BRAIN AVM EMBOLIZATION WITH ONYX

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CERTIFICATE

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INTRODUCTION

Arteriovenous malformations of the brain (brain AVMs) are disease characterized by a network of abnormal direct vascular channels between the arterial feeder and the draining vein without an intervening capillary network. These are relatively rare central nervous system lesions that results in significant long-term morbidity and mortality. These were first described about a century ago and have been considered as difficult entity to be treated.

AVMs can clinically present with seizures, headache, focal neurodeficits and life threatening intracranial hemorrhage. In the symptomatic group, AVMs are increasingly being recognized as a possibly treatable cause of various neurologic manifestations produced. More and more clinically silent AVMs are also being diagnosed due to advances in Imaging. Annual average risk of hemorrhage in such cases stated is 1-2%.

Current treatment options include microvascular neurosurgery, stereotactic radiation (radiosurgery), and endovascular embolization. Embolization is an important, well-established modality for brain AVM treatment that can be used alone or in combination with surgery or stereotactic radiosurgery. Embolization is, however, associated with significant risks and limitations that must be carefully balanced against the potential benefits in each patient.

Luessenhop and Spence first introduced the embolization of brain AVMs in 1960. Since then, this modality is rapidly evolving due to advances

in angiography equipment, development of newer microcatheter and embolising agents resulting in overcoming its technical limitations and risk to a significant extend. Various agents have been used for embolization in past including silk threads, coils, ethanol, PVA particles with limited success and high rates of recurrence. In the recent years, use of liquid embolic agents such as NBCA was in vogue with relatively better embolization and practically no recurrence. However, NBCA requires significant technical skill and poor control during injection. In 1990 Taki, et al., developed the original formulation of Onyx (Onyx Liquid Embolic System; Micro Therapeutics, Inc., Irvine, CA) which is a new co-polymer (EVOH) with proclaimed better penetration and controlled, prolonged injection. This new agent has made embolization technically less demanding and is claimed to have better nidus obliteration rates.

Available data which is mostly western has been generally applied to our context regarding clinical presentation. Management strategies also differ as economic and technical considerations are different. The study will highlight any clinical and radiological similarities and differences in Indian population regarding onyx embolization of AVM as compared to available data which is western. There are no large series from India till date about this novel agent used in AVM embolization and SCTIMST is one of the institutes in India doing maximum number of AVM embolization. The study will also try to formulate revised workup and management protocol of the Institute (SCTIMST) for these patients in light of the results.

AIMS AND OBJECTIVES

This is a prospective and retrospective study to analyze clinical & radiological characteristics, efficacy of management by embolization using onyx and complications (if any) in patients with brain arterio-venous malformations (AVMs) who reported to SCTIMST between 1 Jan 2008 and 31 May 2014.

1. To describe clinical and radiological features in patients with brain AVM for better understanding the natural history of AVM.
2. To assess the effectiveness of embolization for brain AVM.
3. To find out difficulties and complications during management of AVM
4. To evaluate radiologic & clinical outcome in patients treated with onyx embolization.

REVIEW OF LITERATURE

INTRODUCTION

Brain arteriovenous malformations (AVMs) are relatively rare central nervous system lesions that are the cause of significant long-term morbidity and mortality. They were first described about a century ago and have been considered to be difficult entity to be treated. AVMs can clinically present with seizures, headache, focal neurodeficits and life threatening intracranial hemorrhage. In the symptomatic group, AVMs are increasingly being recognized as a possibly treatable cause of various neurologic manifestations produced. More and more clinically silent AVMs are also being diagnosed due to advances in Imaging. Annual average risk of hemorrhage in such cases stated is 1-2%. Current therapeutic options include microvascular neurosurgery, stereotactic radiation (radiosurgery), and endovascular embolization. Embolization is an important, well-established modality for brain AVM treatment that is usually combined with surgery or stereotactic radiosurgery. Embolization is, however, associated with significant risks that must be carefully balanced against the potential benefits in each patient. Embolization performed by experienced interventional neuroradiologists in appropriately selected cases improves the overall safety and efficacy of brain AVM treatment.

CLASSIFICATION AND PATHOGENESIS OF CEREBRAL VASCULAR MALFORMATIONS

Cerebral vascular malformations have been studied since the 18th century. Nonetheless, clinically useful classification schemes have only been developed recently. Initially, vascular malformations were categorized by their gross pathological appearance, resulting in confusing and contradictory nomenclature that created a barrier to understanding their etiology, natural history, and clinical management[1].

A new biological classification for vascular lesions was proposed in 1982[2]. Two major categories were identified: hemangiomas and vascular malformations. Lesions with growth potential shown by proliferation of endothelial cells with active DNA synthesis were defined as hemangiomas and were considered vascular neoplasms. Lesions without endothelial cell proliferation or active DNA synthesis and displaying proportionate growth were named vascular malformations and were thought to be hamartomas rather than neoplasms. Vascular malformations were subdivided into arterial, capillary, venous, lymphatic and combined types[2].

Four categories of intracranial vascular malformations have been defined on the basis of gross and microscopic pathological data: AVM, capillary telangiectasia, cavernous malformation, and venous malformation[3].

A mixed malformation also has been described[4]. These have been considered congenital lesions, present from birth without the potential for significant cellular proliferation or de novo postnatal development.

Brain AVMs have cerebral arterial feeders directly connected to the venous system without an intervening capillary bed, resulting in high-flow arteriovenous (AV) shunts. The nidus (Latin for nest) contains the direct AV connections. The vessels in the nidus vary in size and histology from relatively well-differentiated arteries and veins to thick and thin walled, hyalinized, malformed vessels that are neither. Dilated segments of vessels commonly occur. There is gliotic brain parenchyma within and around the nidus. Gross or microscopic calcification may be present with the vascular walls or in the gliotic parenchyma. Hemosiderin is commonly present, indicative of some degree of prior hemorrhage. The gross pathological appearance has been aptly described as a ‘‘bag of worms’’.

Most brain AVMs occur sporadically; however, they also are associated with a number of congenital or hereditary syndromes, including: Rendu-Osler-Weber syndrome (hereditary hemorrhagic telangiectasia), Klippel-Trenaunay syndrome, Parks-Weber syndrome, Wyburn-Mason syndrome, and Sturge-Weber disease[5]. Rare familial cases not associated with syndromes also have been described.

There is recent evidence that not all brain AVMs are congenital in origin[5]. Although the large majority probably occurs congenitally because of the failure of capillary formation during early embryogenesis[6], some brain AVMs appear to form in response to a postnatal stimulus of angiogenesis, particularly in younger patients. The de novo development of brain AVMs in a child[7] and in an adult[8] has been reported. Also, brain AVMs has recurred in children after complete surgical resection[9].

EPIDEMIOLOGY OF BRAIN AVMs

Most of the estimates of the prevalence of brain AVMs are flawed and potentially inaccurate. The widely quoted prevalence estimates of 500 to 600/100,000 were based on biased autopsy data. Another erroneous estimate of 140/100,000 was based on an inappropriate analysis of the Cooperative Study of Intracranial Aneurysm and Subarachnoid Hemorrhage data. These estimates may represent greater than 10-fold overestimates of the true prevalence[10]. A comprehensive review of the published literature performed in 2001 identified only three population based studies of the incidence and/or prevalence of brain AVMs, all retrospective in nature[11]. The Mayo Clinics identified a total of 48 intracranial vascular malformations in the population of Olmstead County, Minnesota, over a period of 27 years, from 1965 to 1992. The brain AVM detection rate was 1.11 (95% CI, 0.7–1.5) per 100,000 person-years[12]. The incidence of symptomatic brain AVMs was 1.1 (95% CI,

0.6–1.8) per 100,000 patient-years in the Leeward Islands of the Netherlands Antilles between 1980 and 1990[13]. A retrospective study in the Lothian region of Scotland found a minimum point prevalence of 15 symptomatic brain AVMs per 100,000 in unselected living adults[14]. In 2003, a prospective population based study of brain AVMs in the New York Islands (Manhattan, Staten Island, and Long Island) with 9.4 million residents reported an AVM detection rate of 1.34 (95% CI, 1.18–1.49) per 100,000 person-years. The estimated prevalence of brain AVM hemorrhage within the detected cases was 0.68 (95% CI, 0.57–0.79) per 100,000[15]. The currently available data do not suggest that there is a large reservoir of asymptomatic brain AVMs in the general population, but that most brain AVMs become symptomatic during life.

NATURAL HISTORY OF BRAIN AVMs

The risks of treating a brain AVM must be weighed against the natural history of the disease, in particular the possibility that a brain AVM will bleed or re-bleed if it is not treated and the associated potential clinical consequences. Unfortunately, little unbiased natural history data are available, in part, because brain AVMs are relatively rare and quite heterogeneous and also because most undergo some form of treatment. No level I or level II natural history studies have been published[16]. Data on specific predictors for the clinical course of a specific brain AVM are even more limited. In many

natural history studies there is a selection bias toward untreatable AVMs. In addition, natural history outcomes usually have not been correlated with the type of presentation, the analyses have differed and follow up periods have been short.

Despite these limitations, some general observations can be made about the natural history of brain AVMs. Clinical presentation can occur at any age, with the mean age of presentation in the fourth decade of life. There is an essentially equal distribution between sexes[11]. Brain AVMs most commonly present with intracranial hemorrhage, epilepsy, headache, or a focal neurological deficit, although they are occasionally found incidentally[11]. Intracranial hemorrhage is the most common form of clinical presentation. In a prospective population-based study published in 1996, 65% of patients newly diagnosed with a brain AVM presented with intracranial hemorrhage[17]. Intraparenchymal hemorrhage occurred in 41% of these cases, subarachnoid hemorrhage in 24%, intraventricular hemorrhage in 12%, and a combination of these types in 23% of cases. The more recent prospective population-based study of brain AVMs in the New York Islands reported that 38% of patients with newly found AVMs presented with intracranial hemorrhage[15].

Hospital-based case series have been retrospectively analyzed to identify risk factors for brain AVM hemorrhage[11]. These findings have not been confirmed by prospective population-based studies. The features most

consistently associated with an increased risk of hemorrhage include deep venous drainage, a single draining vein, venous stenosis, and high-feeding mean arterial pressure[11]. These may share the common hemodynamic mechanism of associated high intranidal pressures[18]. Less consistent risk factors for hemorrhage are a small AVM size, feeding artery and intranidal aneurysms, and deep or posterior fossa locations[11]. Sex and pregnancy do not appear to increase the risk of hemorrhage[19].

Features that may be associated with a decreased risk of hemorrhage include a large AVM size[20], arterial stenosis and ectasia[21], dural arterial supply[22], venous recruitment[23], and angiogenesis[24].

The second most common form of clinical presentation is epilepsy. In one retrospective population-based study, 19% of newly discovered AVMs presented with seizures[17]. In two retrospective hospital-based studies, 18% and 27% of AVMs presented with seizures, respectively[25, 26].

Other less common brain AVM presentations include headache (1% and 11% in two hospital-based series)[25, 26], focal neurological deficit (7% and 5% in two hospital-based series) [25, 26] and as an incidental finding in an asymptomatic individual (15% in one population-based study, 0% and 3% in two hospital based series) [25, 26].

There are extremely limited data on the natural history of brain AVMs following the initial diagnosis. An annual 2% to 4% risk of first-ever hemorrhages from a brain AVM is widely quoted on the basis of a few hospital-based series[27, 28]. No prospective, population-based study of the clinical course of unruptured brain AVMs has been published[11]. After an initial bleed, the risk for recurrent hemorrhage may be as high as 18% in the first year[26]. This appears to subsequently decrease to the baseline 2% to 4% annual risk of hemorrhage over time[29].

Fatality rates from brain AVM hemorrhage range from 0% to 18% during the first year[26, 28]. Weigele et al. reported long-term annual fatality rates are 1% to 1.5%. Ondra et al. prospectively evaluated 166 untreated symptomatic brain AVM patients over a mean follow-up period of 23.7 years. There was a 4.0% annual rate of hemorrhage and a 1.0% annual mortality rate. The combined rate of mortality and major morbidity was 2.7% per year. Over the follow up period, 23% of the patients died from hemorrhage. There was no difference in the incidence of re-bleeding or death regardless of presentation with or without evidence of hemorrhage in his study. The mean interval between initial presentation and subsequent hemorrhage was 7.7 years[28].

In another hospital-based study, 47% of patients with a first-ever hemorrhage sustained no neurological defect and 37% experienced no

significant disability despite symptoms (Rankin 1)[30]. Parenchymal hemorrhage had a greater likelihood (52%) of producing a neurological defect.

To provide evidence based answers to many of the management issues associated with the AVMs, a randomized multicenter trial ARUBA (A Randomized trial of Unruptured Brain Arteriovenous malformations) was done with the support of NINDS. ARUBA aims to compare the risk of death and symptomatic stroke in patients with an unruptured brain arteriovenous malformation who are allocated to either medical management alone or medical management with interventional therapy. Adult patients (≥18 years) with an unruptured brain arteriovenous malformation were enrolled into this trial at 39 clinical sites in nine countries. Patients were randomized (by web-based system, in a 1:1 ratio, with random permuted block design, stratified by clinical site) to medical management with interventional therapy (i.e., neurosurgery, embolization, or stereotactic radiotherapy, alone or in combination) or medical management alone (ie, pharmacological therapy for neurological symptoms as needed). The primary outcome is time to the composite endpoint of death or symptomatic stroke. Randomization was started on April 4, 2007, and was stopped on April 15, 2013, when a data and safety monitoring board appointed by the National Institute of Neurological Disorders and Stroke of the National Institutes of Health recommended halting randomization because of superiority of the medical management group (log-

rank Z statistic of 4·10, exceeding the pre-specified stopping boundary value of 2·87). At this point, outcome data were available for 223 patients (mean follow-up 33·3 months [SD 19·7]), 114 assigned to interventional therapy and 109 to medical management. The primary endpoint had been reached by 11 (10·1%) patients in the medical management group compared with 35 (30·7%) in the interventional therapy group. The risk of death or stroke was significantly lower in the medical management group than in the interventional therapy group (hazard ratio 0·27, 95% CI 0·14–0·54). No harms were identified, other than a higher number of strokes (45 vs12, p<0·0001) and neurological deficits unrelated to stroke (14 vs1, p=0·0008) in patients allocated to interventional therapy compared with medical management. Thus, ARUBA trial showed that medical management alone is superior to medical management with interventional therapy for the prevention of death or stroke in patients with unruptured brain arteriovenous malformations followed up for 33 months. The trial is continuing its observational phase to establish whether the disparities will persist over an additional 5 years of follow-up[31].

ANGIOGRAPHY AND ANGIOARCHITECTURE OF BRAIN AVMs

(A) Selective and Superselective Cerebral Angiography

Brain AVMs demonstrate AV shunting on angiography, resulting in early opacification of the draining veins and a decrease in the AV transit time[32]. This shunting is the result of a direct connection between the arterial and venous sides of the cerebral circulation without an intervening capillary bed. There may be two types of AV connections: fistulous and plexiform[33]. A fistulous nidus contains large-caliber direct AV connections. A plexiform nidus consists of a conglomerate of multiple smaller and more numerous vascular channels supplied by one or more arterial feeders. These are collected into one or more draining veins. A plexiform nidus can contain one or more direct fistulas (mixed plexiform-fistulous nidus)[33, 34].

The complete angiographic evaluation of a brain AVM consists of:-

(1) ***Selective*** evaluation of the AVM and the entire cerebral circulation using 4 or 5 French (Fr) diagnostic catheters and (2) ***Superselective*** angiographic evaluation of the feeding arterial pedicles, the nidus, and the venous drainage using microcatheters advanced into distal aspects of the arterial feeders[32].

The goals of the selective angiographic evaluation are listed in Table 1. This provides an important assessment of the arterial supply to the AVM, the general characteristics of the nidus, the venous drainage of the AVM, and the rest of the intracranial circulation. Selective angiography, however, has significant limitations. Rapid AV shunting often superimposes the arterial feeders, the nidus, and the draining veins obscuring important features, such as small arterial feeders, distal feeding pedicles, nidal aneurysms, direct AV fistulas, and small accessory draining veins[32].

The goals of superselective angiography are listed in Table 2. Such detailed anatomic information from superselective angiography concerning the distal arterial feeders, the nidus, and the proximal draining veins is critical for planning and performing endovascular embolization[32].

Table 1 Goals of Selective Angiographic Evaluation of Brain AVMs

1. Arterial territories supplying the AVM
2. Feeding pedicles
3. High-flow arteriopathy (stenoses, ectasias, flow-related aneurysms)
4. Nidus (size, shape, location, flow, fistulas, ectasias, aneurysms)
5. Venous drainage (territories, deep, superficial)
6. Individual draining veins
7. High-flow venous angiopathy (dural sinuses, venous stenoses, occlusions, and varices)
8. Venous drainage of normal brain parenchyma
Abbreviation: AVM, arteriovenous malformation.

Table 2 Goals of Superselective Angiographic Evaluation of Brain AVMs

1. Distal feeding pedicles (anatomy, aneurysms, geometry, hemodynamics)
2. Arterionidal junction
3. Nidus (compartments, direct AV fistulas, plexiform regions, intranidal ectasias, and aneurysms)
4. Venonidal junction
5. Proximal aspects of the draining veins
Abbreviations: AVM, arteriovenous malformation; AV, arteriovenous.

(B) Classification of Brain AVMs[32]

Brain AVMs are categorized into

1. Superficial Cortical AVMs

a. sulcal,

b. gyral,

c. Mixed (sulcogyral).

2. Deep AVMs

a. subarachnoid,

b. deep parenchymal,

c. plexal,

d. Mixed.

A sulcal AVM nidus occupies the subpial space of the sulcus. The nidus may remain contained within the sulcus or variably extend through the sulcus into the cerebral cortex, into the subcortical white matter, and into the deep white matter to the ventricular wall.

Sulcal AVMs assume a conical or pyramidal shape conforming to the sulcal space. Their most superficial aspect is covered by the meninges, not by parenchyma. Because of this, meningeal arterial supply to their superficial aspect is common. Pial arteries are their primary supply. These end in the nidus after providing cortical and medullary branches to adjacent gyri (terminal feeders). This terminal supply is usually amenable to safe embolization. Larger sulcal AVMs also receive supply from basal perforating arteries[32].

Gyral AVMs are covered by cortex and are typically spherical. The gyrus usually is enlarged and adjacent sulci are compressed. A large gyral AVM may extend into the subcortical white matter toward the ventricular wall. The arterial supply is primarily from pial branches that continue beyond the AVM to supply normal parenchyma (indirect feeders). Meningeal supply typically is absent because the overlying cortex is positioned between the nidus and the meninges. Basal perforating arteries may supply the deeper extension of a large gyral AVM[32].

Mixed (sulcogyral) types usually are large AVMs that combine both sulcal and gyral features. The AVM typically involves gyri and sulci, extending into the subcortical white matter to the ventricular wall. The arterial supply combines meningeal arteries and terminal pial branches from the sulcal component, non-terminal pial branches from the gyral component, and basal perforating arteries[32].

Deep AVMs are relatively rare. They can be subdivided into subarachnoid, deep parenchymal, plexal, and mixed types. Subarachnoid AVMs are found in the basal cisterns and fissures, supplied by the subarachnoid portions of the choroidal and perforating arteries. Deep parenchymal AVMs are located in deep gray and white matter such as the thalamus, basal ganglia, and corpus callosum. Basal perforators, choroidal arteries, basal circumferential arteries, and medullary pial branches supply them. Plexal AVMs are intraventricular, primarily supplied by the choroidal arteries. Mixed deep AVMs are typically larger, combining subarachnoid, deep parenchymal, and plexal features. Venous drainage is predominately into the deep venous system; however, transmedullary cortical venous drainage also is seen[32].

(C) Angioarchitecture of Brain AVMs

The routine use of superselective angiography in addition to conventional selective cerebral angiography in recent years has added considerably to the understanding of brain AVM angioarchitecture.

1. Feeding Arteries

The classification of the arterial feeders to a brain AVM using *anatomic, geometric, and hemodynamic* criteria is essential for planning and performing endovascular embolization.

Anatomically, pial supply may be provided by extracortical (subpial), cortical, medullary, and/or corticomedullary branches. Meningeal supply may be direct or through transdural pial anastomoses. Collateral supply can occur through leptomeningeal and subependymal anastomoses. Choroidal artery supply can arise from the extraventricular (fissural, parenchymal) or intraventricular portions[33, 34].

Geometric classification of arterial feeders defines the relationship of the distal feeder with the nidus and normal parenchyma. Three types are defined on super selective angiography[33, 34]:

1. Terminal,
2. Pseudoterminal, and
3. Indirect.

The terminal feeder ends within the nidus distal to branches supplying normal brain. Terminal feeders are usually large, facilitating their superselective catheterization[33, 34].

The pseudoterminal feeder appears to end in the nidus, but actually continues beyond to supply normal brain. The distal segment is not angiographically visible because of the high flow (sump effect) into the nidus. Its presence must be inferred on an anatomic basis. Changing hemodynamic conditions during embolization of a pseudoterminal feeder can cause the embolic material to occlude the distal portion to normal brain, resulting in an ischemic complication[33, 34].

The indirect feeder (feeder *en* passage) is a branch to the nidus arising from an artery that passes in proximity to the nidus while continuing on to supply normal brain. Indirect feeders are typically smaller and shorter, usually originating at an acute or right angle from the parent vessel. Superselective catheterization is often feasible, but more difficult. The parent vessel may be enlarged up to the origin of the indirect feeders and smaller beyond[33, 34].

Hemodynamically, feeding arteries may be characterized into dominant or supplementary feeders according to the amount of flow most cerebral AVMs contain a combination of both types of feeders[32].

High-flow angiopathy results in stenoses in the feeding arteries in up to 20% of brain AVMs. These may be isolated, proximal stenoses intrinsic to the vessel wall or rarely caused by extrinsic compression. Diffuse stenoses with a moyamoya appearance are occasionally seen in younger patients[34]. Arterial

stenoses associated with decreased distal tissue perfusion may result in a shift in the watershed zone toward the nidus (watershed transfer), occurring in up to 30% of superficial (cortical) AVMs. Cortical arteries and leptomeningeal collaterals are recruited to supply more of the territory distal to the AVM. This shift in arterial supply may perfuse just the normal parenchyma or also include the distal aspect of the AVM nidus. Angiogenesis can occur with watershed transfer in response to chronic parenchymal ischemia. It may be mistaken for part of the nidus; however, angiogenesis has no AV shunting and is not a true AVM component[34].

2. AVM Nidus

The nidus is considered the region between very distal aspects of the readily identifiable arterial feeders and the proximal aspects of the draining veins. AV shunting occurs at this site and represents the primary target of embolization. Complete obliteration of the nidus results in a cure[33, 34].

Most brain AVMs has a ***compact,*** well-defined nidus with well-demarcated borders, discrete feeding arteries, and draining veins. A minority has ***diffuse*** and ill-defined margins. Angiogenesis associated with watershed transfer may mimic a diffuse nidus.

Nidal ***sizes*** vary tremendously. Yasargil classified into micro AVMs (< 1cm), small (1-2), Moderate (2-4cm), Large (4-6cm) and Giant (> 6cm).

Their ***shapes*** tend to conform to their anatomic environments. Sulcal AVMs are usually conical, gyral and subcortical white matter AVMs tend to be spherical, and deep AVM shapes vary with location (callosal, cisternal, etc.). Larger AVMs have more complex shapes reflecting their involvement with multiple anatomic structures[32].

Superselective angiography has led to the concept of the nidal ***vascular compartment***, referring to an intranidal vascular unit consisting of one or more feeding arteries supplying the region of AV shunting with a unique draining vein. A nidus may be composed of one or multiple vascular compartments of varying sizes and flow patterns. The AV connections within a given compartment may be plexiform, fistulous, or mixed. These compartments are often hemodynamically interconnected, so occlusion of the compartmental feeders without occlusion of the compartmental zone of AV shunting may allow the compartment to continue to fill from neighboring units. Compartmental vein occlusion can increase the risk of nidal rupture. Hence, careful characterization of the compartmental angioarchitecture is essential for planning an embolization[32].

Histological studies have described the nidus as a complex system of coiling and intercommunicating vascular channels emptying into tortuous thin walled collecting veins. ***Three zones*** have been described within the nidus: arterial, intermediate, and venous. The ***arterial zone*** consists of a plexus of

interconnecting thick-walled vessels. The ***intermediate zone*** is very heterogeneous, containing coiled, interconnected channels ranging from 0.15 to 1.0 mm in diameter. ***The venous zone*** consists of 1- to 3-mm thin-walled vessels converging into the draining veins. AV shunting is thought to occur between the arterial and intermediate zones[35].

3. Draining Veins

The location of a brain AVM usually predicts the pattern of venous drainage; however, there are frequent variations. Cortical AVMs (sulcal and gyral) typically drain through cortical veins into the nearby dural sinuses. Those with subcortical or ventricular extension often have both *superficial* (cortical) and *deep* (subependymal) venous drainage. Central AVMs usually drain into the deep venous system. However, unexpected patterns, such as transcerebral cortical venous drainage of a deep AVM or deep venous drainage of a cortical AVM, may be seen approximately 30% of the time. These variants may represent venous collaterals that developed after occlusion of the original venous drainage system[34].

Important aspects of the nidal venous drainage include venous anatomic variations, collateral venous drainage, and high-flow angiopathy. Anatomic variations in venous drainage develop in response to hemodynamic effects, such as persistence of embryonic veins and variations in the cerebral veins and dural sinuses. Collateral venous drainage is acquired as a response to

obstruction including ipsilateral, contralateral, and transcerebral rerouting of venous drainage. This may be due to mechanical venous compression or intrinsic venous stenoses or thromboses due to high-flow angiopathy. Insufficiently developed collateral venous drainage may result in venous hypertension, venous aneurysms, and venous ectasia (varix) proximal to the obstruction, especially in high-flow AVMs. Clinical symptoms may result from direct compression of the brain or cranial nerves by the varix, seizures or neurological deficits from venous hypertension, and hemorrhage from AVM rupture[32, 34].

4. Aneurysms Associated with Brain AVMs

(a) Introduction. The association of aneurysms with brain AVMs has been reported for many years although until recently little was known regarding the frequency or clinical implications of their concomitant occurrence. The publication of relatively large series has enabled study and understanding of some aspects of the association between these two cerebrovascular lesions.

(b) Classification. Classification of aneurysms associated with AVMs was first proposed by Hayashi et al. in 1981[36]. These authors included only aneurysms external to the AVM nidus in their classification. They divided extranidal aneurysms into three groups, depending on whether they were located proximally or distally on vessels giving supply to the AVM or were located on vessels unrelated to the AVM supply.

In 1994, the Tew's classification (Table 3) divided AVM-associated aneurysms into four groups based on their relationship to the AVM nidus and feeding arteries[37]. This classification also includes intranidal aneurysms (Type IV). This comprehensive and relatively straightforward classification has the advantage of suggesting potential mechanisms for aneurysm formation based on location. In addition, it has proven useful in attempts to relate aneurysm types to clinical behavior. These often overlap and have included aneurysms unrelated to the AVM supply; flow-related aneurysms, which have been subdivided into those, located either proximally or distally on arteries supplying the AVM; and intranidal aneurysms[38, 39, 40]. Nevertheless, definitions of AVM-associated aneurysms similar to those outlined in the Tew's classification have become relatively standardized with publication of ''Reporting Terminology for Brain Arteriovenous Malformation Clinical and Radiographic Features for use in Clinical Trials'' in Stroke journal 2001[41].

Table 3 Tew's Classification of AVM-Associated Aneurysms

Type I Dysplastic or remote, not related to AVM supply
Type II Proximal, arising from the circle of Willis or origin of a vessel supplying the AVM
Type III Pedicular, arising from the midcourse of a feeding pedicle
Type IV Intranidal, within the AVM nidus
Abbreviation: AVM, arteriovenous malformation.

(C) Epidemiology. The reported prevalence of aneurysms associated with AVMs varies widely among series. In an early examination of the subject, the First Cooperative Study of Intracranial Aneurysms and Subarachnoid Hemorrhage found intracranial aneurysms associated with 6.2% of 545 AVMs. Similarly, in a large series of 600 AVMs, Thompson et al. identified 7.5% patients whose AVMs were associated with extranidal aneurysms[42]. Other series have noted prevalence of extranidal aneurysms as high as 17.6%[43]. In 1994, Turjman et al., using superselective angiography, demonstrated a considerably higher prevalence, which included a group of aneurysms located within the angiographic boundaries of the AVM nidus and which filled prior to filling of significant portions of the nidus. These intranidal aneurysms were identified in 58% of 100 consecutive AVMs[44]. Meisel et al. evaluated 662 AVM patients and identified 46% with associated aneurysms. Among 305 patients having both aneurysms and AVMs, 372 of the aneurysms were identified as intranidal, with 313 located on vessels supplying the AVM[40]. Redekop et al., however, found a somewhat lower frequency and identified aneurysms in association with 16.7% of 632 AVMs of which 5.5% were intranidal aneurysms[45].

Overall, the reported prevalence of AVM- associated aneurysms falls generally into the range of 15% to 25%. Nevertheless, prevalence in individual series varies 10-fold, from 5.8% to 58% in different series.

Most series indicate that AVM-associated aneurysm prevalence is similar in men and women. The frequency of AVM-associated aneurysms has been noted, however, to increase with patient age, as well as flow rate and size of the AVM nidus. Reported multiplicity of AVM-associated aneurysms is common but also quite variable. Ezura et al., for example, found multiple aneurysms in 18 of the 25 patients (72%) to be AVM-associated aneurysms in their series, while Meisel et al. found 67% of their AVM-associated aneurysm cases to have multiple aneurysms[46, 47]. Data suggest that close to half of patients with AVM-associated aneurysms will have more than one aneurysm, and a significant proportion will have more than two aneurysms.

(d) Pathogenesis of AVM-associated aneurysms. Three major theories have addressed the association of AVMs and aneurysms. These include

- incidental occurrence,
- underlying congenital vascular defect responsible for both lesions, and
- Flow-related or hyperdynamic theory.

(e) Clinical implications. The natural history of AVMs associated with aneurysms has been the subject of considerable controversy. Some data suggest that increased rates of both initial and recurrent hemorrhage occur in patients who have AVMs with concomitant aneurysms. Piotin et al. found that 50% of their patients with AVM-associated aneurysm presented with

intracranial hemorrhage. Of these, 80% had bled from their aneurysms[55]. Similarly, Batjer et al. found that for patients who harbored both lesions and presented with intracranial hemorrhage, 78% had bled from the associated aneurysms[56]. Cunha e Sa et al. identified the source of intracranial hemorrhage in patients with AVM-associated aneurysms as the aneurysm in 46% of their series[53]. Brown et al. emphasized the long-term risk of harboring an aneurysm in association with an AVM. They found that patients with AVM-associated aneurysms had an annual hemorrhage risk of 7% at five years following diagnosis. This was significantly higher than the 1.7% annual hemorrhage rate for those AVM patients without coexisting aneurysms[43].

Studies of clinical behavior also suggest that important differences may characterize different types of AVM-associated aneurysms. Intranidal aneurysms have been associated with a higher incidence of initial hemorrhage as well as with multiple episodes of recurrent bleeding. For example, Redekop et al. noted intracranial hemorrhage associated with 38% of their series of 632 AVMs. Presentation with intracranial hemorrhage occurred in 72% of patients with intranidal aneurysm; 36% without aneurysm; and 40% with flow-related or unrelated aneurysms. These authors also found an annual hemorrhage rate of nearly 10% among patients with intranidal aneurysms who were not treated[45]. Despite the difficulty in formulating risk profiles associated with AVM-associated aneurysms in general, aneurysms seem to present more of a

risk of hemorrhage when located closer to or within the AVM nidus. Given this information, a number of management approaches to patients identified as having AVM-associated aneurysms have been suggested.

(f) Treatment approaches. Specific management recommendations for patients having both aneurysm(s) and an AVM are difficult to formulate because of the relatively sparse and often conflicting data. General guidelines have been suggested, however. For patients presenting with hemorrhage, the first step is to determine which lesion was responsible for the hemorrhage. It is that lesion toward which the initial treatment should be directed. When no determination can be made as to the source of hemorrhage, the greater morbidity and higher chance of repeat hemorrhage from an aneurysm dictates that the aneurysm be addressed as a first priority. In cases where the AVM is identified as the source of hemorrhage, initial treatment is directed at that lesion. Most data indicate that intranidal aneurysms associated with AVMs presenting with hemorrhage should be strongly considered to be the source of hemorrhage and treatment initially directed at this feature of the AVM[40]. The specific treatment depends on the overall treatment plan for the AVM. Endovascular treatment should be targeted to close the feeding pedicle from which the aneurysm originates first in order to minimize the chance of subsequent hemorrhage. Differing recommendations have been made with respect to prophylactic treatment of feeding artery aneurysms in conjunction

with AVM hemorrhage (i.e. in cases of unbled aneurysms/AVMs).Thompson et al. found that of 45 aneurysms identified in their 600 patients (7.5%), five bled prior to treatment while two bled within three weeks following AVM treatment. Their experience led them to recommend treatment of aneurysms on feeding vessels prior to definitive treatment of the AVM[42]. Similarly, Ezura et al. treated feeding artery aneurysms endovascularly prior to treating the AVM with either resection or radiosurgery[46]. However, others suggest that decreasing flow through the AVM results in frequent regression of extranidal aneurysms without the need for direct treatment [40, 45].

ANGIOGRAPHIC GRADING SYSTEMS FOR BRAIN AVMs

Because of the tremendous variability of brain AVMs with respect to their anatomy and biological behavior, a number of studies have attempted to correlate specific criteria of AVM characteristics with therapeutic outcomes to guide clinical decision-making. Most of these grading systems have focused on surgical management. Luessenhop and Gennarelli were the first to assign a grade to a brain AVM in an effort to predict operability and outcome. Grading was based on the number of arteries feeding the AVM and the vascular territory that was involved. Other criteria such as size, anatomic location, degree of vascular steal, and venous drainage were not included, limiting the system's utility[55].

In 1986, two new grading systems were proposed. Shi and Chen categorized AVMs on the basis of four criteria: (1) size, (2) location and depth, (3) complexity of the arterial supply, and (4) complexity of the venous drainage. Each criterion was attributed a grade of I to IV on the basis of a detailed analysis that was related to the operative risk. A composite grade was assigned on the basis of the grades for the individual criteria. This complex system did not gain widespread usage[56].

Spetzler and Martin also proposed a grading system for brain AVMs in 1986 that has become the most widely utilized. The authors sought a system that was simple and applicable to all brain AVMs providing a reasonable estimate of operative morbidity and mortality. They considered a number of parameters, including the AVM size, the number of feeding arteries, the anatomic location, the operative accessibility, the amount of flow, degree of vascular steal, the eloquence of nearby brain parenchyma, and the venous drainage pattern[57].

Recognizing that a grading system that attempted to incorporate all of the potential parameters would be too complex to be practical, and that many of those variables were interrelated, they proposed a simplified grading system based on three criteria: the AVM size, the venous drainage pattern, and the eloquence of the adjacent brain parenchyma. The AVM size was divided into three categories: small (<3 cm), medium (3 to 6 cm), and large (>6 cm). The

venous drainage was designated as superficial only if all of the venous drainage emptied into the cortical venous system. If any or all of the venous drainage egressed through deep veins (internal cerebral, basal veins, precentral cerebellar vein) it was categorized as deep. An AVM was considered to be adjacent to eloquent brain parenchyma if it was next to the sensorimotor cortex, language areas, visual cortex, hypothalamus, thalamus, internal capsule, brain stem, cerebellar peduncles, or deep cerebellar nuclei[57].

When using the Spetzler-Martin grading system, points are assigned for the AVM size, the venous drainage pattern, and the location relative to eloquent brain (Table 6). The points for each parameter are added for the total score (1–5) that corresponds to the Spetzler-Martin grade (I–V). AVMs with no possibility of surgical resection (e.g., diffuse brain stem or holo hemispheric involvement) are assigned a grade of VI[57].

Following resection of Spetzler-Martin grade I and II AVMs, the authors' retrospective evaluation of their personal surgical experience found a low incidence of minor deficits (0%, 5% in grade I AND II, respectively) and no major neurological deficits; grade IV and V AVM resections were associated with significant incidences of both minor deficits (20%, 19% in grade IV and grade V, respectively) and major deficits (7%, 12% in grade IV and grade V, respectively)[57].

A subsequent prospective evaluation confirmed the accuracy of the Spetzler-Martin grading system for predicting both new-temporary and new-permanent neurological deficits[58]. A recent analysis demonstrated interobserver variability between neuroradiologists and a neurosurgeons performing Spetzler- Martin grading in 27.7% of patients; however, this variability did not diminish the predictive value of the Spetzler-Martin scale[59].

Table 4- Spetzler-Martin grading system for brain AVMs

AVM Feature Points	
Size of nidus	
<3 cm (small)	1
3–6 cm (medium)	2
>6 cm (large)	3
Eloquence of adjacent brain	
Noneloquent	0
Eloquent	1
Venous drainage	
Superficial	0
Deep	1

EMBOLIZATION OF BRAIN AVMs

(A) Historical Background

In a landmark publication in 1960, Luessenhop and Spence reported the first therapeutic embolization of a brain AVM[60]. Because this report predated the development of selective cerebral angiography, the authors injected Silastic spheres directly into a surgically accessed cervical internal carotid artery. Their technique relied on the much greater rate of blood flow to the AVM to direct the spheres into the nidus rather than into normal cerebral branches; however, this flow-dependent embolization was unreliable and was associated with a significant risk of causing an ischemic infarct. Another problem was that the relatively large spheres lodged in the proximal feeders and did not penetrate into the nidus. The nidus remained unoccluded and could recruit deep perforating arteries that were much more difficult to control during surgery[61].

In 1974, Serbinenko was the first to report superselective cerebral artery catheterization and embolization using a detachable balloon attached to a flexible, flow-directed catheter[62]. Superselective catheterization of the target vessel with the balloon catheter was not always technically feasible because it depended on the arterial geometry and hemodynamics. Similar to the problem with the flow-directed Silastic spheres, the detachable balloons occluded the proximal arterial feeders inducing the nidus to recruit new blood supply from

other branches that were often more difficult to control during surgery. This early experience suggested the AVM nidus should be the target of therapeutic embolization.

In 1976, Kerber set the stage for the development of modern therapeutic brain AVM embolization techniques. He reported the use of a microcatheter with a calibrated-leak balloon to super selectively catheterize cerebral arteries and to deliver a liquid embolic agent [isobutyl-2-cyanoacrylate (IBCA)] into the AVM nidus[63]. However, both the catheter and the embolic agent had serious limitations. Calibrated-leak balloon catheters were difficult to use and were associated with multiple complications including vascular injuries. The catheters also could be permanently glued into the AVM[64]. In addition, the IBCA transformed the AVM into a hard, incompressible mass with ill-defined borders and containing embolized vessels that were difficult to surgically cut or coagulate[64]. IBCA also was reported to be carcinogenic and associated with toxic reactions[65].

These pioneering efforts provided the foundation and stimulus for the development of the microcatheters, guide wires, and embolic agents that are currently used for AVM embolization. This early experience also established the concept of targeting the nidus for embolic occlusion, and defined the risks of embolising too proximally (the arterial feeders) and too distally (the venous outflow).

(B) Embolization Indications

Current therapeutic options for brain AVMs include embolization, microvascular surgery, stereotactic radiation (radiosurgery), and various combinations. The goal of any combined therapy is to decrease the overall morbidity and mortality of AVM treatment. In many centers, brain AVM embolization is most commonly performed before microsurgical resection.

Embolization is also performed prior to radiosurgery. In this setting, the goal is to permanently occlude enough of the nidus so that stereotactic radiation can target the rest with a higher dose and a better chance for cure. Less frequently, embolization is used as a stand-alone curative technique, especially for small, surgically difficult lesions. Occasionally, embolization is employed for the palliation of symptoms from an otherwise untreatable AVM. Ideally, a multidisciplinary team consisting of a microvascular neurosurgeon, an interventional neuroradiologist, and a radiation therapist collectively evaluates and formulates an individualized plan for each patient.

(i) Presurgical Embolization

Microvascular surgery has been the oldest and still principle method to treat brain AVMs at many centers. Neurosurgical outcomes have improved with advances in stereotactic guidance, electrophysiological monitoring, barbiturate anesthesia, intraoperative angiography, and aggressive

perioperative blood pressure control. Many small, superficial brain AVMs can be surgically resected without preoperative embolization with minimal morbidity and mortality[58]. Nonetheless, preoperative embolization results in improvements in overall treatment outcomes for many brain AVMs.

Brain AVM embolization can improve surgical outcomes through several mechanisms. Often, the most valuable contribution is the elimination of deep or surgically inaccessible feeders. Preoperative embolization of the deep arterial supply can allow an otherwise inoperable AVM to be successfully resected[66]. Also, embolization can decrease the size of the nidus and the amount of blood flow through the AVM resulting in shorter surgical times and less blood loss. Embolized vessels also are easily identified during surgery. Finally, preoperative embolization of feeding vessel and nidal aneurysms can eliminate those angioarchitectural risk factors for perioperative hemorrhage. Proximal feeding artery aneurysms are at risk for rupture after AVM resection because elimination of the AV shunt causes a sudden increase in arterial pressure. These proximal aneurysms may be impossible to access through the craniotomy for the AVM resection, and preoperative embolization eliminates the need for a second craniotomy[66].

There is a general consensus that many superficial Spetzler-Martin grade I and II AVMs can be surgically resected with minimal morbidity and mortality without preoperative embolization. In these cases, the additional

risks of embolization may not be justified. There are, however, exceptions such as a grade I or II AVM with a deep feeder that is difficult to access surgically[67]. Also, some experts advocate embolising an intranidal aneurysm in a Spetzler- Martin grade I or II AVM presenting with acute hemorrhage to stabilize the nidus until surgery[67]. Embolization is used frequently for Spetzler-Martin grade III AVMs, particularly for those in central and eloquent locations and those with deep feeders. Pre-operative embolization (often staged) is commonly employed for those Spetzler-Martin grades IV and V AVMs considered for resection.

(ii) Pre-radiosurgical Embolization

There is a wide variability at different institutions in the use of combined embolization and radiosurgery. Stereotactic radiosurgery primarily is employed at some centers for small brain AVMs that have a high surgical risk because they are deep-seated or are located in the eloquent cortex. Other centers frequently use embolization to render large brain AVMs amenable to stereotactic radiosurgery. In this setting, embolization is used to reduce the size of the AVM to increase the probability of a radiosurgical cure[68]. The rate of cure after stereotactic radiosurgery significantly decreases as the volume of AVM being treated increases[69]. Radiosurgical cure is more likely after embolization has reduced the residual AVM volume to less than 10 cc[68, 70]. Embolization is also performed prior to radiosurgery to occlude nidal

aneurysms that represent a risk for hemorrhage until the radiosurgically induced obliteration occurs and also to occlude high-flow fistulas that may be refractory to radiosurgery[68]. Repeat embolization or surgery also can be used to treat residual AVM persisting after radiosurgery.

(iii) Curative Embolization

There is currently a limited role for curative embolization of brain AVMs. Although embolization can successfully obliterate some small AVMs that have limited feeders, it rarely cures large, complex AVMs. Most of the AVMs that have a relatively high probability of cure with embolization are amenable to complete surgical removal with negligible morbidity and mortality. Therefore, justifying the risks of an attempted curative embolization is often questionable[58]. Small deep central AVMs with limited feeders are exceptions where curative embolization can play an important role. However, in carefully selected cases with small nidus and good vascular access restricted to one or few feeders, a curative goal may be attained.

(iv) Palliative Embolization

Palliative embolization does not appear to improve on conservative medical management of most patients with incurable AVMs and may even worsen the subsequent clinical course. There are, however, appropriate goal-directed roles for palliative embolization in select circumstances. Palliative

embolization can alleviate symptoms due to vascular steal and mechanical compression and obliterate specific aneurysms responsible for repeated hemorrhages. Embolization of meningeal supply can improve intractable headaches.

(C) Embolization Tools and Technique

(i) Microcatheters and Guide wires

Microcatheters are classified into over the wire, flow-directed and steerable microcatheters. Generally flow directed microcatheters are used for AVM embolization.

The flow-directed microcatheters currently used for embolization with liquid agents are designed for safe and reliable navigation into the very distal aspects of the intracranial circulation. They have several segments of progressive softness. The proximal segments are relatively stiff and thick-walled to transmit longitudinal motion and torque efficiently. The transitional middle segments have thinner walls and progressively increase in flexibility but remain ‘‘pushable.’’ The distal segments are small (1.3 to 1.8 F outer diameters), thin walled and extremely soft and supple. They provide no intrinsic transmission of longitudinal force. The catheter tips are slightly bulbous so blood flow will pull them forward. The microcatheters have hydrophilic surface coatings to decrease thrombogenicity, facilitate movement

through small tortuous vessels, and prevent adhesion of embolic agents. Recently, microcatheters with detachable tip are introduced with an aim to allow sustained and prolonged onyx injection without the risk of catheter gluing.

Guide wires designed for use in the cerebral arteries (0.007–0.014 inch) have very flexible distal segments and soft, shapeable platinum tips. They also are covered with a hydrophilic coating to reduce friction between the catheter and guidewire. They remain ‘‘torquable’’ even after they have gone through several curves. Only the smallest guidewires, such as the 0.008-inch Mirage (EV3, Plymouth, Minnesota, U.S.), will pass through the flow-directed microcatheters commonly used with liquid embolic agents[79].

(ii) Vessel Selection

Current techniques for brain AVM embolization require advancing a suitable microcatheter into the very distal aspect of an arterial feeder supplying the nidus. A guide catheter (e.g., Envoy, Cordis Endovascular, Miami Lakes, Florida, U.S. or Vista Brite) first is placed in the distal cervical aspect of the appropriate internal carotid or vertebral artery. A 6-Fr guide catheter is preferred for easier contrast injections while the microcatheter is inserted; however, a 5-Fr guide catheter may be safer in a small vertebral artery. A rotating hemostatic valve is used for coaxial placement of a microcatheter and to continuously flush the guide catheter with heparinized saline. Intravenous

heparin is administered on an individual basis to prevent thromboemboli if there are small feeders or there is slow flow. A microcatheter (1.5- or 1.8-Fr Spinnaker Elite, Boston Scientific Corporation, Natick, Massachusetts, U.S.; Marathon or Ultraflow, EV3, Sonic (Balt, Montmorency, France), Apollo (Coviedien) with a small steam-shaped distal curve (e.g., 1-mm radius distal ‘‘J’’ shape) is navigated through the cerebral arteries under continuous subtracted fluoroscopic (road-map) imaging. There are two primary techniques for intracranial navigation: flow directed and guidewire assisted. Flow-directed navigation uses arterial blood flow to drag the very flexible distal catheter segment and slightly bulbous catheter tip forward. The tip will preferentially tend to advance into the vessel with the highest flow, which is usually the desired feeder to the AVM. Directional control also is facilitated by gentle injections of contrast to redirect the curved tip into the desired branch. For guidewire-assisted navigation, a 0.008-inch Mirage (EV3) guidewire is advanced into the distal segment of the microcatheter to augment its ‘‘pushability’’ and to change shape of the catheter tip. Advancing and withdrawing the guidewire in the distal segment also changes its elasticity often prompting the catheter tip to spring forward. When necessary, the Mirage guidewire can be extended beyond the microcatheter tip to navigate difficult anatomy; however, this must be done with caution to avoid arterial perforation or dissection.

(iii) Embolic Agents

There are three general categories of currently available embolic agents: solid occlusive devices (coils, silk threads, balloons), particulates [polyvinyl alcohol (PVA) particles], and liquids (cyanoacrylates, Onyx, ethanol) [80]. Solid occlusive devices primarily are used to occlude large direct AV fistulas. Particulate embolization using PVA particles has been replaced by liquid embolization with N-butyl cyanoacrylate (NBCA) at most centers. Onyx is a new liquid embolic agent recently approved by the Food and Drug Administration (FDA) [81]. Although absolute ethanol and silk threads have been used to embolized brain AVMs, limited results have been published.

(a) Polyvinyl alcohol particles. PVA particles were commonly used for brain AVM embolization before liquid agents such as NBCA and Onyx became more widely used. PVA particles are supplied in various size ranges from 50 to 1000 mm. They are non-radiopaque and are mixed with iodinated contrast for delivery. PVA particles were often used in combination with coils or silk threads to facilitate their retention, especially in larger AV shunts[82]. Typically, larger (e.g., 3-Fr) over-the-wire microcatheters have been required for larger PVA particles (>500 mm) resulting in more proximal embolization of the arterial feeders rather than the nidus[67].

PVA particles have several disadvantages as compared to liquid embolic agents. They can occlude the small, flow-directed microcatheters that

can be most reliably advanced into the distal feeder. Also, since the particles are radiolucent, it is not possible to identify where they deposit. There is evidence they often aggregate and frequently occlude the arterial feeder rather than the nidus. The nidus can then recruit collateral blood supply and regrow. This may explain why Sorimachi et al. found 43% of brain AVMs partially embolized with PVA particles demonstrated an increase in the size of the nidus on follow-up angiograms[82]. In addition, a histopathological analysis revealed PVA embolized vessel lumens contained clumps of particles intermixed with thrombus rather than solid luminal packing with PVA. Eighteen percent of the embolized vessels were partially recanalized[83]. This may explain why AVMs that appears completely obliterated on angiography after PVA embolization can reappear on follow-up exams[82]. This conclusion is supported by the observation that 15% to 20% of AVM patients undergoing PVA embolization prior to radiosurgery had recanalization two to three years later on follow-up angiography[70].

(b) N-Butyl cyanoacrylate. Cyanoacrylates have been used for brain AVM embolization for more than 20 years. The FDA approved NBCA (Trufill, Cordis endovascular) for brain AVM embolization in 2000. NBCA has been the most commonly used embolic agent for this purpose in the United States before the advent of Onyx. The liquid NBCA monomer undergoes a rapid exothermic polymerization catalyzed by nucleophiles found in blood and on

the vascular endothelium to form an adhesive, non-biodegradable solid. The vessel is permanently occluded when the polymer completely fills the lumen. NBCA provokes an inflammatory response in the wall of the vessel and surrounding tissue leading to vessel necrosis and fibrous ingrowth. These histological responses also may contribute to the permanency of NBCA occlusions[84, 85].

The NBCA polymerization rate can be adjusted to satisfy specific requirements. The goal of the embolization is to form a solid intranidal NBCA cast, avoiding early polymerization in the arterial feeder or late polymerization in the venous outflow. Pure NBCA polymerizes almost instantaneously at the catheter tip. Although this may be necessary to occlude a direct high-flow fistula, immediate polymerization will not allow the NBCA to penetrate optimally into a plexiform nidus. The addition of ethiodol slows the polymerization rate, allowing better nidal penetration. The polymerization rate progressively decreases as more ethiodol is added. The objective is to use an ethiodol /NBCA mixture with a polymerization time optimally matched to the individual AVM's angioarchitecture and hemodynamics. The AV transit time on superselective angiography is subjectively evaluated as a guide to formulating the mixture. This is far from an exact science and is highly dependent on experience. The concept of a ''wedged'' catheter position, where forward flow is controlled by the rate of injection, theoretically allows

slower, more controlled injections of a more dilute NBCA/ethiodol mixture with a longer polymerization time[86].

Many experts believe portions of the AVM nidus that are well cast with NBCA can be considered permanently obliterated[86]. Wikholm followed 12 brain AVMs totally occluded with NBCA for 4 to 78 months and found no angiographic evidence of recanalization[87]. In another study, six patients with complete obliteration of the AVM nidus had no angiographic evidence of recurrence at 17 to 32 months[88]. NBCA embolization therefore has the potential to transform inoperable AVMs into surgically respectable lesions and to reduce the size of an AVM nidus sufficiently to make radiosurgery possible. Some small AVMs can be cured by embolization alone. A solid NBCA cast in the nidus is essential to assure permanent obliteration of the AVM[86].

Table-5- Clinical and anatomical results of the endovascular treatment of brain AVMs using NBCA

Series	Year	Number	Hemorrhagic complications	Morbidity	Mortality	Complete occlusion
n-BCA trial[67]	2002	52	13.0 %	-	2.0 %	-
Ozanne[71]	2005	283	5.3 %	5.6 %	1.1 %	-
Klurfan[72]	2005	155	-	5.9 %	0.8 %	30.0 %
Raymond[73]	2005	227	6.0 %	2.0 %	7.0 %	16.0 %
Bhattacharya[74]	2005	127	3.1 %	7.9 %	0.8 %	-
Campos[75]	2005	106	-	3.0 %	2.0 %	24.0 %
Goto[76]	2005	177	-	3.9 %	1.1 %	5.6 %
Li[77]	2005	469	0.9 %	2.1 %	0.5 %	33.3 %

(c) Onyx

Onyx (ev3, Irvine, California) is a premixed, liquid embolic agent consisting of ethylene-vinyl alcohol copolymer (EVOH) and tantalum powder (35% weight per volume -for radio-opacity) dissolved in dimethyl sulfoxide (DMSO). EVOH contains 48-mol/L ethylene and 52-mol/L vinyl alcohol[89]. Taki et al. were the first to describe the use of EVOH, mixed with metrizimide powder (for radiopacity), and dissolved in DMSO to embolise brain AVMs in 1990[90]. Subsequent studies led to a multicenter randomized trial that demonstrated noninferiority of Onyx compared to NBCA in achieving greater than or equal to 50% volume reduction for presurgical brain AVM embolization, resulting in FDA approval of Onyx for brain AVM embolization in 2005[81].

Onyx is a cohesive, nonadhesive liquid embolic agent. The copolymer holds together as it is injected, but it does not adhere to the endothelium. When the mixture contacts an aqueous solution such as saline or blood, the DMSO diffuses away rapidly, causing the copolymer to precipitate into a soft, spongy solid. The precipitation progresses from the outer surface inward, forming a skin with a liquid center that continues to flow as the solidification continues. During the injection, the column of Onyx advances into the path of least resistance. The rate of precipitation of the copolymer is proportional to the concentration of EVOH in the solution. Onyx is available in ready-to-use

vials of 1.5 mL in 3 different viscosities, Onyx 18, 20, and 34 (concentrations of EVOH in centipoise: 6%, 6.5%, and 8% respectively). Onyx 18 travels farther distally and penetrates more deeply into the nidus because of its lower viscosity and slower precipitation rate. Onyx 18 is used for distal feeding pedicle injections into a plexiform nidus, whereas Onyx 34 is recommended for embolising high-flow fistulas. Complete solidification of both formulations occurs within five minutes.

DMSO was chosen as the solvent because it rapidly diffuses in aqueous solution and its physiological properties in humans are well known[90]. DMSO is angiotoxic, however, with adverse effects that include vasospasm, angionecrosis, arterial thrombosis, and vascular rupture[91]. These undesirable consequences are related to the volume of DMSO infused and the endothelial contact time. Severe angiotoxic effects do not occur when the DMSO infusion rate does not exceed 0.25 mL/90 sec.

Only specifically approved microcatheters (Ultraflow, Marathon, Echelon, Sonic and Apollo) can be used with Onyx because the DMSO will dissolve incompatible catheters. Patients may notice a garlic-like taste for several hours, and their skin and breath may have a characteristic odor due to the DMSO for one to two days after an embolization with Onyx.

The cohesive and nonadhesive properties of Onyx provide several advantages compared to NBCA. Because Onyx is nonadhesive and it solidifies

more slowly than NBCA, typical injections are performed over much longer time intervals (minutes) and are easier to control. This procedure results in a much more leisurely embolization, providing time to analyze progress with interval angiography, if desired, and involving less risk of refluxing the embolic agent too proximally in the arterial feeders or extending too distally into the venous outflow . It is also possible that a more complete and solid casting of the nidus may be obtained with Onyx compared to NBCA. This may result in an increased rate of cure, but this remains to be proven. In addition, the catheter also can be repositioned into a second pedicle and another embolization can be performed, a maneuver that is not possible with NBCA. Finally, Onyx does not cause inadvertent gluing of the catheter tip to the vessel as fast as NBCA[81].

The available data on use of Onyx for brain AVM have been published and appears very encouraging. Histopathological examination of the resected specimens showed mild inflammation one day after embolization and chronic inflammatory changes after four days. Angionecrosis was seen in two patients, but the vessel wall integrity was maintained in all specimens[81]. In another study, the surgical handling characteristics of Onyx were compared with NBCA in embolized swine rete mirabile[92]. Onyx was softer and handled better than NBCA during surgical resection. The permanency of Onyx embolization is as yet unknown. Short-term angiographic follow-up (1–100 days) did not

reveal recanalization[81]; however, no long follow-up studies have been published. Many other hospital series have firmly established the safety and efficacy of Onyx - so much so that it has nearly replaced NBCA as agent of choice for AVM embolization.

Onyx Technique:

Patients can experience pain during embolization with Onyx; therefore, general anesthesia is used more frequently than with NBCA. An Onyx compatible microcatheter is positioned in the desired location using flow-directed and guide-wire-assisted navigation. After positioning of the microcatheter, a superselective angiogram is obtained. The Onyx solution must be vigorously shaken for 20 minutes to fully suspend the micronized tantalum powder. Mixing is continued until just before the embolization. Failure to do this may result in inadequate radiopacity[89]. The manufacturer provides an adapted Vortex-Genie (Scientific Industries, Inc., Bohemia, New York, U.S.) to mix the Onyx. The catheter is flushed with normal saline and the dead space is loaded with pure DMSO solvent. The Onyx mixture is drawn into a DMSO-compatible 1-cc syringe, the syringe is connected to the microcatheter and a slow, steady injection is begun at a rate of 0.25 mL/90 sec to displace the DMSO in the dead space with Onyx. Subtracted fluoroscopy is begun just before the dead space volume has been replaced by the injection. A slow, steady injection usually results in optimal nidal penetration. Changes in

the injection rate tend to cause proximal reflux. The injection rate should not be allowed to exceed 0.25 mL/90 sec to prevent angiotoxicity. If proximal reflux occurs, the injection is paused 30 seconds and restarted. This allows a plug to solidify around the catheter tip that prevents further reflux and promotes forward flow. This ‘‘plug and push’’ technique can be repeated multiple times as required. Proximal reflux around the catheter tip should be limited to 1 cm to avoid causing difficulty with the catheter retrieval. As a circumferential plug forms around the catheter tip, the injection can be paused for as long as two minutes to allow the plug to solidify. This will establish proximal flow arrest when the injection is restarted so that the subsequent flow will move distally. Similarly, if Onyx begins to fill a draining vein, a pause in the injection will allow that material to solidify, and when the injection is restarted the additional Onyx usually fills new areas of the nidus. The injection should never be paused for more than two minutes to prevent Onyx from precipitating in the catheter lumen. If there is resistance, the injection should be discontinued to avoid rupturing the catheter.

Other techniques have also been described for onyx injection. Some of the described techniques include:

-Wedged technique: A microcatheter is gently flow directed into a vascular channel in the nidus no bigger than the catheter tip, effectively blocking the blood flow beyond the tip. Onyx is then slowly injected, filling the nidus.

-The pressure cooker technique (PCT) was designed to create an anti-reflux plug by trapping the detachable part of an Onyx-compatible microcatheter with coils and glue in order to obtain wedge-flow conditions, thereby enabling a better understanding of macrofistulous AVMs and a more comprehensive, forceful and controlled Onyx embolization. The PCT might enlarge the range of AVMs amenable to endovascular cure[93].

-The 2-microcatheter technique uses two separate microcatheters at different feeders of same AVM. Using 2 catheters for delivery of Onyx has allowed a more efficient and complete embolization of complex AVMs. The operator should stop injecting when reflux is noted in the parent vessel. Having another catheter in position allows the operator to immediately resume injection in another site of the AVM. This back-and-forth movement between the catheters makes the procedure more dynamic and efficient because the AVM nidus is being occluded from different directions. The technique allows for less reflux of Onyx. The potential drawbacks with this technique are need for bilateral femoral artery access and possible thromboembolic and hemorrhagic complications from multiple microcatheters should be weighed against the benefits of having access to 2 AVM pedicles for embolization with Onyx[94].

There are two catheter retrieval techniques for safe retrieval of catheters after onyx embolisation. The slow ‘‘traction’’ method uses incremental catheter withdrawal (cm by cm) with sustained moderate Tension on the

catheter. The quick ‘‘wrist-snap’’ technique is to withdraw the catheter enough (3–5 cm) to create slight tension and then quickly snapping the wrist (not the entire arm) 10 to 20 cm left to right. Pulling too far or hard runs the risk of causing a catheter separation.

Post procedural Care

Patients are observed in the neurointensive care unit for 24 hours and usually discharged to home on the second postembolization day. Mild hypotension (mean arterial pressure ~90% of normal) may be induced for 24 hours if a large; high-flow AVM has been embolized. Additional embolization sessions for large, high-flow AVMs are staged every three to four weeks.

Results and complications of onyx embolisation:

The literature on outcomes for brain AVM treatments predominantly consists of uncontrolled, single institution case series. Many of these have demonstrated an important role for brain AVM embolization in selected patient populations. Nonetheless, they have relatively small sample sizes, and tremendous variability in selection criteria, techniques, patient evaluation, and follow-up. Recently published multicenter prospective series from Europe, BRAVO, also confirmed the suitability of Onyx for brain AVM embolization. BRAVO is the largest multicenter study to independently evaluate the safety and efficacy of Onyx embolization for brain AVMs. It shows that this

treatment is associated with acceptable mortality (4.3 %) and morbidity (5.1 %) with a 100 % occlusion rate in 23.5 % of patients and most patients with incomplete embolisation amenable to a complementary treatment (82.3 %)[109].

W.J.VanRooji et al. achieved average 75% (median 80%, range 40%–100%) nidal obliteration using onyx in their study group of 44 patients. They achieved total embolization in 16%[104]. V. Panagiotopoulos et al. reports complete obliteration rate of 24.4 %(30/82) at the end of all endovascular procedures and an average of 75% (range, 30%–100%) volume reduction. An average of 2.6-mL Onyx was used per patient and procedure-related permanent disabling morbidity and mortality were 3.8% and 2.4% respectively[97]. Isil saatcI et al. in their series of 350 patients reports angiographically confirmed obliteration achieved in 179 patients (51%) with only endovascular treatment; 1 patient died due to intracranial hemorrhage after the treatment. Twenty-two patients underwent resection, and 136 patients were sent to radiosurgery after endovascular treatment. In all 178 surviving patients who had angiographically confirmed AVM obliteration by embolization alone, 1–8 years of control angiography (mean 47 months) confirmed stable obliteration, except for 2 patients in whom a very small recruitment was noted in the 1st year on control angiography studies, despite initial apparent total obliteration (recanalization rate 1.1%). In the entire series,

5 patients died; the mortality rate was 1.4%. The permanent morbidity rate was 7.1%[108].

Literature regarding experience of onyx embolisation using detachable tip microcatheter is also coming forth. S Maimon et al reports 55% complete embolization using detachable tip catheter in patients who concluded treatments (16/29) in their total study population of 43. They also achieved complete embolization in 37% of the whole cohort (16/43). They were able to inject significantly larger amount of onyx using detachable tip catheter than that injected with the non-detachable microcatheters (mean volume, 2.5 +/- 2.2 versus 1.7 +/-1.3 mL, respectively, P< .05, t test). They observed 7 clinical complications in a total of 76 embolization sessions (9.2%)[98].

In the only available publication from India by S.Joseph et al attained complete AVM nidus obliteration in 2 out of 5 patients.

Table-6 - Clinical and anatomical results of the endovascular treatment of brain AVMs using Onyx

Series	Year	Number	Hemorrhagic complications	Morbidity	Mortality	Complete occlusion
Perez-Higueras[101]	2005	45	8.9 %	15.5 %	2.0 %	22.2 %
Song[102]	2005	50	6.0 %	10.0 %	0.0 %	20.0 %
Van Rooij[104]	2007	44	6.8 %	4.6 %	2.3 %	16.0 %
Weber[105]	2007	93	-	12.0 %	0.0 %	20.0 %
Mounayer[100]	2007	94	8.5 %	8.5 %	3.2 %	49.0 %
Katsaridis[106]	2008	101	5.9 %	8.0 %	3.0 %	53.9 %
Pierot[103]	2009	50	8.0 %	8.0 %	2.0 %	8.3 %
Panagiotopoulos[97]	2009	82	12.2 %	3.8 %	2.4 %	24.4 %
S.Maimon etal[98]	2010	43	13.9%	6.9%	-	37%
Xu[107]	2011	86	7.0 %	3.5 %	1.2 %	18.6 %
Isil Saatci[108]	2011	350	4.0 %	4.3 %	1.1 %	50.9 %
BRAVO[109]	2013	127	8.5 %	5.1 %	4.3 %	23.5 %

In NBCA series, the rate of complete occlusion is slightly lower (5.6–33.3 %) compared with the Onyx series. Indeed these indirect comparisons have limited value singularly because patients, AVMs, treatment techniques and follow-up techniques are not the same. In the randomised trial, the efficacy of Onyx and glue (pre-surgical volume reduction of brain AVMs ≥50%) was 96.0% and 85.2% respectively[99]. There was no difference between the glue and the Onyx group with regard to operative blood loss and resection time.

Safety comparisons between Onyx and glue for brain AVM embolisation are mostly indirect as only one small, randomised trial was conducted comparing embolisation with Onyx and glue for the presurgical treatment of brain AVMs[99]. Selecting NBCA (N-butylcyanoacrylate) studies after the year 2000, the ranges of haemorrhagic complications (0.9–13.0 %), morbidity (2.0–7.9 %) and mortality (0.5–7.0 %) are comparable to those observed with Onyx. Similarly, in the randomised trial, the rate of adverse events and serious adverse events was not significantly different in patients treated with Onyx or glue[99].

Complications

1. Periprocedural hemorrhage: There are a number of causes of periprocedural hemorrhage from brain AVM embolization. Technical factors include catheter or guidewire-induced arterial perforations, dissections, rupture of aneurysms, vascular injuries during catheter retrieval, and accidental embolization of venous outflow[86]. Physiological factors include venous outflow thrombosis, hemodynamic changes in the setting of impaired cerebrovascular reactivity, and hemodynamic stresses on angioarchitectural weak sites such as feeder, nidal, and venous aneurysms. Embolization can markedly reduce flow through a fistulous nidus causing stagnation in the draining veins. This can result in venous outflow thrombosis, nidal congestion, and a delayed hemorrhage or a venous ischemic infarct[110, 111]. Normal perfusion pressure breakthrough is another important physiological cause of hemorrhage following AVM treatment. The ‘‘sump effect’’ of a large shunt causes low pressure in the arterial feeders and nearby parenchymal branches. The high flow through the nidus elevates venous pressures. The result is a chronically low cerebral perfusion pressure that can impair cerebrovascular auto regulation. If the shunt is suddenly therapeutically disrupted, there is an immediate increase in arterial pressure and a decrease in venous pressure, with a resulting dramatic increase in the cerebral perfusion pressure. If cerebrovascular auto regulation is impaired, resulting parenchymal

hyperperfusion can cause cerebral edema or hemorrhage. Spetzler et al. called this normal perfusion pressure breakthrough and found it was associated with large, high-flow AVMs, poor angiographic filling of normal cerebral arteries, extensive collateral flow (steal), external carotid supply, and progressive or fluctuating neurological deficits[112]. The risk of normal perfusion pressure breakthrough–induced hemorrhage can be minimized by stepwise reduction in the degree of shunting in large, high-flow AVMs through multiple embolizations staged every three to four weeks, facilitating the gradual recovery of normal vascular reactivity[112]. Prompt surgical evacuation of an embolization induced cerebral hematoma results in a good outcome in most cases. Jafar and Rezai reported the emergent surgical evacuation of acute intracerebral hematomas from brain AVMs in 10 patients experiencing acute neurological deterioration, including eight cases occurring after embolization. They employed immediate intubation, hyperventilation, osmotic diuresis, barbiturate anesthesia, and surgery. Postoperative cerebral perfusion pressure was maintained above 55-mm Hg with mannitol and barbiturates. Nine of the 10 patients had good to excellent outcomes[113].

2. Ischemic stroke Technical causes of acute stroke during embolization include the showering of NBCA/ onyx droplets from the catheter tip as it is removed, catheter or guidewire-related arterial dissections and thromboemboli, the embolization of en passage or pseudoterminal supply to

normal brain parenchyma distal to the nidal supply, and the inadvertent reflux of embolic material into normal branches proximal to the catheter tip. Ischemic stroke can result from retro-grade thrombosis in stagnant feeding arteries propagating into branches to normal brain. Delayed venous thrombosis can cause a venous infarct. Careful attention to the angioarchitecture on superselective angiography and to an optimal embolization technique will minimize these events[111].

3.Retained microcatheter: Embolization with cyanoacrylates has caused permanent adhesion of the microcatheter tip to the embolized vessel in a small percentage of cases. This incidence has decreased significantly in recent years with the use of NBCA and now Onyx, rather than isobutyl cyanoacrylate, a wedged microcatheter position to prevent proximal reflux, more dilute NBCA/ethiodol mixtures with slower polymerization rates, and more durable microcatheters with hydrophilic coatings. Recently introduced detachable tip microcatheters also helps in significantly reducing instances of stuck catheters.

4. Pulmonary emboli (PE) have been reported with both particulate and liquid embolic agents. Most are asymptomatic, although respiratory distress and death have occurred.

Multistage angiographic and embolization procedures result in significant radiation doses. Temporary alopecia has been reported, which typically occurs after a short-term radiation dose of 3 to 6 Gy[114].

MATERIALS AND METHODS

This is a prospective and retrospective study to analyze clinical & radiological characteristics, efficacy of management by embolization using onyx, either alone or in combination, and complications (if any) in patients with brain arterio-venous malformations (AVMs) who reported to SCTIMST between 1 Jan 2008 and 31 May 2014. There were a total of 86 cases included in the study.

The clinical data of the patients was obtained by reviewing their case sheets obtained from the Medical Records Department & the imaging data was obtained from the DSA lab archive. From these, the data regarding clinical presentation, imaging, angiographic characteristics, details of the embolization procedure, post procedural status and the follow up was collected.

All patients underwent a baseline neurological evaluation prior to the procedure. All the patients had a baseline imaging done – either a CT or MRI of the brain. Subsequently, the patients underwent a complete four vessel diagnostic cerebral angiogram. All the studies were performed on Advantx digital substraction angiography unit (GE Milwaukee, USA) or Innova biplane flat panel digital subtraction angiography unit (GE Milwaukee, USA).

Diagnostic angiographies were done under local anesthesia when they were performed separate from interventional procedure or performed as a check angiography for follow up. The interventional procedure was done under general anesthesia. Premedication (Inj. Pethidine/ Tramodol 25-50mg i.m & Inj. Phenergan12.5- 25mg i.m) was given before the local procedures. Post procedure these patients were managed in the wards when angiography was performed under local anesthesia. For procedures carried out under general anesthesia, the patient was monitored in the neurointervention intensive care unit.

After discharge, the patients were followed up with clinical evaluation for improvement in their symptoms. Follow up imaging or angiograms were evaluated, 1-2months after endovascular embolization and after one year of radiotherapy.

A complete evaluation of the patient including demographic profiles (age, sex), clinical presentation, imaging features, treatment method and outcome including complications and follow up was carried out as per the proforma attached.

Technique of embolisation:

All procedures were performed via the transfemoral route using the Seldinger technique. The guiding catheters used during the procedure were

continuously flushed with heparinized saline (2000 units /L) with systemic heparinisation of 3000- 5000 IU as bolus and 1000 IU every hour monitoring the ACT.

The procedures were performed under general anesthesia. A guiding catheter was placed in the main feeding arteries In anterior feeders, guiding catheter was usually placed in vertical portion of distal ICA and then feeders were selectively cannulated with microcather, In posterior feeders, guiding catheter was placed in V2 segment and then feeders were cannulated and embolized using coil or glue.

Superselective catheterizations and embolic injections were performed, using DMSO compatible microcatheters, Marathon in earlier cases for onyx injection and later detachable tip microcatheters, Sonic and Apollo were also used. Flow guided microcatheters, Spinnaker or Ultraflow were used in cases were glue, PVA particles or absolute alcohol was used in addition to Onyx.

Decisions regarding injection of embolic material were taken following anatomic evaluation of superselective angiograms and pre-embolisation MR and with the conviction that all brain areas are eloquent.

The techniques of catheterization and embolisation used throughout this series are described in detail later.

The catheters and wires used for the purpose are shown in table 1.

Table-7 : MATERIAL USED FOR ANGIOGRAM AND EMBOLIZATION

1.	Sheath – Radiofocus, Cordis	4,5, 6, 7 French size
2.	Diagnostic catheters – Vertebral glide (Terumo), Right coronary (Cordis), Simmons (Cordis)	5, 4 French size
3.	Guide wire – Terumo exchange length, Terumo standard,	150 cm – Standard 260 cms - Exchange
4.	Guiding catheters – Vistabrite, Launcher (Cordis), Envoy, Neuron	6, 7 French size
5.	Microcatheters – Spinnaker, Ultraflow, Mararthon, Sonic, Apollo	1.5 to 1.8 French
6.	Microguidewires – Transcend, Mirage, and Hybrid wire, Traxcess.	.008, .010, 0.014 of varying length (190-205cm)
7.	Embolic materials –Glue (N-Butyl Cyanacrylate - NBCA), Absolute alcohol, Onyx	Onyx-18

Immediate post embolisation brain CT was done in those cases with suspicion of complication. Patients with AVMs in which a complete obliteration was achieved, had follow up DSA following the last embolization session at variable intervals ranging from 1 month to 2 years. Follow up data from all patients were obtained from hospital case record, during their OPD visit and also telephonic conversation with patients or their immediate relatives.

RESULTS

Demographic profile

Age and sex

There were total of 86 cases. The age of the patients ranged between 8-65 years (mean 30 years, median 28yrs) and male to female ratio was 50: 36.

Table-8: Age distribution

AGE	NUMBER
0 to 10	4
11 to 20	25
21 to 30	20
31 to 40	17
41 to 50	14
51 to 60	5
61 to 70	1

Clinical Features

Half (50%) of the patients in the study group presented with intracranial bleed. Other common presentations were with seizure (35 patients, 40.1%) and headache (27 patients, 31.4%). 8 patients had focal neurological deficits. One patient had tinnitus. 2 were incidentally detected.

Table-9: clinical presentation

PRESENTATION	FREQUENCY
BLEED	43
SEIZURE	35
HEADACHE	27
INCIDENTAL	2
FND	8
OTHER	1

Angioarchitecture

Location

AVM locations were classified on the lobe were predominant part of nidus located. Most common locations were frontal (24.4%) and parietal lobe (25.6%) followed by occipital (19.8%) and temporal lobe (15.1%). Cerebellar AVM was seen in 9 (10.5%) and corpus callosal AVM in 3 patients (3.5%). One had intraventricular AVM nidus. None of patient had brainstem AVM.

Table-10: Location of AVM

LOCATION	NUMBER	%
FRONTAL	21	24.4
PARIETAL	22	25.6
TEMPORAL	13	15.1
OCCIPITAL	17	19.8
CORPUS CALLOSUM	3	3.5
BRAIN STEM	0	0
CEREBELLAR HEMISPHERE	9	10.5
VERMIS	0	0
INTRAVENTRICULAR, CHOROIDAL	1	1.2
TOTAL	86	

Table-11: Plane of lesion

PLANE	NUMBER	%
SUPERFICIAL	24	28
DEEP	46	53.5
PERIVENTRICULAR	15	17.4
INTRAVENTRICULAR	1	1.2
TOTAL	86	

Majority of nidus were located deep (53.5%). In 28% nidus location was superficial. It was in periventricular location in 17.4% and intraventricular in 1 patient.

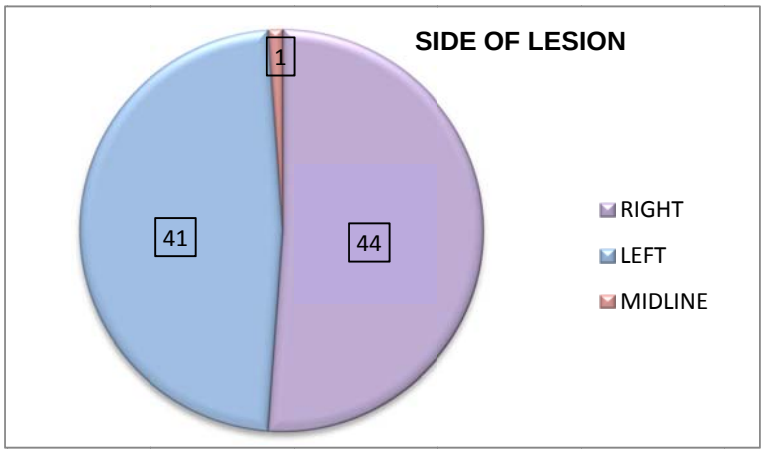
Eloquent *vs* non-eloquent

Lesions of 51patient (59.3%) were in non-eloquent areas whereas that of 35 patients (40.7%) were in eloquent location.

Side of lesion

Majority of lesions were right sided (44patients- 51.2%). In 41 patients (47.7%), nidus was left sided. In 1 patient it had midline corpus callosal location. There were three patients with corpus callosal AVM, but in other two it was predominantly towards one side.

Figure-1: Side of AVM nidus



Size of nidus

Majority (52.3%) of the case were of moderate size (3 to 6cm). 45.3% of cases were less than 3cm and 2 patients had lesion more than 6cm.

Size was comparable between bled and un-bled group.

Table-12: Size of AVM nidus in total, bled and unbled groups

NIDUS SIZE	TOTAL	BLED	UNBLED
0-3CM	39(45.3%)	19(44.2%)	20(46.5%)
3-6CM	45(52.3%)	24(55.8%)	21(48.8%)
>6CM	2(2.3%)	0	2(4.7%)
Total	86	43	43

Nidus type

Majority were compact nidus type AVM.

Table-13- Type of AVM nidus

NIDUS TYPE	NUMBER	%
COMPACT	78	90.7
DIFFUSE	8	9.3
TOTAL	86	

AVM related aneurysms

AVM related aneurysms were classified on the basis of Tews' classification. 18 patients had AVM related aneurysms. Most of them were intranidal (in 14 patients). One patient had type-3 and type-4 aneurysm co-existing. One had type-1 aneurysm and none had type-2 aneurysms.

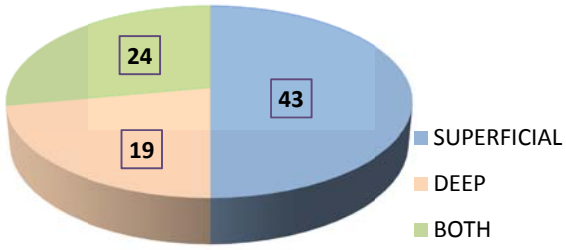
Table-14: Frequency distribution of AVM related aneurysms

ANEURYSM	NUMBER
TYPE-1	1
TYPE-2	0
TYPE-3	4
TYPE-4	14
NIL	68

Venous drainage

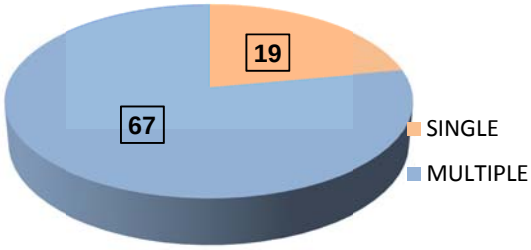
50% of patient had superficial venous drainage. 19 patients (22.1%) had deep venous drainage and 24 patients (27.9%) had both superficial and deep pattern of drainage.

Figure-2: Venous drainage pattern



Majority (67%) had multiple draining veins. 19% had single draining vein.

Figure-3: Number of draining veins



Venous ectasia was seen in 23 patients and stenosis in three patients. Sinus thrombosis was seen in two patients.

Table-15: Venous changes

VENOUS CHANGES	NUMBER
STENOSIS/ OCCLUSION	3
ECTASIA	23
NORMAL	60

Grading

Spetzler Martin grading was applied to these AVMs based on location, size and venous drainage pattern on evaluation of angiographic images. 30patients each were in grade 2 and 3 (34.9% each). 7 (8.1%) had grade-1 lesion. 18 patients (20.9%) had grade-4 lesions and one had grade-5 lesion.

Table-16: Frequency distribution of SM grade

SM- GRADE	NUMBER	%
1	7	8.1
2	30	34.9
3	30	34.9
4	18	20.9
5	1	1.2

Management

A Total of 86 patients were embolized during the period. 3 patients required 3 sittings of embolization. 21 patients required 2 sittings of embolization and rest 62 patients underwent embolization in single sitting.

Embolising agent

Embolisation was performed with onyx alone in 70 patients (81.4%). Onyx was used along with glue in 12 patients and with ethanol in 3 patients. In one patient, onyx, glue and ethanol were used. Majority of cases where glue and ethanol were used in addition to onyx were in initial half of study period.

Table-17: Frequency distribution of embolising agent used

MATERIAL	NUMBER
ONYX	70
ONYX + GLUE	12
ONYX + ETHANOL	3
ONYX + G + E	1
TOTAL	86

Microcatheter

Most frequently used microcatheter was Marathon, followed by sonic detachable tip microcatheter. Ultraflow was used in 12 patients. Apollo detachable tip microcatheter was used in 4patients.

Table-18: Frequency distribution of microcatheter used for embolisation

MICROCATHETER	NUMBER
MARATHON	57
ULTRAFLOW	12
SONIC	23
SPINNACKER	2
APOLLO	4

Obliteration of nidus

In 6 patients, we could achieve 100% obliteration of nidus. In 23 patients 90 to 99% obliteration was achieved. Hence, 29 patients (33.7%) got >90% obliteration of nidus. In 60.5% of patients, more than 70% obliteration of nidus was achieved.

In 18% of patients, we could achieve only <40% obliteration of nidus, most of them of SM grade more than 3 and embolization were targeted to angiographic weak points.

Table-19: % obliteration of nidus

NIDUS OBLITERATION	NUMBER	%
0-9%	1	1.2
10 to 19%	3	3.5
20 to 29%	5	5.8
30 to 39%	7	8.1
40 to 49%	6	7
50 to 59%	7	8.1
60 to 69%	5	5.8
70 to 79%	16	18.6
80 to 89%	7	8.1
90 to 99%	23	26.7
100%	6	7
Total	86	

The mean nidus obliteration rate obtained in the whole study group was 66.23%. It is about 67.2% in the subgroup where onyx was used alone.

Average onyx injected per session was about 2.46ml and average amount injected per person was about 2.93ml (excluding the two patients whose data is not available). Average injection time per session was about 51.3minutes. 13minutes was the smallest recorded injection time and 130minutes the maximum recorded injection time per session.

Average onyx injection time per person was about 60.4minutes.

Largest amount injected person was 16ml in 220minutes. This was given in two sessions 6ml and 10ml in sessions of duration 90minutes and 130minutes respectively. This patient achieved about 85% obliteration of nidus without any complication.

Complications

We had eight instances of intracranial hemorrhage post-procedure. Half of them required surgical evacuation. All of them survived. There was no mortality procedure related mortality in our group.

Table-20: Complications encountered

COMPLICATIONS	NUMBER
PUNCTURE SITE HEMATOMA	1
STUCK CATHETER	10
IC HEMORRHAGE	8
VENOUS THROMBOSIS	1
NIL	60

All instances of hemorrhage occurred when procedure was done in single stage, except in two cases when it occurred in first sitting when complete obliteration was targeted. These occurred mainly in first half of study period. In later period we opted to stage the embolisation and there were no instances of bleed.

Instances of stuck microcatheter were encountered in 10 instances. This complication was significantly reduced when we started using detachable tip microcatheter. There was only one instance of stuck micro catheter when a detachable tip microcatheter was used. This was in a case where Sonic was used and about 1.5ml onyx was injected over 40minutes.

Poor percolation was seen in 11 patients.

Post-procedure outcome

There was no procedure related mortality. Post procedure outcome was Glasgow outcome score 5 in 84/86 patients. One patient had moderate disability and one had severe disability post procedure. Both of them had post embolisation intracranial bleed, requiring evacuation. One underwent radiation subsequently for residue and has only very minimal residue on last check angiogram. Other patient with severe disability lost to follow-up.

Table-21: Post-procedure outcome

GOS	NUMBER
1	0
2	0
3	1
4	1
5	84

Adjuvant treatment

37 patient received radiation following embolisation. 7 underwent surgery. 1 received both surgery and radiation. This patient has post-procedural bleed, which was evacuated with partial excision of AVM nidus. Follow-up angiogram showed residue for which she received radiation.

Table-22: Adjuvant treatment received

ADJUVANT	NUMBER
NIL	41
RT	37
SURGERY	7
RT + SURGERY	1

Final outcome

Final outcome data is available in 32patients. Of these 20 (62.5%) attained complete obliteration of AVM nidus. More than 90% obliteration was achieved in 26 out of these 32 (81.3%).

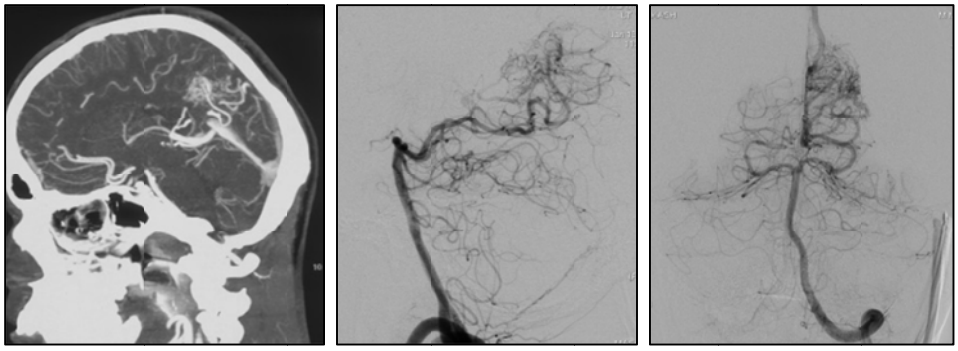
REPRESENTATIVE CASES

Case - 1

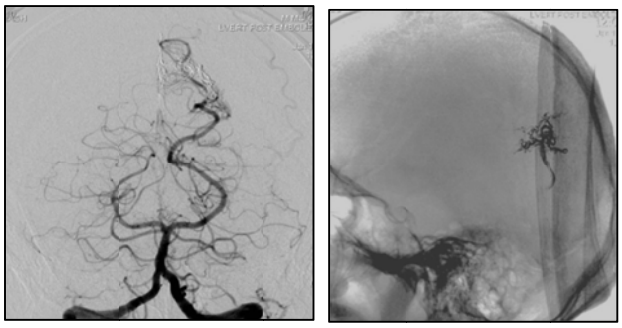
18year right handed male without any significant comorbidities, apparently normal till 27th Feb 2011, when he felt sudden onset severe headache followed by loss of consciousness. Immediately he was taken to local hospital and CT scan done. CT Brain done on 27/02/2011 showed acute intracerebral hemorrhage in left parietal region measuring 4.3 X 2.3cm. He remained in ICU for about one week in altered conscious state. He gradually improved over days. He came to SCTIMST for definitive treatment. On examination, there were no significant neurodeficits.

CT cerebral angiogram done on 28 April 2011 showed AVM with nidus measuring about 25 X 18 X 18mm in left parietal lobe

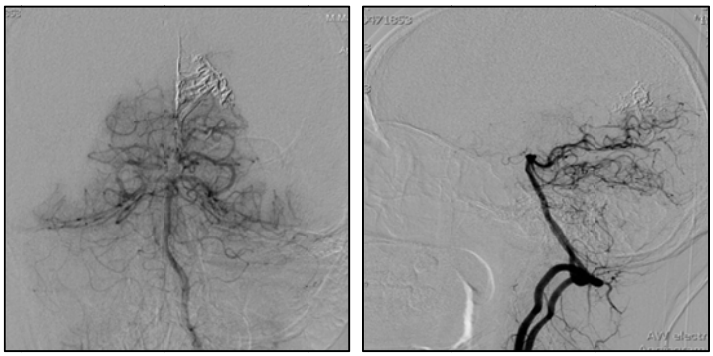
DSA done on 13/1/2012 showed diffuse nidus AVM with nidus measuring 22 X 20 X 16mm in medial left parietal region fed by multiple small feeders from parieto-occipital branch of left PCA. Venous drainage is through dilated cortical vein-> Superior sagittal sinus and also through deep veins to Vein of Galen-> Straight sinus. No feeding artery or intranidal aneurysm.



Embolization was done achieving 80-90% obliteration of nidus done on 18/01/2012.



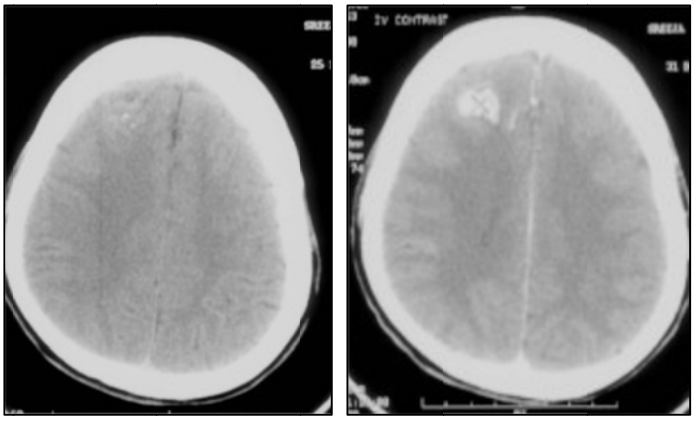
Subsequently he was referred for radiotherapy. Radiotherapy was completed in April 2012. Check DSA done on April 2014 showed complete obliteration of AVM nidus.



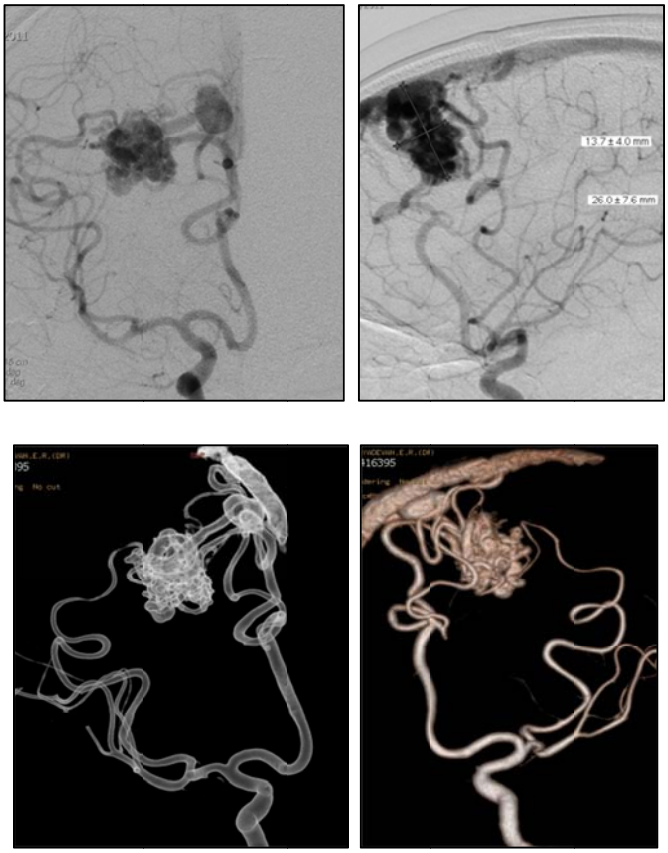
Case - 2

This 33 year old female without any known co-morbidities presented with history of intermittent, mild to moderate, non-radiating, parieto-occipital region headache with no specific diurnal variation, occasionally associated with vomiting. She also has history extra temporal complex partial seizures from Dec 2010 after which regular antiepileptic medications. Seizures continued despite taking AEDs regularly. On examination, there were no significant neurodeficits.

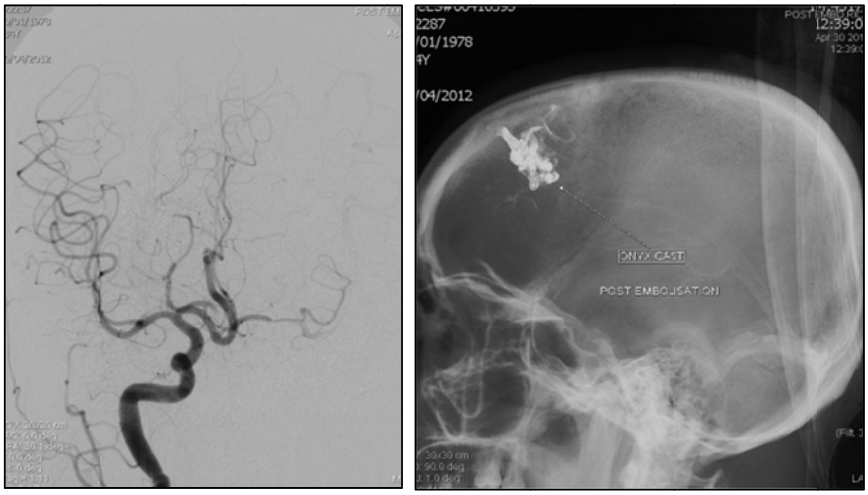
CT scan done in Dec 2012 showed a calcified lesion in right frontal lobe surrounded by prominent enhancing vascular channels.



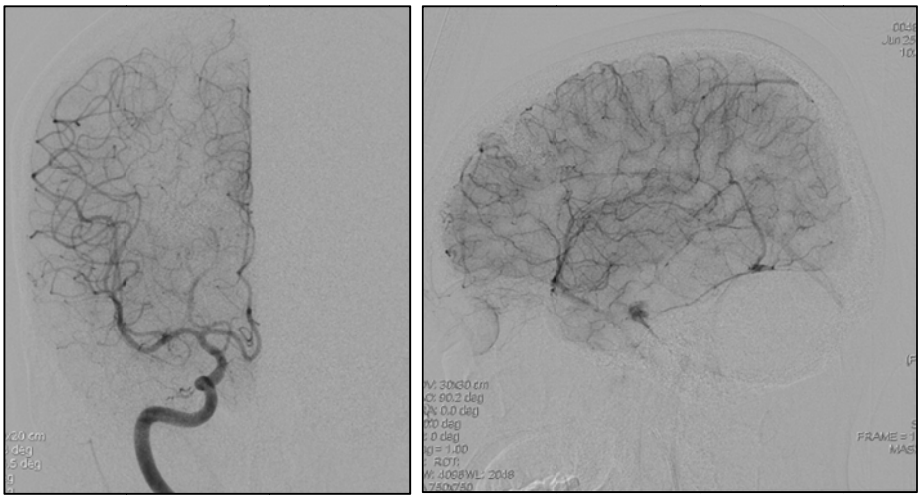
DSA done on Jan 11 showed compact AVM with nidus measuring 26 X 18 X 14 mm seen in right frontal lobe fed by anterior internal branch of Right ICA and precentral branch of right MCA. Venous drainage is to anterior aspect of SSS. No associated aneurysm



She underwent embolisation using about 3.3ml Onyx achieving complete obliteration of nidus on April 2012.

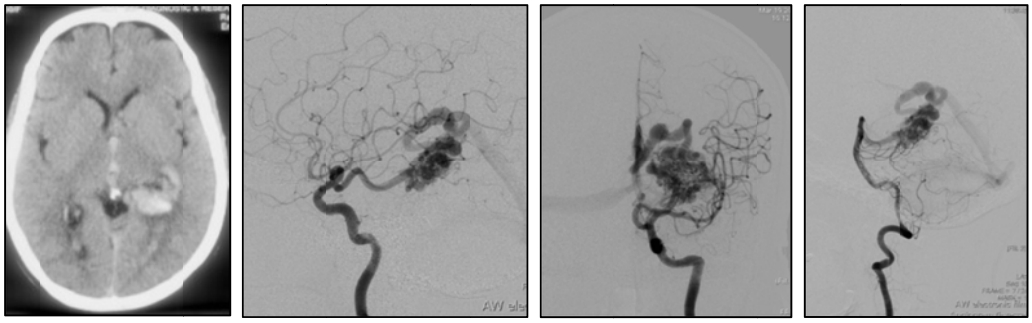


Follow-up DSA was done on June 2013 which shows no recurrent or residual lesions. She is on tapering AEDs.

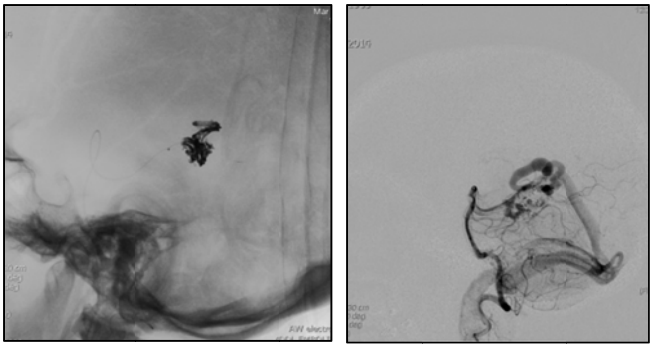


Case - 3

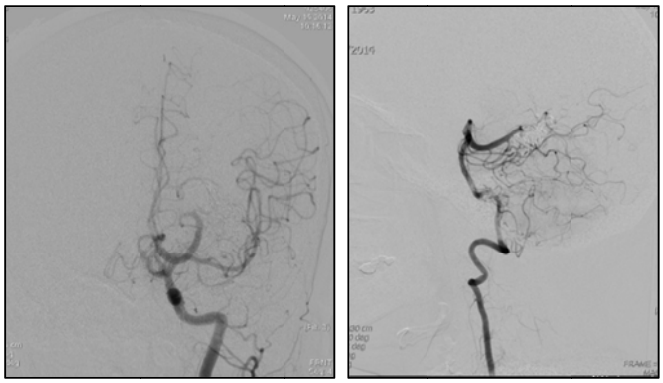
50yr old female, was apparently well till 26/5/13 when she developed sudden onset of giddiness which was associated with multiple episodes of vomiting. There is no history of headache/LOC/seizures/weakness of limbs. She was initially treated elsewhere and evaluation revealed with CT showed left temporal hematoma with hemorrhage in all ventricles. Further evaluation revealed left peritrigonal AVM. She was managed conservatively and referred to us for definitive treatment. There were no significant neurodeficits on examination. DSA done on 12/7/13, which revealed SM grade 3 left choroidal and peritrigonal AVM.



She underwent Onyx embolisation of AVM with about 60% obliteration of nidus on 19/3/14. Subsequently developed draining vein thrombosis. She was managed conservatively. No adjuvant treatment received.



Check DSA done in Sep 2014 showed complete obliteration of AVM nidus.

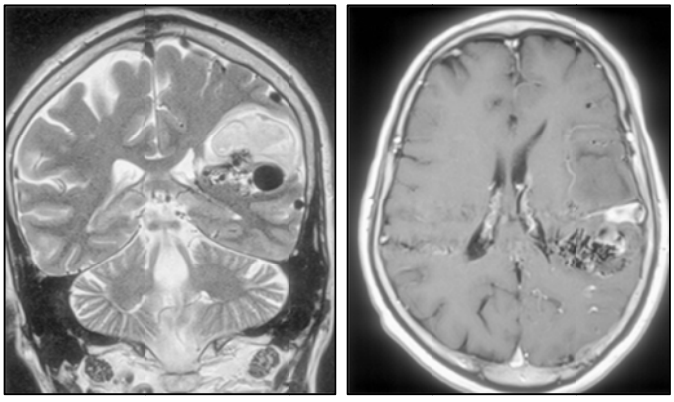


Case - 4

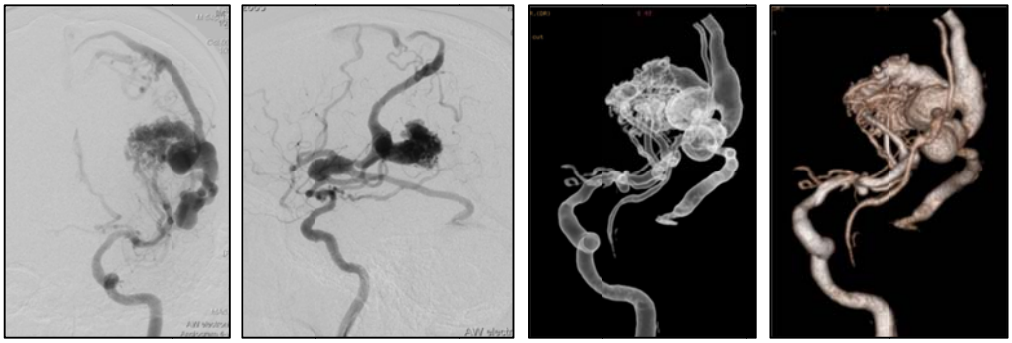
This 66year old male, smoker, without any known comorbidities, presented with sudden onset of weakness of right side of body on 20/07/2012. He found difficulty in taking objects in hand, difficulty in standing and walking associated with difficulty in speech. There was no h/o headache, loss of consciousness, vomiting, trauma or seizures. Imaging showed intracranial bleed. Symptomatically, he was improving gradually, and on admission, he was able to walk without support. Speech was also gradually improving.

On examination, general and systemic examinations were normal. CNS- Motor system- Normal bulk and tone. 4+/5 power in right upper and lower limb. Normal 5/5 power on left side. Reflexes normal. Plantar- bilateral flexor. Rest of neurological examination was normal.

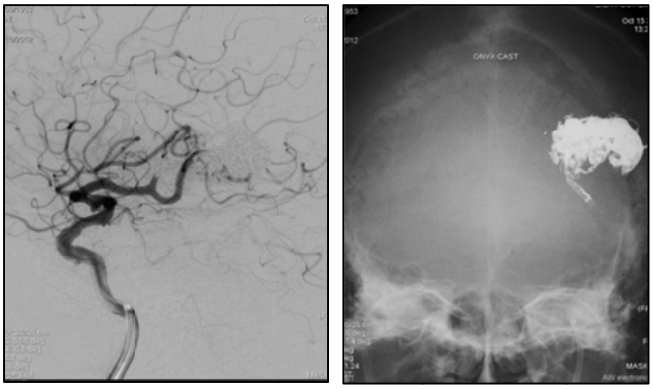
MRI done on 20/07/2012 showed left parietal lesion with multiple flow-voids and prominent draining vein s/o AVM with hematoma.



He underwent DSA on 09/10/2012 which showed a compact AVM nidus located in left parietal lobe and operculum with nidus size measuring 23.8 x 30.2 x 22.2 mm (AP x TR x CC). Arterial feeders are from the post central and parietal branch of left MCA. A wide neck saccular posteriorly directed flow related aneurysm is seen in left M1 MCA measuring 3.1 x 3.4 mm. There is a small intranidal aneurysm measuring 1.4 mm in size in superior and medial aspect of the nidus. Significant fistulous component is seen in the AVM nidus. Venous drainage is via (a) Vein of Trolard into superior sagittal sinus (b) Vein of Labbe into left transverse and sigmoid sinus (c)Dilated SMCV with a venous sac within it and reflux into the cortical vein (d) through small branches into VOG--> straight sinus.



He underwent endovascular intervention on 15/10/2014. Near-total obliteration of AVM nidus was achieved using 7.5ml of onyx. In single sitting. post embolisation 3D CT done showed no e/o any intracranial bleeds.

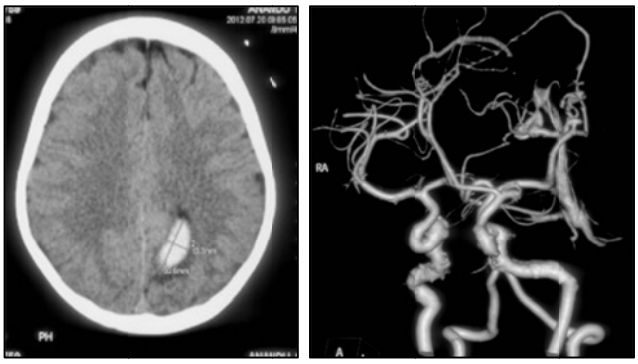


Post procedure he was observed in ICU and he was noted have slurred speech and mild disorientation in the evening and emergent CT showed a large acute bleed in the left temporo-parietal region with fluid levels. Emergent neurosurgery consultation was sought and immediate evacuation of the hematoma was done. Post evacuation, he was observed in ICU with all supportive measures. Tracheostomy was performed and he was slowly weaned from the ventilator. He had right side hemiplegia which was gradually improving. He was discharged after about 20 days of procedure. He had gradual improvement in higher mental functions and right hemiplegia.

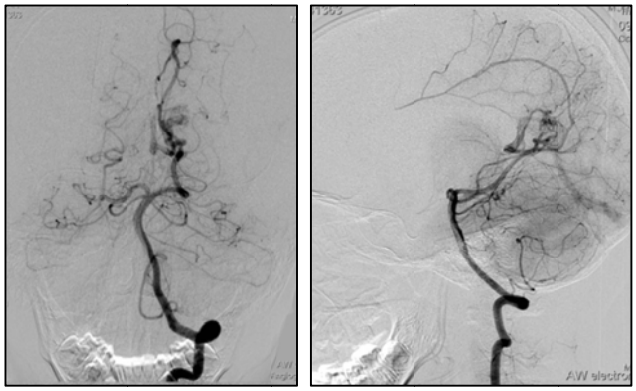
Case - 5

10 year old boy presented with complaints of sudden onset severe holocranial headache on 17/07/2012 when child was playing in school followed by multiple episodes of vomiting. He was taken to the local hospital where he had one episode of generalized tonic-clonic seizure. No history of loss of consciousness, visual disturbances, limb weakness, gait disturbances.

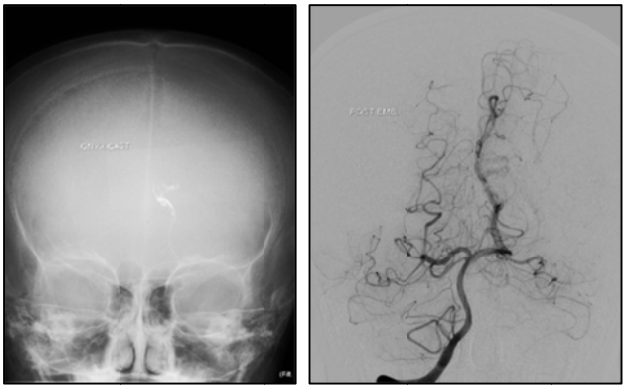
CT followed by CTA was done immediately which showed left occipital lobe hematoma with 1 x 1 cm size AVM nidus



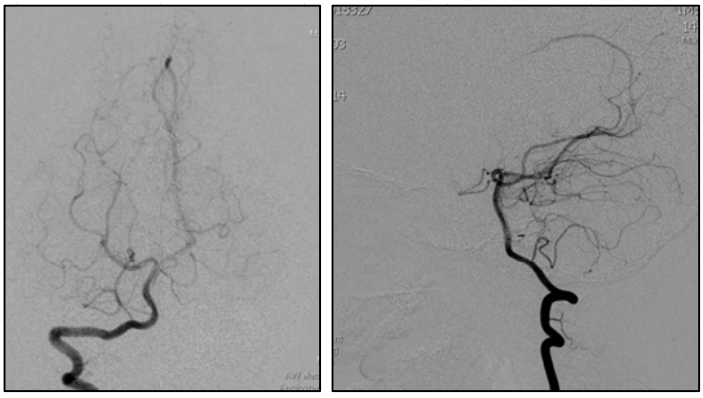
Patient was then evaluated with a DSA on October 2012 which showed small compact nidus left occipital AVM, feeders from parieto-occipital branch of left PCA and venous drainage into the Vein of Galen-> Straight sinus. No intranidal aneurysm



He underwent embolisation on Dec 2012 using about 0.8ml of Onyx achieving 90% obliteration of AVM nidus.

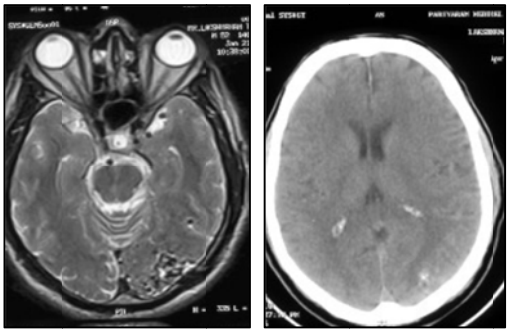


He subsequently underwent radiotherapy in Mar 2013. Check DSA done on March 2014 showed complete obliteration of AVM.

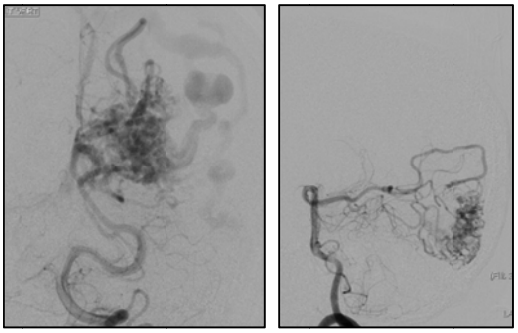


Case - 6

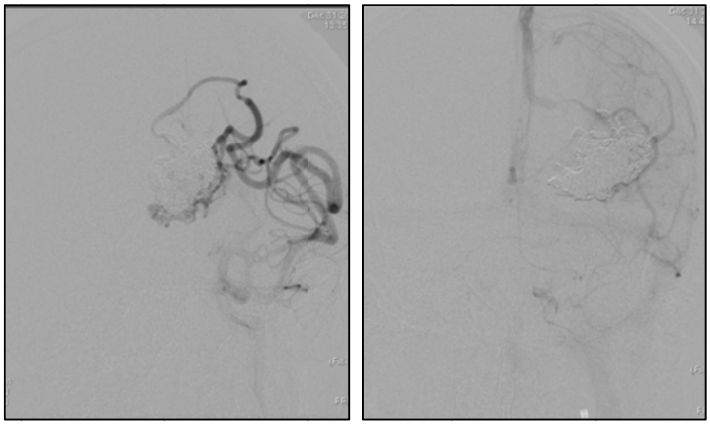
54-year-old male patient had presented with recurrent episodes of (4 episodes in last 2 months) seizures. Seizures were GTCS in nature with post-ictal drowsiness. He also has been complaining of headache associated with visual symptoms and nausea since last 25 years. He was evaluated with imaging and diagnosed to have a left parieto-occipital AVM



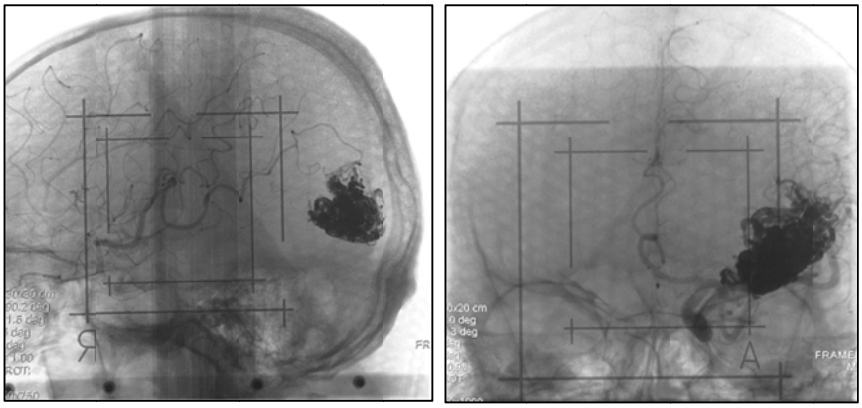
DSA showed evidence of AVM nidus 3.6x2.6x2.7cm. Feeders are from parieto-occipital branch of left PCA and parietal branches from left MCA. Venous drainage to SSS/TS.



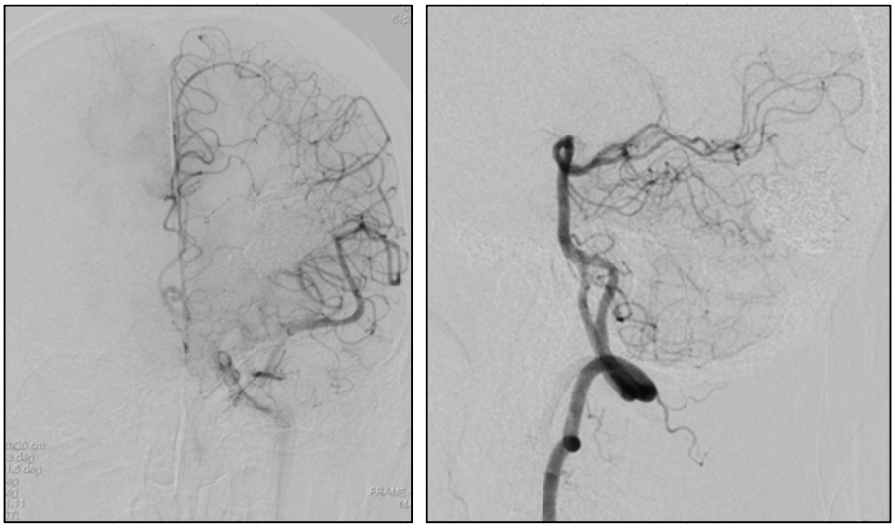
He underwent embolization with about 6ml of onyx achieving 95% nidus obliteration on Dec 2010.



He underwent SRS with DSA planning on August 2012.



Check DSA done on Sep 2013 showed complete obliteration of AVM nidus. He has discontinued AEDs on his own since last 10 months without any further episodes of seizures.



DISCUSSION

This is a prospective and retrospective study to analyze clinical & radiological characteristics, efficacy of management by embolization using onyx and its complications in patients with brain arterio-venous malformations (AVM) with a focus to generate data in Indian context as most of the extensively published data has been from the western literature.

The study group included patients with brain AVM who reported to SCTIMST between 1 Jan 2008 and 31 May 2014 and treated with onyx, alone or in combination with other agents. There were a total of 86 cases included in the study.

The age of our study group ranged between 8-65 years (mean 30 years, median 28yrs). In a recently published systematic review and meta- analysis by Van Beijunum et al (JAMA, 2008), the median age among 13698 patients was 34 years (range 10-54 years)[95]. In another large series of 1289 patients published by Las Jaunias et al (Stroke, 2000), the median age was 31.2 years (range 0-60 and above)[96]. Hence our findings are in concordance with available data; our mean age being 30years.

One important observation to note is that we had 4 patients in first decade. All these cases presented with bleed. This is in different from the

aforesaid meta-analysis and support the congenital etiology of AVM. This also supports the theory that more cases can be diagnosed early with increased awareness about this condition in general practitioners and improving diagnostic facilities.

The male to female ratio (50:36 – 1.39:1) in our study showed a slight male preponderance. This is in concordance with both the above quoted large studies which showed only slight male preponderance (male to female ratio was 1.2:1)

The clinical presentation of the AVMs can be classified broadly into hemorrhagic and non-hemorrhagic which determines the urgency and necessity to treat them to a significant extent. In a prospective population-based study published in 1996, 65% of patients newly diagnosed with a brain AVM presented with intracranial hemorrhage[17]. The more recent prospective population-based study of brain AVMs in the New York Islands reported that 38% of patients with newly found AVMs presented with intracranial hemorrhage[15]. The Lasujaunias group (ii) reported 51% of their patients presenting with hemorrhage. 50% patients (43 out of 86) in our study group presented with hemorrhagic manifestations. This is in concordance with the above mentioned literature data.

The second commonest manifestations seen in our study were seizures (35 patients, 40.1%). In the literature also, the second most common form of clinical presentation is seizure. In one retrospective population-based study, 19% of newly discovered AVMs presented with seizures[17]. In two retrospective hospital-based studies, 18% and 27% of AVMs presented with seizures, respectively[25, 26]. In the series published by Las Jaunias et al *(ii)* seizures were seen in 40%, Our study group included more number of patients presented with seizures. This may be because our institute having a well-established comprehensive epilepsy center, having largest number of epilepsy surgery performed in India.

Table-23: Location in patients presenting with seizures

LOCATION	NUMBER	%
FRONTAL	13	37.1
PARIETAL	11	31.4
TEMPORAL	5	14.3
OCCIPITAL	5	14.3
BRAIN STEM	0	0
CEREBELLUM	1	2.9

Among patients, presented with seizures, most of them were located in frontal and parietal lobe and only 5 in temporal lobe. Also patients with seizures were equally distributed along superficial and deep locations. Francis

Turjman et al observed cortical location to be predictive of epilepsy. In his analysis of 100 patients, common location for AVM were temporal followed by parietal and frontal[115]. Discordance in our observation might be due the fact that the study group limited by AVM patients who underwent endovascular treatment, which might not be representative to make a valid observation in this regard.

Table-24: Plane of lesion in patients presenting with seizures

PLANE	NUMBER
SUPERFICIAL	17
DEEP	18
PERIVENTRICULAR	0
INTRAVENTRICULAR	0

Other less common brain AVM presentations include headache (1% and 11% in two hospital-based series)[25, 26], focal neurological deficit (7% and 5% in two hospital-based series)[25, 26], and as an incidental finding in an asymptomatic individual (15% in one population-based study, 0.5% and 3% in two hospital based series)[17, 25, 26]. In the series published by Lasjaunias et al neurodeficits occurred in 14% and headache in 7% patients. The other manifestations seen in our study were head ache (27patients, 31.4%) and focal neurological deficits (8 patients, 9.3%). Only two AVMs were incidentally detected. It is important to note that the prevalence rates for these less

common manifestations are as such significantly variable in literature as mentioned above.

As far as angioarchitecture features are concerned, most of the AVMs in our series were in frontal and parietal location (24.4 & 25.6% respectively) followed by occipital (19.8%) and temporal (15.1%). The current available data on location and plane of AVM is varying and our study group is small to make any interpretations in this regard. Also it included only limited patients who underwent endovascular embolisation with onyx.

Majority (53.5%) of nidus were located deep. In 28% nidus location was superficial. It was located in periventricular location in 17.4% and intraventricular in 1 patient. Compared with un-bled group, bled group had more AVMs at periventricular location and less AVMs in superficial location in our group.

Table-25: Comparison of plane of lesion in bled and unbled group

PLANE	BLED	UNBLED
SUPERFICIAL	7(16.3%)	17(39.5%)
DEEP	22(51.2%)	24(55.8%)
PERIVENTRICULAR	14(32.6%)	1(2.3%)
INTRAVENTRICULAR	0	1(2.3%)

13 patients in bled group had intranidal aneurysm, compared with 5 in unbled group.

We have more patients in bled group with deep drainage, compared with unbled group, in consistence with available data.

Table-26: Comparison of venous drainage pattern in bled and unbled group

VEIN S/D	UNBLED	BLED
SUPERFICIAL	23(53.5%)	20(46.5%)
DEEP	7(16.3%)	12(28%)
BOTH	13(30.2%)	11(25.6%)

But in our group, more patients in unbled group had single draining vein compared with bled group. This observation is different from the evidence currently available which considers single draining as a predictor of bleed[11]. Also we observed 2 cases with venous stenosis in unbled group compared with one in bled group. These differences with currently available data are likely due to small study group and it included only patients underwent endovascular treatment with onyx.

Table-27: Number of draining veins in bled and unbled group

VEIN S/M	UNBLED	BLED
SINGLE	11 (25.6%)	8 (18.6%)
MULTIPLE	32 (74.4%)	35 (81.4%)

In our group who underwent onyx embolisation, majority were in SM grade 2 or 3. We treated most of patients in single stage of embolisation (62 out of 86). 21 patients were treated as two sittings and three in 3sittings. We observed significantly fewer instances of hemorrhagic complications in the group who underwent treatment in multiple sittings rather than in single stage.

In 6 patients, we could achieve 100% obliteration of nidus. In 23 patients 90 to 99% obliteration was achieved. Hence, 29 patients (33.7%) got >90% obliteration of nidus. In 60.5% of patients, more than 70% obliteration of nidus was achieved.

Average injection time per session was about 51.3minutes. 13minutes was the smallest recorded injection time and 130minutes the maximum recorded injection time per session.

Average onyx injection time per person was about 60.4minutes.

Table- 28: Results of the endovascular treatment of brain AVMs using Onyx

Series	Year	Number	Complete occlusion
Perez-Higueras[101]	2005	45	22.2 %
Van Rooij[104]	2007	44	16.0 %
Weber[105]	2007	93	20.0 %
Mounayer[100]	2007	94	49.0 %
Katsaridis[106]	2008	101	53.9 %
Pierot[103]	2009	50	8.3 %
Panagiotopoulos[97]	2009	82	24.4 %
S.Maimon etal[98]	2010	43	37%
Xu[107]	2011	86	18.6 %
Isil Saatci[108]	2011	350	50.9 %
BRAVO[109]	2013	127	23.5 %
Present study	2014	86	7%

Our complete obliteration rate was less compared with rest of literature, mostly because our target was usually to reduce size of nidus for facilitating adjuvant treatment for complete cure and reduce complications. This is reflected in our comparison of complications with other studies.

BRAVO is the largest multicenter study to independently evaluate the safety and efficacy of Onyx embolization for brain AVMs. It shows that this treatment is resulted in 100 % occlusion rate in 23.5 % of patients and most patients with incomplete embolisation amenable to a complementary treatment (82.3 %)[109].

W.J.VanRooji et al. achieved average 75% (median 80%, range 40%–100%) nidal obliteration using onyx in their study group of 44 patients (our average nidal obliteration rate is 67.2%). They achieved total embolization in 16%[104]. V. Panagiotopoulos et al. reports complete obliteration rate of 24.4 %(30/82) at the end of all endovascular procedures and an average of 75% (range, 30%–100%) volume reduction. An average of 2.6-mL Onyx was used per patient (160). Average amount injected per person in our group was about 2.93ml[97].

Literature regarding experience of onyx embolisation using detachable tip microcatheter is also coming forth. S.Maimon et al reports 55% complete embolization using detachable tip catheter in patients who concluded treatments (16/29) in their total study population of 43. They also achieved

complete embolization in 37% of the whole cohort (16/43). They were able to inject significantly larger amount of onyx using detachable tip catheter than that injected with the non-detachable microcatheters (mean volume, 2.5 +/- 2.2 versus 1.7 +/-1.3 mL, respectively, P< .05, t test). In our subgroup of patients where detachable tip microcatheters were used, we achieved an average obliteration rate of about 62.8%, which is less than the average rate in whole group (66.23%). But we were able to inject slightly more onyx with detachable tip microcatheters (2.98ml compared with 2.93 per patient in whole group). Less than expected results in our group might be due to more number of larger AVMs[98].

Isil saatcI et al. in their series of 350 patients reports angiographically confirmed obliteration achieved in 179 patients (51%) with only endovascular treatment; 1 patient died due to intracranial hemorrhage after the treatment. In the entire series, 5 patients died; the mortality rate was 1.4%. The permanent morbidity rate was 7.1%. We had eight instances of intracranial hemorrhage post-procedure. Half of them required surgical evacuation. All of them survived. There was no mortality procedure related mortality in our group. Only two patients had procedure related significant morbidity.

The complications associated with AVM embolization have produced variable morbidity and mortality with better results in the recent years with introduction of onyx. A summary of morbidity and mortality rates on literature review is shown in table below

Table-29: Clinical and anatomical results of the endovascular treatment of brain AVMs using Onyx

Series	Year	Number	Haemorrhagic complications	Morbidity	Mortality
Perez-Higueras[101]	2005	45	8.9 %	15.5 %	2.0 %
Song[102]	2005	50	6.0 %	10.0 %	0.0 %
Van Rooij[104]	2007	44	6.8 %	4.6 %	2.3 %
Weber[105]	2007	93	-	12.0 %	0.0 %
Mounayer[100]	2007	94	8.5 %	8.5 %	3.2 %
Katsaridis[106]	2008	101	5.9 %	8.0 %	3.0 %
Pierot[103]	2009	50	8.0 %	8.0 %	2.0 %
Panagiotopoulos[97]	2009	82	12.2 %	3.8 %	2.4 %
S.Maimon etal[98]	2010	43	13.9%	6.9%	-
Xu[107]	2011	86	7.0 %	3.5 %	1.2 %
Isil Saatci[108]	2011	350	4.0 %	4.3 %	1.1 %
BRAVO[109]	2013	127	8.5 %	5.1 %	4.3 %
Present study	2014	86	9.3%	2.3%	0

Among other complications, catheter gluing was seen in 10 patients, which significantly reduced after started using detachable tip microcatheters. In series published by C. Mounayer etal of the use of onyx in AVM embolisation, using standard microcatheter, they achieved 49% (26/53) angiographic cure. They had four instances for trapping of catheter tip (162). Only available case series of Sonic use is by S.Maimon et al from Tel Aviv which achieved 55% cure rate in patients who concluded treatments (16/29) and 37% in the whole study group (16/43). Average Onyx volume injected by this group is 2.5ml using detachable tip microcatheter and 1.7ml using non-detachable tip microcatheter (160). They had no instances of stuck catheter.

Our morbidity rate and mortality rate were significantly less compared to most of the series quoted in literature above.

CONCLUSION

Brain AVM management remained always complex and controversial. With more and more literature evidences coming in recent few years, and improvement in treatment techniques, brain AVM treatment has significantly improved with better outcomes and reduces treatment related complications. Even though there are larger series about brain AVM from western literature, larger studies from Indian subcontinent is currently not available.

Brain AVM requires multimodality treatment after careful evaluation of clinical and angiographic profile of lesions. Our group comprised neurologist, neurosurgeon, interventional neuroradiologists and radiation experts. This study, largest group from Indian population, showed that the clinical and angiographic profile of brain AVM is almost in concordance with available evidence. In our group, 33.7% of patients with brain AVMs could be near-completely (>90%) embolized, with a morbidity of 2.3%, without any instances of mortality. Further, with adjuvant treatment, complete obliteration achieved in 62.5% and near-complete obliteration in 81.3%.

Embolization has a significant role in the multimodality treatment of brain AVMs, by either enabling or facilitating subsequent microsurgical or radiosurgical treatment. Results of AVM treatment have shown better outcomes with use of Onyx. Appropriately targeted embolization in otherwise untreatable AVMs represents a reasonable form of palliative treatment for

either ameliorating the clinical condition of the patient or reducing the potential risk of hemorrhage.

This series also helped us in reaching following inferences regarding practical management based on observations and outcomes on analysis of data -

1. The clinical and radiological features of brain AVM in our Indian study group was generally in concordance with the available literature evidence from abroad except few observations.
2. Periventricular and deep location, deep venous drainage, AVM related aneurysms etc. increased the risk of bleed in our study group also in concordance with available literature, but single draining vein doesn't seems to increase bleeding risk.
3. Among patients who had seizure, our study observed more AVMs in frontal and parietal lobes rather than temporal lobes and also they were equally distributed in superficial cortical and deep planes.
4. In carefully selected patients, we may aim for curative embolization whereas in others, only pre surgical /pre RT embolization, targeted or palliative embolization may be carried out. The rate of complete obliteration of AVM with nidus with endovascular treatment alone was less in our group compared with majority of other studies, this is probably because our target was size reduction to facilitate adjuvant treatment rather than complete endovascular obliteration. We got

overall better final outcome with multimodality treatment along with significantly reduced complication rate.

5. Onyx shows better nidus obliteration rates as compared to previously used agents and should be the embolic agent of choice as far as possible. It gave good control on nidal percolation and reduced overall procedure time.
6. Advances in technology should be carefully used to the maximum, to reduce complications rate and improve results. For example, detachable tip catheters significantly helped us in reducing the instances of stuck microcatheter.
7. Techniques should also be tailored based on experience, as literature evidence AVM management is only emerging. In our case, we found it beneficial to stage embolisation and targeting size reduction rather than complete embolisation to significantly reduce complications, especially in unbled AVMs (also considering ARUBA trial results). We didn't experience any significant increase in AVM bleed after partial and targeted embolisation.

To conclude, rather than angiographic cure, treatment aim should be always a good final outcome for the diseased. It should be done by utilizing all available treatment options appropriately, so as to avoid complications and finally resulting in a fruitful productive life.

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ANNEXURES

Annexure 1: PROFORMA

1. Clinical
   a) Presentation
      i) Incidental
      ii) Hemorrhage
      iii) Seizure
      iv) Focal neurological deficit
      v) Headache
      vi) Other
   b) Date of presentation (date)
2) Location and size
   a) Lesion side
      i) Right
      ii) Left
      iii) Midline
   b) BAVM size (mm)
   c) BAVM location

i)	Cortical	viii)	Internal capsule
ii)	Subcortical	ix)	Intraventricular
iii)	Periventricular	x)	Corpus callosum
iv)	Frontal	xi)	Cerebellar hemisphere
v)	Temporal	xii)	Vermian (paramedian)
vi)	Parietal	xiii)	Deep cerebellar nuclei
vii)	Occipital	xiv)	Brain stem
viii)	Basal ganglia		

   d) BAVM eloquence

   i) Eloquent
   ii) Non eloquent

e) BAVM haemorrhage

i) Bled
ii) Unbled

f) Hemorrhage location

i) Ventricular
ii) Parenchymal
iii) Subarachnoid

3) Venous drainage

a) Superficial vs deep venous drainage

i) Both superficial and deep
ii) Superficial only
iii) Deep only

b) Number of draining veins leaving nidus:

c) Venous stenosis/occlusion:

d) Venous ectasia (dilatation) (yes/no):

e) Sinus thrombosis/occlusion:

4) Arterial supply

i)	Anterior cerebral	viii)	Posterior inferior cerebellar
ii)	Middle cerebral	ix)	External carotid
iii)	Posterior cerebral	x)	Other internal carotid branches
iv)	Anterior choroidal	xi)	Basilar
v)	Posterior choroidal	xii)	Vertebral
vi)	Superior cerebellar	xiii)	Other a.
vii)	Anterior inferior cerebellar		

5) Nidus:

   a) Type-

      i) Compact

      ii) Diffuse

6) AVM related aneurysms

      i) Number of aneurysms:

      ii) AVM-related aneurysms location

- Intranidal
- Flow-related
  (a) Proximal
  (b) Distal
- Not flow-related

2) Treatment

   a) Endovascular

      i) Number of sessions:
      ii) Date:
      iii) Feeder:
      iv) Guidecatheter:
      v) Microcatheter:
      vi) Onyx quantity:
      vii) Injection time:
      viii) Other agents:
      ix) Percentage obliteration:

   b) Complications:

      i) Outcome: Glasgow Outcome Scale:

1.	Dead
2.	Vegetative State (meaning the patient is unresponsive, but alive; a "vegetable" in lay language)
3.	Severely Disabled (conscious but the patient requires others for daily support due to disability)
4.	Moderately Disabled (the patient is independent but disabled)
5.	Good Recovery (the patient has resumed most normal activities but may have minor residual problems)

c) Other treatments:

   i) Radiation:
   ii) Surgery:

d) Imaging follow-up:

   i) Available- yes/no

   ii) If yes- modality-

   iii) Residual/ recurrence- Yes/no

   iv) If yes, size-

e) Clinical follow-up:

   i) Symptomatic/ asymptomatic:

   ii) Any new symptoms:

MASTER CHART

SL NO	AGE	SEX	CLINICAL PRESENTATION						IMAGING			DSA								SM GRADE	EMBOLISATION						COMPLICATIONS	GOS	ADJUVANT TREATMENT	FINAL OUTCOME
												NIDUS				VENOUS DRAINAGE															
			BLEED	SEIZURE	HEADACHE	INCIDENTAL	FND	OTHER	PLANE	LOCATION	ELOQUENCE	SIDE	TYPE	SIZE	ANEURYSM	S/D	S/M	CHANGES	SINUS THROMBOSIS		STAGES	MATERIAL	%REDUCTION	QUANTITY OF ONYX (ml)	TIME (mts)	MICROCATHETER				
1	38	M	0	0	1	0	0	0	2	4	1	1	2	2	0	3	2	0	0	4	3	2	40	3.8	100	2	0	5	0	NA
2	13	M	0	0	1	0	0	0	3	6	1	1	2	2	0	3	2	0	0	4	1	2	40	1.8	60	2	0	5	0	NA
3	34	F	0	1	0	0	0	0	2	3	0	2	2	3	0	3	2	2	0	4	1	1	70	7	115	1	0	5	1	REDUCTION
4	52	M	1	0	0	0	0	0	1	8	1	1	1	1	0	1	2	0	0	2	2	3	30	1.9	45	1	1,2,3	5	0	NA
5	21	F	1	1	0	0	1	0	1	1	0	2	1	2	0	1	2	0	0	2	3	4	95	3,7	52, 80	2	4	4	3	MIN RESIDUE
6	30	M	0	1	0	0	0	0	1	4	1	2	1	1	0	1	2	0	0	2	2	3	95	1	40	2	0	5	0	NA
7	30	F	1	0	0	0	1	0	2	3	0	1	1	2	1	3	2	0	0	3	2	1	25	0.5, 0.5	15, 25	1	2,3	5	2	COMPLETE
8	43	M	0	0	1	0	0	0	4	10	0	1	1	1	0	2	2	0	0	2	1	1	90	2.4	45	1	0	5	0	NA
9	23	F	1	1	1	0	1	0	1	2	1	2	1	2	0	1	1	0	0	3	1	2	30	0.4	20	1	0	5	0	NA
10	15	M	0	1	0	0	0	0	2	1	0	2	1	1	0	3	2	0	0	2	2	2	20	0.5	15	1	3	5	0	NA
11	16	F	0	1	1	0	0	0	1	2	1	1	1	2	0	1	2	0	0	3	2	1	60	2.5	55	1	4	5	0	NA
12	25	F	0	1	1	0	0	0	2	2	1	1	2	2	0	3	2	0	0	4	2	2	70	3	70	2	0	5	0	NA
13	18	M	1	1	0	0	0	0	2	1	1	1	1	2	0	3	2	0	0	4	2	2	45	1.2	20	1	2	5	1	NA
14	34	M	0	1	0	0	0	0	1	3	0	1	1	1	0	1	1	0	0	1	2	1	80	2.8, 4		1,2	2	5	0	NA
15	23	M	0	0	1	0	0	0	1	2	1	2	1	1	0	1	2	0	0	2	1	1	100	1.2	40	1	0	5	0	COMPLETE
16	36	F	0	0	0	1	0	0	2	1	0	1	1	2	0	1	2	0	0	3	1	1	50	4	120	2	2,4	5	0	NA
17	41	M	0	0	1	0	0	0	2	4	1	2	1	2	0	3	2	0	0	4	2	1	70	3.2, 1.3	80, 35	2	0	5	0	NA
18	41	M	0	0	0	0	1	0	1	4	1	2	1	1	0	1	2	0	0	2	1	1	70	2.5	50	2	4	5	2	COMPLETE
19	32	F	1	0	1	0	0	0	3	4	1	2	1	2	0	2	1	2	0	4	2	1	70	4,1	100, 20	1,2	3	5	1	NA
20	12	M	0	0	1	0	0	0	1	1	1	2	1	2	0	3	2	0	0	4	3	1	98	2,7.5, 5.5	30, 110, 75	1	2	5	0	NA
21	42	F	0	1	0	0	0	0	2	3	0	2	1	1	0	1	2	0	0	1	1	1	100	1.6	40	1	0	5	0	COMPLETE
22	35	M	1	0	0	0	0	0	2	8	1	1	1	1	0	2	2	0	0	3	2	2	50	3.5	45	1	0	5	1	NA
23	8	M	1	0	0	0	0	0	2	3	1	2	1	2	4	3	2	0	0	3	1	1	95	6.5	125	1	4	5	2	COMPLETE
24	26	M	0	0	1	0	0	0	1	4	1	2	1	1	0	1	2	0	0	3	1	1	100	4	95	2	0	5	0	COMPLETE

SL NO	AGE	SEX	CLINICAL PRESENTATION						IMAGING			DSA								SM GRADE	EMBOLISATION						MICROCATHETER	COMPLICATIONS	GOS	ADJUVANT TREATMENT	FINAL OUTCOME
												NIDUS				VENOUS DRAINAGE															
			BLEED	SEIZURE	HEADACHE	INCIDENTAL	FND	OTHER	PLANE	LOCATION	ELOQUENCE	SIDE	TYPE	SIZE	ANEURYSM	S/D	S/M	CHANGES	SINUS THROMBOSIS		STAGES	MATERIAL	%REDUCTION	QUANTITY OF ONYX (ml)	TIME (mts)					
25	21	F	1	0	0	0	0	0	3	6	0	3	1	2	0	1	1	2	0	2	1	1	80	1.7	25	1	0	5	1	MIN RESIDUE
26	24	F	1	0	0	0	0	0	1	2	0	1	1	1	4	1	1	2	0	1	1	1	95	0.4	15	2	0	5	1	COMPLETE
27	17	M	0	1	0	0	0	0	1	2	1	2	1	2	0	1	1	2	0	3	1	1	30	1.9	60	1	0	5	0	NA
28	13	M	0	1	0	0	0	0	1	4	1	1	1	2	0	1	1	2	0	3	2	2	95	2.8, 1.6	120, 35	1	0	5	1	NEARCOMPLETE
29	17	F	0	1	0	0	0	0	1	1	1	1	1	1	0	1	1	0	0	2	2	1	85	2.6, 1.2	48, 25	1	0	5	1	NA
30	49	M	1	1	0	0	0	0	1	2	1	2	1	2	0	1	2	0	0	3	1	1	75	3.4	85	1	0	5	0	NA
31	17	M	0	1	1	0	0	0	1	2	1	1	1	1	4	1	2	2	0	2	1	1	95	1.5	35	1	0	5	0	NA
32	35	F	1	0	0	0	0	0	3	2	0	2	1	1	3	2	2	2	0	2	1	1	70	0.5	25	1	0	5	1	COMPLETE
33	9	M	1	0	0	0	0	0	2	8	1	1	1	2	0	3	2	0	0	4	1	1	50	0.4	15	1	0	5	1	PARTIAL
34	14	M	0	1	0	0	0	0	1	2	0	1	1	1	4	2	1	0	0	2	1	1	90	0.4	32	1	0	5	0	NA
35	30	M	1	0	1	0	0	0	3	4	1	1	1	2	3	1	2	0	0	3	1	1	25	1.5	45	3	0	5	0	NA
36	42	M	1	1	0	0	0	0	2	1	1	1	1	2	0	1	2	0	0	3	1	1	100	0.5	13	1	0	5	0	COMPLETE
37	52	M	0	1	1	0	0	0	2	4	1	2	1	1	0	1	1	0	0	2	1	1	95	6	90	1	0	5	1	COMPLETE
38	18	F	1	0	1	0	0	0	2	1	1	1	2	2	0	1	2	0	0	3	1	1	10	0.6	20	1	4	5	0	NA
39	43	M	0	1	1	0	0	0	2	8	1	1	1	3	0	2	2	2	0	5	2	3	85	6,10	90, 130	1	0	5	0	NA
40	11	F	0	1	0	0	0	0	1	1	1	1	1	2	0	1	1	0	0	3	1	1	30	0.8	30	1	2,3	5	1	NA
41	36	F	1	1	0	0	0	0	2	2	1	2	1	2	0	3	2	0	0	4	2	1	80	4,3	47,35	1	0	5	1	NA
42	55	M	1	0	1	0	0	0	2	4	1	2	1	1	0	1	2	1,2	0	2	1	1	70	0.8	20	1	0	5	0	NA
43	20	F	1	0	0	0	0	0	2	1	1	2	1	1	0	1	2	2	0	2	1	1	98	1	30	1	2	5	0	NA
44	35	F	0	1	1	0	0	0	2	1	1	1	1	1	0	1	2	0	0	2	1	1	100	3.3	55	1,3	0	5	0	COMPLETE
45	28	M	0	1	1	0	0	0	2	1	1	1	1	2	4	1	1	2	0	3	1	1	50	3.5	56	3	0	5	0	NA
46	43	M	0	1	0	0	0	0	2	1	1	2	1	1	4	3	2	0	0	3	1	1	40	3.4	67	3	0	5	1	NA
47	18	M	1	0	0	0	0	0	2	2	0	2	1	1	0	3	2	0	0	2	1	1	90	1.3	42	3	0	5	1	COMPLETE
48	15	F	1	0	0	0	0	0	2	8	1	1	1	2	0	2	2	0	0	4	1	1	30	1	40	1	2	5	0	NA
49	10	F	1	0	0	0	0	0	2	3	0	2	1	2	0	1	2	0	0	2	1	1	60	2.1	40	1	0	5	2	COMPLETE

SL NO	AGE	SEX	CLINICAL PRESENTATION						IMAGING			DSA								SM GRADE	EMBOLISATION						COMPLICATIONS	GOS	ADJUVANT TREATMENT	FINAL OUTCOME
												NIDUS				VENOUS DRAINAGE														
			BLEED	SEIZURE	HEADACHE	INCIDENTAL	FND	OTHER	PLANE	LOCATION	ELOQUENCE	SIDE	TYPE	SIZE	ANEURYSM	S/D	S/M	CHANGES	SINUS THROMBOSIS		STAGES	MATERIAL	%REDUCTION	QUANTITY OF ONYX (ml)	TIME (mts)	MICROCATHETER				
50	28	M	0	1	0	0	0	0	2	2	1	2	1	2	0	3	2	0	0	4	1	1	0	0.5	15	1	3	5	0	NA
51	39	F	0	0	1	0	0	0	2	3	0	1	1	1	0	2	2	0	0	3	1	1	70	1	55	1	4	5	1	PARTIAL
52	23	F	0	1	1	0	0	0	2	2	1	1	1	2	0	1	2	0	0	3	2	1	70	4.5,2	55, 80	1,3	3	5	1	NA
53	26	M	1	0	0	0	0	0	3	2	0	1	1	1	0	2	2	0	0	2	1	2	70	0.3	10	1	0	5	1	NA
54	40	M	0	0	0	1	0	0	2	8	1	1	1	2	0	2	2	0	0	4	1	1	10	0.2	15	1	3	5	1	NA
55	28	F	1	0	0	0	0	0	3	4	0	1	1	1	0	2	2	0	0	2	1	1	70	2.4	48	3	0	5	1	COMPLETE
56	45	M	1	0	0	0	1	0	2	8	1	2	1	1	0	1	2	0	0	2	1	1	70	NA	35	1,3	0	5	0	NA
57	46	F	1	0	0	0	0	0	2	1	1	2	1	2	4	1	1	2	0	3	1	1	60	2.4	45	1	0	5	0	NA
58	25	F	1	0	0	0	0	0	3	3	0	2	1	1	0	2	2	0	0	2	1	1	90	NA	NA	1	0	5	0	NA
59	46	M	1	1	0	0	0	0	1	1	0	2	1	2	4	3	2	2	0	3	1	2	40	2.7	60	1,4	0	5	1	PARTIAL
60	30	F	0	0	1	0	0	0	1	1	0	2	1	1	0	3	2	0	0	2	1	1	95	3.5	60	1	0	5	1	NEARCOMPLETE
61	22	M	1	0	0	0	0	0	2	2	1	1	1	1	0	1	2	0	0	2	1	1	95	2	57	3	0	5	1	NA
62	17	F	1	0	0	0	0	0	2	1	0	2	1	1	0	2	2	0	0	2	1	1	90	0.4	15	3	0	5	1	COMPLETE
63	32	M	0	1	0	0	0	0	1	1	1	1	1	2	0	1	2	2	0	3	2	1	90	4,4.4	80, 80	1,3	0	5	1	NA
64	48	M	0	0	1	0	0	0	2	8	1	2	2	2	3	2	2	0	0	4	1	1	10	1	25	3	0	5	1	NA
65	38	M	1	1	0	0	0	0	1	1	0	1	1	1	0	1	2	2	0	1	1	1	100	0.6	20	1	0	5	0	COMPLETE
66	49	M	0	0	0	0	1	0	2	3	0	1	2	2	0	2	1	2	0	3	1	1	50	3	60	1	0	5	1	NA
67	36	F	0	0	0	0	1	0	2	8	1	1	1	1	0	3	2	0	0	3	1	1	80	2	45	1	0	5	1	NA
68	40	F	1	0	1	0	0	0	3	2	0	1	1	1	4	1	2	0	0	1	1	2	90	4	90	3,4	0	5	1	PARTIAL
69	37	F	0	0	1	0	0	TINI	2	2	0	2	1	2	0	1	1	2	0	3	2	1	80	1.7	38	5	0	5	0	NA
70	28	M	1	0	0	0	0	0	2	4	1	2	1	2	0	1	2	0	0	3	1	1	95	9.1	120	3	0	5	0	NA
71	9	M	1	1	0	0	0	0	2	4	1	2	1	1	0	2	1	0	0	3	1	1	90	0.4	15	1	0	5	1	COMPLETE
72	19	M	1	0	0	0	0	0	2	4	1	2	1	1	4	1	2	0	0	2	1	2	95	0.6	15	1	0	5	1	NA
73	20	M	0	1	0	0	0	0	1	3	0	2	1	1	0	1	1	2	0	1	1	1	65	2.4	60	1	0	5	2	COMPLETE
74	55	M	1	0	0	0	0	0	3	4	0	2	2	2	0	3	2	0	0	4	1	1	30	1.8	41	3	0	5	0	NA

SL NO	AGE	SEX	CLINICAL PRESENTATION						IMAGING			DSA								SM GRADE	EMBOLISATION						MICROCATHETER	COMPLICATIONS	GOS	ADJUVANT TREATMENT	FINAL OUTCOME
												NIDUS				VENOUS DRAINAGE															
			BLEED	SEIZURE	HEADACHE	INCIDENTAL	FND	OTHER	PLANE	LOCATION	ELOQUENCE	SIDE	TYPE	SIZE	ANEURYSM	S/D	S/M	CHANGES	SINUS THROMBOSIS		STAGES	MATERIAL	%REDUCTION	QUANTITY OF ONYX (ml)	TIME (mts)					
75	59	M	1	0	0	0	0	0	2	2	0	2	1	2	3,4	3	2	2	0	4	1	1	95	7.5	100	1,3	4	3	2	NA
76	12	F	1	0	0	0	0	0	3	4	1	1	1	2	0	3	2	0	1	4	1	1	60	2.5	45	3	0	5	1	REDUCTION
77	65	M	1	0	0	0	0	0	2	2	0	1	1	2	4	1	2	2	0	2	2	1	30	0.9,1	30, 30	1,3	0	5	0	NA
78	16	M	0	1	1	0	0	0	2	1	0	1	1	2	0	1	2	1	0	2	1	1	70	3.8	70	1	0	5	0	NA
79	28	F	1	0	0	0	0	0	3	2	0	1	1	1	4	2	1	2	0	2	1	1	20	0.6	15	3	3	5	1	90%
80	13	F	1	0	0	0	0	0	3	3	0	1	1	2	4	2	1	2	0	3	2	1	70	1, 1.5	40, 84	1,3	3	5	1	NA
81	17	M	0	1	0	0	0	0	2	2	1	1	1	2	0	1	2	0	0	3	1	1	40	2.7	55	5	0	5	0	NA
82	20	M	0	1	0	0	0	0	2	3	1	1	1	1	0	3	2	1	0	3	1	1	50	1.3	48	5	0	5	1	NA
83	39	F	0	0	1	0	1	0	2	1	0	1	1	1	0	1	2	1,2	0	1	1	1	20	0.6	35	3	3	5	1	NA
84	15	F	1	0	0	0	0	0	3	6	0	2	1	1	0	3	2	0	1	2	1	1	50	1.5	40	3	2	5	1	90%
85	50	F	1	0	0	0	0	0	3	3	0	2	1	2	0	2	2	0	0	3	1	1	70	2.3	55	5	5	5	0	COMPLETE
86	19	M	0	1	0	0	0	0	1	4	1	2	1	2	0	3	2	0	0	4	2	1	95	2, 1.8	45, 50	1,3	0	5	2	COMPLETE

CODES TO MASTER CHART

PLANE	No.
CORTICAL	1
DEEP	2
PERIVENTRICULAR	3

ANEURYSM	No.
TYPE-1	1
TYPE-2	2
TYPE-3	3
TYPE-4	4

NIDUS SIDE	No.
RIGHT	1
LEFT	2
MIDLINE	3

VENOUS CHANGES	No.
STENOSIS/ OCCLUSION	1
ECTASIA	2

SINUS THROMBOSIS	No.
PRESENT	1
ABSENT	0

COMPLICATIONS	No.
PUNCTURE SITE HEMATOMA	1
STUCK CATHETER	2
POOR PERCOLATION	3
IC HEMORRHAGE	4
VENOUS THROMBOSIS	5

LOCATION	No.
FRONTAL	1
PARIETAL	2
TEMPORAL	3
OCCIPITAL	4
BASAL GANGLIA	5
CORPUS CALLOSUM	6
BRAIN STEM	7
CEREBELLAR HEMISPHERE	8
VERMIS	9
INTRAVENTRICULAR, CHOROIDAL	10
SEPTUM	11

NIDUS SIZE	No.
0-3CM	1
3-6CM	2
>6CM	3

NIDUS TYPE	No.
COMPACT	1
DIFFUSE	2

MATERIAL	No.
ONYX	1
ONYX + GLUE	2
ONYX + ETHANOL	3
ONYX + G + E	4

PLANE	No.
SUPERFICIAL	1
DEEP	2
PERIVENTRICULAR	3
INTRAVENTRICULAR	4

VEIN S/D	No.
SUPERFICIAL	1
DEEP	2
BOTH	3

VEIN S/M	No.
SINGLE	1
MULTIPLE	2

NIL	0
RT	1
SURGERY	2
RT + SURGERY	3

Anterior choroidal a.	1
ACA. cortical branches	2
ACA. penetrators	3
MCA. cortical branches	4
MCA. penetrators	5
Other ICA. branches	6
ICA. penetrators	7
PCA. Cortical branches	8
PCA. penetrators	9
Posterior choroidal a	10
Superior cerebellar a.	11
AICA	12
PICA	13
ECA branches	14
Basilar a. penetrators	15
Vertebral a. branches	16
Vertebral a. penetrators	17
Other a	18

MICROCATHETER	No
MARATHON	1
ULTRAFLOW	2
SONIC	3
SPINNACKER	4
APOLLO	5

GLASSGOW OUTCOME SCALE	
1	Dead
2	Vegetative State
3	Severely Disabled
4	Moderately Disabled
5	Good Recovery