EVALUATION OF CEREBRAL HEMODYNAMICS USING FUNCTIONAL NEAR INFRARED SPECTROSCOPY IN PATIENTS WITH INTRACRANIAL DURAL ARTERIOVENOUS FISTULA

THESIS

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CERTIFICATE

This is to certify that the work incorporated in this thesis titled ***"Evaluation of Cerebral Hemodynamics Using Functional Near Infrared Spectroscopy in Patients with Intracranial Dural Arteriovenous Fistula"*** *for the degree of* ***DM NEUROIMAGING AND INTERVENTIONAL NEURORADIOLOGY*** *has been carried out by* ***DR. SANTHAKUMAR*** *under our supervision and guidance. The work done in connection with this thesis has been carried out by the candidate himself and is genuine.*

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CONTENTS

INTRODUCTION

Advances in the structural MRI have given us enough capabilities in understanding the characterization of various structural lesions. There are still various caveats in the analysis of vascular structural abnormalities as there will be artefacts from the embolizing agents, more so with arterio-venous shunting disorders. The cognitive aspect of such disorders is not adequately assessed. The advent of functional neuroimaging helps to fill this lacuna. Nevertheless, it comes with various disadvantages, specific to closed, fixed environment.

In the understanding of various neurological and psychiatric disorders, a portable technology has emerged to better analyse the abstract neurological abnormalities in various neurological and psychiatric disorders.

Near infrared spectroscopy (NIRS) has evolved over the last two decades from a purely research tool to a potential tool in the evaluation of clinical neurologic disorders. Having multiple advantages over other functional neuroimaging techniques, with respect to its portability, a minimal motion artefacts, silent technique and high temporal resolution, this technique has now increasingly being used in clinical medicine.

There are various types of functional NIRS available globally, however continuous wave (CW) FNIRS is the most common type being used in the clinical medicine (1). The distance between the source and the detector determines the pathlength of the light travelled. The pathlength of the travelled light is generally half the source-detector distance. The usual custom is to have a source-detector distance of about 3 cm, such that the NIR light penetrates about 1.5 cm depth (2).

Evaluating the hemodynamics of cortical parenchyma remains the cornerstone of NIRS. It involves measurement of oxyhaemoglobin (HbO), deoxyhaemoglobin (HbR), total haemoglobin (HbT) and regional oxygen saturation (O2Sat). The changes in haemoglobin concentration is obtained by calculating the changes in the absorption spectra for these two chromophores. HbO absorption is higher for $\lambda > 800$ nm while HbR absorption is higher for $\lambda<800$ nm. Thus, two different wavelengths (650 and 830 nm) are used for obtaining changes in HbO and HbR (1).

The main disadvantage of FNIRS include lower spatial resolution and poor depth penetration, compared to other functional neuroimaging techniques. Despite having a less penetration of NIR light, it is still adequate to image the cortex (5-10 mm of cortex), as the depth of the cortex from the skin surface varies between 1-1.5 cm (2).

Dural arteriovenous fistula are abnormal arteriovenous shunts located in the dural venous sinus. Dural venous sinuses are seen between the periosteal and meningeal dura, thus superficial to the cerebral cortex. Dural AV fistula are classified into nonaggressive and aggressive types. Aggressive type usually shows cortical venous reflux and it has high risk of bleeding into the cerebral parenchyma.

Besides the aggressive symptoms like hemorrhage which has been well studied previously, there are other symptoms which cause significant morbidity such as cognitive complaints (behavioural disturbances, dementia) and seizures (3). These symptoms occur due to venous congestion and subsequent raised intracranial tension. Except for a few case reports, there no large studies that addressed these cognitive symptoms using functional neuroimaging techniques. This was evident from variably altered neuropsychological tests in dural AV fistula (4). Additionally, these cognitive complaints appear to be reversible with treatment (5).

The research in terms of cognitive evaluation of patients with intracranial dural AV fistula is limited. Therefore, in order to understand more about pre-treatment and post-treatment functional neuroimaging, we explored the effects of functional NIRS in evaluating the cognitive domain of angiographically proven dural AV fistula and also to compare between pre-treatment and post-treatment effects.

To the best of our knowledge, a similar study was not undertaken to assess the cognitive domain assessment in dural AV fistula using functional NIRS.

AIMS AND OBJECTIVES

HYPOTHESIS:

Cognitive evaluation with functional NIRS can reliably predict hemodynamic changes in patients with intracranial DAVF and since cognitive alterations can potentially reverse with treatment, functional NIRS can be a useful bedside tool for monitoring treatment response.

AIMS AND OBJECTIVES:

- To establish the role of cerebral hemodynamics in patients with intracranial dural arteriovenous fistula using optical imaging
- To observe cerebral hemodynamic changes using optical imaging before and after the treatment.
- To study if there is correlation between the clinical symptoms, cognitive domain and cerebral hemodynamics.

REVIEW OF LITERATURE

3.1 PHYSICS BEHIND FUNCTIONAL NEAR INFRA-RED SPECTROSCOPY:

The basis of spectroscopy relies on the three physical properties of light. These properties are absorption, reflection, and scatter. The process absorption refers to the deposition of the energy of travelling photon into the absorbing material and conversion into the internal energy of the medium. Absorption depends on the material's properties.

There are various materials encountered by the incident infrared light. These include water, lipids, haemoglobin, melanin, and cytochrome C. All these materials absorb light at different wavelengths. Water constitutes about 70% and with its minimal absorption rate, allows NIR light to travel through the tissue. Hemoglobin is the most dominant absorbing chromophore in the NIR spectrum.

Oxyhemoglobin (HbO) and deoxyhemoglobin (HbR) absorb NIR light at different wavelengths. Absorption coefficient of HbO is <800 nm, while that of HbR is >800 nm. Therefore, we exploit this property of varying absorption coefficients of oxy and deoxyhemoglobin and thereby measuring the change in absorption. Absorption spectra of oxyhemoglobin and deoxyhemoglobin with demonstration of iso-bestic point is shown in fig.1

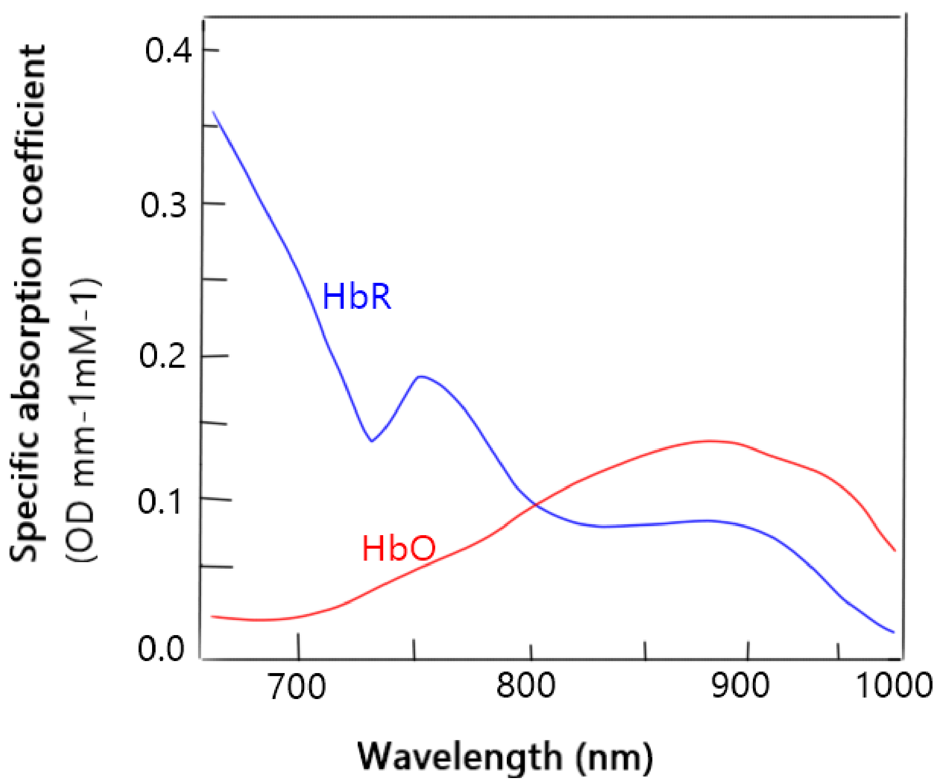


Fig 1. Absorption spectra of oxy- and deoxy- hemoglobin (HbO & HbR).

Maximum absorption of light by these chromophores is found between 690-900 nm and iso-bestic point is seen at 800 nm.

Brain neural activity, when increased by a task, leads to increase in the metabolic demand. This in turn increases the vascular supply, thus increasing the cerebral blood flow (CBF), as the metabolic demand is increased. This functional hyperemia in response to the increased neural firing is known as neurovascular coupling (NVC). NVC occurs by increase of oxyhemoglobin in the venous and capillary blood vessels due to activation (6). This activation and the related signal are more in the involved area than the neuronal metabolic demand (7). Activation results in reduction of deoxyhemoglobin. This HbR reduction further causes more uniformity of the magnetic field and eventually results in increase in the MR signal obtained.

f-NIRS, too, works on the same principle of neuronal activation and neurovascular coupling. Task related changes in neural activity and the indirect effect on hemodynamics are shown in fig.2.

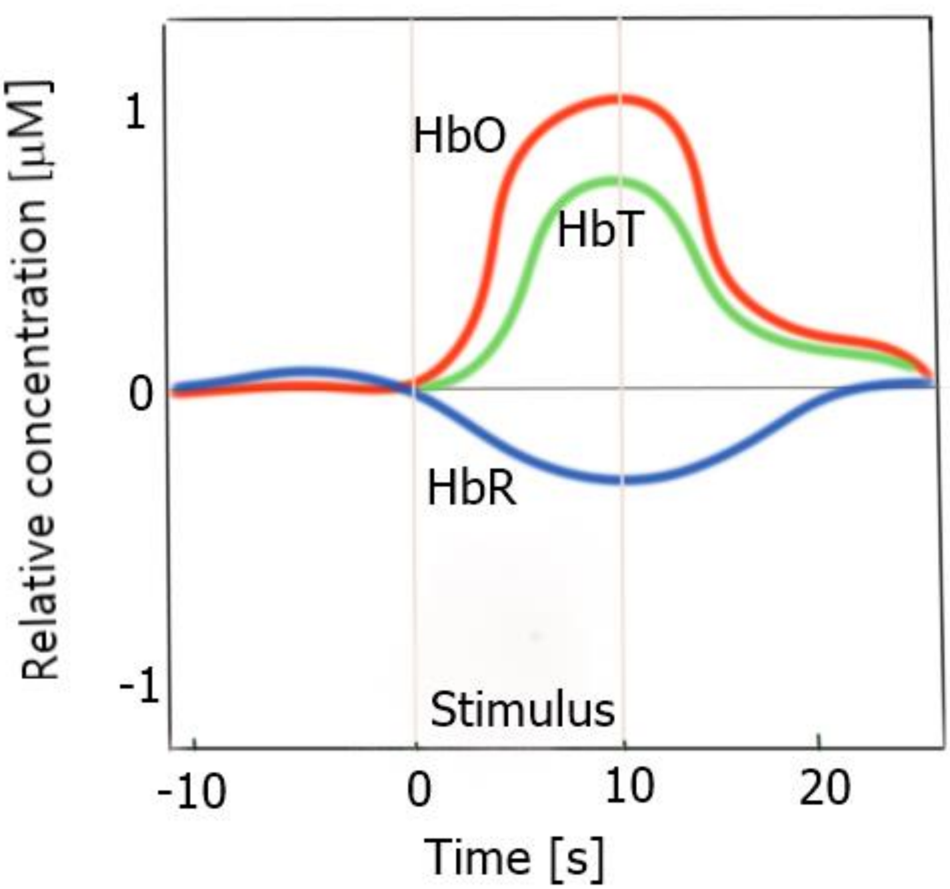


Fig.2: Task based f-NIRS hemodynamic changes.

Maximum peak of HbO is 4 to 5 times higher than the fall in HbR.

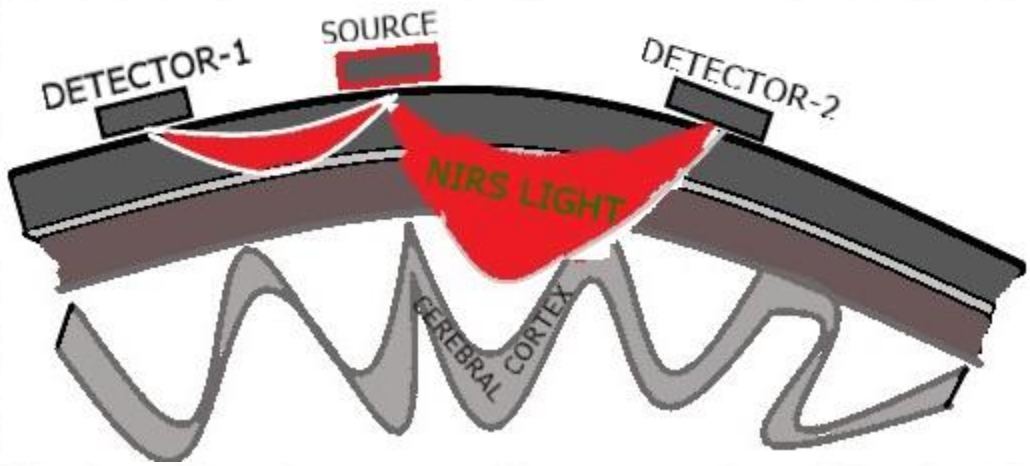
3.1 TYPES OF FUNCTIONAL NEAR INFRA RED SPECTROSCOPY:

3.2.1 Continuous-Wave NIRS:

In CW-NIRS, silicon photodiodes and light emitting diodes are used as detectors and sources, respectively. Elastic band acts as a velcro to hold them in place and placed in such a way that, sources and detectors are placed at about a distance of 3 cm. At this distance, light penetration depth and spatial resolution obtained are 1.5 and 2 cm, respectively.

This term "Continuous wave" implies that the instrument's sole measurement is the light intensity, especially the intensity of the diffusely reflected light. Instruments were simpler in the earlier days when they measured the light intensity at a specific location. It suffered a disadvantage to find out the precise location in the head to make such measurement.

Then, it was designed to obtain topographic information from a relatively larger portion of the head. This had quite a few advantages like localizing the brain activity and precise sensor localization is



trivial. This technology known as functional near infrared imaging, came a big way as measuring brain activity from a larger area is important and quantification of the values is insignificant as only the measurement of change in the brain activity is of utmost importance.

Fig. 3: Penetration of light based on the source- detector distance. Light pathway follows a banana shaped path.

3.2.1.1 Hardwares used in CW-NIRS:

Light sources: Commonly used sources are LED bases diodes and Laser diodes (LD). Comparison between those two groups of diodes are presented in table 1. CW-NIRS systems usually emit light at two different wavelengths. The wavelengths selected are usually close to 800 nm, as that wavelength is considered as isobestic point. As per recommendations made by Yamashita et al, one of the wavelength should be around 830 nm and another wavelength should be <780 nm to increase the

SNR (8). Water absorbs NIR light at around 1000 nm so the second wavelength should not be above 950 nm (9).

Features	LED based diodes	Laser diodes
1. Emission	Spontaneous	Stimulated
2. Light	Incoherent	Coherent
3. Bandwidth	Wide (35 nm)	Narrow (<1 nm)
4. Intensity adjustment	Easy	Difficult
5. Size	Small	Large
6. Colours	Many	Limited
7. Fibre coupling	Possible	Easy
8. Cost	Low	High
9. Safety	High	Low(Laser radiation to eyes)

Table 1: Differences between the LED based and Laser diodes

Photodetectors: They work on the principle of internal or external photoelectric effect. The three types of photodetectors, that are being used are, photodiodes (PD), avalanche photodiodes (APD) and photomultiplier tubes (PMT). Comparison of important properties between the different types of photodetectors are summarized in table 2 (9). High dynamic range of PD enables lack of need for stabilized voltage supply or cooling, which helps in giving them in small packages. APDs requires a few (upto 100) volts thus it mandates the need for stabilized power supplies and cooling (10,11). PMT is not commonly used in fNIRS, but it is the gold standard. It is large, require high voltages and susceptible to magnetic fields. To overcome these disadvantages of PMT recently silicon photomultipliers (SiPMT) were discovered. It uses APDs in Geiger mode. The advantages of SiPMT includes photon counting capabilities, small package, lower operative voltage and not vulnerable to ambient light or magnetic fields (12).

Features	PD*	APD	PMT
1. Gain	High	Moderate	Large
2. Dynamic range	High (100dB)	Moderate	Moderate
3. Size	Small	Small	Bulky
4. Operating voltage (Vop)	1V	100V	1kV
5. Speed	Medium (100MHz)	Fast	Fast
6. Robustness to ambient light	Good	Medium	Medium
7. Susceptibility	No	No	Yes

Table 2: Differences between various commonly used detectors. ***PD:** Photodiodes, APD: Avalanche photodiodes, PMT: Photomultiplier tubes

Probe design: Optical fibres guide the light into the scalp, and they are fixed by manufacturer provided fibre holders. Source fibres are thin (i.e. 0.5 mm). Detector fibres, which guide the light from the scalp are larger (about 3 mm) to receive more light. Disadvantages of the optical fibre system is added weight and inertia, fibre loss and reduced subject mobility (13). The more the light is received, the SNR would be high. This light coupling depends on the hair colour, density, and skin pigmentation, thus underscoring the importance of displacing the hair from the field, to improve the SNR (10).

3.2.1.2 Analysis of FNIRS Signal:

There are two methods to determine the HbO and HbR. They are i) Modified Beer Lambert Law (MBLL) and ii) Multi-distance approaches.

MBLL (14) is the extension of the Beer-Lambert Law with inclusion of scattering coefficient. But this method suffers from a disadvantage that the changes in the chromophore concentration are homogenous and they occur in a homogenous tissue. So, the error that stems out from this pitfall is, quantification error, as the changes in concentration could be underestimated (10). This can be corrected by taking partial differential wavelengths (15). This provides the differential path length factor (DPF) which is added to the equation of Beer Lambert Law to obtain the chromophore concentration.

3.2.2 Frequency domain Spectroscopy: In this type, modulation of emitted light intensity and the reflected light measurement will be done with the measurement of phase shift to provide the absolute chromophore concentration (9).

3.2.3 Time domain Spectroscopy: This method extremely short pulse of light is emitted, and the arrival time of the emerged photons is measured. The highest amount of information is obtained but the method is overly complex and expensive.

3.3 APPLICATIONS OF NEAR INFRARED SPECTROSCOPY:

3.3.1 ***Traumatic Brain Injuries:***

f-NIRS has its role in early detection of intraparenchymal bleed, epidural hematoma, and subdural hematomas. Previous study by Gopinath et al revealed the earlier detection of delayed but surgically important hematomas after TBI (16). A recent study was done in TBI using stroop task and assessed frontal lobe connectivity. They concluded f-NIRS was capable of identifying frontal lobe inefficiency after TBI (17).

3.3.2 ***Epilepsy:***

In complex partial seizures, increase in the blood volume and oxygenated hemoglobin concentration was noted, thus clearly emphasized the importance of utility of f-NIRS in epilepsy. The role of f-NIRS in differentiating various seizure types, especially complex partial seizures (CPS) from secondary generalized variety, as CPS tend to have increase in oxygenated hemoglobin concentration (18). Watanabe et al concluded that f-NIRS, when combine with ictal-SPECT is a potential non-invasive device for epileptic focus diagnosis (19).

3.3.3 ***Alzheimer's Disease:***

Reduction in HbO and HbT was observed by Hock et al. The findings were clearly more pronounced in the parietal cortex than the frontal cortex in patients with Alzheimer's disease (20). Various cognitive tasks were used, some of which were verbal fluency test (VFT), Go-No Go task, Stroop task, pattern recognition task etc.

f-NIRS is particularly suitable for neurodegenerative disorders, as, a modality which can continuously monitor the hemodynamic activity would be better suited to assess the progression of severity of the disease.

3.3.4 ***Parkinson's Disease:***

The effects of frontal lobe oxygenation were earlier studied by Muratani, Sakatani et al as early as 1999 and concluded that stimulating thalami or globus pallidum tend to increase the prefrontal lobe oxygenation, as measured by single-channel f-NIRS (21). Recent multi-channel f-NIRS studies by Morishita et al, signified relative increase in the primary motor area activity ipsilateral to the hemisphere that had undergone deep brain stimulation (DBS). Clinical improvement was divulged by HbO changes in the same study (22). Based upon these studies, the novel near infrared light treatment (at a wavelength between 600-1070 nm) is being used as an alternative treatment to medical and surgical therapy in parkinson disease (23).

3.3.5 *Stroke Rehabilitation:*

f-NIRS studies by Arun et al assessed the resting state functional connectivity (rs-FC) in patients who had evolved stroke. They concluded the rs-FC changes during the rehabilitation help in prediction of extent of recovery from motor deficits caused by the cerebrovascular accident (24).

Apart from these neurological applications, there were also a variety of psychiatric applications in schizophrenia (25), mood disorders (26), and anxiety disorders.

3.4 DURAL ARTERIOVENOUS FISTULA:

3.4.1 EMBRYOLOGY:

Dural arteriovenous fistula are arteriovenous shunts which occur within the epidural

venous space (between two layers of dura mater). As shown in fig.4 dural sinus is usually sandwiched between osteal dural (derived from ectomeninx) and dura propria (derived from neural crest cells). The dural fistula are also grouped into neural crest (NC) group and mesodermal (MS) group. NC group fistula are usually located at the superior sagittal sinus (SSS), transverse sinus (TS), torcula, cavernous sinus (CS), sigmoid sinus and anterior condylar confluence. MS group includes tentorial, anterior ethmoidal, superior petrosal sinus, foramen magnum fistula (27).

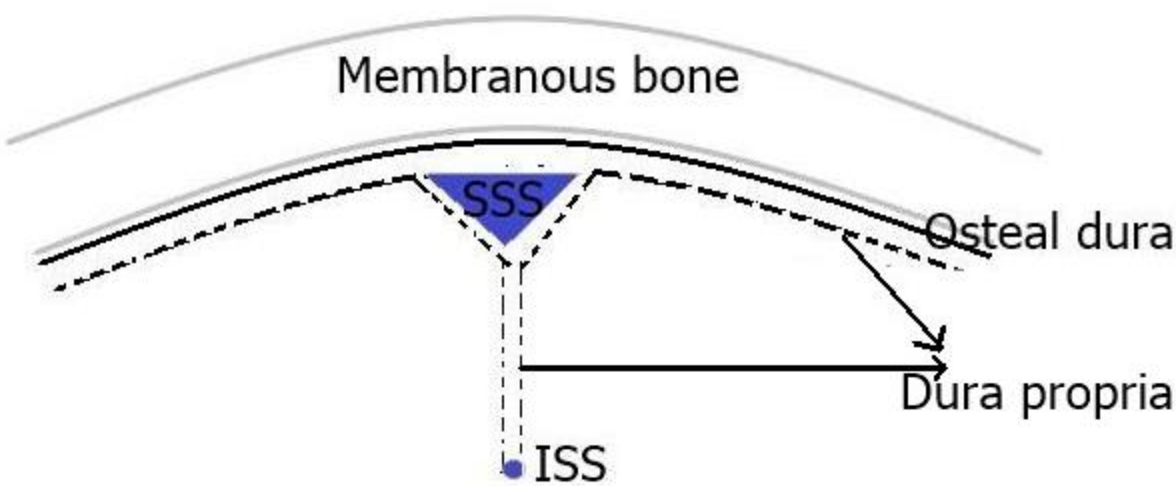


Fig 4. Embryology of dural sinus.

Mesoderm (MS) derived sinuses are usually seen between osteal dura and dural propria, while Neural crest (NC) derived sinuses are seen between two layers of dura propria.

3.4.2 CLASSIFICATION:

The two most widely used classification systems are Borden-Shucart and Cognard grading (presented in tables) . Borden-Shucart grading is based on venous drainage. Cognard grading is based on shunt location, venous drainage pattern and venous outflow characteristics. Zipfel modified Borden grading by subclassifying grades 2 and 3 as 2A, 2S, 3A and 3S. Subcategory "A" represents fistula with cortical venous drainage (CVD) but patient remaining asymptomatic or symptoms related to high flow like tinnitus, ophthalmological manifestations). Subcategory "S" represents fistula with CVD and symptoms like intracerebral hemorrhage (ICH) or NHND (non-hemorrhagic neurological deficit) (28).

They are broadly classified into non-aggressive and aggressive categories. Aggressive fistula is the one which tend to have cortical venous drainage. They have higher risk of hemorrhage hence required to be treated immediately on diagnosis.

3.4.3 NATURAL HISTORY OF DURAL AV FISTULA:

Dural AV fistula constitute about 10-15% of the total intracranial arteriovenous

shunting (27)

<u>Low grade DAVFs:</u> They generally have a benign natural history. Long term ICH or NHND is low and the risk of ICH or NHND is only around 0-0.6%. Annual mortality is calculated to be about 0.0% (29-32). The only major long-term consequence from these fistula is up-grading of the low grade DAVF. Cognard et al (33) noted this upgrading in seven patients who were put on conservative management or palliative treatment. Satomi et all (29) observed this up-grading in two of their patients. Similarly, Shah et al (30) found this similar finding in 2 patients. Annual rate of this up-conversion was found to be about 0.8%. This up-grading occurred more often with concomitant change in the patient's symptoms.

<u>High grade DAVFs:</u> It is a well-accepted fact that DAVF with CVD tend to have a poorer outcome due to hemorrhage or NHND, if left untreated. (34-37). Duffau et al (38) was the first one to signify a re-bleeding risk of about 35% in a shorter follow up period within only 20 days. A study on 20 patients by Van Dijik et al (39) depicted an annual event rate of 8.1% and 6.9% respectively for ICH and NHND, respectively. The same study yielded cumulative annual risk score was calculated at about 15% and annual mortality risk rate was calculated to be about 10.4% (39).

Among the patients who present with aggressive DAVFs, those who present with ICH or NHND tend to have a higher rate of new events than those who present asymptomatically or with minimum symptoms like tinnitus or ophthalmological manifestations. Studies by Soderman et al (40) and Storm et al (41) exhibited higher annual risk of new neurological deficit in patients who presented with aggressive symptoms (7.5 and 19% vs 1.5 and 1.4% respectively). Various studies also examined the effect of venous ectasia on natural history of DAVF and a study by Gross and Du (31) found significantly higher risk of having hemorrhage in the presence of venous ectasia with an incidence risk ratio of 6.07 (by both fixed effects and random effects model).

The bottom-line from these studies implies the fact that this subgroup of patients with aggressive DAVFs portend high risk of having a first time hemorrhage and also have a higher annual risk of new events (ICH or NHND) who already presented with ICH or NHND.

3.4.4 MODE OF PRESENTATION:

From our understanding of the natural history of the disease process, the clinical

features can broadly be classified into

1) Aggressive symptoms : Intracerebral hemorrhage (ICH) and non-hemorrhagic neurological deficit (NHND). These are primarily related to cortical venous hypertension (cortical venous drainage is mandatory for the development of these features). NHND include seizures, focal deficits, cognitive impairment (including dementia), cranial nerve palsies (trigeminal neuralgia), Parkinsonism, cerebellar dysfunction, aphasia, manifestations due to raised ICP (intracranial pressure) and myelopathy (DAVF with perimedullary venous drainage).
2) Non-aggressive symptoms: Mainly due to increased drainage through the affected sinus. These symptoms include tinnitus, chemosis, proptosis, episcleral congestion with corkscrew vessels.

Symptoms can also be classified by location, as shown in fig.5

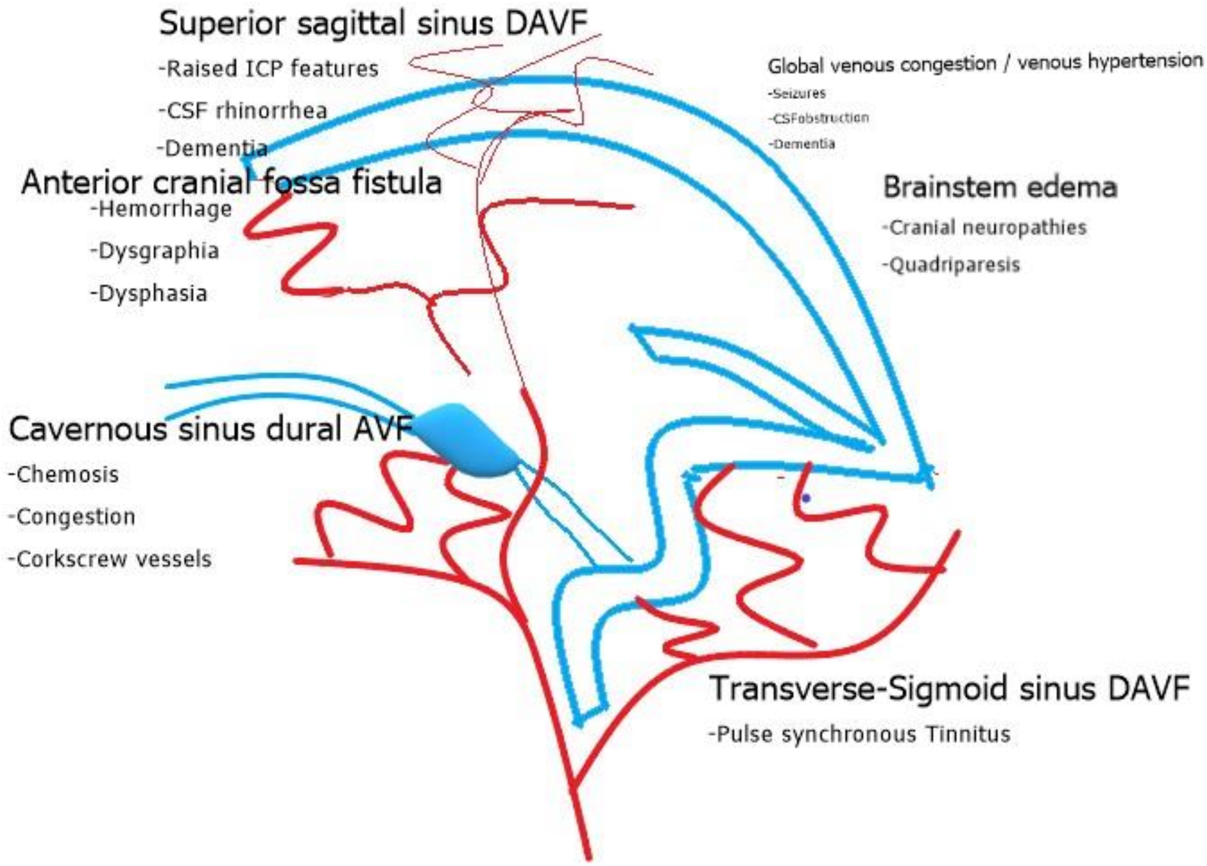


Fig.5. Clinical Manifestations of dural AVF based on the location of the fistula.

3.4.5 IMAGING:

The role of CT in DAVF is limited and helps in delineation of hemorrhage and vasogenic edema. Sometimes hyperdense veins in venous congestion may be evident.

MRI is definitely helpful in delineating the anatomy, due to the superior resolution between the fistula and surrounding neural structures. Conventional T1 and T2 sequences help in showing the flow voids associated with the pathology and vasogenic edema especially bithalamic edema in thalamic dementia. MR angiogram depicts the fistula sometimes and any tortuous vessel surrounding the sinus in an appropriate patient, warrants further investigation with dynamic angio-imaging.

Digital subtraction angiogram is the reference standard for the diagnosis. Additionally, it is important for us to evaluate the angioarchitecture, fistula site and number, feeder vessel anatomy, venous drainage, occlusion or stenosis of the drainage pathway and venous ectasia. Venous hypertension too is identified by engorged pial veins (pseudophlebitic pattern), tortuous veins, and prolonged circulation time.

3.4.6 TREATMENT:

This alarming rate of ICH and NHND (7.4-19%) and mortality (3.8%) per year is the clear indication for the treatment of aggressive DAVF on diagnosis. Non-aggressive DAVF may be conservatively managed and intervened based on careful patient selection. When this subgroup of patients is on conservative management, they have to be carefully scrutinized with follow up imaging in view of possibility of up-grading of the lesion.

Treatment of DAVF can be classified into endovascular, surgical, radiosurgery and combination. Endovascular embolization remains the mainstay of treatment. The main goal of embolization is to completely eliminate the fistula, as there is possibility of up-grading of fistula if residual is present. Significant embolization means when there is complete elimination of the venous hypertension features.

3.5 LACUNA:

The presence of hemorrhage can be ascertained by the conventional imaging

sequences . Angiogram depicts features of venous hypertension, but the procedure is invasive. Apart from hemorrhage, the other major cause of morbidity in these patients is non-hemorrhagic neurological deficit (NHND), which is related to the venous congestion.

To assess venous congestion noninvasively, functional neuroimaging has evolved in a big way. SPECT (especially $_{123}$I iodoamphetamine SPECT) (49) showed perfusion abnormalities in the region of engorged leptomeningeal veins away from the site of fistula. The pathophysiology described in those studies were: the engorged veins due to venous hypertension prevent the further inflow of arterial blood (CBF) thus showing low perfusion in those areas. Studies using these perfusion imaging modalities (SPECT and ASL) (6,7) showed low perfusion in these areas and also signified total reversibility after complete embolization of the DAVF.

The treatable aspect of this morbidity warrants a definite investigation to assess it before the procedure and also to assess the treatment response after the procedure.

MRI, though non-invasive, non-radiating and with an excellent spatial resolution, has a few demerits. These include lack of bedside evaluation, less temporal resolution, difficult to use in uncooperative patients (especially patients with DAVF may have some cognitive impairment which limits the patient from providing full cooperation for the procedure).

SPECT emits radiation, lacks portability, has moderate spatial resolution, but better temporal resolution. In addition, MRI and SPECT are extremely sensitive to motion and even a slight patient motion may not be tolerated.

f-NIRS appears to offer a non-invasive neuroimaging with a limited depth resolution and assess the changes in the neuronal activity and resulting neurovascular coupling. It tends to indirectly measure the CBF by measuring the tissue oxy-hemoglobin (HbO), deoxy-hemoglobin (HbR) and regional tissue oxygen saturation (rSO_2).

The advantages of f-NIRS are multi-fold and that include better temporal resolution, portability, ability to record the findings more physiologically (able to record even when the subject does his routine activities through the recent wireless f-NIRS technology), non-invasive, patient friendly, robust to motion artefacts, and able to overlay the data on the MNI template like in f-MRI.

To the best of our knowledge, there is only a single case report assessing the dural AV fistula using f-NIRS. There are no major studies pertaining to this.

3.6 NEUROPSYCHOLOGY EVALUATION:

Various neuropsychological tests are available to evaluate different aspects of cognitive

domains. Nonetheless, MMSE (Mini Mental Status Examination) and ACE-III (Addenbrooke Cognitive Examination- III Scale) examination scales are widely used.

3.7 RESEARCH QUESTION:

This led us to the following research questions.

a) What is the feasibility of f-NIRS in evaluating the cerebral hemodynamics pertaining to the venous hypertension in patients with intracranial dural arteriovenous fistula?

b) Is there a significant change in the cerebral hemodynamics before and after the embolization procedure in patients with intracranial dural arteriovenous fistula, such that can the treatment response be assessed at the bedside?

c) Can the f-NIRS data be compared with the neuropsychology scores in patients with intracranial dural arteriovenous fistula?

3.8 HYPOTHESIS:

We hypothesized that, f-NIRS may be a feasible, non-invasive, cost-cutting and safe bedside tool in assessment of venous hypertension in patients with intracranial dural arteriovenous fistula. There may be a significant change in the cerebral hemodynamics before and after the embolization procedure, such that it may be a useful tool in assessment of treatment response.

MATERIALS AND METHODS

4.1 ***INCLUSION AND EXCLUSION CRITERIA:***

The design of the study was a case-control type whereby twenty-seven consecutive patients who visited the interventional neuroradiology out-patient department were included in the study. The recruitment was under the supervision of the consultant neuroradiologist. The inclusion and exclusion criteria for the study are given in the table

S.No.	INCLUSION CRITERIA	EXCLUSION CRITERIA
1.	Patients with imaging proven dural arteriovenous fistula	Children less than 18 years of age
2.	Control group who are healthy and age-matched	Patients with severe neurological improvement who has significant difficulty in comprehending the commands.

Table 3: Table showing the inclusion and exclusion criteria for the patients and controls in the study. All the patients (27 in number) underwent task- based NIRS evaluation once before and after the procedure. The f-NIRS procedure is explained in detail (including the data processing steps) below. Healthy controls (23) also underwent this f-NIRS evaluation only once. Changes in the HbO, HbR, regional oxygen saturation were recorded, for each patient before and after the embolization procedure.

Patients underwent complete neuropsychology evaluation before and after the procedure. Controls underwent neuropsychology evaluation once. Neuropsychology evaluation yielded the MMSE scores.

4.2 NIRS EVALUATION (PROCEDURE AND DATA ANALYSIS)

4.2.1 ***EXPERIMENT DESIGN:***

The study was conducted as three parts. The first part was: a rest period of 3 minutes was given to the patient and patient was made to look into a fixation point on the computer screen. Then task-based f-NIRS was done as two trials. The task was designed as a block paradigm with intervening periods of activity and rest. The activity period lasted for 20 seconds, with an equal time interval was given for resting period also. The readings were recorded simultaneously. Then a repeat trial of similar task was given, and the readings were recorded. During the task phase, words with different colours will be shown and the patients is asked to name the colour of the displayed words, but he/she must not read the displayed word.

This experiment was performed on the patients twice, the first time before the embolization and the second time, one month after the embolization. It was done only once on the controls.

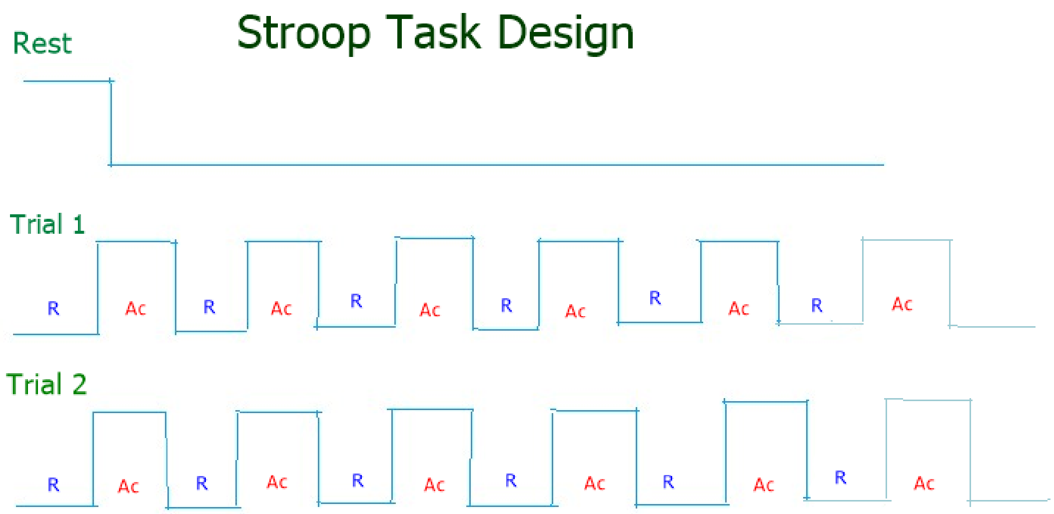


Fig.6: Schematic diagram showing the stroop task used for the patients and controls in the study. R- Rest, Ac- Active

4.2.2 ***PARADIGM DESIGN:***

The task-based measurement using f-NIRS was acquired with the help of paradigm designed using NIRSTIM 4.0 software provided by NIRX LLC. The study was conducted into blocks of active and rest phases. Initially, the rest phase was to ask the patient keep fixated on a particular target in the computer screen, for about 3 minutes. This is followed by two trials, where coloured words are shown in random sequence and the patient was asked to name the colour and specifically instructed not to merely read the word. This was provided in a total of six trials. For obtaining accurate analysis of the activation in brain a synchronised paradigm is required. This is achieved using NIRSTIM software, which has a modular and hierarchical organization and it can be launched from the acquisition software, thus ensuring synchronization of paradigm with the data acquired.

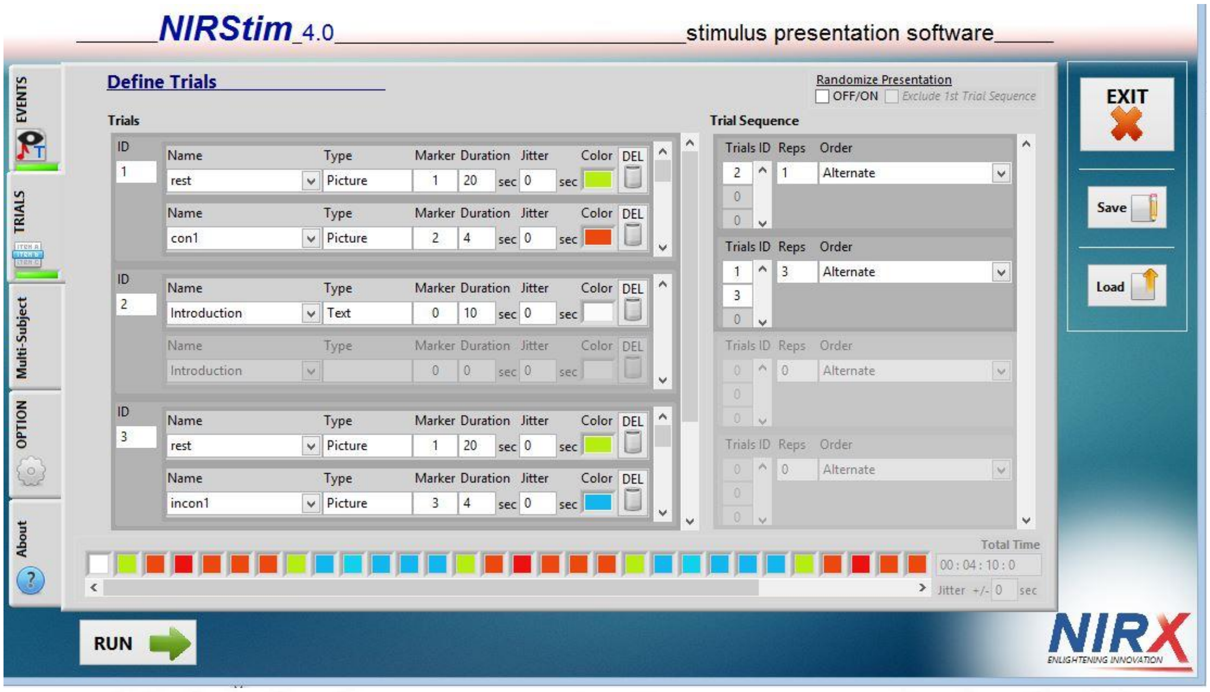


Fig 7. Photograph of the Stroop task used in the study

4.2.3 ***DATA ACQUISITON:***

4.2.3.1 Equipment:

The data were acquired using NIRSport system (NIRx Medical Technologies LLC, Berlin, Germany) having 8 sources and detectors at a sampling rate of 7.825 Hz. The device emits light at two distinct wavelengths, 760nm and 850nm, for discrimination of two oxygenation states of tissue. The system facilitates illumination of multiple targets in a time multiplexed scanning method. 8 sources and 7 detectors were used to cover area of interest in both the hemispheres in the prefrontal cortex. NIRSport is a portable, multi-channel, continuous wave f-NIRS platform which measures hemodynamic neuroactivation through oxy- and deoxy- hemoglobin changes in the cerebral cortex. NIRSport can measure both topographic and tomographic NIRS data from the entire cortex, yielding 3-Dimensional depth discriminating neural activity. NIRSport system should be connected to the laptop loaded with acquisition software.

4.2.3.2 Subject preparation:

Patient tolerance is not a major concern, thanks to the non-invasiveness, portability of the machine, fast setup and the preparation times. The examinee is seated comfortably in a chair. After measuring the examinee's head, NIRS cap size is determined. The fabric cap is specially crafted for placing the optode holders. Placing the optodes and their contact with the skin play a vital role as the correctly placed optodes are robust to motion and ensures high signal quality. While placing the optodes, the skin must be gently displaced to ensure direct contact between the skin and the optodes and better signal quality.

4.2.3.3 Acquisition software:

The software used in our machine is NIR Star. While configuring the software, we used a prefrontal cortex 8x8 montage provided. The 2D representation of the montage is shown in fig.8

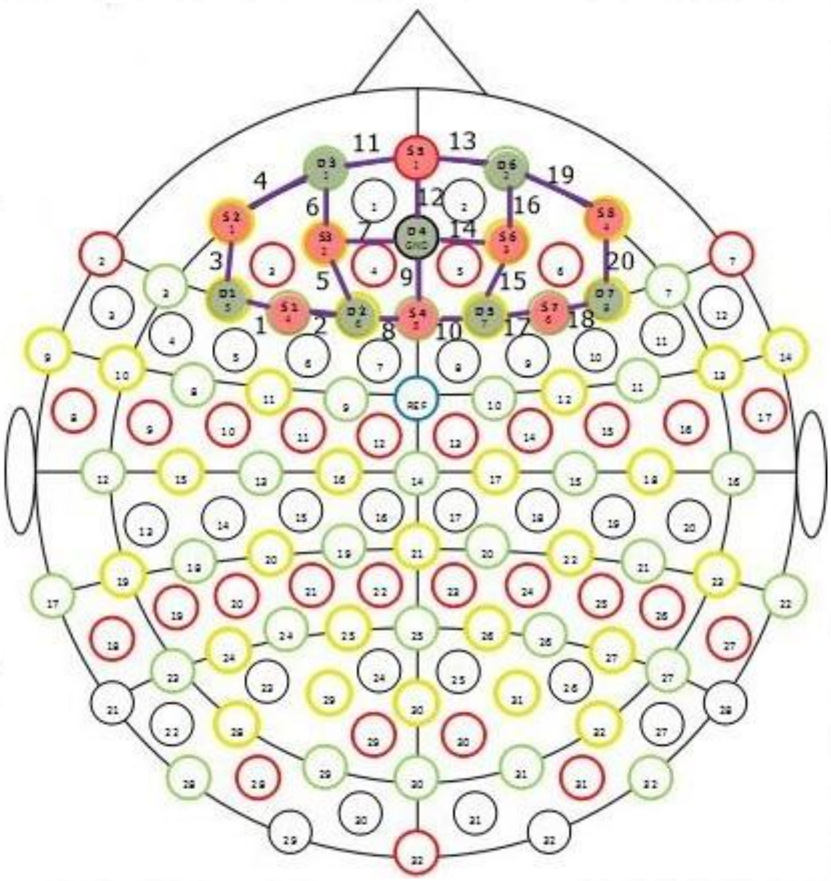


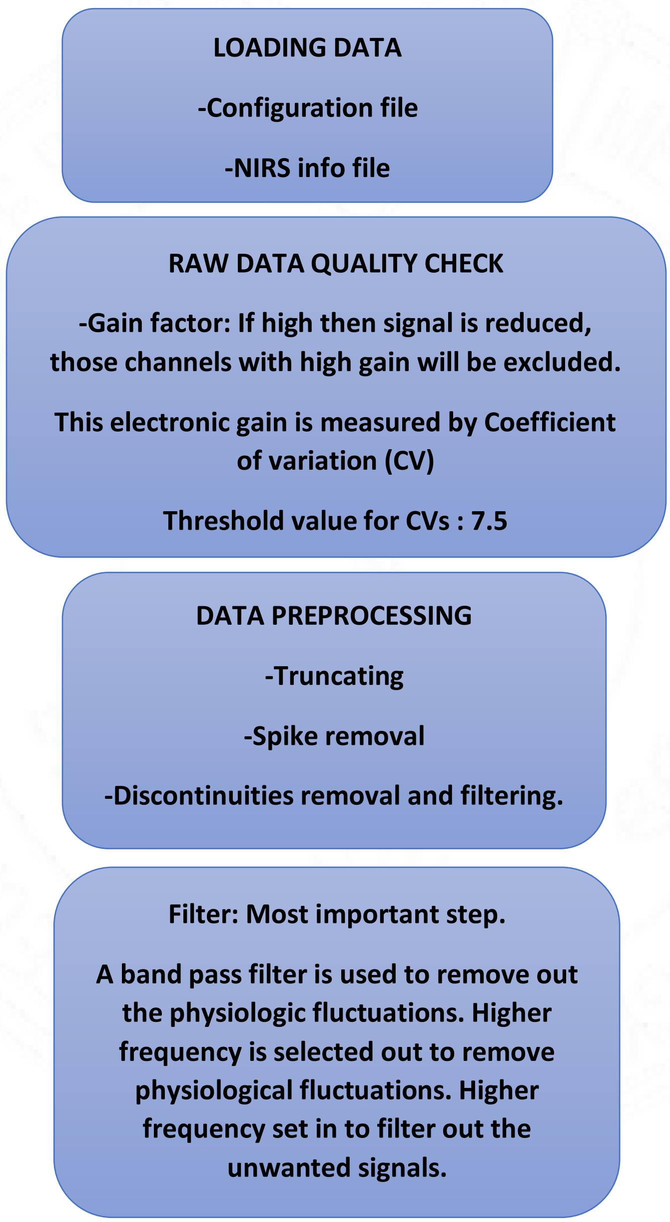
Fig. 8: Photograph of the prefrontal 8x8 montage used in the study. Channels are numbered from 1-20 in the image. Channels correspond to parts of the prefrontal cortex (see text.)

These 8 sources and 8 detectors form a 10-20 channel system. These channels represent the Brodmann areas (BA) (refer fig.8). Channels 1,3 and 7 depict left dorsolateral prefrontal cortex (DLPFC); 9,14,18 and 20 represent right DLPFC; 4,6 and 11 signify left medial prefrontal cortex

(MPFC) and 12,13,16 and 19 denoted right MPFC. The interoptode distance was maintained at 30 mm. After calibration and signal quality is checked, the device is ready for recording the acquisition.

4.2.4 ***DATA ANALYSIS:***

The acquired data are analysed using a Matlab based versatile software analysis environment called NIRSLab software (NIRx Medical Technologies, LCC). Pre-processing steps are shown in the flowchart below



4.2.4.1 Computing Hemodynamic states:

After the above-mentioned pre-processing steps, the data is converted to changes of the hemodynamic states like oxy-hemoglobin (HbO), deoxy hemoglobin (HbR) and total hemoglobin (HbT). Parameters used in modified Beer Lambert Law (MBLL) were set up manually for the calculation of these changes in the hemodynamic states. Following parameters were used.

a) Wavelength

b) Baseline duration

c) Background hemoglobin content in µM.

d) Differential path length factor, which accounts for additional path due to scattering of light.

DPF values are obtained from prior studies (42). Once the parameters are set, hemodynamic states can be computed. Block averages of HbO, HbR and SO_2 can be computed for different tasks.

4.2.4.2 General linear model (GLM):

The GLM has been the method of choice for f-MRI data analysis. Like f-MRI, f-NIRS is also based on neurovascular coupling and this forms the basis for f-NIRS analysis of data. Comparisons among different channels can be done using Level 1 analysis and comparing different subjects can be done using Level 2 analysis. These analysis was done using Statistical Parametric Mapping (SPM).

4.3 EMBOLIZATION PROCEDURE:

4.3.1 ***Preprocedural evaluation:*** After stabilizing the patients, NIRS and neuropsychology evaluations were done according to the above-mentioned standard protocols. Patient would be prepared for the angiograms of bilateral internal carotid arteries (ICA), external carotid arteries (ECA), vertebral arteries, selective injections of bilateral internal maxillary arteries (IMA) and occipital arteries. 3D Rotational angiograms (3DRA) were obtained from IMA injections. Angiograms would usually be done using 5 French vertebral glide catheter (5F VG catheter).

4.3.2 ***Procedure:*** After completing the angiograms, the respective ECA that supplied the DAVF would be cannulated and artery is primed with Nimodipine. Following this, VG catheter will be exchanged for a 6F guide catheter. Microcatheter-microwire combinations would be passed through the guide catheter, to the fistulous site. The fistula was embolized using the permanent liquid embolic agents.

4.3.3 ***Post procedure evaluation:*** After completing the embolization procedure, the patient would be started on intravenous heparin to prevent the cerebral venous thrombosis. The embolization was classified as 1) Complete: considered as "complete" if there was complete resolution of DAVF and complete resolution of venous hypertension, 2) Significant: considered "significant" if there was complete resolution of venous hypertension and cortical venous reflux but residual fistula persisted and was downgraded, 3) Partial: considered "Partial: if there is partial reduction in the fistula and the venous hypertension or cortical venous reflux. These parameters were assessed subjectively. Circulation times were recorded before and after the procedure. Normal circulation time was 7 seconds. Embolization were repeated in the patients with significant residual fistula.

4.4 STATISTICAL ANALYSIS:

Statistical analysis between the pre-procedure f-NIRS data and the post procedure f NIRS data were analysed by paired-t-test. Patients and controls were compared using unpaired-t-test. f-NIRS data and angiographic parameters before and after procedure were analysed using unpaired-t-test.

Non-parametric tests were used for evaluation of neuropsychological data. Pre-embolization neuropsychology data of patients and controls were evaluated using Mann Whitney U test. Pre-embolization and post-embolization neuropsychology data were assessed using Wilcoxon signed rank test.

Neuropsychology scores and f-NIRS data were analysed by Spearman rho correlation test. Dichotomous data like hemorrhage and site of fistula were assessed using chi-square test and Fisher exact test.

All statistical analyses were done using SPSS software version 25.0.

OBSERVATIONS AND RESULTS

DEMOGRAPHICS:

The study included a total of 27 consecutive patients with imaging proven intracranial dural arteriovenous fistula (23 males and 4 females). Additionally, 23 healthy people were included as controls (16 males and 7 females)

DEMOGRAPHICS	PATIENT	CONTROLS	p-value
Age(Mean±S.D.)	48 ± 13 (24-70)*	45 ± 17.8 (20-73)*	0.818
Gender (percentage)	23 males (85.2%), 4 females (14.8%).	16 males (69.6%), 7 females (30.4%).	0.557
Risk factors# (DM, HTN, CVT, Trauma, Hypercoagulable states etc	19/27 (70%)	9/23 (40%)	0.192
MMSE scores# (Median±range)	25±20	30±1	**0.000**
ACE III scores (Median±range)	76±61	94±9	**0.000**

TABLE 4. Demographic details of the patient and cohort population. **MMSE and ACE scores are found to be significant between the patient and controls.**

*range is provided within the parenthesis.

#DM- Diabetes mellitus, HTN- hypertension, CVT- Cortical venous thrombosis, MMSE- Mini Mental Status examination, ACEIII- Addenbrooke Cognitive Examination

CLINICAL FEATURES:

S.no.	Symptoms	Number of patients (n=27)
1.	Headache	19 (70.3%)
2.	Tinnitus	3 (11.1%)
3.	Ocular	7 (25.9%)
4.	Seizures	5 (18.5%)
5.	Cognitive and behavioural disturbances	11 (40.7%)
6.	Aphasia	1 (3.7%)
7.	Slurred speech	2 (7.4%)
8.	Tremors	1 (3.7%)
9.	Incidental	1 (3.7%)
10.	Death (before angiogram)	1 (3.7%)

TABLE 5. Proportion of symptoms attributed to intracranial dural AV fistula.

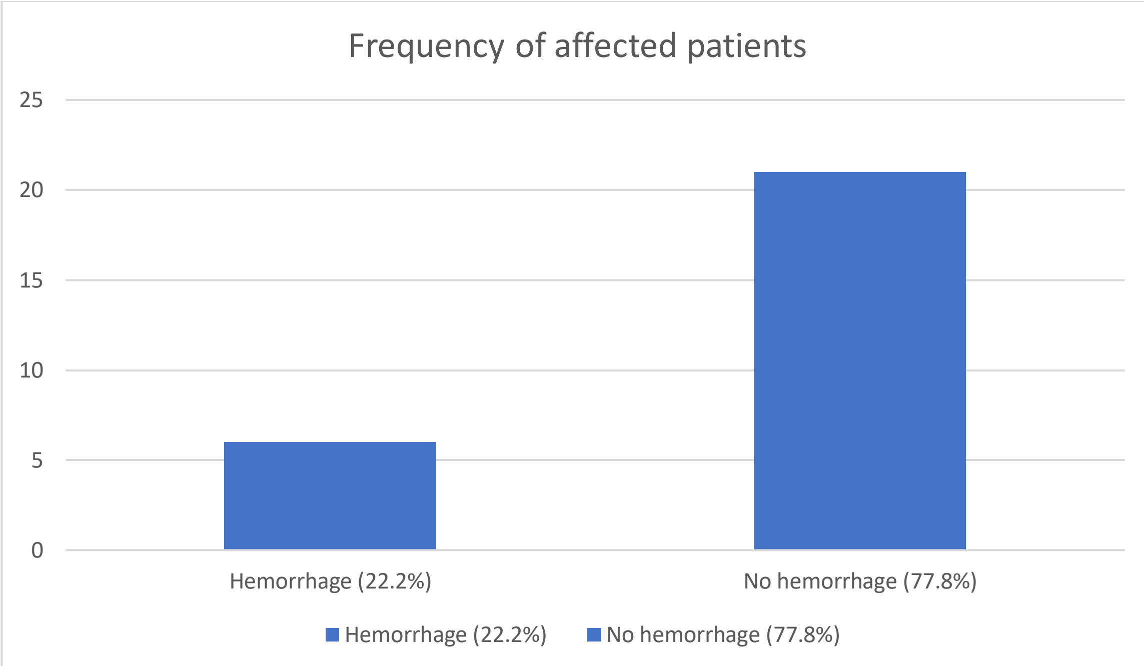


Fig 9. Bar chart describing the frequency of hemorrhage in the affected patients.

Epilepsy and cognitive impairment were grouped together, as disturbance in cognition is known to occur in patients with recurrent seizures.

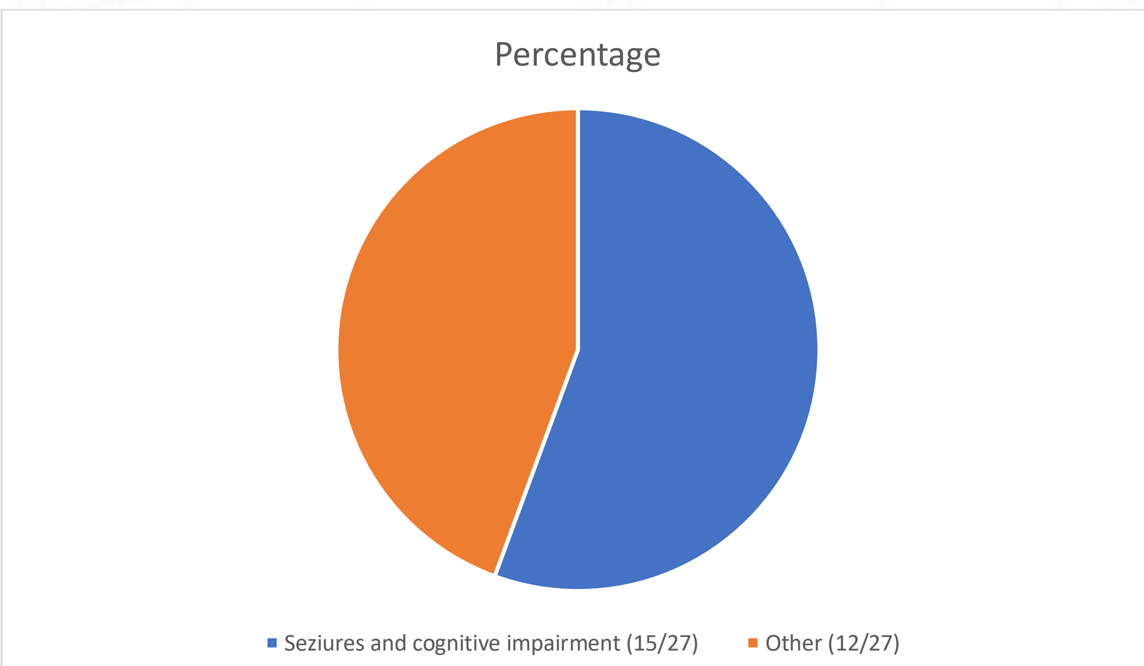


Fig.10 Pie chart depicting the percentage of patients affected by seizures and cognitive impairment.

ANGIOGRAPHIC FINDINGS:

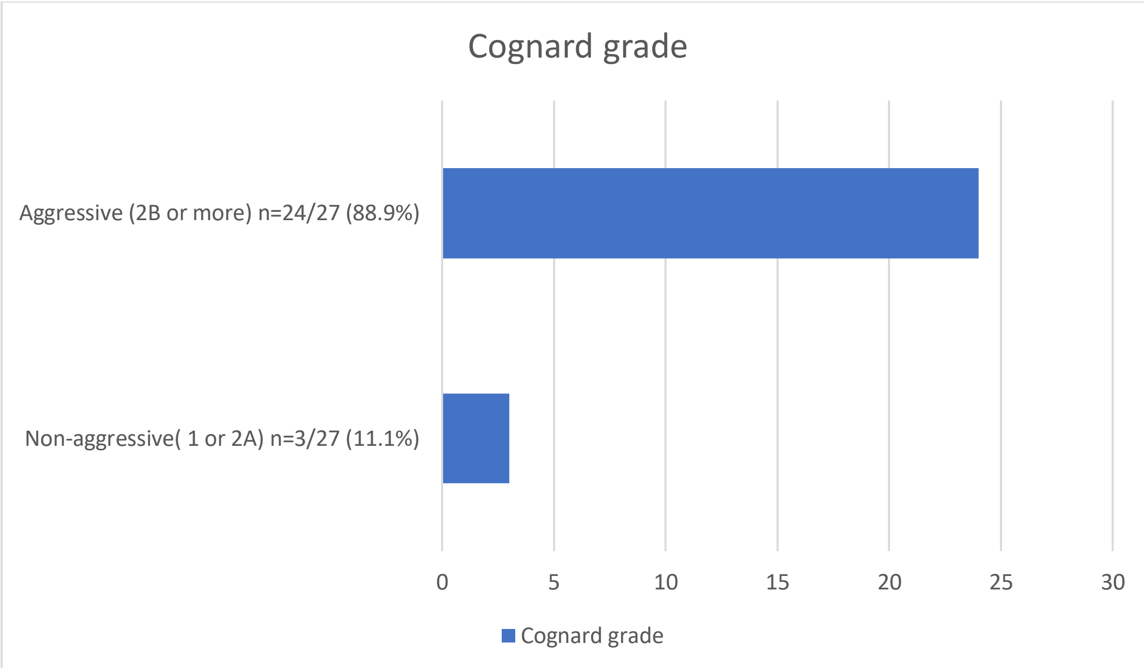


Fig.11 Bar chart explaining the frequency of non-aggressive and aggressive fistula.

SITE OF FISTULA:

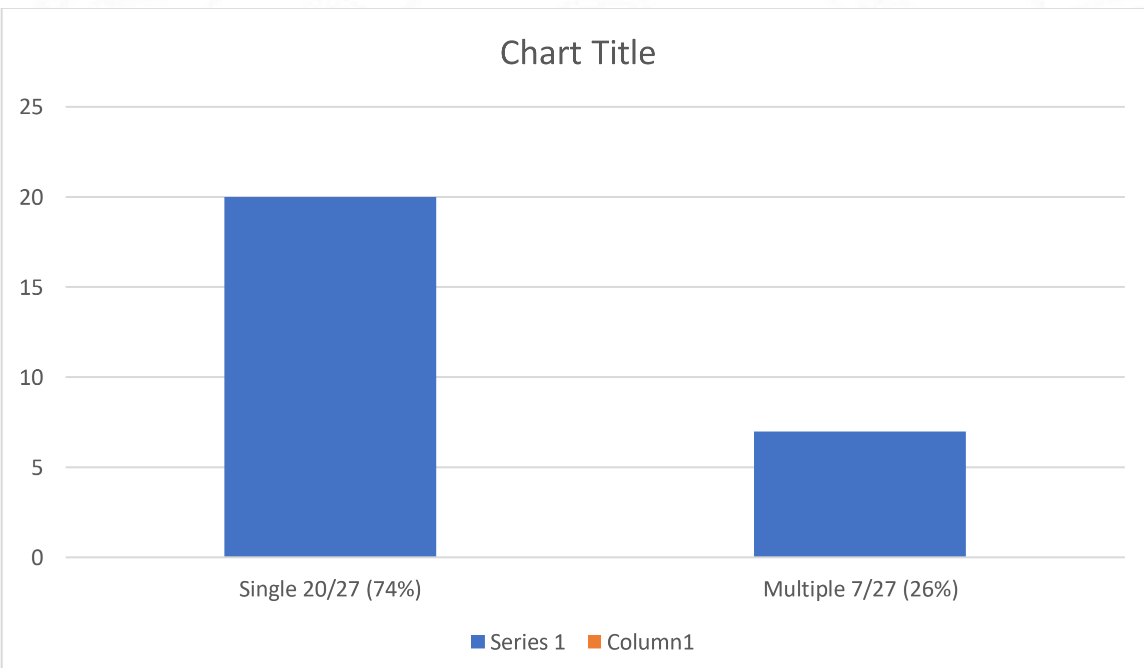


Fig.12 Bar chart divulging the number of fistula in the affected patients

CIRCULATION TIME:

CIRCULATION TIME	FREQUENCY (n=26)
Within normal limits	13 (50%)
Prolonged	13 (50%)

Table. 6: Percentage of patients with prolonged circulation time in the initial angiogram

EMBOLIZATION:

Complete embolization: 18 (66.7%)

Partial: 4 (14.8%)

Significant: 3 (11.1%)

Expired: 1 (3.7%)

Conservative: 1 (3.7%)

FNIRS data:

Pre-embolization (baseline) FNIRS data: available in all the patients.

Postembolization FNIRS data: available only in 22 patients.

Results of cerebral hemodynamics obtained from f-NIRS as :

1. Change in the oxyhemoglobin concentration,

2. Change in the deoxyhemoglobin concentration,

3. Change in the regional oxygen saturation.

TASK-BASED F-NIRS:

1. **COMPARISON OF PATIENTS (PRE-EMBOLIZATION) AND CONTROLS:**

	Task based change in HbO (mM*)		Task based change in HbR (mM)		Task based change in SO_2(%)	
	Mean±2SD	p-value	Mean±2SD	p	Mean±2SD	p
Patients	-2.57E-05±2.13E-04	**0.009**	-3.48E-05±4.66E-05	0.419	2.32E-02±1.04E-01	0.693
Controls	1.09E-04±1.02E-04		-4.81E-05±6.84E-05		3.58E-02±1.20E-01	

Table 7: Task based change in cerebral hemodynamics between the patients and the controls. *mM – millimoles.

f-NIRS that was done for the first time immediately after the diagnosis of DAVF and before the embolization was compared with the controls. ***Changes in the oxyhemoglobin was found to be statistically significant, as can be seen from the table 7.***

2. COMPARISON AMONG PATIENTS BETWEEN F-NIRS PARAMETERS PRE- AND POST-EMBOLIZATION:

	Task based change in HbO (mM)		Task based change in HbR (mM)		Task based change in SO_2(%)	
	Mean±2SD	p	Mean±2SD	p	Mean±2SD	p
Pre embolization	-2.10E-04±2.33E-04	**0.05**	-3.06E-05±5.02E-05	0.210	1.00E-02±1.08E-01	0.245
Post embolization	9.89E-04±1.22E-04		-7.99E-06±5.50E-05		4.18E-02±7.04E-02	

Table 8: Task based change in the cerebral hemodynamics between pre-embolization and post-embolization groups in the study patients. N=22.

Analysis among patients between pre-embolization and post-embolization values were done in a total of 22 patients. ***Oxyhemoglobin changes were found to be statistically significant, with a reduction before embolization was noted and increase in the value was seen after the embolization (ref table 8.).***

If only aggressive fistula (>Cognard 2B) are included, HbO changes are quite significant (p- value 0.001).

F-NIRS CHANGES IN PATIENTS WHO PRESENTED WITH COGNITIVE SYMPTOMS (PRE AND POST EMBOLIZATION)

	Task based change in HbO (mM)		Task based change in HbR (mM)		Task based change in SO_2(%)	
	Mean± 2SD	p-value	Mean± 2SD	p-value	Mean±2SD	p-value
Pre-embolization	-5.41E-05±1.19E-04	**0.001**	-1.32E-05±4.42E-05	0.181	1.00E-02±1.08E-01	**0.008**
Post-embolization	1.05E-04±1.00E-04		-3.97E-06±5.23E-05		4.18E-02±7.04E-02	

Table 9: Changes in the task based cerebral hemodynamics in a subgroup of patients who presented with cognitive abnormalities (N=10)

HbO changes are found to be considerably significant in a subgroup analysis between the patients who presented exclusively with cognitive symptoms (ref table 9).

CEREBRAL HEMODYNAMICS CHANGES VERSUS IMAGING FINDINGS:

<u>SUBGROUP ANALYSIS CONSIDERING CIRCULATION TIME:</u>

	Task based change in HbO (mM)		Task based change in HbR (mM)		Task based change in SO_2(%)	
	Mean±2SD	p	Mean±2SD	p	Mean±2SD	p
Within normal limits	6.10E-05±2.92E-04	**0.07**	-2.03E-05±3.72E-05	0.215	1.01E-02±1.09E-01	0.113
Prolonged Circulation time	-9.51E-05±7.95E-05		-3.14E-06±3.23E-05		2.11E-02±E-024.92	

Table 10: Analysis of cerebral hemodynamics between patients with normal and prolonged circulation times.

HbO changes showed a trend towards significance with reduction in the value in patients with prolonged circulation time (indicating significant venous hypertension) (ref table 10).

<u>BENIGN (COGNARD GRADES 1,2A) VS AGGRESSIVE (COGNARD GRADES 2B AND ABOVE):</u>

Out of a total 27 patients, only 3 patients had non-aggressive fistula, whereas the remaining 24 patients had aggressive fistula. So, a test of statistical significance was not carried out in view of an exceptionally low patients on one study arm. Nonetheless, there was a significant trend in the HbO changes were observed. This finding could be validated in a larger study.

Mean HbO change in patients with non-aggressive fistula: 3.48E-04

Mean HbO change in patients with aggressive fistula: -7.24E-05.

<u>HEMORRHAGE VS NON-HEMORRHAGE ANALYSIS</u>

	Task based change in HbO (mM) Mean±2SD	p	Task based change in HbR (mM) Mean±2SD	p	Task based change in SO_2(%) Mean±2SD	p
Patients with bleed (n=6)	-4.04E-05±1.07E-04	0.97	-1.96E-05±3.09E-05	0.904	2.23E-03±4.50E-02	0.785
Patients with no bleed (n=21)	-3.65E-05±2.71E-04		-2.20E-05±4.40E-05		1.50E-02±1.10E-01	

Table 11: Analysis of cerebral hemodynamics between the patients with and without hemorrhage at the initial presentation.

None of the cerebral hemodynamic parameters showed a significant difference among the patients who had imaging evidence of hemorrhage from those who did not have a bleed (ref table 11).

SINGLE SITE VS MULTI-SITE DAVF:

	Task based change in HbO (mM)		Task based change in HbR (mM)		Task based change in SO_2(%)	
	Mean±2SD	p	Mean±2SD	p	Mean±2SD	p
Patients single site DAVF (n=20)	-1.90E-05±2.74E-04	0.52	-2.26E-05±3.95E-05	0.82	2.14E-02±1.09E-01	0.42
Patients with multi-site DAVF (n=7)	-9.00E-05±1.17E-04		-1.83E-05±4.79E-05		5.81E-02±2.20E-02	

Table 12: Analysing cerebral hemodynamics between patients with single and multi-site davf

None of the cerebral hemodynamic parameters showed a significant difference among the patients who had multi-site fistula from those who had a single site fistula (ref table 12).

NEUROPSYCHOLOGICAL EVALUATION:

Table 13: Comparison of MMSE scores in the patients before and after embolization procedure.

VARIABLE	PREEMBOLIZATION (Median±IQR) (n=19)	POST EMBOLIZATION (Median± IQR) (n=19)	p-value
MMSE	25±20	30±6	**0.001**
ACE	76±61	85±30	**0.001**

NEUROPSYCHOLOGY EVALUATION VS F-NIRS HEMODYNAMICS:

In patients with DAVF, MMSE scores before embolization was compared against changes in HbO, HbR and SO_2.

Changes in HbO and MMSE scores (pre-embolization) was found to be moderately correlating using Spearman Rho correlation test**. Correlation coefficient was calculated to be 0.42.** Thus, there may be a significantly low HbO when the patient has low MMSE scores and a relatively high HbO when the patient has better MMSE scores.

ILLUSTRATIVE CASES

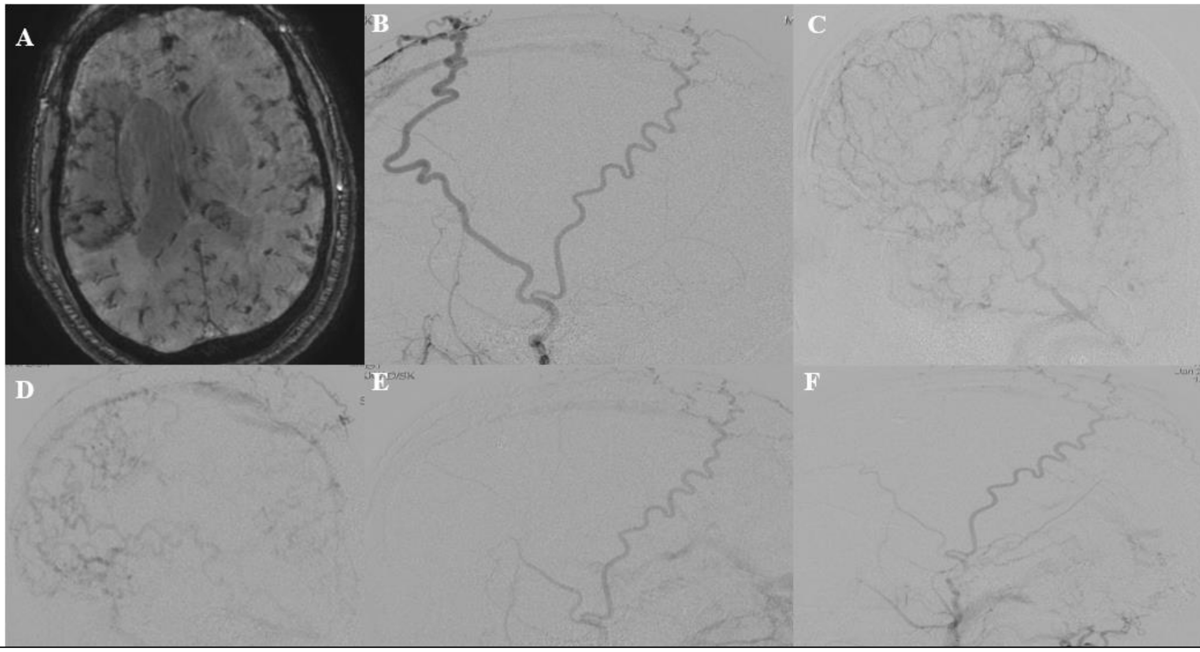


Fig.13. Representative Image of a patient with multisite DAVF. SWI image in (A) denotes right MCA territory chronic infarct with multiple dilated congested veins in brain parenchyma. Angiogram image in (B) depicts the DAVF in anterior Superior sagittal sinus (SSS) fed by frontal branch of hypertrophies superficial temporal artery. Angiogram images in (C&D) represent the congested cortical veins suggesting features of venous hypertension. Images E&F signify the complete embolization of SSS fistula.

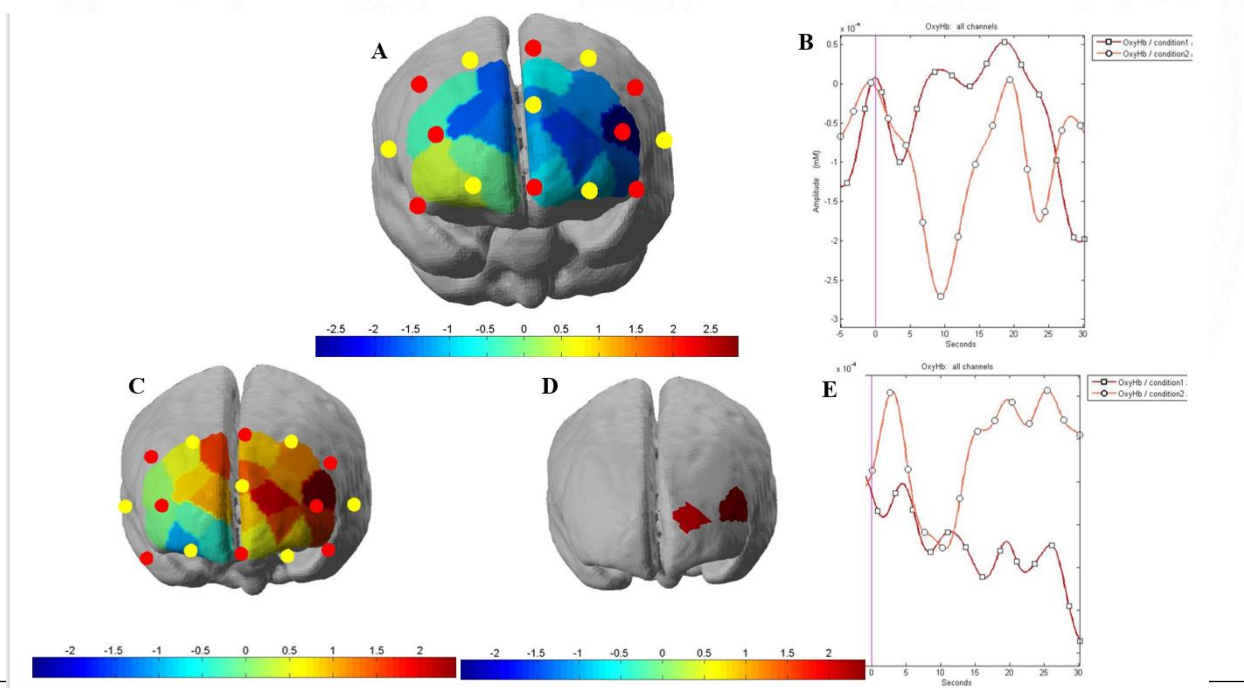


Fig. 14 NIRS Images of the same patient with multisite DAVF: Images (A&B) exhibit pre-procedure HbO images that show decreased concentration of HbO in all the channels of the prefrontal 8x8 montage. Image C depicts post-procedural increase in HbO concentration in many channels. Statistical increase of HbO is seen in channels 3 and 7 (which map to left DLPFC) is shown in image D. HbO plot in image E also signifies post-procedure increase in HbO.

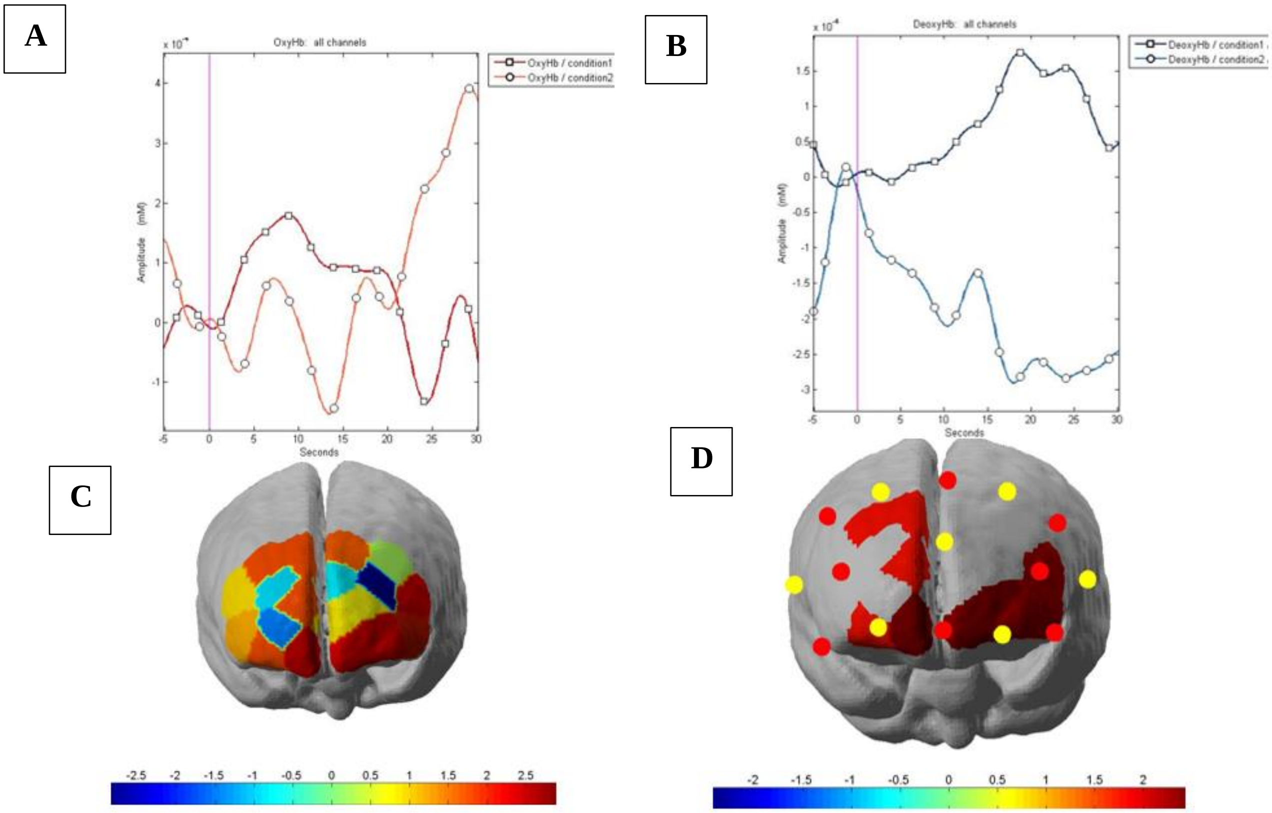


Fig.15. NIRS Images of a healthy control: Image (A) shows the early dip in HbO and later peaking of HbO (stimuli based neurovascular coupling). (B) exhibits the gradual reduction of the HbR. (C) reveals hemoglobin changes in all the channels of prefrontal montage of 8x8 f-NIRS system. Image (D) denotes only channels with statistically significant increase of HbO (at p value of 0.05 and statistical analysis done through GLM). Activates channels are 6,11,13,19,14, 10 and 17- correspond to left MPFC, Right MPFC and right DLPFC

DISCUSSION

This study aimed at understanding the feasibility of functional near infra-red spectroscopy in patients with intracranial dural arteriovenous fistula. Analysing 27 patients and 23 controls involved in the study, the results obtained from study revealed that there were significant hemodynamic changes in patients with intracranial dural arteriovenous fistula. These changes were more pronounced in terms of change in the oxyhemoglobin concentration. Change in HbO (Oxyhemoglobin concentration) was found to be consistently significant between patients and controls, and in addition, HbO changes reverted back to normal in patients after significant embolization (resolution of venous hypertension). While HbO changes reflected a significant alteration in the patient group, deoxyhemoglobin changes (HbR changes) neither depicted any significant alteration between the patient and control cohort nor there was a significance between the pre-embolization and the post-embolization status. Changes in oxygen saturation too, did not signify significant alteration in these groups.

Neuropsychology tests showed significant improvement of the scores among the patients after embolization. Pre-embolization MMSE score showed a moderate correlation with the pre-embolization change in the HbO level.

Previous studies in the context of utility of F-NIRS applications in neurology have been quite less. Studies in general have shown the basic principle of neurovascular coupling as the basis for utilizing f-NIRS in neurological disorders. There may be an initial decline in the oxyhemoglobin and upstroke in the deoxyhemoglobin, after a neural activity, due to rapid increase in the cerebral metabolic rate (43). BOLD-FMRI studies have already shown that after the initial reduction in oxyhemoglobin there is persistent increase in the oxyhemoglobin after a task (6). Unlike FMRI which depends mainly on the reduction in the deoxyhemoglobin (HbR) for the signal increase (6), FNIRS depend mainly on this latter increase of the HbO, to signify the cortical activity.

FNIRS, though had a wide clinical and research utility in psychiatry (44), it did not make a significant impact in neurology per se, save for a few applications in TBI, dementia etc. Dural Arterio-venous fistula (DAVF) is one such neurologically deteriorating condition which was extensively studied in relation to its bleeding (hemorrhage) tendency since hemorrhage tend to have a grave outcome in DAVF patients. The other important NHND in DAVF is cognitive impairment which ranged from subtle to severe (45) and sometimes can be rapidly progressive but many a time it is reversible(46,47).

Early identification of this cognitive impairment due to dural AV fistula is of utmost importance as timely treatment can reduce the morbidity significantly. The central pathogenesis of this cognitive impairment is venous hypertension. Structural neuroparenchymal and vascular imaging (MRI and DSA) could not accurately assess the treatment response, with reference to the resolution of venous hypertension. Moreover, these imaging modalities come with the cost of radiation, lower temporal resolution etc.

ASL and SPECT study in the past showed hyper perfusion in the parenchyma at the fistulous site and hypoperfusion in parenchyma away from the fistulous site (48). The reason mentioned for this lower perfusion was attributed to the retrograde venous drainage (venous congestion) which hampered the arterial inflow (CBF) and thus reducing the perfusion in those areas (rCBF). In the same study this lower perfusion was normalized after treatment of the DAVF.

There is another ^{123}I-iodoamphetamine SPECT study also showed reduced CBF due to the venous congestion in aggressive type of DAVF (49).

Our study too showed comparability with these previous studies, significantly reduced HbO and increased HbR in patients with aggressive DAVF (that is, in patients with cortical venous reflux). This has reversed back to normal after endovascular treatment for DAVF in the same subgroup of patients.

There were only a few studies in the past which assessed the hemodynamic disturbance in DAVF. We could only find a single case report which assessed the cerebral hemodynamics of DAVF utilizing NIRS (50). Their finding was also comparable where there is reduction of HbO in patients affected by

DAVF which subsequently increased partly after partial embolization and completely after complete embolization.

We did not obtain significant alterations in the HbR changes. This may possibly be due to the fact that during neurovascular coupling, after initial transient deactivation, there will be increase in cerebral blood flow and this increase in oxygenation is found to be much more than the focal area of neural activity (6). This disproportionate change in HbO might result in its significant alteration in such disorders.

The same explanation might hold good for lack of significance of the resting state HbO and HbR changes in our study as the only the task would significantly increase the cerebral blood flow and oxygenation through NVC.

We also found that the task based HbO changes were more pronounced in the aggressive grade (Cognard 2B and above) dural arteriovenous fistulas. This again emphasizes the fact that venous hypertension sets in only when the cortical venous reflux occurs, and thus aggressive fistula tend to have a higher amount of venous congestion and pseudophlebitic pattern and hence resulting in reduction in blood flow with eventual reduction in the change in HbO level.

The alteration in the neuropsychology scores were found to be significant, before and after embolization. This result was also found to be comparable with the previous study in dural arteriovenous fistula (48). Additionally, we also found a correlation between change in HbO level (before embolization) and the neuropsychology scores (before embolization). This may imply that the worser the cognition becomes, there may be a significant reduction in the HbO values. However, this needs to be validated at a larger population before its generalizability.

This study has shown the feasibility of functional near infrared spectroscopy in the bedside evaluation of cerebral hemodynamics in patients with intracranial dural arteriovenous fistula. Besides the obvious advantages of f-NIRS like portability, non-invasiveness, radiation free, patient comfort, cost effectiveness, bedside evaluation etc, the most important advantage is the utility of F-NIRS in a very treatable condition. The advantage of bedside monitoring to assess the treatment response at the patient's convenient area will definitely ease the transition of this brain-computer interface tool, from its research to clinical application.

Future studies will be required in this area especially with the newly arrived wearable and wireless FNIRS tool, tools with sophisticated algorithms to measure absolute HbO and HbR like time domain and frequency domain tools and algorithms like Multiple distance (MD) analysis that can eliminate the extracerebral and systemic signals which interfere with cerebral hemodynamic assessment. Study with requirement of a larger sample size in this condition will definitely help in the better significance of the results and make the results more generalizable.

The drawbacks of the FNIRS instrument were, the inclusion of other contaminated signals like extracerebral and systemic signals (including variations in heart rate, respiratory rate etc). This results in inaccurate interpretation of the cerebral hemodynamic assessment (9). This can be corrected by using adaptive filtering (using a band-pass or a low-pass filter), block averaging, using general linear model for statistics. We have used all these methods to correct for these unwanted signals. Other methods of corrections include spatially resolved spectroscopy and self-calibrating method. These methods will also be required for measuring absolute value of SO_2. These methods were not available with us and hence not used in our analysis. The other main demerit of f-NIRS is its inability to measure the whole brain cortex with adequate spatial resolution. Other limitations of this study were limited number of sample size, selection bias (inherent to the case-control study design).

This study had the following advantages such as detailed study of a rare disease, first of its kind, in the evaluation of DAVF using NIRS, incorporation of neuropsychological evaluation, follow up of patients and as a translational research involving development of a diagnostic research tool to clinical medicine.

CONCLUSION:

Dural arteriovenous fistula is a rare disease with altered cerebral hemodynamics, and cognitive evaluation in DAVF remains understated. Utilization of f-NIRS in DAVF as a bedside treatment response tool is feasible to a larger extent, particularly to assess the venous hypertension post intervention. Change in oxy-hemoglobin is found to be a significant parameter in differentiating these patients from controls. Additionally, it also helped to assess treatment response as it normalized after the embolization with the resolution of venous congestion. Moderate correlation was noted between the pre-embolization neuropsychological scores and changes in oxy-hemoglobin, nonetheless it requires a larger study to validate this finding. A multi-centric study with a larger number of participants and with more sophisticated tools and algorithms can help in generalizability of these results and bring in this relatively inexpensive, comfortable, and non-invasive tool for bedside evaluation of dural arteriovenous fistula.

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ANNEXURES

INFORMATION SHEET

PATIENT INFORMATION SHEET AND STUDY CONSENT FORM FOR ADVANCED NEUROIMAGING FROM HEALTHY VOLUNTEERS

Study title: "Evaluation of Cerebral Hemodynamic Assessment Using Functional Near Infra-Red Imaging and Neuropsychological Assessment in Patients with Dural Arterio- Venous Fistula."

Investigators:

Principal Investigator: Dr. Santhakumar.S
Co-investigator: Dr. Santhosh Kumar K
Co-investigator: Dr. Bejoy Thomas
Co-investigator: Dr. Kesavadas.C

Co-investigator: Dr. Ramshekhar.N.Menon
Co-investigator: Mr. Arun K.M.

This consent form is meant to invite you for participation in a research study conducting at Sree Chitra Tirunal Institute for Medical Sciences and Technology on "Evaluation of Cerebral Hemodynamic Assessment Using Functional Near Infra-Red Imaging and Neuropsychological Assessment in Patients with Dural Arterio-Venous Fistula."

Purpose of the study

The study is conducted to explore the utility of Functional- Near Infra-Red Spectroscopy in intracranial dural arterio-venous fistula. It helps to understand the cerebral hemodynamic changes in individuals with dural arterio-venous fistula.

Kindly take time to read this information carefully and to decide whether you wish or not to participate. The Principal Investigator will help you by explaining all the procedures involved in the study to the patient and clear all his/her doubts regarding Functional- Near Infra-Red Spectroscopy within 10-15 minutes. If you have decided to participate, you will be asked to fill in, sign and date this information and consent form and to keep it as useful reference on study details and personal contacts.

Nature of the procedure

Functional- Near Infra-Red Spectroscopy is a portable instrument which uses light to image superficial structures of brain. It helps in assessment of Hemoglobin changes in brain which helps to understand the hemodynamics of intracranial dural arterio-venous fistulas. Understanding it, may help in the treatment of the same in future.

It can be done at bedside, no need for a closed environment, no radiation exposure, no drug administration.

If you take part, what will you have to do?

On the day of the F-NIRS examination, you will be asked to come to a room where the scan is performed or if you are unable to come then the scan can be done at bedside. The scan uses a head cap to cover your head. Small sources and detectors will be placed in specific regions of superficial aspects of scalp to obtain the signal. You will be asked to look at a cross hair in the computer monitor. The scan starts by resting state data acquisition of 6 min during which subject can be in relaxed state and looking onto a fixation cross hair. This can be followed by a task-rest session which includes a simple cognitive paradigm like stroop task. Here the task run will last for 3 minutes which is divided into 7 'rest' and 7 'active' sessions.

Similar type of scan will be done post operatively as detailed above.

The principal investigator will provide you with the necessary instructions and help during the recording.

The information that we obtain from this investigation will help us to better understand the nature of the functional abnormalities, in patients with intracranial dural AV Fistula. However, if we identify any clinically relevant information, it will be communicated to your treating physician for appropriate decision making. Your participation is entirely voluntary, and decision will in no way influence your current treatment at SCTIMST. Absolute confidentiality of data shall be maintained. No expenses shall be incurred as a result of your participation in the study.

Can you withdraw from this study after it starts?

You have right to withdraw consent at any stage of study and this will not affect your usual treatment in this institute in any way.

Contact for Further Information:

In case if the subject wants more information about the study and the participant's right at any time of the research, you will be free to contact any one among the Research team. Please contact the Principal Investigator, Dr.Santhakumar. S, Senior Resident**,** Dept of IS&IR (contact No: Ph: 9442357488) or Co Principal Investigator, Dr.Kesavadas.C or Dr. Mala Ramanathan, Member Secretary, IEC, SCTIMST, (Phone No: 0471-2524234).

We thank you very much for agreeing to participate in this study

.

INFORMED CONSENT FORM

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

I____
son/daughter of____ (Please tick boxes)

- Declare that I have read the above information provided to me regarding the study: "Evaluation of Cerebral Hemodynamic Assessment Using Functional Near Infra- Red Imaging and Neuropsychological Assessment in Patients with Dural Arterio-Venous Fistula" and have clarified any doubts that I had [ ]
- I also understand that my participation in this study is entirely voluntary and that that I am free to withdraw at any time without giving any reason [ ]
- I also understand that the neuroimaging is being done to explore the utility of f- NIRS in cerebral hemodynamic changes of intracranial dAVF [ ]
- I understand that the results of the data obtained will not be disclosed to me. [ ]
- I understand that no expenses will be incurred by me for participating in this study and my identity will not be revealed in any information released to third parties or published [ ]
- I voluntarily agree to take part in this study [ ]
- I received a copy of this signed consent form [ ]

Name:
Signature:
Date:

Name of witness:
Relation to participant:
Date:

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

__________________________________ ____________________

Name and Signature of Principal Investigator with date

കാര്യബോധത്തോടെയുള്ള സമ്മതപത്രം

പങ്കെടുക്കുന്നയാളുടെ പേര്.....................................മകൻ/മകൾ....................... (ദയവായി (ബോക്സുകളിൽ ശരി അടയാളമിടുക)

- ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളുടെ, ഫങ്ഷണൽ നീയർ ഇൻഫ്രാറെഡ് ചിത്രീകരണമുപയോഗിച്ചുള്ള തലയിലെ രക്തചംക്രമണ വ്യവസ്ഥയുടെ വിലയിരുത്തലും ന്യൂറോ മനശാസ്ത്ര വിലയിരുത്തലും എന്ന പഠനസംബന്ധമായി എനിക്കുനൽകിയ വിവരങ്ങൾ വായിച്ചുഎന്നും എനിക്കുണ്ടായ സംശയങ്ങൾ ദുരീകരിച്ചു എന്നും ഞാൻ പ്രസ്താവിക്കുന്നു. [ ]

- എന്റെ ഈ പഠനത്തിലുള്ള പങ്കാളിത്തം സ്വമേധയായുള്ളതാണെന്നും, എനിക്ക് ഒരു കാരണവും കൂടാതെ ഏതുസമയത്തും, എനിക്കുള്ള വൈദ്യശുശ്രൂഷയെയോ നിയമപരമായ അവകാശങ്ങളെയോ ബാധിക്കാതെ പിൻവാങ്ങാമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- തലയോട്ടിക്കുള്ളിലെ ഡിഎവിഎഫിന്റെ പ്രവർത്തിപരമായ ബന്ധത്തിലുള്ള മാറ്റങ്ങൾ കണ്ടെത്തുന്നതിലുള്ള റെസ്റ്റിംഗ് സ്റ്റേറ്റ് എഫ് എംആർഐയുടെ പ്രയോജനക്ഷമത പരിശോധിക്കാനാണ് ന്യൂറോ ചിത്രീകരണം നടത്തുന്നത് എന്നും ഞാൻ മനസ്സിലാക്കി [ ]
- ശേഖരിച്ചവിവരങ്ങൾ എന്നോട് വെളിപ്പെടുത്തില്ലെന്നും, എന്നിരുന്നാലും, ചികിത്സ പരിഷ്ക്കരിക്കാനിടയാക്കുന്ന എന്തെങ്കിലും വിവരങ്ങൾ കണ്ടെത്തിയാൽ അത് വേണ്ടുന്ന തീരുമാനമെടുക്കാനായി ചികിത്സിക്കുന്ന ഡോക്ടർക്ക് നൽകുമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു.
- പഠനത്തിൽ പങ്കെടുക്കുന്നതുകൊണ്ട് എനിക്ക് ചിലവൊന്നും ഉണ്ടാകില്ലെന്നും, മൂന്നാം കക്ഷികൾക്കോ പ്രസിദ്ധീകരണത്തിനോ നൽകുമ്പോൾ എന്റെ വ്യക്തിവിവരങ്ങൾ വെളിപ്പെടുത്തുകയില്ലെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- സ്വമേധയാ പഠനത്തിൽ പങ്കെടുക്കാൻ ഞാൻ സമ്മതിക്കുന്നു. [ ]
- സമ്മതപത്രത്തിന്റെ ഒപ്പിട്ട ഒരു പ്രതി എനിക്ക് കിട്ടി. [ ]

പേര്

ഒപ്പ്/ രോഗിയുടെ വിരലടയാളം/

തീയതി

സാക്ഷിയുടെ പേര്

ഒപ്പ്

തീയതി

രോഗിയുമായുള്ള ബന്ധം

(സമ്മതം വാങ്ങുന്നയാൾ)

മെഡിക്കൽ റിസർച്ച് പ്രോജക്ടിനാവശ്യമായ സമ്മതപത്രത്തിനു വേണ്ടുന്ന എല്ലാ ഘടകങ്ങളും തൃപ്തികരമായി നിർവഹിച്ചിരിക്കുന്നുവെന്ന് ഞാൻ ബോധ്യപ്പെടുത്തുന്നു. പഠനപങ്കാളിയുമായി ഗവേഷണപദ്ധതിയെപ്പറ്റി സാങ്കേതികേതര പദങ്ങളുപയോഗിച്ച് എല്ലാ വിവരങ്ങളെപ്പറ്റിയും ചർച്ച നടത്തുകയും പ്രതീക്ഷിക്കാവുന്ന അപകടസാധ്യതകളും പാർശ്വഫലങ്ങളും വിശദീകരിക്കുകയും ചെയ്തു. പങ്കാളിയെ ചോദ്യങ്ങൾ ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും എല്ലാ ചോദ്യങ്ങൾക്കും ഉത്തരം നൽകുകയും ചെയ്തു എന്നും ഞാൻ സാക്ഷ്യപ്പെടുത്തുന്നു.

സമ്മതപത്രം വാങ്ങുന്ന ആളുടെ പേരും ഒപ്പും

ഡോ ശാന്തകുമാർ എസ് (ഫോൺ. 442357488)

സീനിയർ റസിഡന്റ്

പഠനവുമായി ബന്ധമില്ലാത്ത വ്യക്തിയെ ബന്ധപ്പെടുന്നതിന് ദയവായി സ്ഥാപനത്തിലെ നൈതീക കമ്മിറ്റി മെംമ്പർ സെക്രട്ടറി ഡോ. മാല രാമനാഥനെ ബന്ധപ്പെടാം. ഫോൺ 04712524234, email: iec.mem.sec@sctimst.ac.in

കാര്യബോധത്തോടെയുള്ള സമ്മതപത്രം

പങ്കെടുക്കുന്നയാളുടെ പേര്....................................മകൻ/മകൾ...................... (ദയവായി (ബോക്സുകളിൽ ശരി അടയാളമിടുക)

- ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളുടെ, ഫങ്ഷണൽ നീയർ ഇൻഫ്രാറെഡ് ചിത്രീകരണമുപയോഗിച്ചുള്ള തലയിലെ രക്തചംക്രമണ വ്യവസ്ഥയുടെ വിലയിരുത്തലും ന്യൂറോ മനശാസ്ത്ര വിലയിരുത്തലും എന്ന പഠനസംബന്ധമായി എനിക്കുനൽകിയ വിവരങ്ങൾ വായിച്ചുഎന്നും എനിക്കുണ്ടായ സംശയങ്ങൽ ദുരീകരിച്ചു എന്നും ഞാൻ പ്രസ്താവിക്കുന്നു. [ ]

- എന്റെ ഈ പഠനത്തിലുള്ള പങ്കാളിത്തം സ്വമേധയായുള്ളതാണെന്നും, എനിക്ക് ഒരു കാരണവും കൂടാതെ ഏതുസമയത്തും, എനിക്കുള്ള വൈദ്യശുശ്രൂഷയെയോ നിയമപരമായ അവകാശങ്ങളെയോ ബാധിക്കാതെ പിൻവാങ്ങാമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- തലയോട്ടിക്കുള്ളിലെ ഡിഎവിഎഫിന്റെ പ്രവർത്തിപരമായ ബന്ധത്തിലുള്ള മാറ്റങ്ങൾ കണ്ടെത്തുന്നതിലുള്ള റെസ്റ്റിംഗ് സ്റ്റേറ്റ് എഫ് എംആർഐയുടെ പ്രയോജനക്ഷമത പരിശോധിക്കാനാണ് ന്യൂറോ ചിത്രീകരണം നടത്തുന്നത് എന്നും ഞാൻ മനസ്സിലാക്കി [ ]
- ശേഖരിച്ചവിവരങ്ങൾ എന്നോട് വെളിപ്പെടുത്തില്ലെന്നും ഞാൻ മനസ്സിലാക്കുന്നു.
- പഠനത്തിൽ പങ്കെടുക്കുന്നതുകൊണ്ട് എനിക്ക് ചിലവൊന്നും ഉണ്ടാകില്ലെന്നും, മൂന്നാം കക്ഷികൾക്കോ പ്രസിദ്ധീകരണത്തിനോ നൽകുമ്പോൾ എന്റെ വ്യക്തിവിവരങ്ങൾ വെളിപ്പെടുത്തുകയില്ലെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- സ്വമേധയാ പഠനത്തിൽ പങ്കെടുക്കാൻ ഞാൻ സമ്മതിക്കുന്നു. [ ]
- സമ്മതപത്രത്തിന്റെ ഒപ്പിട്ട ഒരു പ്രതി എനിക്ക് കിട്ടി. [ ]

പേര്

ഒപ്പ്/ രോഗിയുടെ വിരലടയാളം/

തീയതി

സാക്ഷിയുടെ പേര്

ഒപ്പ്

തീയതി

പങ്കാളിയുമായുള്ള ബന്ധം

(സമ്മതം വാങ്ങുന്നയാൾ)

മെഡിക്കൽ റിസർച്ച് പ്രോജക്ടിനാവശ്യമായ സമ്മതപത്രത്തിനു വേണ്ടുന്ന എല്ലാ ഘടകങ്ങളും തൃപ്തികരമായി നിർവഹിച്ചിരിക്കുന്നുവെന്ന് ഞാൻ ബോധ്യപ്പെടുത്തുന്നു. പഠനപങ്കാളിയുമായി ഗവേഷണപദ്ധതിയെപ്പറ്റി സാങ്കേതികേതര പദങ്ങളുപയോഗിച്ച് എല്ലാ വിവരങ്ങളെപ്പറ്റിയും ചർച്ച നടത്തുകയും പ്രതീക്ഷിക്കാവുന്ന അപകടസാധ്യതകളും പാർശ്വഫലങ്ങളും വിശദീകരിക്കുകയും ചെയ്തു. പങ്കാളിയെ ചോദ്യങ്ങൾ ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും എല്ലാ ചോദ്യങ്ങൾക്കും ഉത്തരം നൽകുകയും ചെയ്തു എന്നും ഞാൻ സാക്ഷ്യപ്പെടുത്തുന്നു.

സമ്മതപത്രം വാങ്ങുന്ന ആളുടെ പേരും ഒപ്പും

ഡോ ശാന്തകുമാർ എസ് (ഫോൺ. 442357488)

സീനിയർ റസിഡന്റ്

പഠനവുമായി ബന്ധമില്ലാത്ത വ്യക്തിയെ ബന്ധപ്പെടുന്നതിന് ദയവായി സ്ഥാപനത്തിലെ നൈതീക കമ്മിറ്റി മെംബർ സെക്രട്ടറി ഡോ. മാല രാമനാഥനെ ബന്ധപ്പെടാം. ഫോൺ 04712524234, email: iec.mem.sec@sctimst.ac.in

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ സയൻസ് ആന്റ് ടെക്നോളജി, തിരുവനന്തപുരം

ആധുനീകമായ ന്യൂറോ ചിത്രീകരണത്തിന് രോഗികൾക്കുള്ള വിവരണപത്രം

പഠനശീർഷകം.

ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളുടെ, ഫങ്ഷണൽ നീയർ ഇൻഫ്രാറെഡ് ചിത്രീകരണമുപയോഗിച്ചുള്ള തലയിലെ രക്തചംക്രമണ വ്യവസ്ഥയുടെ വിലയിരുത്തലും ന്യൂറോ മനശാസ്ത്ര വിലയിരുത്തലും.

ഗവേഷകർ

പ്രധാന ഗവേഷകൻ	ഡോ. ശാന്തകുമാർ എസ്
സഹ പ്രധാന ഗവേഷകൻ	ഡോ. കേശവദാസ് സി
സഹ-ഗവേഷകൻ	ഡോ. ബിജോയ് തോമസ്
സഹ-ഗവേഷകൻ	ഡോ. സന്തോഷ്കുമാർ കെന്നത്ത്
സഹ-ഗവേഷകൻ	ഡോ. റാം ശേഖർ മേനോൻ
സഹ-ഗവേഷകൻ	ശ്രീ അരുൺ കെ

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ സയൻസ് ആന്റ് ടെക്നോളജിയിൽ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളുടെ, ഫങ്ഷണൽ നീയർ ഇൻഫ്രാറെഡ് ചിത്രീകരണമുപയോഗിച്ചുള്ള തലയിലെ രക്തചംക്രമണ വ്യവസ്ഥയുടെ വിലയിരുത്തലും ന്യൂറോ മനശാസ്ത്ര വിലയിരുത്തലും എന്ന ഗവേഷണ പഠനത്തിൽ താങ്കളുടെ പങ്കാളിത്തം ക്ഷണിക്കുന്നതിന് ഉദ്ദേശിച്ചുള്ള സമ്മതപത്രമാണിത്.

പഠനത്തിന്റെ ഉദ്ദേശം

തലയോട്ടിക്കുള്ളിലെ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയിൽ, ഫങ്ഷണൽ നീയർ ഇൻഫ്രാറെഡ് സ്പെക്ട്രോഗ്രഫിയുടെ പ്രയോജനക്ഷമത പരിശോധിക്കാനാണ് ഈ പഠനം നടത്തുന്നത്. ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള വ്യക്തികളിലെ രക്തചംക്രമണ വ്യവസ്ഥയുടെ മാറ്റങ്ങൾ മനസ്സിലാക്കാൻ ഇത് സഹായിക്കും.

വിവരങ്ങൾ ശ്രദ്ധാപൂർവ്വം വായിക്കാൻ ദയവായി സമയമെടുക്കുകയും പങ്കെടുക്കണോ വേണ്ടയോ എന്ന് താങ്കൾ തീരുമാനിക്കുകയും ചെയ്യുക. പ്രധാന ഗവേഷകൻ പഠനത്തിലുൾപ്പെട്ടിട്ടുള്ള എല്ലാ നടപടികളും രോഗിയോട് വിശദീകരിക്കുകയും അദ്ദേഹത്തിന് ഫങ്ഷണൽ നീയർ ഇൻഫ്രാറെഡ് സ്പെക്ട്രോഗ്രഫിയെപ്പ റ്റിയുള്ള സംശയങ്ങൾ 10-15 മിനിട്ടിനകം ദുരീകരിക്കുകയും ചെയ്യും. താങ്കൾ പങ്കെടുക്കാൻ തീരുമാനിച്ചാൽ, ഈ കാര്യവിവരണ സമ്മതപത്രം പൂരിപ്പിക്കുകയും ഒപ്പും തീയതിയും നൽകുകയും പഠന വിശദാംശങ്ങളുടെയും വ്യക്തിബന്ധങ്ങളുടെയും ഗുണകരമായ ആധാരമായി സൂക്ഷിക്കുകയും ചെയ്യുക.

നടപടിയുടെ സ്വഭാവം

ഫങ്ഷണൽ നീയർ ഇൻഫ്രാറെഡ് സ്പെക്ട്രോഗ്രഫി തലച്ചോറിന്റെ പുറമേയുള്ള ഘടനകളുടെ ചിത്രീകരണം പ്രകാശമുപയോഗിച്ച് ചെയ്യുന്ന കൊണ്ടുനടക്കാവുന്ന ഒരുപകരണമാണ്. തലച്ചോറിലെ ഹീമോഗ്ലോബിൻ വ്യതിചലനങ്ങൾ വിലയിരുത്തുന്നതിനെ സഹായിച്ച് ഡ്യൂറൽ ആർട്ടീരിയോ വീനസ് ഫിസ്റ്റുലകളുടെ രക്തചംക്രമണ വ്യവസ്ഥ മനസ്സിലാക്കാൻ സഹായിക്കുന്നു. അത് മനസ്സിലാക്കുന്നതിലൂടെ ഭാവിയിൽ ചികിത്സയെ സഹായിച്ചേക്കാം.

ബഡ്ഡിന് അരികിൽ ഇത് ചെയ്യാനാകും, അടഞ്ഞ പരിതസ്ഥിതി ആവശ്യമില്ല, റേഡിയേഷൻ ഉണ്ടാവില്ല, ഒരുമരുന്നും നൽകേണ്ടതില്ല.

പങ്കെടുക്കുന്നു എങ്കിൽ താങ്കളെന്ത് ചെയ്യണം

എ്- എൻഐആർഎസ് പരിശോധനാ ദിവസം താങ്കളോട് സ്കാൻചെയ്യുന്ന മുറിയിലേക്ക് വരാൻആവശ്യപ്പെടും, താങ്കൾക്ക് അവിടെ വരാൻ കഴിയില്ലെങ്കിൽ താങ്കളുടെ ബഡ്ഡിനരികിൽ സ്കാൻ ചെയ്യാനാകും. സ്കാൻനിനായി താങ്കളുടെ തലമൂടുന്ന തൊപ്പി ഉപയോഗിക്കും. ചെറിയ പ്രഭവകേന്ദ്രങ്ങളും, സ്പർശനികളും, സിഗ്നലുകൾ ലഭിക്കാൻ തലയിലെ ഉപരിതലത്തിലുള്ള ഘടനകളുടെ നിർദ്ദിഷ്ട സ്ഥാനങ്ങളിൽ വയ്ക്കും. താങ്കളോട് കമ്പ്യൂട്ടർ മോണിറ്ററിലുള്ള ഒരു ക്രോസ് വയറിലേക്ക് നോക്കാനാവശ്യപ്പെടും. സ്വസ്ഥമായ അവസ്ഥയിലുള്ള (റെസ്റ്റിംഗ് സ്റ്റേറ്റ്) വിവരങ്ങൾ ശേഖരിച്ചുകൊണ്ട് സ്കാൻ ആരംഭിക്കും, 6 മിനിട്ട് ദൈർഘ്യമുള്ള വിവരശേഖരണസമയത്ത്, രോഗി സ്വസ്ഥമായി ക്രോസ് വയറിലേക്ക് നോക്കിക്കൊണ്ടിരിക്കും. ഇതിനേ തുടർന്ന് ലളിതമായ ചലന മാതൃക യുടെ പ്രവർത്തി- വിശ്രമ ഘട്ടവും. ഇതിൽ പ്രവർത്തി ഘട്ടം 3 മിനിട്ട് നീളും അതിൽ 7 വിശ്രമത്തിന്റെയും 7 സജീവതയുടെയും ഘട്ടമുണ്ട്. അത് ഇടതുകൈ, വലതു കൈ രണ്ട് കൈകളും എന്നിങ്ങനെ ആവർത്തിക്കും.

മുകളിൽ വിശദീകരിച്ചതുപോലെയുള്ള സ്കാൻ ശസ്ത്രക്രിയക്കുശേഷവും ആവർത്തിക്കും.

സ്ക്ാൻരേഖപ്പെടുത്തുന്ന സമയത്ത് പ്രധാന ഗവേഷകൻ വേണ്ടുന്ന നിർദ്ദേശങ്ങൾ നൽകുകയും താങ്കളെ സഹായിക്കുകയും ചെയ്യും.

ഈ പരിശോധനയിൽനിന്നും ലഭിക്കുന്ന വവരങ്ങൾ തലയോട്ടിക്കുള്ളിൽ ഡിഎവിഎഫ് ഉള്ള രോഗികളുടെ പ്രവർത്തനപരമായ അസാധാരണത്വം മനസിലാക്കാൻ ഞങ്ങളെ സഹായിക്കും. എന്നിരുന്നാലും വൈദ്യശാസ്ത്രപരമായി പ്രസക്തമായ എന്തെങ്കിലും വിവരങ്ങൾ ഞങ്ങൾ കണ്ടെത്തിയാൽ താങ്കളെ ചികിത്സിക്കുന്ന ഡോക്ടർക്ക് വേണ്ടുന്ന തീരുമാനമെടുക്കാനായി അത് നൽകും. താങ്കളുടെ പങ്കാളിത്തം തികച്ചും സ്വമേധയായും തീരുമാനം താങ്കളുടെ SCTIMST യിലെ ഇപ്പോഴത്തെ ചികിത്സയെ ഒരുവിധത്തിലും ബാധിക്കില്ല. വിവരങ്ങളുടെ പരിപൂർണ്ണ രഹസ്യ സ്വഭാവം നിലനിർത്തും.പങ്കെടുക്കുന്നതുകൊണ്ട്. താങ്കൾക്ക് ഒരു ചിലവുമുണ്ടാകില്ല.

പഠനം ആരംഭിച്ചശേഷം താങ്കൾക്ക് പിൻമാറാമോ

പഠനത്തിന്റെ ഏത് ഘട്ടത്തിലും താങ്കൾക്ക് സമ്മതം പിൻവലിക്കാം, അത് താങ്കളുടെ സാധാരണ ചികിത്സയെ ഒരു വിധത്തിലും ബാധിക്കില്ല.

കൂടുതൽ വിവരങ്ങൾക്ക് ബന്ധപ്പെടാൻ

രോഗിക്ക് പഠനത്തെപ്പറ്റിയും പങ്കാളിയുടെ അവകാശങ്ങളെപ്പറ്റിയും കൂടുതൽ വിവരങ്ങൾ ആവശ്യമെങ്കിൽ ഗവേഷണ സംഘത്തിലെ ഏതൊരാളെയും ബന്ധപ്പെടാം.

ദയവായി പ്രധാന ഗവേഷകനെ ബന്ധപ്പെടുക. ഡോ. ശാന്തകുമാർ എസ്, സീനിയർ റസിഡന്റ്, ഡിപ്പാർട്ടമെന്റ് ഓഫ് ഐഎസ് & ഐആർ (ബന്ധപ്പെടാനുള്ള ഫോൺ നമ്പർ. 9442357488) email. santhakumar@sctimst.ac.in, സഹ- പ്രധാനഗവേഷകൻ ഡോ. കേശവദാസ് സി,

ഡോ. മാല രാമനാഥൻ മെമ്പർ സെക്രട്ടറി ഐഇസി (ഫോൺ നമ്പർ 0471-2524234)

പഠനത്തിൽ പങ്കെടുക്കാൻ സമ്മതിച്ചതിന് താങ്കൾക്ക് വളരെ നന്ദി

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ സയൻസ് ആന്റ് ടെക്നോളജി, തിരുവനന്തപുരം

ആധുനീകമായ ന്യൂറോ ചിത്രീകരണത്തിന്, ആരോഗ്യമുള്ള സന്നദ്ധപ്രവർത്തകർക്കുള്ള വിവരണപത്രം

പഠനശീർഷകം.

ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളുടെ, ഫങ്ഷണൽ നീയർ ഇൻഫ്രാറെഡ് ചിത്രീകരണമുപയോഗിച്ചുള്ള തലയിലെ രക്തചംക്രമണ വ്യവസ്ഥയുടെ വിലയിരുത്തലും ന്യൂറോ മനശാസ്ത്ര വിലയിരുത്തലും.

ഗവേഷകർ

പ്രധാന ഗവേഷകൻ	ഡോ. ശാന്തകുമാർ എസ്
സഹ പ്രധാന ഗവേഷകൻ	ഡോ. കേശവദാസ് സി
സഹ-ഗവേഷകൻ	ഡോ. ബിജോയ് തോമസ്
സഹ-ഗവേഷകൻ	ഡോ. സന്തോഷ്കുമാർ കെന്നത്ത്
സഹ-ഗവേഷകൻ	ഡോ. റാം ശേഖർ മേനോൻ
സഹ-ഗവേഷകൻ	ശ്രീ അരുൺ കെ

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ സയൻസ് ആന്റ് ടെക്നോളജിയിൽ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളുടെ, ഫങ്ഷണൽ നീയർ ഇൻഫ്രാറെഡ് ചിത്രീകരണമുപയോഗിച്ചുള്ള തലയിലെ രക്തചംക്രമണ വ്യവസ്ഥയുടെ വിലയിരുത്തലും ന്യൂറോ മനശാസ്ത്ര വിലയിരുത്തലും എന്ന ഗവേഷണ പഠനത്തിൽ താങ്കളുടെ പങ്കാളിത്തം ക്ഷണിക്കുന്നതിന് ഉദ്ദേശിച്ചുള്ള സമ്മതപത്രമാണിത്.

പഠനത്തിന്റെ ഉദ്ദേശം

തലയോട്ടിക്കുള്ളിലെ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയിൽ, ഫങ്ഷണൽ നീയർ ഇൻഫ്രാറെഡ് സ്പെക്ട്രോഗ്രഫിയുടെ പ്രയോജനക്ഷമത പരിശോധിക്കാനാണ് ഈ പഠനം നടത്തുന്നത്. ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള വ്യക്തികളിലെ രക്തചംക്രമണ വ്യവസ്ഥയുടെ മാറ്റങ്ങൾ മനസ്സിലാക്കാൻ ഇത് സഹായിക്കും.

വിവരങ്ങൾ ശ്രദ്ധാപൂർവ്വം വായിക്കാൻ ദയവായി സമയമെടുക്കുകയുംപങ്കെടുക്കണോവേണ്ടയോ എന്ന് താങ്കൾ തീരുമാനിക്കുകയും ചെയ്യുക. പ്രധാന ഗവേഷകൻപഠനത്തിലുൾപ്പെട്ടിട്ടുള്ള എല്ലാ നടപടികളും പങ്കാളിയോട് വിശദീകരിക്കുകയും അദ്ദേഹത്തിന് ഫങ്ഷണൽ നീയർ ഇൻഫ്രാറെഡ് സ്പെക്ട്രോഗ്രഫിയെപ്പറ്റിയുള്ള സംശയങ്ങൾ 10-15 മിനിട്ടിനകം ദുരീകരിക്കുകയും ചെയ്യും. താങ്കൾ പങ്കെടുക്കാൻ തീരുമാനിച്ചാൽ, ഈ കാര്യവിവരണ സമ്മതപത്രം പൂരിപ്പിക്കുകയും ഒപ്പും തിയതിയും നൽകുകയും പഠന വിശദാംശങ്ങളുടെയും വ്യക്തിബന്ധങ്ങളുടെയും ഗുണകരമായ ആധാരമായി സൂക്ഷിക്കുകയും ചെയ്യുക.

നടപടിയുടെ സ്വഭാവം

ഫങ്ഷണൽ നീയർ ഇൻഫ്രാറെഡ് സ്പെക്ട്രോഗ്രഫി തലച്ചോറിന്റെ പുറമേയുള്ള ഘടനകളുടെ ചിത്രീകരണം പ്രകാശമുപയോഗിച്ച് ചെയ്യുന്ന കൊണ്ടുനടക്കാവുന്ന ഒരുപകരണമാണ്. തലച്ചോറിലെ ഹീമോഗ്ലോബിൻ വ്യതിചലനങ്ങൾ വിലയിരുത്തുന്നതിനെ സഹായിച്ച് ഡ്യൂറൽ ആർട്ടീരിയോ വീനസ് ഫിസ്റ്റുലകളുടെ രക്തചംക്രമണ വ്യവസ്ഥ മനസ്സിലാക്കാൻ സഹായിക്കുന്നു. അത് മനസ്സിലാക്കുന്നതിലൂടെ ഭാവിയിൽ ചികിത്സയെ സഹായിച്ചേക്കാം.

ബഡ്ഡിന് അരികിൽ ഇത് ചെയ്യാനാകും, അടഞ്ഞ പരിതസ്ഥിതി ആവശ്യമില്ല, റേഡിയേഷൻ ഉണ്ടാവില്ല, ഒരുമരുന്നും നൽകേണ്ടതില്ല.

പങ്കെടുക്കുന്നു എങ്കിൽ താങ്കളെന്ത് ചെയ്യണം

എ്- എൻഐആർഎസ് പരിശോധനാ ദിവസം താങ്കളോട് സ്കാൻചെയ്യുന്ന മുറിയിലേക്ക് വരാൻ ആവശ്യപ്പെടും, താങ്കൾക്ക് അവിടെ വരാൻ കഴിയില്ലെങ്കിൽ താങ്കലുടെ ബഡ്ഡിനരികിൽ സ്കാൻ ചെയ്യാനാകും. സ്കാൻ താങ്കളുടെ തലമൂടുന്ന തൊപ്പി ഉപയോഗിക്കും. ചെറിയ പ്രഭവകേന്ദ്രങ്ങളും സ്പർശനികളും സിഗ്നലുകൾ ലഭിക്കാൻ ഉപരിതലത്തിലുള്ള ഘടനകളുടെ നിർദ്ദിഷ്ട സ്ഥലങ്ങളിൽ തലയിൽ വയ്ക്കും. താങ്കളോട് കമ്പ്യൂട്ടർ മോണിറ്ററിലുള്ള ഒരു ക്രോസ് വയറിലേക്ക് നോക്കാനാവശ്യപ്പെടും. സ്വസ്ഥമായ അവസ്ഥയിലുള്ള (റെസ്റ്റിംഗ് സ്റ്റേറ്റ്) വിവരങ്ങൾ ശേഖരിച്ചുകൊണ്ട് സ്കാൻ ആരംഭിക്കും, 6 മിനിട്ട് ദൈർഘ്യമുള്ള വിവരശേഖരണസമയത്ത്, രോഗി സ്വസ്ഥമായി ക്രോസ് വയറിലേക്ക് നോക്കിക്കൊണ്ടിരിക്കും. ഇതിനേ തുടർന്ന് ലളിതമായ ചലന മാതൃകയുടെ പ്രവർത്തി-വിശ്രമ ഘട്ടവും. ഇതിൽ പ്രവർത്തി ഘട്ടം 3 മിനിട്ട് നീളും അതിൽ 7 വിശ്രമത്തിന്റെയും 7 സജീവതയുടെയും ഘട്ടമുണ്ട്. അത് ഇടതുകൈ, വലതു കൈ രണ്ട് കൈകളും എന്നിങ്ങനെ ആവർത്തിക്കും.

മുകളിൽ വിശദീകരിച്ചതുപോലെയുള്ള സ്കാൻ ശസ്ത്രക്രിയക്കുശേഷവും ആവർത്തിക്കും.

സ്ക്കാൻരേഖപ്പെടുത്തുന്ന സമയത്ത് പ്രധാന ഗവേഷകൻ വേണ്ടുന്ന നിർദ്ദേശങ്ങൾ നൽകുകയും താങ്കളെ സഹായിക്കുകയും ചെയ്യും.

ഈ പരിശോധനയിൽനിന്നും ലഭിക്കുന്ന വവരങ്ങൾ തലയോട്ടിക്കുള്ളിൽ ഡിഎവിഎഫ് ഉള്ള രോഗികളുടെ പ്രവർത്തനപരമായ അസാധാരണത്വം മനസിലാക്കാൻ ഞങ്ങളെ സഹായിക്കും. എന്നിരുന്നാലും വൈദ്യശാസ്ത്രപരമായി പ്രസക്തമായ എന്തെങ്കിലും വിവരങ്ങൾ ഞങ്ങൾ കണ്ടെത്തിയാൽ താങ്കളെ ചികിത്സിക്കുന്ന ഡോക്ടർക്ക് വേണ്ടുന്ന തീരുമാനമെടുക്കാനായി അത് നൽകും. താങ്കളുടെ പങ്കാളിത്തം തികച്ചും സ്വമേധയായും. തീരുമാനം താങ്കളുടെ SCTIMST യിലെ ഇപ്പോഴത്തെ ചികിത്സയെ ഒരുവിധത്തിലും ബാധിക്കില്ല. വിവരങ്ങളുടെ പരിപൂർണ്ണ രഹസ്യ സ്വഭാവം നിലനിർത്തും. പങ്കെടുക്കുന്നതുകൊണ്ട്. താങ്കൾക്ക് ഒരു ചിലവുമുണ്ടാകില്ല.

പഠനം ആരംഭിച്ചശേഷം താങ്കൾക്ക് പിൻമാറാമോ

പഠനത്തിന്റെ ഏത് ഘട്ടത്തിലും താങ്കൽക്ക് സമ്മതം പിൻവലിക്കാം, അത് താങ്കളുടെ സാധാരണ ചികിത്സയെ ഒരു വിധത്തിലും ബാധിക്കില്ല.

കുടുതൽ വിവരങ്ങൾക്ക് ബന്ധപ്പെടാൻ

പങ്കെടുക്കുന്നയാൾക്ക് പഠനത്തെപ്പറ്റിയും പങ്കാളിയുടെ അവകാശങ്ങളെപ്പറ്റിയും കൂടുതൽ വിവരങ്ങൾ ആവശ്യമെങ്കിൽ ഗവേഷണ സംഘത്തിലെ ഏതൊരാളെയും ബന്ധപ്പെടാം.

ദയവായി പ്രധാന ഗവേഷകനെ ബന്ധപ്പെടുക. ഡോ. ശാന്തകുമാർ എസ്, സീനിയർ റസിഡന്റ്, ഡിപ്പാർട്ടമെന്റ് ഓഫ് ഐഎസ് & ഐആർ (ബന്ധപ്പെടാനുള്ള ഫോൺ നമ്പർ. 9442357488) ഇമെയിൽ. santhakumar@sctimst.ac.in, സഹ- പ്രധാനഗവേഷകൻ ഡോ. കേശവദാസ് സി,

ഡോ. മാല രാമനാഥൻ മെമ്പർ സെക്രട്ടറി ഐഇസി (ഫോൺ നമ്പർ 0471-2524234)

പഠനത്തിൽ പങ്കെടുക്കാൻ സമ്മതിച്ചതിന് താങ്കൾക്ക് വളരെ നന്ദി

Study Title: Evaluation of Cerebral Hemodynamics Using Functional Near Infrared Spectroscopy in patients with Intracranial Dural Arteriovenous Fistula

DAVF reporting format for F-NIRS and DSA

a)	Reallocated Anonymized Image identification number: ………………………..
b)	Study / Sequence evaluated: F-NIRS/DSA………………....
c)	Investigator analysing study:…………………………… Date of Image analysis:……………
d)	Quality of image: four-point scale score*: …………………………………………

	Name:
	Age:
	Sex:
	Chief complaints:
A.	Ophthalmological
B.	Seizures
C.	Cognitive complaints
D.	Headache
E.	Others

- **F-NIRS parameters:**

a. Resting state HbO, HbR and SO_2

b. Task based FNIRS evaluation: Change in HbO, Change in HbR and Change in SO_2.

c. GLM (General Linear Model) evaluation of cerebral hemodynamics.

- **DSA parameters:**

a. Lesion side : Right / Left

b. DAVF location

c. Architecture

Type:

Cognard/Borden classification:

d. Feeding artery

e. Unilateral/ bilateral supply …………

f. Venous drainage:

g. Cortical venous reflux : Present/absent

NAME	CLINICAL F	PRESENTA	MRI Bleed	Cognard	Site	Embolization		Risk factor	MMSE	ACE	MMSEPOS	ACEPOST	NS CHANG	NS CHANG	HbO chan	HbR chang	Osat chan
1	Headache	1	2	3 Rt parac	1	Complete	Improved	1	26	54							
2	Headache	2	2	2B(torcula	2	Signficant	Improved	1	23	53							
3	Headache	1	2	1 (Left TS-	1	Conservative		2	30	88							
4	Headache	1	2	1 Left TS-S	1	Partial	Improved	1+	28	76	30	85	2	9	-8.12E-04	1.18E-04	-2.14E-04
5	Ocular	1	2	2A+B(torc	2	Signficant	Improved	1+	30	83	30	96	0	13	1.54E-04	5.90E-05	6.40E-03
6	Headache	1	2	3(Rt TS)	1	Complete	Improved	1	24	78	30	92	6	14	1.82E-04	1.37E-05	-1.24E-02
7	Headache	1	2	2A+B(mid	1	Complete	Improved	1	24	56	28	78	4	22	2.65E-05	-2.85E-05	3.69E-02
8	Headache	1	2	2A+B(Torc	1	Signficant	Improved	1+	26	78	30	84	4	6	-4.50E-05	7.23E-05	-8.28E-02
9	Headache	1	2	2A midSSS	1	Complete	Imprvoed	1	28	87							
10	Headache	1	2	2B Tentori	1	Complete	Improved	2	30	98	30	98	0	0	8.30E-05	-7.61E-05	1.03E-01
11	Headache	2	2	3 Rt pariet	2	Complete	Improved	1+	24	74							
12	Headache	3	2	3 SSS 2A+E	2	Complete	Improved	1	24	72							
13	Headache	3	2		2	Partial	Improved	1	28	83	28	85	0	2	4.10E-05	1.70E-06	1.45E-02
14	Headache	3	2	2A+B Rt TS	2	Partial	Improved	2	26	80	30	87	4	7	1.69E-04	-1.50E-04	-2.60E-01
15	Memory d	3	2	4 Tent	1	Complete	Improved	2	19	37							
16	Headache	3	1	2B- Left TS	1	Complete	Improved	2	18	57	26	79	8	22	6.00E-06	1.61E-05	-1.25E-02
17	Headache	3	1	2B Rt TS-S	1	Complete	Improved	1	27	77	29	90	2	13	1.55E-04	1.88E-04	1.33E-01
18	Tremors, r	3	2	2A+B Rt TS	1	Complete	Tremors ir	1+	10	40	26	68	16	28	9.30E-05	7.80E-06	3.07E-02
19	Memory d	3	2	2B Mid SS	2	Complete	Improved	1+	23	70	26	84	3	14	9.42E-05	-1.06E-04	1.36E-01
20	Headache	2	2	2B MidSSS	1	Complete	Improved	1	28	76	30	84	2	8	5.19E-05	6.59E-06	1.50E-02
21	Slurred sp	2	2	3 Lt paraca	1	Complete	Improved	1	21	65	24	83	3	18	3.71E-04	-5.64E-05	2.01E-01
22	Slurred sp	1	1	2B Left TS-	1	Complete	Improved	2	26	80	30	87	4	7	1.99E-04	1.08E-05	7.05E-02
23	GTCS and	3	1	2A+B Rt TS	1	Complete	Improved	2	25	86	30	92	5	12	-1.20E-06	2.16E-05	5.21E-02
24	Headache	1	1	3 Lt sphen	1	Complete	Improved	1	23	78	29	87	6	9			
25	Headache	5	1	3 Torcula-	1	Expired		1	17	46							
26	Incidental	4	2	3 Lt pariet	1	Complete	Improved	2	30	98	30	98	0	0	-8.77E-05	-7.50E-06	-2.84E-02
27	Memory d	3	2	2A+B Post	1	Partial	LTFU	1	20	54	26	74					

NAME	hbopre	mmsepre	ACEpre	hbopost	mmsepost	ACEpost	hbrpre	osatpre	resthbopr	resthbopo	resthbr	resthbrpo	resto2sat	restosatpo	NP score M	NP score A
1	6.18E-05	26	54				-5.20E-05	-5.53E-02	-6.52E-05	-8.92E-05	3.13E-05	2.20E-05	1.00E+00	-5.64E-02	2.60E+01	5.40E+01
2	-2.25E-04	23	53				-4.23E-05	-3.29E-02	4.62E-05	-5.55E-05	5.37E-05	1.20E-04	-3.29E-02	-1.17E-01	2.30E+01	5.30E+01
3	1.90E-04	30	88				-4.50E-05	8.97E-02	-1.31E-04		3.48E-05		8.97E-02		30	88
4	8.14E-04	2.80E+01	7.60E+01	1.97E-06	30		-1.02E-04	4.22E-01	-7.38E-04	-6.20E-05	1.31E-04	-8.27E-05	-4.18E-01	5.20E-02	2.80E+01	7.60E+01
5	-2.33E-04	2.40E+01	8.30E+01	-7.89E-05	30		-1.86E-05	-7.54E-02	8.56E-05	3.51E-06	5.29E-05	-2.27E-05	-1.51E-02	2.26E-02	3.00E+01	8.30E+01
6	-1.33E-04	2.40E+01	7.80E+01	4.86E-05	30		-3.30E-05	4.98E-02	9.47E-05	-4.67E-06	2.77E-05	7.65E-06	-9.27E-03	-9.02E-03	2.40E+01	7.80E+01
7	-1.88E-05	2.40E+01	5.60E+01	-1.27E-02	28		9.08E-06	-1.60E-02	-6.80E-06	-3.32E-05	-1.46E-05	5.45E-05	1.08E-02	6.43E-02	2.40E+01	5.60E+01
8	-8.20E-05	2.60E+01	7.80E+01	-1.27E-04	30		-3.85E-05	4.34E-03	1.07E-06	-1.20E-05	-4.77E-05	-3.73E-05	4.61E-02	2.99E-02	2.60E+01	7.80E+01
9	1.10E-04	2.80E+01	8.70E+01				-2.72E-05	1.51E-02	-2.70E-04	-6.92E-05	4.80E-05	-5.07E-07	-1.52E-01	-2.73E-02	2.80E+01	8.70E+01
10	-2.33E-04	3.00E+01	9.80E+01	-1.50E-04	30		5.78E-05	-1.46E-01	1.21E-05	3.97E-05	-1.51E-05	-2.50E-05	1.83E-02	3.90E-02	3.00E+01	9.80E+01
11	-8.98E-05	2.40E+01	7.40E+01				-3.44E-05	-3.87E-03	1.13E-04	-5.89E-06	4.09E-05	-1.94E-05	6.94E-03	1.57E-02	2.40E+01	7.40E+01
12	-9.97E-05	2.40E+01	7.20E+01				-3.47E-05	1.12E-02	1.99E-06		-1.11E-05		4.30E-03		2.40E+01	7.20E+01
13	1.04E-04	2.80E+01	8.30E+01	1.45E-04	28		-3.60E-05	7.52E-02	-1.92E-04	-1.33E-04	2.21E-05	1.84E-05	-9.74E-02	-7.05E-02	2.60E+01	8.10E+01
14	-6.95E-05	2.60E+01	8.00E+01	1.00E-04	30		-5.04E-05	1.99E-02	-1.10E-05	-1.11E-04	3.84E-05	1.44E-04	7.95E-02	-1.81E-02	2.60E+01	8.00E+01
15	-2.87E-04	1.90E+01	3.70E+01				-8.93E-05	-2.63E-02	-4.05E-05	-6.03E-05	3.37E-05	1.59E-05	-4.79E-02	-3.90E-02	1.90E+01	3.70E+01
16	1.28E-04	1.80E+01	5.70E+01	1.34E-04	26		-1.62E-05	6.64E-02	-6.65E-05	-1.65E-05	-3.88E-07	1.37E-05	-2.62E-02	-1.96E-02	1.80E+01	5.70E+01
17	-1.79E-05	2.70E+01	7.70E+01	1.37E-04	29		-1.29E-05	4.71E-03	-1.48E-06	-1.53E-04	5.84E-06	5.73E-05	-6.18E-03	-1.14E-01	2.70E+01	7.70E+01
18	-4.99E-05	1.00E+01	4.00E+01	4.31E-05	26		3.10E-06	-2.29E-02	-9.76E-05	-5.82E-05	-4.81E-05	-6.90E-05	5.66E-03	4.22E-02	1.00E+01	4.00E+01
19	-1.68E-05	2.30E+01	7.00E+01	6.53E-05	26		8.81E-05	-9.33E-02	-1.10E-04	-1.36E-04	6.79E-05	-5.91E-06	-1.07E-01	-4.91E-02	2.30E+01	7.00E+01
20	6.21E-05	2.80E+01	7.60E+01	1.14E-04	30		-1.31E-05	3.71E-02	-4.54E-05	-8.78E-05	1.91E-05	4.23E-07	-3.61E-02	-3.54E-02	2.80E+01	7.60E+01
21	-4.68E-05	2.10E+01	6.50E+01	3.24E-04	24		-1.66E-05	-4.17E-03	1.23E-05	2.43E-04	4.19E-05	2.15E-04	-3.64E-02	-9.44E-02	2.10E+01	6.50E+01
22	-2.47E-05	2.60E+01	8.00E+01	1.74E-04	30		-1.12E-05	4.99E-04	1.84E-05	-1.16E-04	2.24E-05	-1.34E-05	-1.36E-02	-3.40E-02	2.60E+01	8.00E+01
23	-2.06E-04	2.50E+01	8.60E+01	-2.18E-05	30		-1.35E-05	-6.92E-02	9.24E-05	9.56E-05	7.01E-06	-5.23E-06	3.10E-02	4.30E-02	2.50E+01	8.60E+01
24	-6.67E-05	2.30E+01	7.80E+01				1.44E-05	-1.54E-02	1.34E-05		-1.17E-05		-4.01E-02		2.30E+01	7.80E+01
25							-7.84E-05	2.64E-02	7.31E-05		5.79E-05		-2.48E-02		1.70E+01	4.60E+01
26	1.53E-04	3.00E+01		6.53E-05	30		-2.81E-05	8.76E-02	-1.19E-04	-7.68E-05	1.10E-05	5.07E-06	-5.79E-02	-3.53E-02	3.00E+01	9.80E+01
27															2.10E+01	5.50E+01

KEYS TO MASTER CHART:

1. Presentation**:** 1. Headache, ocular, Tinnitus, 2. Seizures, 3. Cognitive impairment, 4. Incidental, 5. Death
2. MRI Bleed: 1- Yes, 2- No
3. Site: 1- Single, 2- Multiple
4. Risk factors: 1- Having one or multiple risk factors, 2- No risk factors, 1+ (Included in #1): Had CVT.

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ABBREVIATIONS*:

NIRS- Near Infrared Spectroscopy

F-NIRS- Functional Near Infrared Spectroscopy

HbO- Oxyhemoglobin

HbR- Deoxyhemoglobin

SO_2- Oxygen saturation

*- Other relevant abbreviations and expansions are included in the text, wherever applicable.