secondary to infarcts of the AICA.

DISCUSSION

DISCUSSION

The present study is a retrospective analysis of the medical, imaging and treatment related records of all patients with brain AVMs who underwent liquid embolization at our institution between January 1st, 2010 to July 31st, 2017 with an aim to study the efficacy and safety of detachable tip microcatheters as compared conventional microcatheters in the endovascular treatment of this disease entity.

A **116 patients** with brain AVMs who underwent liquid embolization primarily with EVOH based embolic agents were included in the study. This is a relatively large sample size with only 2 other studies by Peirot et al[17] and Saatci et al[51] who included 117 and 350 patients respectively in their series on the efficacy of Onyx embolization having larger study populations(table 1) The only other study to compare detachable tip and conventional microcatheters by Maimon et al had a much smaller sample of 43 patients[37]. Strauss et al. did not compare different types of microcatheters, but merely described their experience with the Sonic in their cohort of 92 patients, 68 of whom had completed treatment.

Most patients (58.6%) **presented with** hemorrhagic stroke, consistent with natural history studies of AVMs. Most natural history studies in the 1980s reported a hemorrhagic presentation of over 70%[62,63], a trend that has persisted, albeit at a reduced rate after the introduction of non-invasive imaging at 45-72% (median 52%) in more recent large series[8,64,65]. This is also consistent with the most common age group to which patients belonged which was the 3rd and 4th decade, when hemorrhage was most likely to occur[66].

The study population was **divided into 2 groups**: those who underwent embolization exclusively or predominantly with detachable tip microcatheters (*group 1*) and those who underwent embolization exclusively or predominantly with conventional

microcatheters (*group 2*). These groups were subdivided on the basis of exclusive use of each type of microcatheter (group 1a and 2a), predominant use of each type of microcatheter (group 1b and 2b) and those for whom adjunctive targeted glue embolization was also performed (group 1c and group 2c). No significant difference in the Spetzler-Martin grade or size grade was found between the 2 major groups on statistical analysis – an important consideration when comparing results between these 2 groups.

Overall, patients underwent embolization over an **average** of 1.42 **sessions** with 1.75 **feeders**. This is largely consistent with most studies reporting between 1.2 to 2.5 sessions per patient[13]. When comparing only group 1a and 2a (i.e. embolized exclusively using EVOH agents and either detachable tip or conventional microcatheters only), fewer sessions and feeders were required (1.07 sessions and 1.14 feeders versus 1.13 sessions and 1.58 feeders). However, the overall number of sessions required and feeders cannulated in Group 1 (1.63 and 1.86) was slightly higher as compared to Group 2 (1.21 and 1.65). This could be explained by the fact that in general, more feeders were cannulated in the other groups due to multiple factors such as poor percolation, cannulation of smaller supplementary feeders and multiple targeted glue injections. Importantly it must be noted that the number of sessions or feeders need not necessarily be a good indicator of the efficacy of embolization since a staged embolization is considered prudent in order to avoid ischemic or hemorrhagic complications, particularly in large AVMs[26].

49 **feeders** were cannulated using the Apollo microcatheter, 32 with the Sonic microcatheter while 76 feeders were cannulated using the Marathon microcatheter. This is the largest series to involve using the Apollo microcatheter to date, while the only other large series to use the Sonic microcatheter were Maimon et al with 93 cannulations in 43

patients[37] and Strauss et al with 233 cannulations in 92 patients[20]. Most other large series have used the Marathon microcatheter[38,51].

Onyx-18 was the chief **embolic agent** used in 72 (62.6%) of patients as compared to Squid 12/18 which was used in 42 (36.5%) of patients. A single patient was embolized using both embolic agents. This is the largest case series as yet to utilize Squid with the only other descriptions being that of small series of multiple vascular lesions and tumors[67] and single case reports[68] all of whom recorded no complications related to the embolic agent. The use of Onyx in the embolization of brain AVMs has been well established[13,36]. We included at total of 12 patients, (4 in group 1, 8 in group 2), who underwent targeted embolization with NBCA glue since in all cases this did not result in a significant degree of nidal obliteration. The only study to compare detachable tip and conventional microcatheters also used adjunctive glue in a small number of their cases (3 of 43 patients)[37].

The **Spetzler-Martin grade** of an AVM is an important predictor of curative embolization, with lower grades having a higher chance of complete obliteration[13,20]. The percentage of SM grades I/II/III/IV/V distributed amongst the entire study population was 18.2/31.3/31.3/18.2/0.8%. The majority were SM grade II and III with equal numbers in each, while the rest were equally distributed in SM grades I and IV with only 1 case of SM grade V. This distribution is largely consistent with most other studies(table 27), however, Maimon et al and Strauss et al had a larger proportion of high grade SM IV and V AVMs[20,37].

Study	SM Grade (I/II/III/IV/V) Distribution (%)
He et al, 2005[52]	0/23/46/23/9
Mounayer et al, 2007[26]	5/37/41/17/1
Katsaridis et al, 2008[38]	7/18/39/33/4
Panagiotopoulous et al, 2009[56]	59 (I, II) / 16 (III) / 7 (IV, V)
Maimon et al, 2009[37]	7/12/21/32/28
Xu et al, 2011[58]	3/15/52/22/7
Abud et al, 2011[59]	18/29/35/18/0
Saatci et al, 2011[51]	15/30/28/20/7
Pierot et al, 2013[17]	17/38/24/21/1
Strauss et al, 2013[20]	30 (I, II) / 24 (III) / 46 (IV, V)
Present study	18/31/31/18/1

Table 27

The SM grade utilizes the **maximal dimension** of an AVM to classify them as small (<3cms), medium (3-6cms) and large (>6cms) with an aim to predict risk of surgical morbidity[69]. This classification of maximal size is also a predictor of curative embolization[17,70]. However, considering this important variable, a few recent studies mention this in their description of AVMs in their study populations. However, amongst the studies that do mention size, not all of them ascribe to this same classification. Mounayer et al graded the maximal diameters of AVMs not as per the SM system, but by a size of <2cms, 2-4cms and >4cms[26]. A smaller volume of an AVM, <6cc, is also considered a predictor of curative embolization[18]. However, instead of using volume as a rather obscure predictor of obliteration, we calculated an idealized spherical diameter calculated from the volume[60,61]. We adopted a classification of this idealized diameter into <2, 2-4 and >4cms since a volume of 6cc calculates into an idealized diameter of 2.25cms. We also classified AVMs as per the SM grade classification. A near equal number of AVMs in our study were <3cms (49.5%) and between 3-6cms (48.6%) in size with only 2 niduses that were larger than 6cms (1.7%). With regards to **idealized spherical diameter**, a majority of niduses were between 2-4cms in diameter (57.3%) with the remaining being <2cms (38.2%)

and >4cms (4.3%). Both in terms of maximal dimension and idealized spherical diameter no statistically significant difference was present between group 1 and 2, thus allowing a comparison of results between these 2 cohorts.

We classified a **good angiographic outcome** as those that achieved complete obliteration (100%) and near complete obliteration (>80%) similar to Katsaridis et al[38]. Additionally, in all cases of near-total obliteration, similar to the findings of Mounayer et al, we found that the residual niduses were ≤2cms in size, a dimension that corresponded with a higher rate of success of stereotactic radiosurgery (SRS) without an increased risk of poorer clinical or radiographic outcomes[26,71,72]. This classification of good angiographic outcome is hence apt for our study since the primary intent of embolization in our institute is predominantly adjunctive, with the residues being treated by stereotactic radiosurgery (SRS) or microsurgery.

We achieved **complete obliteration** of the nidus in a total of 11/116 patients (9.2%), with a higher number reached in group 1 (8/66, 12.1%) than in group 2 (2/40, 4.1%), although this difference was not statistically significant. All AVMs were in SM grades I-III. This obliteration rate is at the lower end of the spectrum of most other studies that utilized Onyx which averaged around a 30% rate of curative embolization with a range between 13-54% (table 1)[17,20,51-55,57,58]. This may be explained by our less aggressive approach with a primarily adjunctive embolization of brain AVMs. Ten of these 11 patients who achieved complete embolization underwent follow-up angiographies at an average of 6.4months (range 1-14months) post-treatment with **no recurrences** in this patient group. This rate of permanent cure by embolization is better than most other studies who reported recurrences usually of 1.1%[51] to 20%[53,56] to as high as 100%[52].

We achieved **near-complete obliteration** in 36/116 (31.1%) of patients in our study, concordant with similar rates achieved by Katsardis et al[38] of 34.6% and Mounayer et al[26] of 38%.

Thus, in total, we achieved a **good angiographic outcome** of 40.5%. This outcome was statistically better in group 1 than in group 2 with rates of 50% and 28.6% respectively (p=0.02, Fischer test). No other study compares the angiographic outcomes between these 2 types of microcatheters. Maimon et al was the only other study to compare detachable tip (specifically Sonic) microcatheters to conventional microcatheters focused instead on the volumes of onyx injected by each microcatheter type and not efficacy[37]. Strauss et al, also used the Sonic microcatheter in the majority of their cases, but did not compare obliteration rates between the two[20].

When **subclassified by SM grade,** no significant differences were seen between the obliteration rates (good angiographic outcome) with only a trend seen with SM grade II and III lesions, i.e. predominantly low grade lesions. This is consistent with similar results of higher rates obliteration with lower grade AVMs as found by Strauss et al[20] and Jordan et al[70].

When **subclassified by maximal dimension,** a statistically significant difference was found in rates of good angiographic outcome for medium sized (3-6cms) AVMs with 39.7% achieved with detachable tip microcatheters as compared to 13.6% with conventional microcatheters (p=0.03). A similar result was found when outcomes were **subclassified by idealized spherical diameter** of the AVMs with a statistically higher proportion of AVMs having a good angiographic outcome with detachable microcatheters (39.4%) rather than conventional microcatheters (16.6%)(p=0.03). This information may have important financial connotations especially in resource poor environments. No other studies have

compared the efficacy between the different types of microcatheters with regards to the sizes of AVM niduses.

A statistically higher **volume of liquid embolic agent** was injected via detachable microcatheter (2.18±1.26cc) than conventional microcatheters (1.26±1.41cc)($p<0.001$). This is consistent with the results of Maimon et al who had comparable volumes of onyx injected with Sonic and Marathon (2.5±2.2ml and 1.7±1.3ml respectively, $p<0.05$)[37]. We found a similar result with regards to the duration of injection with longer durations with detachable tip microcatheters than conventional microcatheters (54.05 ± 27.9mins vs 33.65 ± 28.34mins, $p<0.001$). This has not been compared in the study by Maimon et al. However, this duration of injection is higher than prior studies with durations of injection with conventional microcatheters varying between 3-72 minutes (mean 24 minutes)[26].

The Sonic microcatheter detached in 36.3% of embolizations with Onyx or Squid, while the Apollo microcatheter detached in 59.1% of cannulations. In the 2 cases of retention of the Sonic microcatheter, both were due to excessive reflux reaching beyond the detachment zone during our initial experience with this microcatheter. Both patients were started on single antiplatelet therapy with no clinical consequences. While both Maimon et al and Strauss et al, the 2 largest studies involving the use of the Sonic microcatheter do not report detachment rates, both had reported the same single case of Sonic retention similar to our case, where reflux extended beyond the detachment zone[20,37]. Ozturk et al also did not have detachment of the tip of the Sonic microcatheter after 16 minutes of NBCA injection in their case report[41]. The small case series involving the use of the Apollo microcatheter by Altschul et al and Paramasivam et al reported detachment in 25.9% and 45% of cases respectively[46,47].

We had a total of 11 **technical complications** in a 116 patients, with 162 cannulations (feeders) (9.4% per patient, 6.7% per cannulation). The most common complications was unintended catheter entrapment in 8 patients with no clinical consequences. These entrapments were more common when we embolized medium sized AVMs but this was not statistically significant. The microcatheter was in situ of for an average of 34.3minutes (range 15-55 minutes) to inject an average of 1.2ml (range 0.4 to 2.5ml) of onyx or squid. One case of premature detachment occurred with the Apollo microcatheter. No clinical consequences. Catheter blockage with a Marathon microcatheter occurred in the same patient. Maimon et al reported that catheter entrapments tended to occur in their cohort more commonly if they injected for a period of >50 minutes[37]. Permanent clinical morbidity in the form of mild cerebellar ataxia occurred in one patient with rupture of a Marathon microcatheter leading to non-target embolization of the vertebrobasilar arteries necessitating mechanical retrieval with a Solitaire stentriever. Fewer technical complications occurred when using the detachable microcatheter (4.3% vs. 9.7% with conventional microcatheters), suggestive of a better safety profile, but this was not statistically significant (p=0.228, Fischer test).

Clinical complications occurred in 6 patients, with 4 of these being intraparenchymal hemorrhages, 2 of them resulting in mild permanent neurological deficits. None were related to catheter entrapment with one case likely being due to normal pressure perfusion breakthrough in the post-procedure period. The other 2 clinical complications were those of strokes, with both patients developing mild clinical neurological deficits. One occurred due to unintended parent vessel embolic agent leakage due rupture of a Marathon microcatheter.

Thus the total **morbidity rate** in our cohort was 3.4% per patient. No mortalities occurred. This favors comparably with most other studies whose morbidity/mortality rate ranged between 6.8 to 17.7%[22,26,38,45,53,56].

Adjuvant treatment: 21 patients underwent stereotactic radiosurgery (SRS) with 9 patients confirmed to have nidus obliteration, while 3 underwent complete surgical resection of residues. These rates of obliteration with SRS and surgery are compatible with prior studies[73].

When we analyze the mode of our treatment approach to our patients with AVMs, we adopted relatively less aggressive strategy of primarily adjunctive embolization prior to radiosurgery or microsurgery. While our rates of curative embolization were relatively low at 9.2%, our rates of good angiographic outcome of nidal obliteration >80% was at 41%. Commensurate with our conservative approach we had a relatively low morbidity rate of 3.4% per patient, which is lower than that of most studies utilizing Onyx, and significantly lower than that of the often criticized ARUBA trial which had morbidity and mortality rates of 30.7%[10]. As noted by Jayaraman et al., surgery and radiosurgery both have higher cure rates of near 100% and up to 70% respectively with complication rates of 10-15% and <10% respectively, and therefore cautioned the universal application of curative intent in the embolization of AVMs[73]. Our results compare favourably both with the safety profile of other modalities as well as the natural history of the disease.

Limitations.

This analysis includes but does not account for learning curves of the interventionists in our institute with the use of both new embolic agents as well as the detachable tip microcatheters.

CONCLUSION

CONCLUSION

In summary, our retrospective analysis of a 116 patients showed that a statistically higher rate of good angiographic outcome was reached with the use of detachable tip microcatheters than with conventional microcatheters in the adjunctive liquid embolization of brain AVMs. Detachable tip microcatheters also allowed higher volumes of embolic agent to be injected over more prolonged durations with fewer technical and clinical complications. Further detachable tip microcatheters allowed significantly better obliteration rates particularly in medium sized AVMs rather than in small sized AVMs.

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ANNEXURES

PROFORMA

Sree Chitra Tirunal Institute for Medical Sciences & Technology

Proforma for "A Comparative Study of Detachable Tip Microcatheters Versus Conventional Microcatheters In Liquid Embolization of Brain AVMs."

General Instructions

- Please fill in all the questions.
- Write Yes / No/ NA wherever applicable.
- If the response is not known please write UK
- If additional info is available please elaborate
- Please use separate proforma for each admission
- If admission is for a post operative / intervention complication please go to section E after completing the general information

A. GENERAL INFORMATION: Anonymized Patient ID:

B. CLINICAL DETAILS

Mode of Presentation :

[Intracranial hemorrhage/ Seizures/ Headaches/ incidental/ others]

Examination findings

On initial examination

- GCS :
- Extraocular movements :
- Cranial nerve palsies :
- Weakness (if yes, specify) :

- Any other neurological findings :

C. INVESTIGATIONS

D. Management

1) Protocol initiated :

(Endovascular / Radiotherapy / Surgical) (state reason for choice if relevant)

2) If endovascular,

Date of procedure:

Which sitting of embolization:

3) Preprocedure work up:

Cross Sectional Imaging (CT / MRI) :

Nidus:

- Location :
- Type (Compact / Sparse) :
- Size :

Other factors:

- Hemorrhage (present / sequelae of past) :
- Gliosis :

4) Brief description of procedure:

- **Selective Angiographic Evaluation:**
  i. Arterial territories supplying the AVM
  ii. Feeding pedicles
  iii. High-flow arteriopathy (stenoses, ectasias, flow-related aneurysms)
  iv. Nidus (size, shape, location, flow, fistulas, ectasias, aneurysms)

v. Venous drainage (territories, deep, superficial)
vi. Individual draining veins
vii. High-flow venous angiopathy (dural sinuses, venous stenoses, occlusions and varices)
viii. Venous drainage of normal brain parenchyma.

- **Superselective Angiographic Evaluation:**
  i. Distal feeding pedicles (anatomy, aneurysms, geometry, hemodynamics)
  ii. Arterionidal junction
  iii. Nidus (compartments, direct AV fistulas, plexiform regions, intranidal ectasias, and aneurysms)
  iv. Venonidal junction
  v. Proximal aspects of the draining veins
- **Embolization Data**
  i. Intent of embolization (i.e. Presurgical, Preradiotherapy, curative or palliative)
  ii. Number and final selection of arterial feeder(s) through which embolization is attempted.
  iii. Choice of Embolization device used & its viscosity
  iv. Choice of Microcatheter used
  v. Nidus Obliteration achieved
  vi. Total volume of EVOH Co-polymer injected per session & per patient
  vii. Total time of injection of EVOH Co-polymer injected per session & per patient
  viii. Technical difficulties (catheter related and embolic device related) encountered during embolization – both by documentation in the operational records and by interview of the operating interventionist (in prospectively evaluated cases)
  ix. Number of sessions till complete embolization or till alternate modality used.

5) Technical Difficulties

- Catheter Related
  - Navigability
    - Time taken for navigation
    - Spasm induced?
    - Change of microcatheter

        - If changed, reason for change
    - Liquid Embolization Injection related
        - Clogging present
        - Extent of reflux around microcatheter tip
        - Percolation
    - Retrieval Related
        - Ease of retrieval (subjective)
        - Degree of cast movement (subjective)
        - Time taken for retrieval
- Liquid Embolic Device related
    - Time taken for Precipitation
    - Clogging
    - Percolation through nidus

5) Intra-procedural complications:

Catheter Related

- Microcatheter puncture
- Microcatheter fracture
- Catheter tip premature dissociation
- Failure of microcatheter tip non-dissociation

Liquid Embolization related

- Accelerated precipitation

Intraprocedural hemorrhage / Extravasation of contrast

E. POST PROCEDURE COMPLICATIONS (elaborate if needed)

Clinical Status for first 24 hours post procedure :

- Headache (Mild / Moderate / Severe)
- Other symptoms
- Electrolyte imbalance (if yes, specify) :
- Neurological deficit (if yes, specify) :

- Response to treatment : Complete recovery/ partial recovery/No improvement/ worsened
- Post-procedure intracranial hemorrhage :
- If yes, Surgery required for hematoma evacuation? :

Other Complications :

Total Hospital Stay :

Treatment Plan at discharge? : Clinical Follow-up alone / Further embolization / Radiotherapy /Surgery

In case of Death :

- Time from initial presentation:
- Direct cause of death:
- Pre-treatment or post treatment:
- Whether death due to treatment related complication:
- If yes , elaborate the complication and duration of survival after treatment:

F. FOLLOW-UP OUTCOMES:

Clinical Follow Up:

- Subsequent OPD Follow Up record (as available):

Radiological Follow-Up:

- Date of Procedure:
- DSA findings:

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DEPARTMENT OF IMAGING SCIENCES & INTERVENTIONAL RADIOLOGY

CONSENT FORM

TITLE OF THE STUDY: ***A Comparative Study of Detachable Tip Microcatheters Versus Conventional Microcatheters In Liquid Embolization of Brain AVMs.***

Study number: ***80.***

You are being requested to join this study as you have a rare condition that results in abnormal connections between blood vessels (arteries and veins) called an ArterioVenous Malformation (shortform: AVM) within the brain. As per the treatment options outlined, you will be undergoing liquid embolization with a substance that will block these abnormal connections.
The aim of this study is to evaluate the efficacy of embolization using different types of catheters. This study does not affect the type of treatment that you will receive, but will only assess observe and analyse the treatment procedure and outcomes. For this purpose, the data from your clinical records, investigations, Embolization procedures and follow up investigations will be accessed and analysed. This is to help refine and improve treatments for people with the same kind of disease.
The treatment procedure and risks will be explained to you separately by the doctors performing the procedure. If you like any more detailed information, we will be glad to discuss further with you. We hope to include about 80 people from this hospital in this study.

What is this study for?
Liquid embolization of AVMs uses a long tube called a microcatheter that goes all the way from the artery in your leg (where we usually put the needle) to the blood vessels of your brain. After a safe position has been reached close to the AVM, a glue like substance is injected into the AVM which solidifies and blocks the abnormal connections.
One of the risks associated with the older conventional type of catheters was that the catheter tip itself may sometimes get stuck in the glue like substance, which makes retrieval of the catheter difficult or impossible resulting in complications or need for surgery.
A newer type of catheter, one with a detachable tip has been recently made that has the advantage that the catheter can still be retrieved even if glued to the AVM, leaving only a small portion behind.
This project aims to study the efficacy and safety of these newer catheters in treatment of AVMs.

How will I know what kind of catheter is being used for me?
All patients since the 2013 are being treated using the newer kind of detachable catheters since we believe it to be safer. However this yet to be proven convincingly and hence our project will be studying the safety and efficacy of these newer catheters in comparison to patients in previous years, who were treated with older conventional catheters.

If you take part what will you have to do?
If you agree to participate in this study, you will not have to anything apart from the usual protocol that is required for routine treatment. No change will be made in your treatment.

Your personal identification will be kept confidential. We only require your permission to access data and images of your treatment and progress.

Can you withdraw from this study after it starts?
Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?
The risks associated with treatment of AVMs will be explained by the doctor before your procedure. This study does not change the treatment that is being given and is only an observational study. Any complications that arise during the course of embolization will be treated as per hospital protocol.

Will you have to pay for the catheters?
Yes, you will have to pay for the use of catheters, as they are approved for and already being routinely used in the treatment of AVMs. This study only analyses the efficacy and safety of these newer catheters.

What happens after the study is over?
This study will only review the details of treatment and its outcomes. You will asked to follow-up with the hospital only as per routine treatment protocol.

Will your personal details be kept confidential?
The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask Dr. Chinmay Nagesh (8547992347), Dr. Santhosh Kannath or Dr. Jayadevan ER (0471-2528369/304) or email: chinmay@sctimst.ac.in

Participant's name: Date of Birth / Age (in years):

I_____ _____,

son/daughter of _____ (Please tick boxes).

[ ] Declare that I have read the above information provide to me regarding the study: ***A Comparative Study of Detachable Tip Microcatheters Versus Conventional Microcatheters In Liquid Embolization of Brain AVMs*** and have clarified any doubts that I had.

[ ] I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights.

[ ] I also understand that the newer detachable catheters are used routinely in this hospital for the treatment of AVMs and that this study will only observe its efficacy and outcomes.

[ ] I also understand that as these catheters are part of routine treatment, I still have to pay for their use.

[ ] I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access

[ ] I understand that my identity will not be revealed in any information released to third parties or published.

[ ] I voluntarily agree to take part in this study.

[ ] I received a copy of this signed consent form.

Name:	Name of witness:
Signature:	Relation to participant:
Date:	Date:

(Person Obtaining Consent)
I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

_____ _____
Name and Signature of Person Obtaining Consent

PLAGIARISM CHECK

Plagiarism Checker X Originality Report

A Comparative Study of Detachable Tip Microcatheters Versus Conventional Microcatheters In Liquid Embolization of Brain AVMs

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MASTERCHART

Demographics					Location			Presentation	Angioarchitecture						Microcatheter		Embolic Agent				Complication			Adjuvant Therapy	Check DSA		
					1=F, 2=P, 3=O, 4=T, 5=C, 6=IV 7=BG, thal,cc	1=Superficial, 2=Deep, 3=Both	1=y 0=n	1=ICH 2=Sz 3=Headache 4=Incidental 5=Other	12345	A=<2.99cm, B=3-5.99cm, C>6cms	cm	a = 0-1.99cm, b= 2-3.99cms, c = >4cms	cm	cc	1= Marathon, 2=Ultraflow, 3=Sonic, 4=Apollo 5=Spinnaker 6=others	1=Yes, 0=No	1=Squid, 2=Ony, 3=Glue 4=alcohol 5=PVA 6=coils	ml		1 = <50%, 2=50-80%, 3=80-100%, 4=100%	0=None, 1=Retained, 2=Abandoned 3=Premature Dtach 4=Blockage 5=cath rupture	1=ICH 2=non-h'gic FND 3=Sz	0=Nil 1=fnd, 2=tia, 3=death	0 = Nil, 1=SRS, 2=S 3=Awaiting embo 4=Conservative	0=not done 1=awaited 2=Done	1=nil residue 2=recurrence 3=residue	months
Pt. No	Session no.	Feeder No	Age	Sex	territory	Location	Eloquence	Presentation	SM Grade	Ma Grade	Largest dia	Dia Grade	Calc Dia	Vol	Microcatheter	Detachment of Tip?	Embolization Material	Volume of Embolic Agent	Time	Final EmboObliteration grade	Technical Complications	Clinical Complication	Outcome	Adjuvant Therapy	Check DSA	Check DSA	Check DSA Months after Embo/srs
Group 1 (D)																											
1	1	1	22	1	3	1	1	2	1	A	2.7	b	2.27	6.19	3	1	2	3.4	85	4	0	0	0	0	2	1	3
2	1	1	24	0	2	1	0	1	1	A	1.7	a	1.18	0.88	4	1	1	2.6	90	4	0	0	0	0	2	1	4
3	1	1	30	1	3	1	0	1	1	A	2.4	a	1.79	3.02	4	1	1	1.5	55	3	0	0	0	1	1		
4	1	1	41	1	4	1	0	1	1	A	2.5	a	1.84	3.3	4	0	1	2	50	3	0	0	0	3	0		
5	1	1	48	0	3	1	0	1	1	A	2	a	1.8	3.06	4	1	1	2.4	45	3	0	0	0	1	1		
6	1	1	14	0	3,4	1	0	1	1	A	1.8	a	1.3	1.15	4	1	2	1.3	55	4	0	0	0	0	2	1	1
7	1	1	20	1	2,4	1	0	2	1	A	2.2	b	2.02	4.35	4	0	2	2.4	60	2	0	0	0	2	2	1	12
8	1	1	43	0	4	2	0	1	1	A	1.2	a	0.89	0.37	4	0	1	0.4	30	2	0	0	0	1	1		
9	1	1	28	1	2	3	0	1	1	A	2.6	a	1.8	3.09	4	1	1	1.4	55	2	0	0	0	1	1		
10	1	1	34	0	2	1	0	1	1	A	2.6	a	1.61	2.19	4	0	2	1.25	50	3	0	0	0	1	1		
11	1	1	11	1	2	1		4	2	A	2.5	b	2.11	4.98	4	0	2	3.95	120	3	0	1	1	2	1		
12	1	1	18	1	2	2	0	1	2	A	2.2	a	1.96	3.96	3	0	2	1.3	30	3	0	0	0	1	2	1	15
13	1	1	25	0	2	2	0	1	2	B	4.3	b	3.42	21.07	3	1	2	2.1	100	2	0	0	0	3	0		
14	1	2	28	1	3,4	1	0	1	2	B	3.1	b	2.67	10.04	3	0	2	3.3	75	3	0	0	0	-			
															3	0	2	5.8	100		0	0	0	3	0		
15	1	1	12	0	3	2	0	1	2	A	2.5	b	2.22	5.77	3	1	2	2.5	70	2	0	0	0	1	2	1	46
16	1	1	28	0	2	2	0	1	2	A	2.2	a	1.96	3.96	3	1	2	0.6	35	1	0	0	0	1	2	3	16
17	1	1	39	0	1	2	0	3	2	A	2.6	b	2.42	7.48	3	1	2	0.6	12	1	4	0	0	1	2	3	39
18	1	1	32	1	2	1	1	2	2	A	1.7	a	1.57	2.04	4	1	2	2	70	4	0	0	0	0	2	1	1
19	1	1	24	1	1	1	1	1	2	A	2	a	1.62	2.24	4	1	1	3.5	80	4	0	3	0	0	2	1	4
20	1	1	37	0	2	1	1	3	2	A	2.6	b	2.21	5.72	4	1	2	1.7	40	3	0	0	0	3	1		
21	1	1	31	0	1	1	1	2	2	A	2	a	1.58	2.08	3	0	1	0.75	25	2	0	0	0	3	0		
22	2	2	17	1	3,4	3	1	1	2	B	3.1	b	2.81	11.68	4	0	1	2.8	70	3	0	0	0	-			
															4	1	1	3.4	70		0	0	0	1	1		
23	1	1	26	1	2	1	0	1	2	A	1.8	a	1.67	2.44	4	0	1	1.9	60	3	0	0	0	1	1		
24	1	1	20	1	4	0	1	3	2	A	2.5	b	2.11	4.98	4	0	2	1.3	80	2	0	0	0	1	0		
25	1	1	24	1	2,4	1	1	1	2	A	2	a	1.69	2.56	4	1	1	2.45	65	4	0	0	0	0	0		
26	2	2	7	0	3	1	1	1	2	A	2.6	b	2.14	5.2	4	0	1	3.6	65	3				-			
															4	0	1	0.35	15		0	0	0	1	1		
27	1	1	27	1	1,2	2	1	3	2	A	2.7	b	2.52	8.43	4	1	1	3	55	3	0	0	0	3	0		
28	1	1	34	0	3,4	1	1	2	2	A	1.4	a	1.24	1	4	1	1	0.35	20	2	0	0	0	1	2	1	13
29	1	1	21	0	2	2	0	1	2	A	2.1	a	1.89	3.59	4	0	1	0.65	30	1	0	0	0	3	0		
30	1	1	14	0	2	1	0	1	2	B	3.6	b	2.43	7.52	4	1	1	2.9	80	2	0	0	0	1	1		
31	1	1	30	1	2,3	2	1	1	3	B	4.1	b	3.66	25.7	3	0	2	1.5	45	1	0	0	0	3	0		
32	1	1	27	1	1	3	1	2	3	B	5.5	c	4.14	37.2	3	0	2	3.5	60	2	0	0	0	3			
33	1	1	28	0	6	2	0	1	3	B	3.7	b	2.53	8.54	3	0	2	2.4	50	3	0	0	0	1	2	1	18
34	1	1	16	0	1	2	0	1	3	A	1.23	a	1.12	0.75	3	0	2	0.4	15	3	0	0	0	1	2	1	18
35	1	1	15	0	6	2	0	1	3	B	3.3	b	2.02	4.38	3	0	2	1.5	50	3	1	0	0	1	2	1	38
36	1	1	8	0	7	2	1	1	3	A	2.1	a	1.78	2.99	3	0	1	0.4	12	1	0	0	0	1	2	3	12
37	1	1	50	0	6	2	0	1	3	B	3	b	2.18	5.46	4	0	2	2.3	70	4		0	0	0		1	11
38	1	1	22	1	2	1	1	1	3	A	2.1	a	1.46	1.64	4	1	1	1	45	3	0	0	0	1	1		
39	1	1	14	0	3	1	1	1	3	A	1.8	a	1.53	1.89	4	1	1	1.5	45	4	0	0	0	0	2	1	3
40	1	2	42	0	5	1	1	5, IHT	3	B	4	b	3.01	14.4	3	0	1	0.7	15	2				-			
															3	0	1	2	45					-			
41	1	1	36	1	1	3	0	1	3	B	5.5	b	3.14	16.33	4	1	1	2.35	70	1	0	0	0	3	0		
42	1	1	12	0	5	2	1	1	3	A	2.6	b	2.42	7.43	4	0	1	0.4	6	1	0	0	0	1	2	3	5
43	1	1	16	1	1	2	1	2	3	B	4.2	b	2.94	13.44	4	0	2	3.8	75	2	0	0	0	3	2	3	25
44	2	2	17	1	1	1	1	2	3	B	4.8	b	3.81	29.01	4	0	2	2.7	60	3	0	0	0	-			
															4		1	3.8	65		0	2	2	1	2	3	18
45	1	1	31	0	4	3	0	2	3	B	3.2	b	2.63	9.6	4	1	1	1.7	130	2	0	0	0	3	0		
46	1	1	23	0	1	1	1	1	3	B	3.7	b	3.16	16.65	4	1	2	2	80	2	0	0	0	-	1		
47	2	2	27	1	4	2	0	1	3	B	3.9	b	2.85	12.18	4	0	1	2.75	60	3	0	0	0	-			
															4	0	1	2	55		0	0	0	1	1		
48	1	1	43	1	1	1	1	2	4	B	3.1	b	2.78	11.34	3	1	2	3.4	60	1	0	0	0	1	1		
49	1	1	48	1	5	1	1	2	4	B	3.4	b	2.79	11.39	3	0	2	1	30	1	0	0	0	1	2	1	27
50	1	1	55	1	??	2	0	1	4	B	5.4	b	3.56	23.65	3	0	2	1.8	40	1	0	0	0	3	2		
51	1	1	46	0	5	3	1	1	4	B	3.4	b	3	14.14	4	1	1	0.9	25	1	0	0	0	1	1		
52	2	2	32	1	1	3	1	5, IHT	4	C	7.8	c	4.55	49.5	4	1	1	3.7	90					-			
															4	0	1	3.7	80	1	0	0	0	-	0		
53	1	1	17	1	2,3	2	1	1	4	B	3.1	b	2.42	7.44	4	1	2	1.6	50	2	0	0	0	-	1		
54	1	1	46	1	3	1	1	2	4	B	3.2	a	1.7	2.64	4	1	1	2.75	50	3	0	0	0	3	2	3	1
55	2	2	21	1	4	3	1	2	4	B	4.8	b	3.57	23.97	3	0	1	2	20	2	1	0	0	-			
															4	1	1	2.8	90		0	0	0	1	1		
56	1	1	26	1	1	3	1	2	4	B	4.3	b	3.69	26.31	4	1	1	3.5	90	2	0	0	0	3	2	3	1
Group 1b (D>C)																											
57	1	2	33	0	1	1		2	1	A	1.8	a	1.37	1.35	3	0	2	3	45	4				-			
															1	x	2	0.3	10		0	0	0	-	2	1	14
58	3	4	13	0	6	2	0	1	2	A	2.3	a	1.58	2.07	1	x	2	0.4	20	2	0	0	0	-			
															1	x	2	0.6	15		0	0	0	-			
															3	1	2	0.5	15		0	0	0	-			
															4	0	2	0.8	20		0	0	0	1	1		
59	2	2	27	1	2	1	0	CCF like orbit	2	B	3.2	b	2.83	11.9	4	1	1	1.3	30	2	0	0	0	-			
															1	x	1	0.5	10		0	0	0	1	1		
60	1	2	59	1	2	2	1	1	4	B	3.1	b	2.5	8.19	3	1	2	6	90	3				-			
															1	x	2	1.5	45		0	1	1	2	0		
61	2	2	19	1	3	1	1	2	4	B	3	b	2.28	6.24	3	0	2	2	60	3	0	0	0	-			
															1	x	2	1.7	35		0	0	0	2	0		
62	2	3	42	1	3,4	2	1	1	4	B	3.4	b	2.68	10.09	4	1	1	1.65	40	3	0	0	0	-			
															1	x	1	0.5	15		0	0	0	-			
															1	x	1	0.5	6		0	0	0	1	1		
Group 2a (C.)																											
63	1	1	36	0	5	1	0	5, ataxia	1	A	2.3	a	1.78	3	1	x	2	2	35	2	0	0	0	4	2	3	42
64	1	1	14	1	2	1	0	2	1	A	1.4	a	1	0.5	1	x	2	0.4	30	3	0	0	0	0	0		
65	1	1	42	1	1	1	0	1	1	A	0.8	a	0.61	0.12	1	x	2	0.5	30	3	0	0	0	0	0		
66	1	1	20	0	2	1	0	1	1	A	1.1	a	0.98	0.5	1	x	2	1	35	3	1	0	0	0	0		
67	1	1	42	0	4	1	0	2	1	A	1.7	a	1.36	1.32	1	x	2	1.6	40	4	0	0	0	0	2	1	12
68	1	1	38	1	1	1	0	1	1	A	1.8	a	1.63	2.3	1	x	2	0.6	20	4	1	0	0	-		1	6

Demographics					Location			Presentation	Angioarchitecture						Microcatheter		Embolic Agent				Complication			Adjuvant Therapy	Check DSA			
				1=F, 2=P, 3=O, 4=T,	1=Superficial,		1=ICH 2=Sz 3=Headache 4=Incidental 5=Other	12345	A=<2.99cm, B=3-5.99cm, C>6cms	cm	a = 0-1.99cm, b= 2-3.99cms, c = >4cms	cm	cc	1= Marathon, 2=Ultraflow, 3=Sonic, 4=Apollo 5=Spinnaker 6=others	1=Yes, 0=No	1=Squid, 2=Ony, 3=Glue 4=alcohol 5=PVA 6=coils	ml		1 = <50%, 2=50-80%, 3=80-100%, 4=100%	0=None, 1=Retained, 2=Abandoned 3=Premature Dtach 4=Blockage 5=cath rupture	1=ICH 2=non-h'gic FND 3=Sz	0=Nil 1=fnd, 2=tia, 3=death	0 = Nil, 1=SRS, 2=S 3=Awaiting embo 4=Conservative	0=not done 1=awaited 2=Done	1=nil residue 2=recurrence 3=residue		months
Pt. No	Session no.	Feeder No	Age	Sex	territory	Location	Eloquence 1=y 0=n	Presentation	SM Grade	Ma Grade	Largest dia	Dia Grade	Calc Dia	Vol	Microcatheter	Detachment of Tip?	Embolization Material	Volume of Embolic Agent	Time	Final EmboObliteration grade	Technical Complications	Clinical Complication	Outcome	Adjuvant Therapy	Check DSA	Check DSA	Check DSA	Check DSA Months after Embo/srs
69	1	2	17	1	2	1	0	2	1	A	2.2	b	2.03	4.4	1	x	2	0.7	40	3	0	0	0	-				
															1	x	2	0.8	20		0	0	0	4	0			
70	1	1	55	1	3	1	1	1	1	A	2	a	1.51	1.82	1	x	2	0.8	20	2	0	0	0	-	0			
71	2	4	17	1	1	1	1	2	2	A	2.9	b	2.08	4.71	1	x	2	1.8	40	2	0	0	0	-				
															1	x	2	0.8	20		0	0	0	-				
															1	x	2	0.8	15		0	0	0	-				
															1	x	2	1.2	30		0	0	0	1	0			
72	1	1	60	1	6	2	0	1	2	A	2.7	b	2.42	7.45	1	x	1	0.8	25	1	0	0	0	1	2	3	13	
73	1	1	18	0	1	3	0	1	2	B	4.6	b	2.8	11.59	1	x	2	0.6	20	1	0	1	0	3	2	3	4	
74	1	2	11	0	1	3	0	2	2	B	3.3	b	2.66	9.9	1	x	2	0.2	10	1				-				
															1	x	2	0.4	15		1	0	0	1	0			
75	1	1	34	0	2	1	0	1	2	B	3.6	b	2.74	10.8	1	x	1	0.4	20	1	0	0	0	1	1			
76	1	2	21	0	1	2	0	1	2	B	4.1	b	3.12	16.05	1	x	2	0.9	35	2	0	0	0	-				
															1	x	2	0.8	30		0	0	0	1	2	1	21	
77	1	2	25	0	7, cc	2	0	1	2	A	1.8	a	1.51	1.83	1	x	2	0.5	35	3	0	0	0					
															1		2	0.5	25		5	2	1	1	0			
78	1	1	43	1	3	1	1	1	2	A	2.4	a	1.87	3.45	1	x	1	0.35	15	1	0	0	0	1	2	3	13	
79	1	1	28	1	1	1	1	1	2	A	2.8	a	1.74	6.3	1	x	1	0.4	10	1	0	0	0	-				
80	1	1	25	0	6	2	0	1	2	A	2.1	a	1.96	3.99	1	x	2	0.4	40	2	1		0	1	0			
81	1	1	53	1	6	2	0	1	3	B	3.4	b	3.14	15.75	1	x	2	0.35	7	1	0	0	0	1	1			
82	2	2	36	0	4,3	1	0	2	3	B	4.1	b	3.34	19.61	1	x	2	4	35	2	0	0	0	-				
															1	x	2	3	35		0	0	0	1	0			
83	1	1	52	1	3	3	0	3	3	B	3.6	b	2.86	12.36	1	x	2	6	150	3	0	0	0	1	2	1	13	
84	1	1	9	1	3	1	1	1	3	A	1	a	0.81	0.28	1	x	2	0.4	25	3	0	0	0	1	2	1	12	
85	1	2	30	0	1,2	1	1	3	3	A	2.5	a	2.11	4.95	1	x	2	3	35	3				-				
															1	x	2	0.5	40		0	0	0	1	2	1	43	
86	1	1	9	1	5	3	0	3	3	B	3.5	b	3.04	15.22	1	x	2	0.4	15	1	0	0	0	1	2	3	19	
87	1	1	19	0	3	2	1	1	3	A	2.5	b	2.2	5.62	1	x	1	0.25	10	1	0	0	0	0	0			
88	1	1	50	0	2,4	3	0	1	3	B	3.5	b	2.7	10.39	1	x	1	1.05	70	1	0	0	0	1	1			
89	1	1	30	1	6	2	0	1	3	B	3.1	b	2.04	4.47	1	x	1	0.45	20	1	0	0	0	1	1			
90	1	2	51	1	2	1	1	1	3	B	3.4	b	2.26	5.78	1	x	2	0.9	35	2	0	0	0	-				
															1	x	2	2.5	55		1	0	0	4	0			
91	1	1	30	1	6	2	0	1	3	B	3.1	b	2.04	4.47	1	x	1	0.45	20	1	0	0	0	1	1			
92	1	1	15	0	5	3	1	1	3	B	3.3	b	2.94	13.36	1	x	2	1	40	1	1	0	0	3	0			
93	2	3	11	1	6	2	0	3	3	B	3.3	a	1.25	1.03	1	x	1	0.5	15	2	0	0	0	-				
															1	x	1	0.3	5		0	0	0	-				
															1		1	0.2	5		0	0	0	1	1			
94	2	3	41	1	3	3	1	3	4	B	3.6	b	3.27	18.36	2	x	2	2	45	3				-				
															2	x	2	1.2	35					-				
															2	x	2	1.3	30		0	0	0	4	0			
95	2	3	32	0	1,2	1	1	1	4	B	3.6	b	2.84	12.09	1	x	2	3	70	2				-				
															2	x	2	1	25		2	0	0	-				
															1	x	2	1	40					1	0			
96	1	1	28	1	2	3	1	2	4	B	4	b	3.6	24.5	1	x	2	0.5	15	1	0	0	0	3	0			
97	1	1	40	1	5	3	1	5, trigeminal neuralgia	4	B	3.2	b	2.72	10.56	1	x	2	0.2	15	1	0	0	0	3	0			
98	1	1	49	1	4	3	1	2	4	B	4.3	b	3.23	17.8	1	x	2	3	55	1	0	0	0	1	1			
99	1	2	14	0	2,3	3	1	3	5	C	8.8	c	6.63	153.12	1	x	2	1.3	40	1				-				
															1	x	2	0.6	10		0	0	0	4	0			
Group 2b (C>D)																												
100	2	3	65	1	2	1	0	1	2	B	4.8	c	4.08	35.64	3	0	2	0.4	10	1	4	0	0	-				
															1	x	2	0.5	15		4	0	0	-				
															1	x	2	1	45		0	0	0	3	0			
101	1	2	22	1	2	1	1	1	2	A	2	a	1.68	2.52	3	1	2	2	40	3				-				
															1	x	2	0.4	10		0	0	0	1	0			
102	1	1	27	0	4	3	0	1	3	B	5.1	c	4.01	33.91	1	x	2	8.8	160	2	0	0	0					
103	1	2	22	0	1,2	1	1	2	3	B	3.5	b	3.27	18.37	1	x	2	4.5	45	2				-				
															3	0	2	2	30		0	0	0	1,2	0			
Excluded from Group Analysis																												
104	1	2	20	1	2	1	1	1	2	A	2.3	a	2.12	5.02	4	1					3	x	0	-				
															1					0	4	x	x	1	1			
EVOH + GLUE Group 1c (D+G)																												
105	1	2	40	0	1	2	1	1	2	A	2.7	a	1.83	3.24	5	x	3	1.2	20	3				-				
		1													3	0	2	4	70		x	x	x	1	2	1	18	
106	3	4	32	1	1	1	1	2	3	B	4.2	b	3.39	20.41	3	0	3			2	x	1	0	-				
		3													3	1	2	4	90		x	x	x	-				
															3	1	2	3.4	75		x	x	x	-				
															1	x	2	1	20		x	x	x	1	0			
107	3	3	43	1	2,4	3	1	1	4	B	4.3	b	3.99	31.6	3	1	1	3	60	1	x	x	x	-				
		2													6	x	1	2.7	110		x	x	x	-				
															1	x	3				x	x	x	3	0			
108	2	3	32	0	5	3	1	3	4	B	3.3	a	2.69	10.24	1	x	3	0.5		3	x	x	x	-				
		2													4	1	2	3	55		x	x	x	-				
															4	1	2	1	25		x	x	x	1	2	3	30	
Group 2c) C+G																												
109	1	2	19	1	3	1	0	1	1	A	1.8	a	1.17	0.86	1	x	2	0.6	30	3	x	x	x	-				
		1													1	x	3	0.2			x	x	x	1	2	3	48	
110	1	2	44	1	2	1	0	1	1	A	2.1	a	1.89	3.59	5	x	3	2		1								
		1													1	x	2	0.3	20									
111	1	2	26	1	2	2	0	1	2	A	1.7	a	1.49	1.76	1	x	3	0.4		2				-				
		1													1	x	2	0.3	7		x	x	x	1	0			
112	2	4	13	1	3,4	1	0	2	2	B	5.2	b	3.26	18.3	1	x	2	2.8	110	3	x	x	x	-				
		3													1	x	2	0.7	25		x	x	x	-				
															5	x	3	2			x	x	x	-				
															1	x	2	1.6	50		x	x	x	1	2	3	24	
113	1	2	43	1	1,4	3	1	2	3	B	3.4	b	2.85	12.24	5	x	3	0.5	3	1				-				
		1													1		2	2.7	45		x	x	x	1	2	3	31	
114	1	2	53	1	7, cc	2	1	2	3	A	2.9	b	2.22	5.78	1	x	1	0.7	25	1								
		1													1	x	3	0.75			x	x	x	3	1			
115	2	2	37	1	1	1	1	2	3	B	4.8	b	2.19	5.5	1	x	3			2				-				
		1													1	x	1	0.4	15		x	x	x	1	1			
116	2	4	44	1	1	1	1	2	4	A	2.8	b	3.7	26.64	5	x	3	2		1	x	x	x	-				
		2													5	x	3	1			x	x	x	-				
															1	x	2	0.5	25		x	x	x	-				
															1	x	2	0.9	30		x	x	x	1	2	3	24	