The Innovation of Multilayered Aneurysm Repair Stents (MARS) in Treatment of Thoraco-Abdominal Aneurysms

Thesis
Submitted in fulfillment for the PhD degree in Biomedical Technology in Vascular Surgery

By

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Aknowledgment

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The Innovation of Multilayered Aneurysm Repair Stents in Treatment of Thoraco-abdominal Aneurysms

Abstract

Background

Morbidity and mortality from Thoraco-abdominal aneurysms are tremendous. Preoperative assessment in predicting cardiac and pulmonary risk factors in order to reduce cardiopulmonary complications, paraplegia, and renal failure are the main determinants of postoperative mortality and therefore gained substantial attention during the last decades.***(Jacobs MJ et al.,2007)***

Left heart by-pass, CSF drainage and epidural cooling have significantly reduced the paraplegia rates. Monitoring MEPs allowed detection of cord ischemia,(spinal cord ischemic injury, SCII) guiding aggressive surgical strategies to restore spinal cord blood supply and reduce neurological deficit. It's believed that these protective measures should be included in the surgical protocol of TAAA repair type II cases. ***(Jacobs MJ et al.,2007)***

Renal and visceral ischemia can be reduced significantly by continuous perfusion during TAAA repair. ***(Jacobs MJ et al.,2007)***

Obviously endovascular modalities have been successfully applied in TAAA patients, the majority apart of hybrid procedures. Technological innovations will eventually cause a shift from open to minimal invasive surgical repair. ***(Jacobs MJ et al.,2007)***

The multilayer aneurysm repair system (MARS) is a flow modulator and part of the fluid smart© technology platform developed by Cardiatis, Isne-Belgium. The MARS is self-expanding and composed of multiple cobalt alloy interconnected braided layers the 3D geometrical configuration gurantees an optimal porosity range for stent from 2 to 50mm in diameter providing unique flow modulating features. The innovative multilayer flow modulating device offers a paradigm shift approach to the treatment of these complicated aneurysms by physiologically (rather than mechanically) excluding aneurysms from the circulation, while keeping branches patent and preserving critical collateral circulation.***(C.Vaislic et al.,2011)***

Its 3D geometrical and structural gives rise to several important hemodynamic and biological effects i.e, in a secular aneurysm it reduces the vortex velocity within the aneurysm sac creating a remodeled organized thrombus, it transforms turbulent flow into laminar flow preserving collateral circulation when over stenting collaterals or in a fusiform aneurysm, it accelerates and channels the flow into a branching aneurysm open branch enhancement and accelerates shear flow along the parent vessel, resulting in inhibition of intimal hyperplasia. ***(C.Vaislic et al.,2011)***

Theoretical basic principles of the device are very attractive and the most important of which is preserving the collaterals and improving their flow. Sac thrombosis and sac shrinkage don't usually occur immediately, several factors could play a role as collateral branches and this should be studied and determined preoperatively.***(M.Henry,2011)***

Preliminary clinical results are satisfactory and promising but larger experience and longer follow up are still needed. ***(M.Henry,2011)***

Hypothesis

The results of endovascular treatment for thoraco-abdominal aneurysms are now comparable with the open surgical procedure. However, endovascular repair in the thoraco-abdominal aorta has been limited due to the complexity of keeping the side branches (intercostals ,renal, visceral) perfused. Attempts are being made to adapt endoluminal stent-graft by using custom fenestrations and branched graft. While preliminary data showed concept feasibility, this technique is still investigational and requires highly skilled operator and custom made devices for each patient.

Aim of the work

1- To study the availability of the new technique in management of TAAA.

2- To shed lights on the technique of deploying the new device.

3- To review the outcome and complications of this new device before introducing this technique as a standard utility.

4- To shed lights over the new evolving biomedical technology in vascular surgery

This will be supported by the French STRATO trial and by a number of cases done at multi-european centers

Keywords

Thoraco-abdominal aneurysms, Multilayer Aneurysm Repair System (MARS)

Intimal hyperplasia, Sac shrinkage, Sac thrombosis, Ischemia

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1- Jacobs MJ, Mommertz G, koeppel TA, Langer S, Nijenhuis RJ, Mess WH, Schurink GW. Surgical repair of TAAA. J Cardiovasc Surg Torino(2007) Feb; 48 (1) :49-58

2- C.Vaislic, A.Benjelloun ,J.-N.Fabiani, J.-F.Bonneville, S.Chocron. multilayered flow modulator treatment of thoraco-abdominal aortic aneurysms.Controversies and vascular updates (2011)JAN;74:443-449

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INTRODUCTION

The Innovation of Multilayered Aneurysm Repair Stents in Treatment of Thoraco-abdominal Aneurysms

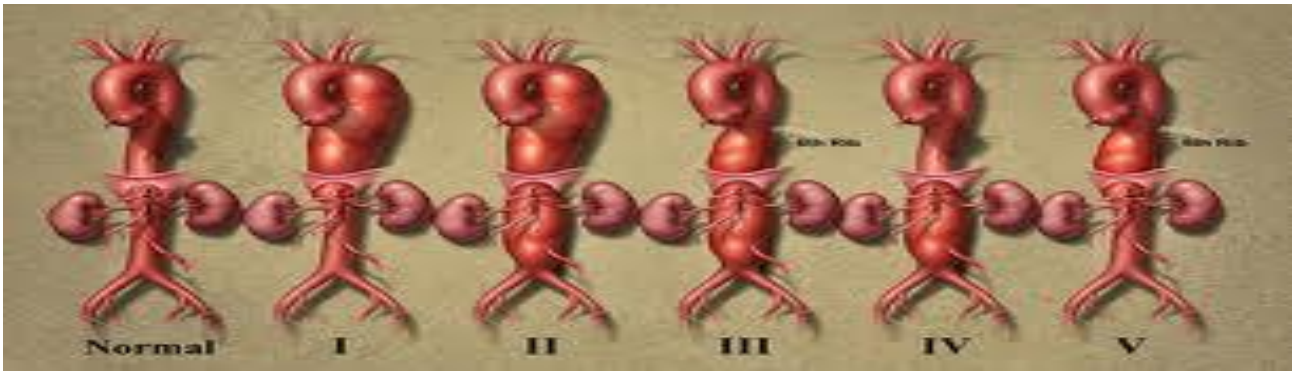
Introduzione

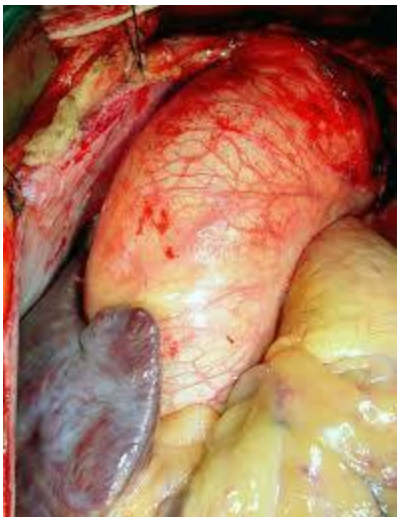
La morbidità e mortalità degli aneurismi toraco addominali è molto alta. La valutazione preoperatoria .

Nelle ultime decadi grande importanza è stata data alla valutazione dei fattori di rischio cardiaci e polmonari al fine di ridurre le complicanze cardiolmonari, la paraplegia e l'insufficienza renale, che sono i principali determinanti della mortalità post operatoria.

Il by pass ventricolare sinistro il CSF drenaggio e il raffreddamento epidurale hanno significativamente ridotto la frequenza della paraplegia. Le strategie chirurgiche aggressive sono guidate con monitoraggio MEPs che permette l'individuazione dell'ischemia spinale per ristabilire il flusso spinale riducendo i deficit neurologici . Queste misure protettive dovrebbero essere incluse nei protocolli chirurgici delle riparazione dei TAAA di tipo II.***(Jacobs MJ et al.,2007)***

Crawford classificazione di TAAA





The figure shows intraoperative detection of TAAA

CTA showing a TAAA

Durante la riparazione TAA l'ischemia renale e viscerale può essere ridotta in modo significativo mantenendo la perfusione continua degli organi . (Jacobs MJ et al., 2007).

Per questa ragione il trattamento endovascolare è stato applicato con successo in questi pazienti nella maggioranza dei casi come parte di procedure ibride.

Le continue innovazioni tecnologiche stanno determinando uno spostamento verso il trattamento endovascolare con minima chirurgia invasiva. (Jacobs MJ et al., 2007)

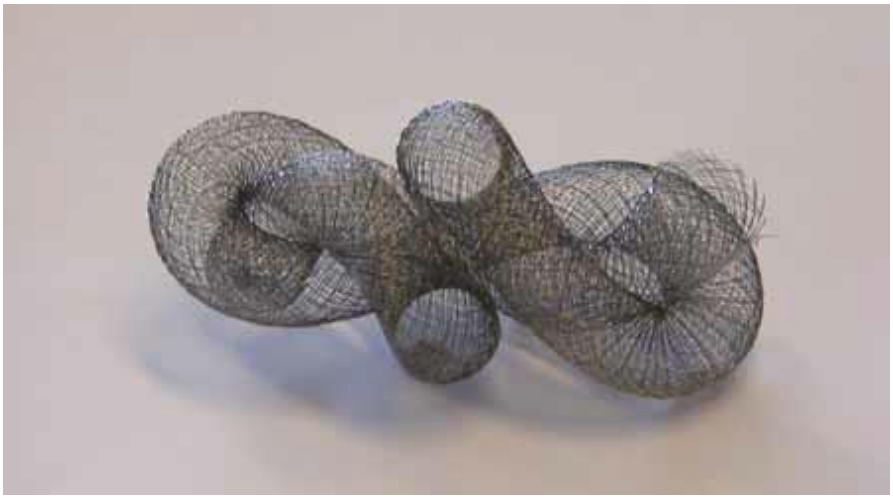
Il sistema di riparazione multistrato per gli aneurismi (MARS) è un modulatore di flusso (the fluid smart technologyes) con piattaforma tecnologica sviluppata da Cardiatis, Isne-Belgio. Il MARS è un device auto-espandibile composto da più strati di lega di cobalto interconnesso ed intrecciato con configurazione geometrica 3D, che garantisce un range ottimale di porosità per gli stent da 2 a 50 mm di diametro fornendo un innovativa capacità di flusso modulante..Questo innovativo dispositivo multistrato di modulazione di flusso, offre un paradigmatico spostamento dell'approccio al trattamento degli aneurismi fisiologicamente complicati (più che meccanicamente), escludendo l'aneurisma dalla circolazione mantenendo le branche laterali pervie e preservando i circoli collaterali (C.Vaislic et al., 2011)

La sua geometria e struttura tridimensionale determina diversi importanti effetti emodinamici e biologici. Negli aneurismi sacciformi riduce la velocità di vortice (flusso spiraliforme) all'interno della sacca determinando un rimodellamento del trombo organizzato che trasforma il flusso turbolento in flusso laminare che preserva la pervietà dei collaterali quando vengono coperti dallo stent. Negli aneurismi fusiformi accelera e dirige il flusso dentro l'aneurisma branched e accelera il flusso di taglio nel vaso nativo determinando un inibizione della proliferazione intimale (C.Vaislic et al., 2011) .

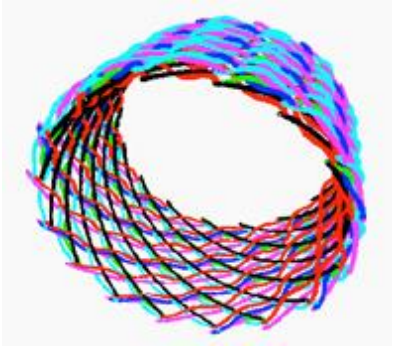
I principi teorici di base del dispositivo sono molto attraenti, il più importante dei quali è la preservazione dei collaterali e il miglioramento del loro flusso.

La trombosi e la riduzione della sacca di solito non si verificano immediatamente e diversi fattori possono giocare un importante ruolo quali i rami collaterali, che dovrebbero essere studiati accuratamente in fase preoperatoria. (M.Henry, 2011).

I risultati clinici preliminari sono soddisfacenti e promettenti, è ancora necessario avere maggiore esperienza e dati di follow up a lungo termine (M.Henry, 2011)



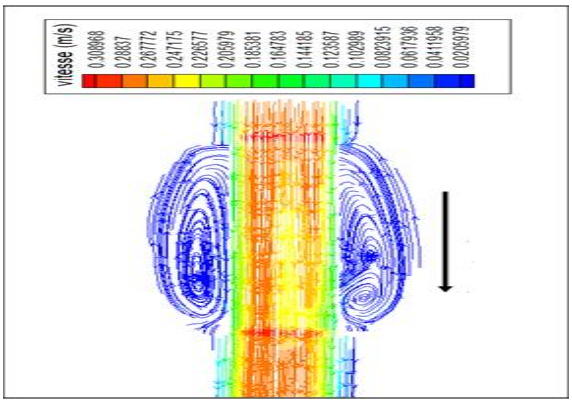
The figure shows high flexibility of CARDIATIS stent



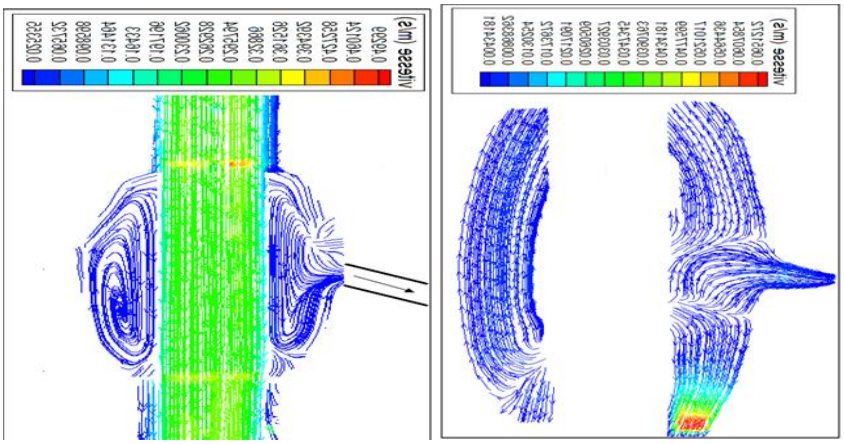
The figure shows virtual 3D geometrical configuration of interconnected braided layers

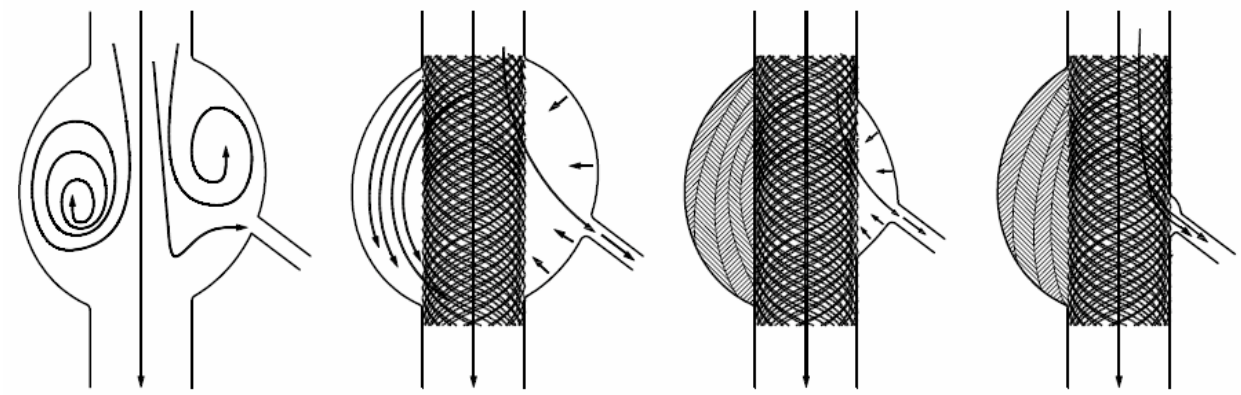
<u>Presupposto Biomedico</u>

- Riduce la velocità spiraliforme di vortice dentro la sacca aneurismatica favorendo il rimodellamento del trombo organizzato



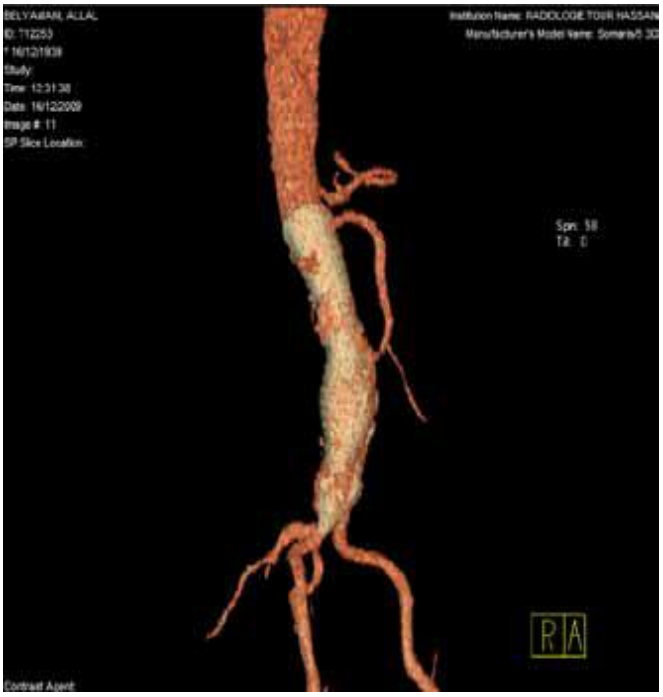
- Trasforma il flusso turbolento in flusso laminare e cosi preserva il flusso attraverso i rami laterali (mantiene la pervietà)**.**





Con stent multistrato una formazione organizzata trombo si verifica con il mantenimento del flusso ramo.

- Accelera il flusso lineare lungo il vaso nativo inibendo la proliferazione intimale.



CTA shows exclusion of TAAA with Cardiatis stent and maintaining the major visceral branches patent

<u>Ipotesi:</u>

Attualmente i risultati della chirurgia tradizionale nel trattamento degli aneurismi toraco addominali sono comparabili a quelli del trattamento endovascolare. Tuttavia il trattamento endovascolare è limitato dalla difficoltà di mantenere pervie e perfuse le branche laterali (intercostali, renali e splancniche). Sono in corso tentativi di adattamento a misura (sartoriali) degli stent graft endoluminali con fenestrazioni e branched.

Sebbene dati preliminari mostrino il concetto di fattibilità queste tecniche sono ancora sotto osservazione e richiedono operatori esperti e dispositivi custom made da adattare a ciascun paziente

<u>Obiettivo del lavoro:</u>

1) Studiare la disponibilità delle nuove tecniche nella gestione e trattamento dei TAAA

2) Per focalizzare l'attenzione sulle tecniche di posizionamento dei nuovi dispositivi e della loro biomeccanica

3) Per rivedere gli outcome e le complicazioni di questi nuovi devices prima di introdurli nella pratica clinica

Indicazione al trattamento

pazienti asintomatici con rapida espansione della sacca , maggiore di 0,5 cm negli ultimi sei mesi

- nei pazienti maschi sintomatici con diametro maggiore di 60-70 mm

- nei pazienti donne sintomatiche con diametro dell'aorta non aneurismatica maggiore del doppio

Tutti i pazienti devono essere meticolosamente esaminati, con anamesi ed esame fisico ed accurata ricerca di associate comorbidità. Dovrà essere valutata la funzione ventricolare sinistra, la presenza di cardiopatia ischemica o valvolare, deficit ischemici neurologici, eventuale presenza di malattia polmonare Particolare attenzione dovrà inoltre esser riservata alla ricerca di segni clinici di claudicatio e di arteriopatia periferica.

Tutti i pazienti dovranno essere valutati riguardo:

- Aspetti demografici (es: età , sesso)

- Fattori di rischio (es: DM, Ipertensione arteriosa, CAD)

- Sintomi (es: dolore toracico, alla schiena, al fianco, addome maniestazioni compressive quali raucedine e disfonia, disfagia, paraplegia e embolizzazione distale

- Substrati anatomici (misurazione e tipo di colletto prossimale, qualità della zona di atterraggio, angolazione del colletto dell'anerisma, calcificazioni, classificazione di Crawford)

Sarà utilizzata una tecnica ibrida in tutti i casi con isolamento chirurgico di un asse femorale e accesso percutaneo di controllo controlaterale

I controlli MSCT dovranno essere eseguiti il primo giorno post operatorio dopo l'angiografia di controllo, dopo una settimana (prima della dimissione), e dopo sei mesi per documentare la riduzione della sacca aneurismatica.

Appendice :

dopo una revisione e analisi della biomeccanica siamo in atttesa di una dimostrazione dai dati dello studio STRATO tenutosi in Francia. In questo studio multicentrico, di tipo prospettico, sono stati arruolati 23 pazienti in un totale di 32 Centri. Il Follow up a 12 mesi è stato portato a termine per 22 pazienti mentre un paziente è andato perduto per abbandono . L'arruolamento è durato dal 7 aprile 2010 fino al 9 Febbraio 2012. Tutti i pazienti sono stati rivalutati con CT MRI a 30 giorni, 6 e 12 mesi.

Sono disponibili anche dati relativi a 5 pazienti trattati all'inizio del 2012 nell'Ospedale IRIS SU (HIS) di Brussel, con follow up molto breve a tre mesi.

Riferimenti

1-Jacobs MJ, Mommertz G, koeppel TA, Langer S, Nijenhuis RJ, Mess WH, Schurink GW. Surgical repair of TAAA. J Cardiovasc Surg Torino(2007) Feb; 48 (1) :49-58

2-C.Vaislic, A.Benjelloun ,J.-N.Fabiani, J.-F.Bonneville, S.Chocron. Multilayered flow modulator treatment of thoraco-abdominal aortic aneurysms.Controversies and vascular updates (2011)JAN;74:443-449

3-M.Henry, The Multilayer Stent. First human study.(2011), ISET presentation.

ANATOMY

ANATOMY

DESCENDING AORTA

The **descending aorta** is divided into two portions, the **thoracic** and **abdominal,** in correspondence with the two great cavities of the trunk in which it is situated**.**

1. The Thoracic Aorta (Aorta Thoracalis)

The thoracic aorta is contained in the posterior mediastinal cavity. It begins at the lower border of the fourth thoracic vertebra where it is continuous with the aortic arch, and ends in front of the lower border of the twelfth at the aortic hiatus in the diaphragm. At its commencement, it is situated on the left of the vertebral column; it approaches the median line as it descends; and, at its termination, lies directly in front of the column. The vessel describes a curve which is concave forward, and as the branches given off from it are small,its diminution in size is inconsiderable.(1)

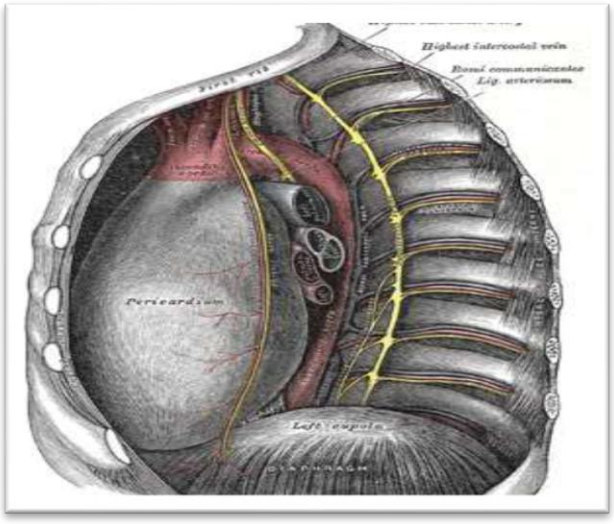


Fig.(1):descending thoracic aorta

Relations.

It is in relation, anteriorly, from above downward, with the root of the left lung, the pericardium, the esophagus, and the diaphragm; posteriorly, with the vertebral column and the hemiazygos veins; on the right side, with the azygos vein and thoracic duct; on the left side, with the left pleura and lung. The esophagus, with its accompanying plexus of nerves, lies on the right side of the aorta above; but at the lower part of the thorax it is placed in front of the aorta, and, close to the diaphragm, is situated on its left side.(1)

Branches of the Thoracic Aorta

Visceral : Pericardial,Bronchial,Esophageal,Mediastinal.

Parietal : Intercostal, Subcostal, Superior Phrenic

The pericardial branches (rami pericardiaci) consist of a few small vessels which are distributed to the posterior surface of the pericardium.

The bronchial arteries (aa. bronchiales) vary in number, size, and origin. There is as a rule only one right bronchial artery, which arises from the first aortic intercostal, or from the upper left bronchial artery. The left bronchial arteries are usually two in number, and arise from the thoracic aorta. The upper left bronchial arises opposite the fifth thoracic vertebra, the lower just below the level of the left bronchus. Each vessel runs on the back part of its bronchus, dividing and subdividing along the bronchial tubes, supplying them, the areolar tissue of the lungs, the bronchial lymph glands, and the esophagus. (1)

The esophageal arteries (aa. æsophageæ) four or five in number, arise from the front of the aorta, and pass obliquely downward to the esophagus, forming a chain of anastomoses along that tube, anastomosing with the esophageal branches of the inferior thyroid arteries above, and with ascending branches from the left inferior phrenic and left gastric arteries below.

The mediastinal branches (rami mediastinales) are numerous small vessels which supply the lymph glands and loose areolar tissue in the posterior mediastinum.

Intercostal Arteries (aa. intercostales).There are usually nine pairs of aortic intercostal arteries. They arise from the back of the aorta, and a redistributed to the lower nine intercostal spaces, the first two spaces being supplied by the highest intercostal artery, a branch of the costocervical trunk of the subclavian. The right aortic intercostals are longer than the left, on account of the position of the aorta on the left side of the vertebral column; they pass across the bodies of the vertebræ behind the esophagus, thoracic duct, and vena azygos, and are covered by the right lung and pleura. The left aortic intercostals run backward on the sides of the vertebræ and are covered by the left lung and pleura; the upper two vessels are crossed by the highest left intercostal vein, the lower vessels by the hemiazygos veins. The further course of the intercostal arteries is practically the same on both sides. Opposite the heads of the ribs the sympathetic trunk passes downward in front of them, and the splanchnic nerves also descend in front by the lower arteries. Each artery then divides into an anterior and a posterior ramus.(1)

The Anterior Ramus crosses the corresponding intercostal space obliquely toward the angle of the upper rib, and thence is continued forward in the costal groove. It is placed at first between the pleura and the posterior intercostal membrane, then it pierces this membrane, and lies between it and the Intercostalis externus as far as the angle of the rib; from this onward it runs between the Intercostales externus and internus, and anastomoses in front with the intercostal branch of the internal mammary or musculophrenic. Each artery is accompanied by a vein and a nerve, the former being above and the latter below the artery, except in the upper spaces, where the nerve is at first above the artery. The first aortic intercostal artery anastomoses with the intercostal branch of the costocervical trunk, and may form the chief

supply of the second intercostal space. The lower two intercostal arteries are continued anteriorly from the intercostal spaces into the abdominal wall, and anastomose with the subcostal, superior epigastric, and lumbar arteries.(1)

Branches.

The anterior rami give off the following branches:

Collateral Intercostal.

Lateral Cutaneous.

Muscular.

Mammary.

The collateral intercostal branch comes off from the intercostal artery near the angle of the rib, and descends to the upper border of the rib below, along which it courses to anastomose with the intercostal branch of the internal mammary.

Muscular branches are given to the Intercostales and Pectorales and to the Serratus anterior; they anastomose with the highest and lateral thoracic branches of the axillary artery.

The lateral cutaneous branches accompany the lateral cutaneous branches of the thoracic nerves.

Mammary branches are given off by the vessels in the third, fourth, and fifth spaces. They supply the mamma, and increase considerably in size during the period of lactation.

The Posterior Ramus runs backward through a space which is bounded above and below by the necks of the ribs, medially by the body of a vertebra, and laterally by an anterior costotransverse ligament. It gives off a spinal branch which enters the vertebral canal through the intervertebral foramen and is distributed to the medulla spinalis and its membranes and the vertebræ. It then courses over the transverse process with the posterior division of the thoracic nerve, supplies branches to the muscles of the back and cutaneous branches which accompany the corresponding cutaneous branches of the posterior division of the nerve.

The subcostal arteries, so named because they lie below the last ribs, constitute the lowest pair of branches derived from the thoracic aorta, and are in series with the intercostal arteries. Each passes along the lower border of the twelfth rib behind the kidney and in front of the Quadratus lumborum muscle, and is accompanied by the twelfth thoracic nerve. It then pierces the posterior aponeurosis of the Transversus abdominis, and, passing forward between this muscle and the Obliquus internus, anastomoses with the superior epigastric, lower intercostal, and lumbar arteries. Each subcostal artery gives off a posterior branch which has a similar distribution to the posterior ramus of an intercostal artery.(1)

The superior phrenic branches are small and arise from the lower part of the thoracic aorta; they are distributed to the posterior part of the upper surface of the diaphragm, and anastomose with the musculophrenic and pericardiacophrenic arteries.

A small aberrant artery is sometimes found arising from the right side of the thoracic aorta near the origin of the right bronchial. It passes upward and to the right behind the trachea and

the esophagus, and may anastomose with the highest right intercostal artery. It represents the remains of the right dorsal aorta, and in a small proportion of cases is enlarged to form the first part of the right subclavian artery. (1)

2-THE ABDOMINAL AORTA (Aorta Abdominalis)

The abdominal aorta begins at the aortic hiatus of the diaphragm, in front of the lower border of the body of the last thoracic vertebra, and, descending in front of the vertebral column, ends on the body of the fourth lumbar vertebra, commonly a little to the left of the middle line, 103 by dividing into the two common iliac arteries. It diminishes rapidly in size, in consequence of the many large branches which it gives off. As it lies upon the bodies of the vertebræ, the curve which it describes is convex forward, the summit of the convexity corresponding to the third lumbar vertebra.(1)

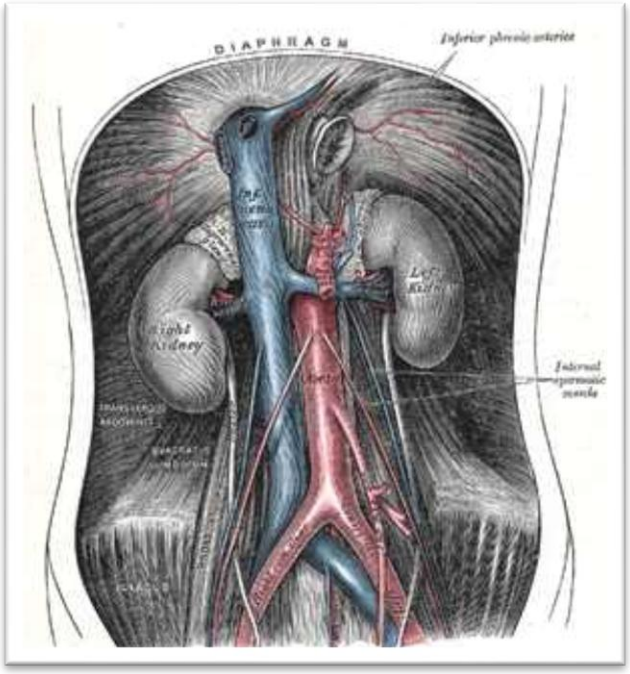


Fig.(2):descending abdominal aorta

Relations.

The abdominal aorta is covered, anteriorly, by the lesser omentum and stomach, behind which are the branches of the celiac artery and the celiac plexus; below these, by the lienal vein, the pancreas, the left renal vein, the inferior part of the duodenum, the mesentery, and aortic plexus. Posteriorly, it is separated from the lumbar vertebræ and intervertebral fibrocartilages by the anterior longitudinal ligament and left lumbar veins. On the right side it is in relation above with the azygos vein, cisterna chyli, thoracic duct, and the right crus of the diaphragm—the last separating it from the upper part of the inferior vena cava, and from the right celiac ganglion; the inferior vena cava is in contact with the aorta below. On the left side

are the left crus of the diaphragm, the left celiac ganglion, the ascending part of the duodenum, and some coils of the small intestine.(1)

Collateral Circulation.

The collateral circulation would be carried on by the anastomoses between the internal mammary and the inferior epigastric; by the free communication between the superior and inferior mesenterics, if the ligature were placed between these vessels; or by the anastomosis between the inferior mesenteric and the internal pudendal, when (as is more common) the point of ligature is below the origin of the inferior mesenteric; and possibly by the anastomoses of the lumbar arteries with the branches of the hypogastric. (1)

Branches

The branches of the abdominal aorta may be divided into three sets: visceral, parietal, and terminal.

Visceral Branches	*Parietal Branches*
Celiac.	Inferior Phrenics.
Superior Mesenteric.	Lumbars.
Inferior Mesenteric.	Middle Sacral.
Middle Suprarenals.	
Renals.	
Internal Spermatics.	Common Iliacs
Ovarian (in the female)	

Of the visceral branches, the celiac artery and the superior and inferior mesenteric arteries are unpaired, while the suprarenals, renals, internal spermatics, and ovarian are paired. Of the parietal branches the inferior phrenics and lumbars are paired; the middle sacral is unpaired. The terminal branches are paired.(1)

AGING OF THE AORTA

Aging of the Aorta

The elasticity and distensibility of the aorta declines with age. such changes are seen even in normal healthy adults,and for unknown reasons, such changes occur earlier and more progressive among men than women.(2)

The loss of elasticity and aortic compliance accounts for the increase in pulse pressure commonly seen in the elderly. Such loss is accelerated among patients with hypertension compared to age matched normotensive patients.(3)

Similarly, patients with hypercholesterolemia and CAD show greater loss of elasticity than do controls.(4)

Histologically, the aging aortic wall exhibits fragmentation of elastin with a concomitant increase in collagen resulting in increased collagen to elastin ratio contributing to loss of distensibility of aortic wall observed physiologically.(5)

In addition, impairement of vasa vasorum flow to the aortic wall results in stiffening of aorta with same histological changes.(6)

HISTOLOGY

Histology

The aorta is composed of 3 layers, thin inner layer, intima ; a thick middle layer, or media ; and a rather thin outer layer,the adventitia.

The strength of the aorta lies in the media, that is composed of laminated intertwining sheets of elastic fibers arranged in spiral manner affording a maximum tensile strength. In contrast to peripheral arteries, the aortic media contains relatively little smooth muscles and collagen between elastic layers. The elastic fibers gives the aorta its distensibility and elasticity, beside its tensile strength.(4)

The aortic intima is thin,delicate,lined by endothelium and easily traumatized

The adventitia contains mainly collagen, and carries vasa vasorum that nourishes the outer half of the aortic wall,including much of the media.(4)

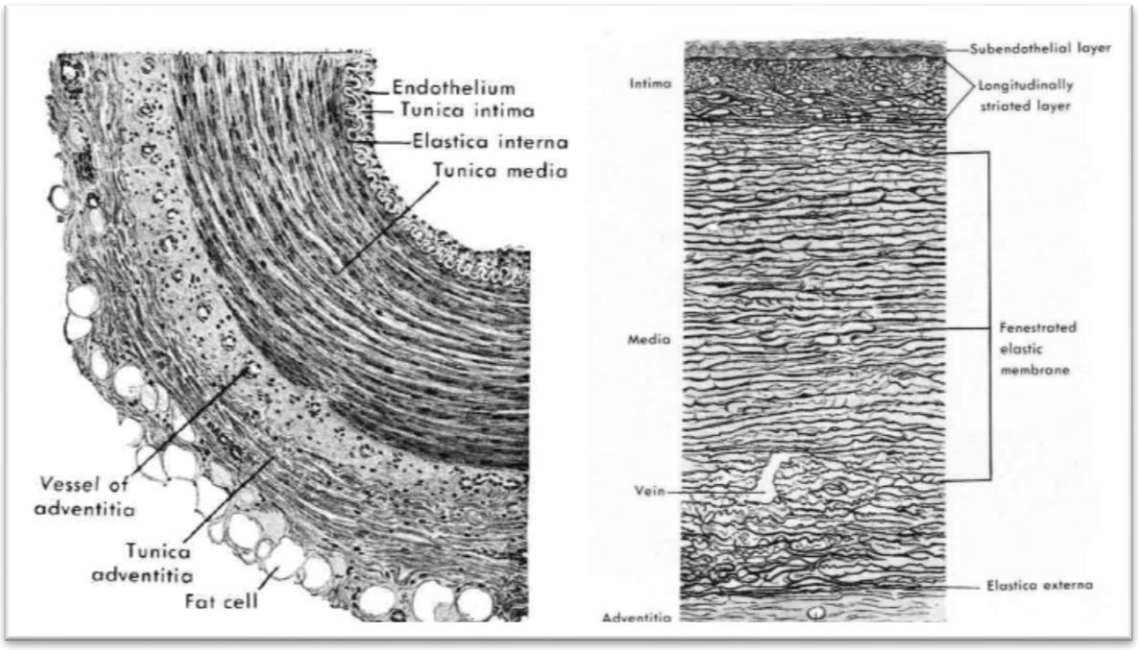


Fig.(3): Histology of the Aorta (quoted from 1)

FUNCTIONS OF THE AORTA

Functions of the Aorta

Appropriately named "the greatest artery" by the ancients,the aorta is admirably suited for its task. In the average lifetime this vessel must absorb the impact of 2.3 to 3 billion heart beats with carrying roughly about 200 million litres of blood through the body.arteries are categorized as resistance or conductance vessels. conductance vessels are blood conduits and aorta is the ultimate conductance vessel.(4)

During the ventricular systole, the aorta is distended by the force of the blood ejected into it by the left ventricle,and in this manner part of the kinetic energy generated by the contracting left ventricle is converted to a potential energy stored in the aortic wall. Then, during diastole, this potential energy stored in the aortic wall recoils, propelling the blood in the aortic lumen distally into the arterial bed. Thus, the aorta plays an essential role in maintaining forward circulation of the blood in diastole after being delivered into the aorta by the left ventricle during systole creating a pulse wave with a milking effect, transmitting blood at a speed 5 m/s to the periphery which is faster than the velocity of the intraluminal blood itself that travels at only 40-50 cm/sec. This is the pumping function of the aorta. (4)

In addition to the previous functions, the aorta plays a role in indirectly controlling the systemic vascular resistance and heart rate. Pressure responsive receptors,analogous to those in the carotid sinus,lie in the ascending aorta and aortic arch and send afferent signals to the vasomotor centre in the brain stem via vagus nerve. Raising the intra-aortic pressure causes reflex bradycardia and reduction of systemic vascular resistance whereas lowering the intra-aortic pressure causes tachycardia and increases the systemic vascular resistance. (4)

PATHOLOGY OF TAAA

Pathology of thoraco-abdominal aneurysms

In the thoracic aorta, a diameter of 3cm or greater is generally considered aneurysmal, although the average size of surgically corrected aneurysms is over 5cm. Thoracic aortic aneurysms (TAAs) can involve the aortic root, ascending aorta, arch, descending aorta, or a combination of these locations. The combination of aortic root dilatation and ascending aneurysm is termed "annuloaortic ectasia." (Anatomically and radiologically, an aneurysm is defined as a dilatation at least 50% above the normal diameter of an artery.) Pseudoaneurysm denotes a ruptured aortic wall with healing of the extravasated blood and formation of the aneurysm wall by fibrous tissue.(7)

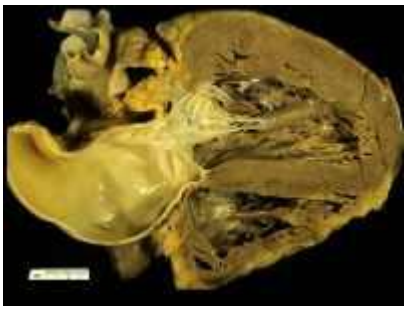


Fig (4): proximal aneurysm of the aorta

Epidemiology

Aortic aneurysms are a leading cause of the death in the United States. With improvements in screening and imaging techniques, the incidence of thoracic aortic aneurysm (TAA) has been increasing steadily in the last decades. Overall, the estimated incidence of TAA is 6 cases per 100,000 person years. Autopsy series have estimated its prevalence at 3-4% in patients over age 65 years.(7)

An approximately 2:1 male predilection for noninflammatory TAA exists;inflammatory TAA is slightly more common in women.(7)

Etiology

Causes of thoracic aortic aneurysm (TAA) include inherited syndromes, atherosclerosis, noninfectious aortitis, and infections; however, a large number have no known cause. Idiopathic, non inflammatory aneurysms are associated with congenital conditions (bicuspid aortic valve) and acquired conditions (hypertension). Pathologically, non inflammatory aneurysms demonstrate degrees of cystic, medial degeneration, depending on etiology or association. The inherited syndromes causing TAA include Marfan syndrome, Loeys-Dietz syndrome, and Ehlers-Danlos syndrome.

Aneurysmal dilatation of the thoracic aorta can occur by various mechanisms. Most commonly, the pathogenesis of the aneurysms is due to non inflammatory, medial degeneration of the elastic aortic wall. However, inflammatory destruction secondary to syphilis, bacterial infection, noninfectious aortitis, or atherosclerosis can result in TAA.

Pseudoaneurysms may result from aortic tears, typically due to blunt chest trauma, with healing of the extravasated blood and formation of fibrous tissue wall.(7)

Aneurysms of the distal arch and descending aorta are typically atherosclerotic. The other common types of aneurysm involving the descending thoracic aorta are healed dissecting aneurysms, infectious (mycotic) aneurysms, and traumatic pseudoaneurysms.

The location of the aneurysm also affects the prevalence of subtypes. Atherosclerotic lesions are most frequent in the descending aorta and the aortic arch. Aneurysms associated with medial degeneration are almost exclusively in the ascending segment, and dissecting aneurysms may be present either in the proximal or descending portion. Patients with aortitis tend to present with involvement of the ascending aorta. Infectious cases (mycotic mainly) are more frequent in the descending aorta.**(7)**

Association with atherosclerosis

The vast majority of descending thoracic aneurysms are associated with atherosclerosis.(8) and the risk factors for aneurysm formation are the same as those for atherosclerosis (eg, hypertension, hypercholesterolemia, smoking).(9)However, it remains unclear whether atherosclerosis is actually responsible for aneurysm formation . It seems likely that there is a multifactorial, systemic, nonatherosclerotic causal process, such as a defect in vascular structural proteins, with atherosclerosis occurring secondarily.(10)

Most theories emphasize the primary role of breakdown of the extracellular matrix proteins elastin and collagen by proteases such as collagenase, elastase, various matrix metalloproteinases, and plasmin (formed from plasminogen by urokinase plasminogen activator and tissue type plasminogen activator) .These proteolytic factors are derived from endothelial and smooth muscle cells and from inflammatory cells infiltrating the media and adventitia.(11)

The combination of protein degradation and mechanical factors are thought to cause cystic medial necrosis, which has the appearance of smooth muscle cell necrosis and elastic fiber degeneration with cystic spaces in the media filled with mucoid material. These changes result in vessel dilatation and subsequent aneurysm formation and possible rupture.(11)

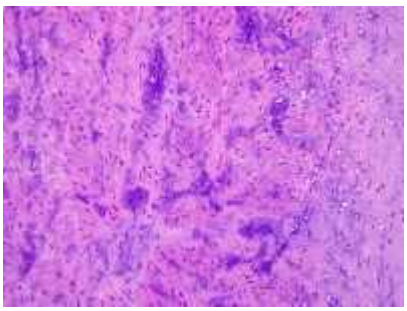
Gross findings

Uncomplicated thoracic aortic aneurysms (TAAs) can be divided grossly into saccular and fusiform. Fusiform aneurysms are most common; they affect the entire circumference of the aorta and have tapered borders (see the images below). Among the types of TAAs, only infectious (mycotic) aneurysms and posttraumatic pseudoaneurysms are typically saccular; both have a propensity for the distal thoracic aorta. Only rarely are aneurysms secondary to medial weakness due to medial degeneration saccular.(11)

Distal thoracic aneurysms are typically atherosclerotic and demonstrate diffuse ectasia of the lumen, with frequent extension across the diaphragm into the abdominal aorta (thoracoabdominal aortic aneurysm). Infectious aneurysms typically erode into adjacent structures with adhesions and tissue edema(11)

Microscopic findings of Non inflammatory TAA

The histopathologic hallmark of noninflammatory thoracic aortic aneurysms (TAAs) is cystic medial degeneration, or the pooling of proteoglycans (mucoid material) and pseudocyst formation in the media, accompanied by extensive loss of elastic lamellae. These changes result in the medial weakening that progresses to aneurysm, dissection, or both. A related histologic finding is so-called medionecrosis, which is also seen in aging aortas and in patients with hypertension. Medionecrosis, or laminar medial necrosis, is defined as coagulative necrosis of medial smooth muscle cells, resulting in loss of nuclei and collapse of the elastic lamellae ,this finding is not specific for any TAA etiology.(11)



Fig(5): at high magnification, the media shows haphazard disorganization, loss of smooth muscle cells, and pools of proteoglycans.

Classification

Aneurysms of the thoracic aorta can be classified into four general anatomic categories, although some aneurysms involve more than one segment.(8)

- Ascending aortic aneurysms arise anywhere from the aortic valve to the innominate artery (60 percent)
- Aortic arch aneurysms include any thoracic aneurysm that involves the brachiocephalic vessels(10 percent)
- Descending aortic aneurysms distal to the left subclavian artery(40 percent)
- Thoracoabdominal aneurysms (10 percent)

Thoracoabdominal aneurysms are further divided according to the Crawford classification (12)

- I. Proximal descending thoracic to proximal abdominal aorta
- II. Proximal descending to infrarenal aorta
- III. Distal descending with abdominal aorta
- IV. Primarily abdominal aorta

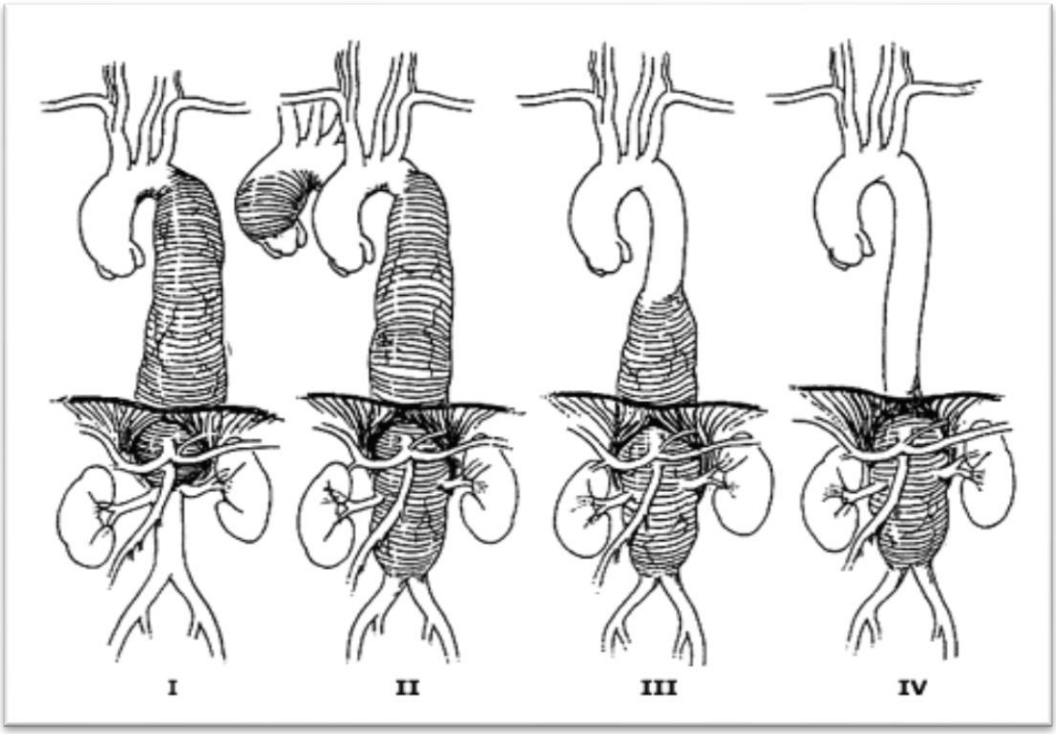


Fig.(6):Crawford classification of TAAA

The Crawford classification is based on the extent of aortic involvement. Extent I aneurysms begin above the sixth intercostal space, usually near the left subclavian artery, and extend down to encompass the aorta at the origins of the celiac axis and superior mesenteric arteries; although the renal arteries may also be involved, the aneurysm does not extend into the infrarenal segment. Extent II aneurysms also arise above the sixth intercostal space, but extend distally into the infrarenal aorta, often to the level of the aortic bifurcation. Extent III aneurysms begin in the distal half of the descending thoracic aorta, below the sixth intercostal space, and extend into the abdominal aorta. Extent IV aneurysms generally involve the entire abdominal aorta from the level of the diaphragm to the bifurcation.(8)

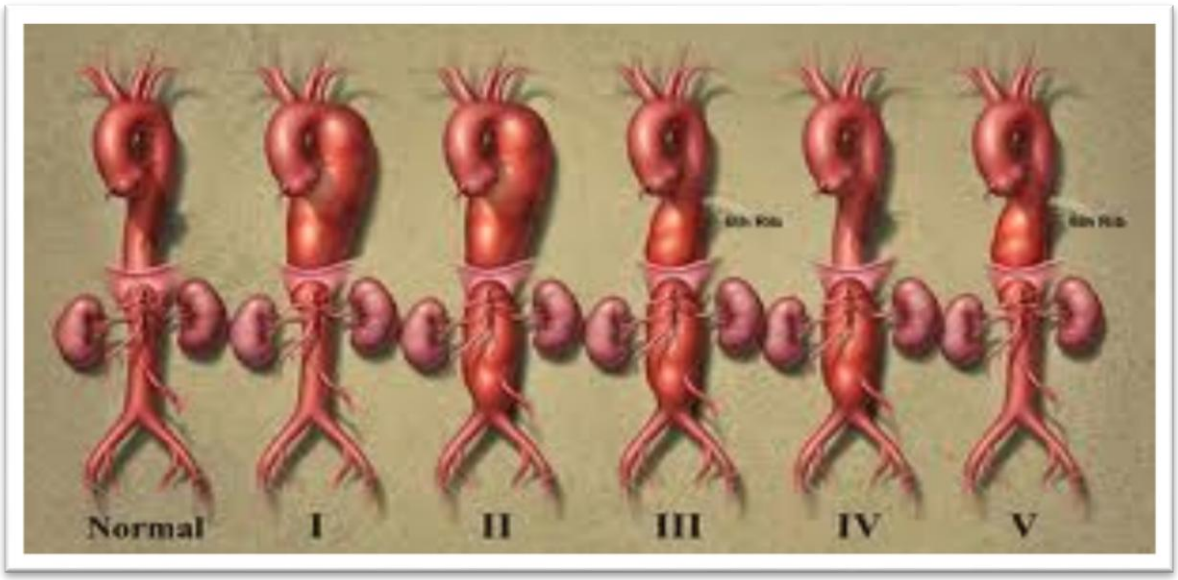


Fig.(7):Safi modification of Crawford classification

CLINICAL PICTURE

Clinical Picture

Patients with thoracic aneurysms are often asymptomatic at the time of presentation.(14)

However, depending upon aneurysm location, chest, back, flank, or abdominal pain can be a presenting symptom. Symptoms are usually attributed to compression or distortion of adjacent structures or vessels, a vascular consequence such as aortic regurgitation, or thromboembolic sequelae.(15)

Ascending aneurysms can present with heart failure due to aortic regurgitation from aortic root dilatation and annular distortion. In addition, compression of a coronary artery can result in myocardial ischemia or infarction, while a sinus of Valsalva aneurysm can rupture into the right side of the heart, producing a continuous murmur and, in some cases, heart failure. Ascending and arch aneurysms can erode into the mediastinum. Such patients can present with one or more of the following: hoarseness due to compression of left vagus or left recurrent laryngeal nerve; hemidiaphragmatic paralysis due to compression of the phrenic nerve; wheezing, cough, hemoptysis, dyspnea, or pneumonitis if there is compression of the tracheobronchial tree; dysphagia due to esophageal compression; or the superior vena cava syndrome. Aneurysmal compression of other intrathoracic structures or erosion into adjacent bone may cause chest or back pain.(15)

Aneurysmal compression of branch vessels or the occurrence of embolism to various peripheral arteries due to thrombus within the aneurysm can cause coronary, cerebral, renal, mesenteric, lower extremity and rarely, spinal cord ischemia and resultant symptoms.(15)

The most serious complications of thoracic aortic aneurysm are dissection or leakage, which can cause pain, or rupture, most often into the left intrapleural space or intrapericardial space .A descending thoracic aortic aneurysm can rupture into the adjacent esophagus, producing an aortoesophageal fistula and presenting with hematemesis. Rupture is often catastrophic, being associated with severe pain and hypotension or shock. Aortic dissection can also occur.(15)

The presensc of abdominal component of TAAA may be asymptomatic in the majority of patients and discovered during routine screening, or symptomatic as **Pulsatile abdominal mass** — Approximately 30 percent of asymptomatic AAAs are discovered when a pulsatile abdominal mass is palpated on routine physical examination. The ability to palpate and estimate the aortic diameter depends upon the patient's body habitus, the size of the aneurysm, and the clinical experience of the practitioner.(15)

Pain — Pain is the most frequent complaint in patients with an AAA. The pain is typically located in the abdomen but can also radiate to the back, flank, or groin. The pain is unaffected by position or movement. Pain from a symptomatic AAA can mimic many other acute conditions such as renal colic, diverticulitis, pancreatitis, inferior wall coronary ischemia, mesenteric ischemia, and biliary tract disease.(15)

Although AAAs can progress to rupture without any intervening symptoms, complaints of new or worsening pain, or findings of tenderness upon palpation of the aorta are suggestive of a rapidly expanding aneurysm or impending rupture.

The manifestations of a ruptured AAA depend in part upon whether or not the rupture is contained. The pathognomonic triad of pain, pulsatile abdominal mass, and hypotension is present in only one-third of patients who present with ruptured AAA.(16)

A contained posterior rupture resulting in a retroperitoneal hematoma can lead to ecchymosis in the flank (Grey-Turner sign) or groin. Such patients can be hemodynamically stable. In contrast, free intraperitoneal rupture is associated with the abrupt onset of pain, abdominal tenderness and distention, hemodynamic instability, and death unless rapidly treated (17)

Thromboembolism — AAA can present with distal thromboembolic events, which may be a sign of rupture of the aneurysm. The thromboemboli can be single or multiple. The manifestations include painful, blue digits and/or a painful, pulseless, cool leg. Rarely, AAA can present with acute thrombosis leading to bilateral lower extremity ischemia. The clinical manifestations of thromboembolic disease are discussed in detail elsewhere.(18)

Disseminated intravascular coagulation — Large or extensive AAAs may be associated with disseminated intravascular coagulation (DIC) causing hemorrhagic and thrombotic complications. The incidence of DIC is reported to be as high as 4 percent.(18)

PHYSICAL EXAMINATION — Any patient with risk factors for or a clinical presentation suggestive of AAA should undergo a thorough abdominal examination.(18)

Abdominal palpation — With the patient supine on the examination table and garments removed from the abdomen, the abdomen should be palpated to identify a widened pulse that suggests the presence of an aneurysm. AAA most often occurs in the segment of aorta between the renal and inferior mesenteric arteries. As a result, palpation between the xiphoid and umbilicus is particularly important.(18)

The vascular examination should include auscultation of the abdomen since the presence of a bruit may indicate aortic or visceral arterial atherosclerotic disease, or rarely an aortocaval or aortoiliac fistula. Palpation of the abdomen to detect AAA is **safe** and has never been reported to precipitate aortic rupture. Most patients will experience mild tenderness with deep palpation of the aneurysm. This finding should **not** be used to brand the aneurysm as symptomatic in order to justify treatment.(19)

Vascular examination — A complete peripheral arterial examination should be performed. Palpation of prominent femoral and/or popliteal pulses warrants further noninvasive evaluation for peripheral and abdominal aneurysm. Iliac aneurysms typically occur in association with AAA. In a study of 10,038 patients with iliac aneurysm, 89 percent had a coexistent AAA A 14 percent incidence of femoral and/or popliteal artery aneurysms was found in another study of patients with AAA. (20)

DIAGNOSIS

DIAGNOSIS

A variety of noninvasive and invasive methods are useful for the diagnosis and evaluation of a thoracic aortic aneurysm.

Chest x-ray

A common way in which asymptomatic aneurysms are detected is on routine chest radiography. The aneurysm produces a widening of the mediastinal silhouette, enlargement of the aortic knob, or displacement of the trachea from midline. Other reported features include displaced calcification, aortic kinking, and opacification of the aorticopulmonary window.(21)

However, chest x-ray cannot distinguish an aneurysm from a tortuous aorta and many aneurysms are not apparent on the chest x -ray. The frequency with which this occurs was illustrated in a series of 36 patients presenting with acute onset of chest or back pain within the prior 14 days who were found to have nondissecting thoracic aortic aneurysms; radiographic abnormalities were detected in only 22 (61 percent) .For this reason as well as better visualization, additional imaging studies are obtained in virtually all patients suspected of having a thoracic aortic aneurysm.(21)

Echocardiography

The 2003 ACC/AHA practice guidelines for echocardiography recommended echocardiography for the diagnosis of aortic aneurysm .Transthoracic echocardiography (TTE) is the preferred procedure with transesophageal echocardiography (TEE) usually being performed only if the examination is incomplete or additional information is needed. There are, however, two settings in which TEE is preferred: for examination of the entire aorta, especially in emergency situations; and for imaging when coexistent dissection is suspected.(22)

Among patients with known bicuspid aortic valves, the 2006 ACC/AHA guidelines on valvular heart disease recommend an initial TTE to assess the diameters of the aortic root and ascending aorta . Patients with aortic root or ascending aorta diameter greater than 4.0 cm should undergo serial evaluation of aortic root/ascending aortic size and morphology by echocardiography, computed tomography or magnetic resonance on a yearly basis.

CT and MRI

Computed tomography (CT) with intravenous contrast and magnetic resonance imaging (MRI) are the preferred tests to detect a thoracic aortic aneurysm, determine its size, and define aortic and branch vessel anatomy. MRI is preferred for aneurysms involving the aortic root.(23)

Among patients with known bicuspid aortic valves, the 2006 ACC/AHA guidelines recommend MRI or CT when morphology of the aortic root or ascending aorta cannot be

accurately assessed by echocardiography .MRI or CT is reasonable in patients with bicuspid aortic valves and aortic root dilatation on echocardiography to further quantify severity of dilatation and involvement of the ascending aorta.(24)

Magnetic resonance angiography (MRA) may be more accurate than CT, but is expensive, time consuming, and may not be available. Conventional arteriography alone does reliably demonstrate the presence of an aneurysm, but it may play a role in planning surgical repair and is essential in performing endovascular repair.(24)

Contrast angiography

Contrast angiography had been the preferred method for evaluation since it provides sharper resolution of luminal characteristics, and is the best method for evaluating branch vessel pathology. However, this procedure is invasive with potential nephrotoxicity from contrast medium, and is unable to discern extraluminal aneurysmal size.(25)

Ultrasonography

When an AAA is suspected based upon the physical examination, abdominal ultrasonography is the initial diagnostic test of choice and is also used to follow small aneurysms over time.

For the detection of AAA (aortic diameter >3.0 cm), abdominal ultrasonography has a sensitivity and specificity approaching 100 percent.(26)

The routine sonographic evaluation involves measuring the anteroposterior (AP), longitudinal, and transverse dimensions of the aorta. Patients are asked to fast prior to undergoing the examination to reduce the presence of overlying bowel gas that can obscure the aorta.(27)

. The main limitation of abdominal ultrasonography is that it is technician and equipment-dependent. If the ultrasound probe is not oriented perpendicular to the center line, the AP diameter of the aorta will be overestimated.(28)

The method of AP measurements included anterior inner wall to posterior inner wall, anterior outer wall to posterior outer wall and midpoint anterior wall to midpoint posterior wall. Interobserver variability in the AP measurement in five of these studies was less than 5 mm; however, four studies reported greater variability (up to 10 mm). The use of a higher frequency transducer (5 MHz) reduces variability and some have suggested that inner to inner wall measurements produce more consistent results]. At times, ultrasound may not give an accurate depiction of the iliac arteries, which may also be aneurysmal .In approximately 1 to 2 percent of cases, the aorta cannot be imaged adequately because of technical difficulties (eg, bowel gas, aortic depth).(29)

Although ultrasonography is generally preferred, computed tomography (CT) can be used for the diagnosis of AAA and for serial monitoring of aneurysm size. CT has the advantage of evaluating the abdomen in more detail, which may be particularly important in patients with a nonspecific clinical problem such as abdominal pain. CT also defines the extent of the aneurysm better than ultrasound and is superior for imaging suprarenal aneurysms].

Limitations of CT compared with ultrasonography are greater cost, the requirement for contrast, and the cumulative risk of radiation with repeated scans .(30)

MANAGEMENT

Management

a-Surgical treatment

Operative therapy is advised if the maximum diameter of the aneurysm is one and half times greater than the caliber of the adjacent normal aorta,or if the aneurysm is ≥ 6 cm in diameter. In smaller aneurysms, indications include rapid rate of expansion or aneurysm associated symptoms.(31)

Thoracic aortic aneurysms are generally resected and replaced with prosthetic sleeve of appropriate size. Cardiopulmonary pypass is necessary for removal of ascending aortic aneurysms, and partial bypass to support the circulation distal to the aneurysm is often advisable in resection of DTAA. (31)

A temporary Gott shunt may be used from the proximal aortato the distal aorta beyond the aneurysm to perfuse the distal circulation while the aortic site is cross-clamped.(31)

Aneurysms of the aortic arch may be successfully excised surgically, but the procedure may be particularly challenging. The brachiocephalic vessels must be removed from the aortic arch prior to its resection and re-implanted to the graft with restoration of cerebral perfusion.(32)

Crowford et al.,1990 (33) has demonstrated that it is possible to successfully replace virtually the entire diseased thoracic and abdominal aorta, a method known as "elephant trunk" technique,carried out in sequential stages of aortic replacement.

Endovascular treatment

Although, the results of surgical treatment for thoracic aortic aneurysms have steadily improved over the past 20-30 years, there is a trend towards developing less invasive procedures to repair these aneurysms in an attempt to further reduce operative risks and complications.(34)

If successful, these techniques may allow one to extend therapy to high risk patients with severe co-existing medical illnesses or who have previously undergone one or more operations for treatment of intrathoracic diseases. (34)

The decreased morbidity of endovascular repair of the thoracic aorta (TEVAR) was detailed in numerous studies1–5 and was the impetus for the multicenter Gore TAG pivotal trial, which led to U.S. Food and Drug Administration (FDA) approval for endovascular repair of descending thoracic aortic aneurysms in March 2005.(35)

The decision to proceed to surgery must weigh the risk of rupture against the risks of the operation and take into account the patient's projected survival. While a size cutoff of 6 cm has traditionally been accepted, surgeons have advocated for treatment of aneurysms as small as 5.5 cm, given the decreased morbidity of this approach compared with open repair. Aneurysms growing >1 cm per year or >5 mm over a 6-month period should also be treated.

Although fenestrated and branched endograft technology is in development, these devices are well away from being approved for general use. Endovascular therapy of these aneurysms is thus hindered by the presence of the intervening visceral segment. Hybrid approaches consisting of ‘‘debranching’’ procedures have been developed to provide separate blood flow to the visceral arteries and allow coverage of the visceral segment. Although debranching procedures are not without morbidity,they may be a suitable option in patients in whom avoiding a thoracotomy or cardiopulmonary bypass is appropriate.(36)

The native thoracic aorta is of larger caliber than that of the infrarenal abdominal aorta, which necessitates the usage of larger-diameter stent grafts. Thoracic grafts are housed in large sheaths, which sometimes preclude conventional transfemoral access and require delivery through the distal common iliac artery, creation of an iliac artery conduit, and, at times, direct delivery through the abdominal aorta. In addition, the high force of blood flow in the thoracic aorta requires a longer seal zone (20 mm) on either end to prevent displacement. The curve of the thoracic aorta at the arch presents special challenges in attempting to achieve adequate proximal fixation and seal. Radial support must be weighed against the need for enough flexibility and conformability within the device to navigate this curve and achieve seal following deployment. The angulation of the aorta often progresses with age, as atherosclerotic changes lead to lengthening and increased tortuosity, adding to the difficulty of accurate device deployment and adequate proximal landing.When device deployment is performed close to or within the arch, the graft must closely appose the ‘‘inner curve’’ of the arch. If the proximal end of the graft is oriented toward the apex of such a curve, ‘‘birdbeaking,’’ where the graft is not apposed to the aortic wall, will occur, increasing the risk of graft collapse, migration, and failure of aneurysm exclusion. With adequate preoperative planning and anticipation of these difficulties, however, these issues can usually be circumvented by landing more proximally and debranching the arch as needed. (36)

The proximal landing zone abuts or involves branch vessels of the arch, namely the brachiocephalic trunk, left common carotid artery, and left subclavian artery. To achieve the 20-mm proximal seal required and to ensure that the graft will sit in close apposition to the inner curve of the arch, debranching procedures can be performed, which essentially ‘‘move’’ the branch vessels to a more proximal location, allowing coverage of the origins of these vessels. When coverage of the left subclavian artery is required, duplex of the vertebral and carotid arteries should be completed to determine whether left common carotid–left subclavian bypass or left subclavian transposition is in order. For more proximal landing zones involving the left common carotid artery or brachiocephalic trunk, antegrade bypass from the ascending aorta/transposition of the great vessels can be performed, or alternatively, extra-anatomic bypass canbe performed to avoid sternotomy.(37)

The distal landing zone also must be at least 20 mm in length. Typically, the celiac axis is spared, although reports of covering the celiac artery in patients with a documented patent pancreaticoduodenal arcade have been successful in achieving up to an additional 25 mm in seal length with nominal incidence of mesenteric ischemia(37)

PREOPERATIVE PLANNING

Computed tomographic angiography (CTA) of the chest, abdomen, and pelvis with three-dimensional reformatting provides accurate and pertinent information regarding the diameter of the aorta to be used for the proximal and distal seal zones, the length of coverage required, the degree of angulation and tortuosity of the aorta, as well as characteristics of the lumen and wall of the aorta, including thrombus burden and calcification. Additionally, the diameter of the external iliacs and the degree of calcification/tortuosity from the femoral vessels, through the iliacs, to the aortic bifurcation should be noted and a decision should be made whether to proceed with transfemoral or alternative access. From this information, the diameter and length of the graft(s) are chosen, keeping in mind the degree of oversizing specified in that device's instructions for use.(36)

AVAILABLE ENDOGRAFTS FOR TEVAR

An overview of the different devices in use is provided below.

The Gore-TAG device is the first stent graft device approved by the FDA for treatment of descending thoracic aneurysms. It is made of expanded polytetrafluoroethylene and an exoskeleton made of nitinol. The proximal and distal ends of the graft have scalloped flares, which are thought to allow for conformity and better apposition to the tortuous aorta.(38)

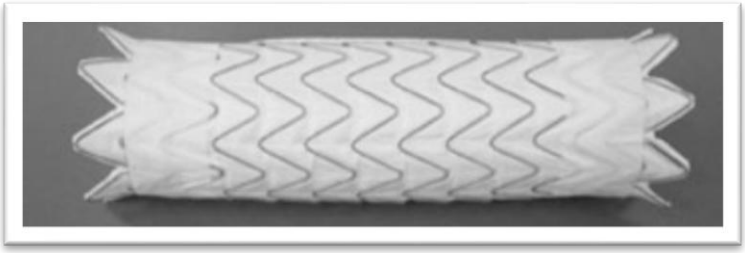


Fig.(8): Gore-TAG device

The Medtronic Talent device was studied in the VALOR I trial (Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aortic Aneurysms), which proved its clinical efficacy. It is made of two components, a proximal straight tubular stent graft with a proximal bare stent configuration, and a distal tapered tubular stent graft with an open web proximal configuration and closed web distal configuration. It consists of a woven polyester graft with a nitinol endoskeleton . The Talent device was widely utilized outside of the United States for several years and spurred the development of its next-generation version, the Valiant endograft, currently being tested for efficacy in the VALOR II trial.(38)

Fig.(9): Medtronic Talent device

The Medtronic Valiant endograft has a modified proximal bare stent configuration with eight bare peak wires compared with the five bare peak wires found in the Talent stent graft. The long connecting bar of the Talent device was removed in the Valiant device to afford better flexibility of the device. Columnar support has also been optimized through stent spacing, and longer covered devices are now an option.(38)

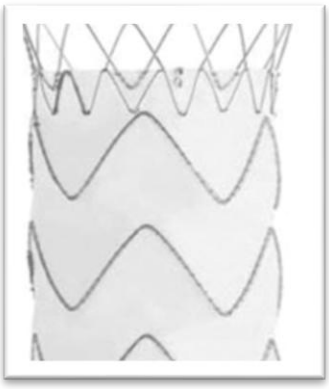


Fig.(10): Medtronic Valiant endograft

The Cook TX2 stent graft is a two-piece modular endograft system made of proximal and distal tubular endografts. The proximal endograft is covered and has stainless steel barbs allowing for active fixation to the aortic wall. The distal component has at its distal end a bare metal stent similar to the suprarenal stent in the Zenith device for endovascular repair of abdominal aortic aneurysm (AAA). This allows active fixation of the device over the origins of the visceral vessels. The TX2 is made of Dacron fabric covered by stainless steel Z-stents. Both the Medtronic Talent and Cook TX2 thoracic endografts were recently approved for commercial use by the FDA.(38)

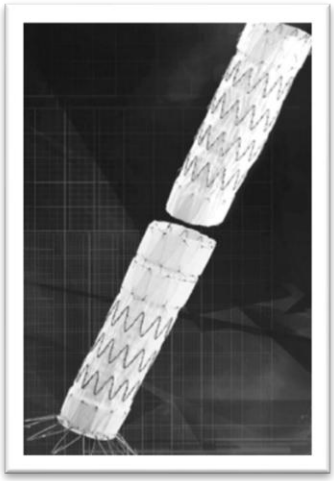


Fig.(11): Cook TX2 stent graft

The Bolton Relay stent graft is a relatively new investigational device used for the treatment of thoracic aortic pathologies. It is composed of self-expanding nitinol stents sutured to a polyester fabric graft with a curved longitudinal nitinol wire intended to provide columnar strength. It has a proximal bare stent, which remains constrained until the endograft is fully deployed.(38)

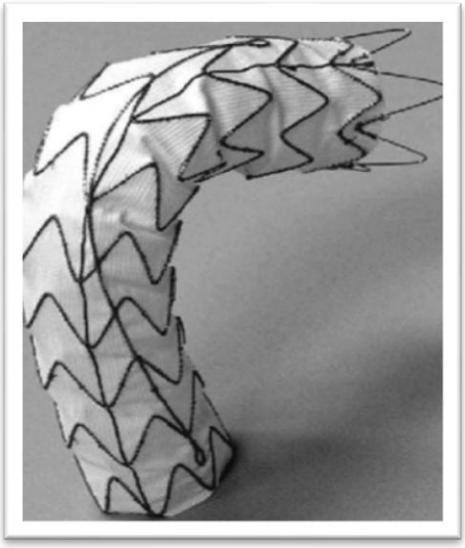


Fig.(12) Bolton Relay stent graft

CONDUCT OF THE OPERATION

The procedure is typically done under general endotracheal anesthesia. A lumbar drain is placed in cases where extensive coverage of the thoracic aorta is anticipated, where interruption of contributing blood supply to the artery of Adamkiewicz (T8–L1) is high, and in cases where the patient has had prior AAA repair. Lumbar drainage of cerebrospinal fluid to decrease the pressure in the subarachnoid space and increase the spinal cord perfusion pressure has been found to be an important adjunct in preventing paraplegia following TEVAR.(38)

Neuromonitoring in the form of somatosensory-evoked potentials (SSEPs) provides real-time functional information about the spinal cord. Any decrease in amplitude of SSEPs during the procedure will prompt maneuvers to increase the mean arterial pressure and cerebrospinal fluid drainage. (38)

Performance of the procedure requires the delivery of a large-bore sheath into the aorta as well as angiographic access. Typically this is accomplished transfemorally, although patients presenting with disadvantaged femoral access sites may require delivery of the sheath through the common iliac artery, an iliac conduit, and so on. To land a device accurately in the arch, positioning of the C-arm in the left anterior oblique position at 45 to 75 degrees will ‘‘splay out’’ the arch branches so that accurate device deployment is achieved. Even with the stent graft perfectly positioned, deployment of the graft can be complicated secondary to the high volume of blood flow in the thoracic aorta and the potential for the ‘‘windsock effect,’’ which describes the tendency for the graft to be pulled distally before deployment is complete. Described maneuvers to circumvent this phenomenon include rapid right ventricular pacing, controlled hypotension, and adenosine- induced cardiac arrest.(39)
Once the device is deployed, the stent graft is typically ballooned at the seal zones and graft junctions, and completion angiography is performed to ensure effective sac exclusion and preservation of essential vessels and to detect any evidence of endoleak.(39)

Type I endoleak: Involves the proximal or distal seal zones. Further ballooning or placement of another graft may be necessary to achieve seal. Vigorous proximal ballooning may be hazardous; retrograde proximal aortic dissection has been reported.(39)

Type II endoleak: Unusual in the thoracic aorta, but due to retrograde flow from intercostal arteries into the sac. Typically resolves with conservative management.

Type III endoleak: Occurs with inadequate overlap and seal between modular components. Usually responds with further ballooning or additional graft or stent placement.

Type IV endoleak: Occurs due to porosity of the graft, which is a rare occurrence with current-generation devices.

Type V endoleak: Otherwise known as ‘‘endotension,’’ occurs in the setting of continued sac expansion despite absence of an identifiable endoleak on subsequent imaging studies.

Once exclusion of the sac has been confirmed, the device sheath is removed, and the arteriotomy is repaired. (39)

COMPLICATIONS

Stroke and Paraplegia

Because the proximal seal zone is in proximity to the carotid arteries, embolic strokes in the distribution of the middle cerebral artery can occur following TEVAR. Risk factors for embolic stroke include the need for proximal deployment of the graft, presence of mobile atheromata in the arch, as well as prior stroke.(40)
In addition, the vertebral arteries arising from the subclavian may be the source for posterior circulation strokes.(41)

Planned coverage of the left subclavian in a patient with a dominant left vertebral, hypoplastic right vertebral, or incomplete circle ofWillis should be preceded by carotid subclavian bypass, as interruption of blood flow in these circumstances has been associated with an increased incidence of stroke and paraplegia. Left upper extremity symptoms occurred in up to 15.8% of patients.(36)

Visceral Ischemia

Visceral ischemia can occur with intentional coverage of the celiac axis, although reports have suggested that documentation of an intact pancreaticoduodenal arcade preoperatively reduces this risk. (37)

Access Complications

Because of the obligatory large sheath size for delivery of the device, passage of the sheath through small-diameter, tortuous, or excessively calcified external iliac artery can lead to iliac artery disruption. Intra-aortic balloon control helps to stabilize the patient until proximal and distal control of the iliac artery and definitive repair can be conducted. Anticipation of the need for adjunctive access measures is thus important and is required in a significant percentage of patients, ranging from 9.4 to 23.8% in published reports.From the percutaneous angiography puncture site, a pseudoaneurysm or hematoma may form.(42)

Postimplantation Syndrome

This syndrome occurs during the early postoperative period and is characterized by leukocytosis, fever, and elevation of inflammatory mediators such as C-reactive protein, interleukin-6, and tumor necrosis factor-a. (43)
It is thought to be due to endothelial activation by the endoprosthesis. For thoracic aortic stent grafts, development of either unilateral or bilateral reactive pleural effusions is not uncommon, with a reported incidence of 37 to 73%.(44)

Device Migration and Endoleak

Migration of the graft (>10 mm) caudally can occur, with a published incidence of 1 to 2.8%.Factors predisposing to migration include excessive oversizing and tortuous seal zone anatomy. The incidence of endoleak following thoracic aortic stent placement is less common that that for EVAR and is estimated at 3.9 to 15.3%.(45)

Other complications

May include myocardial infarction and respiratory/aspiration events, underscoring the predominance of medical comorbidities in the patients with significant vascular disease.(36)

POSTOPERATIVE MANAGEMENT/SURVEILLANCE

The patients are initially monitored in the intensive care unit setting, paying special attention to the neurological exam to detect evidence of stroke or paraplegia, and evidence of visceral ischemia in those individuals who required coverage of the celiac axis for distal landing zone length. Patients are typically transferred from the unit to the floor on postoperative day 3 and discharged within a week. Surveillance consists of CTA at 1 month, 6 months, then annually postoperatively.(36)

CLINICAL OUTCOME

Technical success in various reports has been high, approaching 98%.2,3 Perioperative mortality is low, ranging from 1.9 to 2.1%.This is in contrast to a reported 5.7 to 11.7% in the respective open repair arm.(46)
Perioperative stroke has ranged from 4 to 8%. (47)
Spinal cord ischemia manifesting as paraplegia or paraparesis has been reported to be 3 to 5.6%. (48)
In a recent study in which perioperative morbid events including myocardial infarction, respiratory events, stroke, and paraplegia were combined into a composite score, the percentage of patients who experienced at least one event was over a third lower in the TEVAR group compared with the open repair arm (9.4% versus 33%, $p<0.01$).(49)
The incidence of endoleak at 5-year follow-up with the Gore TAG device was 4.3%, with type I attachment site leaks being the most common type.

Effective aneurysm exclusion was achieved in the majority of patients, with only a 2.8% aneurysm-related mortality at 5 years.(36)

LONG-TERM SURVEILLANCE

Clinical follow-up for thoracic aortic stent grafts is in its infancy, but despite the not insignificant rate of secondary intervention required following stent grafting (3.6 to 4.4%),the greatly decreased morbidity of this approach makes it preferable to open repair in the majority of cases. A CTA is usually obtained within a month of the procedure, followed by an imaging study at 6 months and annually thereafter. Evidence of attachment site endoleak is intervened upon promptly. Type II endoleaks can be observed provided that the sac does not enlarge. MRA can also be used, although it is of limited applicability in patients with ESRD or chronic renal insufficiency. Noncontrast computed tomography allows for measurement of the sac diameter and is sufficient in most circumstances to document effective aneurysm exclusion.(36)

Multi-layered Flow Modulator system (cardiatis design concept) (50)

The use of Multilayer Flow Modulator (MFM) is not only a less invasive procedure, but it can also be applied to patients who may not be candidates for open surgery or endovascular treatment where the vital collateral arteries may be compromised.

It may avoid the complications cited above by:

- preserving the collateral branches deriving from the aorta
- preserving the branch(es) within the aneurysmal sac while retracting its wall

- inducing physiological and stable thrombosis of the aneurysm
- having the device available in an emergency
- a shorter procedure time and under local anaesthesia (45min on average)

Primary and Secondary Functions

The CTMS is biocompatible (comply with the ISO10993-1 requirements and appropriate other parts of the ISO 10993 series) and sterile and should have the following functions:

PRIMARY FUNCTIONS

- Avoid rupture, exclude and reduce the aneurysmal sac from the circulation by an organized thrombus in aneurysm without branch,
- Shrinkage of the aneurysm with branch. The flow is channeled to the branch,

SECONDARY FUNCTIONS

- Preservation of all covered branches,
- Parent vessel integration and Endothelialization (MFM embedded) while keeping the branches patent,
- Ability of the MFM to be visible (under fluoroscopy),
- Ability of the MFM to be consistently accurately and safely deployed,
- Ability of the MFM to ensure effective self fixation and wall apposition,
- Ability of the MFM to maintain its adequate integrity,
- Consistency of the MFM dimensions (elastic recovery) and its design for compatibility for use in specified vessel diameters,
- MRI Compatible

Delivery System and MFM

- Ability of the system to access and reach the intended location.
- Ability of the system to deploy the MFM by preserving the integrity of the system.
- Ability of the delivery system to withdraw easily and safely.
- Haemostasis (ability of the system to minimize blood loss)

CARDIATIS BIOMECHANICS

CARDIATIS STENT BIOMECHANICS

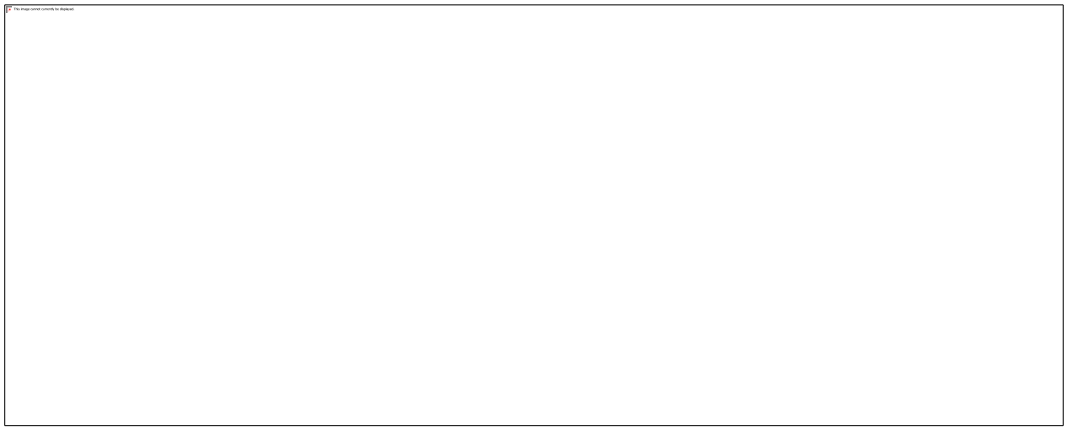
Biomechanics is broadly defined as mechanics applied to biology. Mechanics constitutes the study of motion and associated forces while biology is the study of life. Hence, biomechanics is the interface of two large fields which includes such areas as gait analysis, rehabilitation, sports performance, flight of birds, swimming of sperm, birth labour, surgical devices, biomaterials, plant growth, prosthesis design and invertebrate mechanics to name just a few. In the present context, we shall focus the scope of biomechanics to continuum mechanics as applied to physiology. Physiology is the study of the normal function of living systems, which was originally concerned with the function of the Earth. The physiologist generally seeks to understand the relationship between structure and function. Biomechanics provides the physical and analytical tools to connect structure and function with the major objective to understand problems in physiology with mathematical accuracy. In the context of vascular mechanics, the major objective is to accurately predict the mechanical environment of the cells within the arterial wall, which is the major determinant of cellular homeostasis.(51)

Introduction

In nature, hemodynamic and hydrodynamic principles, by using hedges as windbreaks in crop protection, is well known. Good windbreaks laminate the wind but do not block its passage. In other words a hedge must allow some wind to pass through. (52)

A windbreak is a barrier placed on the land surface that obstructs the wind flow and alters flow patterns both up wind of the barrier (windward) and downwind of the barrier (leeward). As wind approaches a windbreak, a portion of the air passes through the barrier. The remaining air flows around the ends of the barrier or is forced up and over the barrier. As the air moves around or over the barrier, the streamlines of air are compressed. This upward alteration of flow begins at some distance windward of the windbreak and creates a region of reduced wind speed on the windward side. This protected area extends for a distance of 2 H to 5 H, where H is the height of the barrier. A much larger region of reduced wind speed is created in the lee of the barrier. This region typically extends for a distance of 10 H to 30 H. Some wind speed reduction extend as far as 60 H to the lee, but it is unlikely that small reductions at these distances have significant microclimatic or biological impacts. (52)

Pressure on the ground is increased as the wind approaches the barrier and reaches a maximum at the windward edge of the barrier. Pressure drops as the wind passes through the barrier, reaching a minimum just to the lee. Pressure gradually increases, returning to the original condition at or beyond 10H. The magnitude of the pressure difference between the windward and leeward sides of the windbreak is one factor determining the flow modification of the barrier and is a function of windbreak structure.(52)



Barrier characteristics that affect leeward airflow include permeability, height, shape, width, and resilience. Of those, permeability (porosity or density) is most important. Results of many experiments have been presented in terms of permeability.(52)

Wind speed reduction patterns are determined primarily by the porosity and distribution of pores in the barrier. For windbreaks with low porosities, leeward wind speed is minimum near the windbreak and, after reaching minimum, tends to increase more quickly than do wind speeds leeward of more porous windbreaks.(52)

If the 'porosity' is less than 25%, the wind does not get through easily and is deviated towards the top of the hedge, creating turbulence in front and behind the hegde. In general for a hedge to create a protective laminating wind, the mean porosity of the windbreak should be in the 40-50% range, resulting in a lower laminated wind velocity, beneficial over a larger distance.(53)

By applying these physical principles to the technology of MFM,the following data could be assumed.The Porosity is the amount of void space of the device and it is expressed as metal free area /total unit area. The porosity is not measurable& is calculated theoretically Permeability refers to how well blood flows through the mesh of the device. The permeability is measurable it can be quantified as milliliters /minute / cm^2. (50)

For better understanding the figures below show that the pattern is different but the porosity is equal (the same empty space). However the permeability could different, the flow can circulate differently between the two. (50)

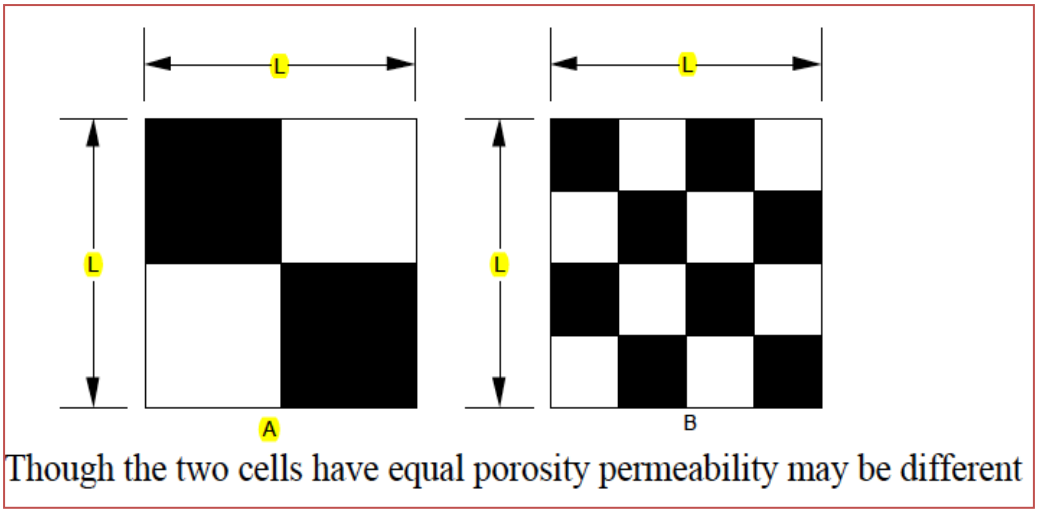


Fig.(13):an example of 2 cells having the same porosity with different permeability

A monolayer stent (1stent thickness) as it is used is characterized by a small amount of metal, consequently high space and then high porosity (90%). High porosity allows more liquid to flow through the mesh, which is quantified by the permeability.(50)

The multilayer stent has more metal (low porosity 65%) and more than 1 thickness, even though the permeability is 90 to 95%. The reason is physical, when a fluid flows through a mesh or grids with many layers its pressure drops and its speed increases. This is important for keeping the branches patent.(50)

In the other hand the low porosity affects the flow velocity when the fluid passes through the mesh into the aneurysm.(50)

The relation between flow modulation and permeability & porosity

The three-dimensional porosity of 50-60% can modulate the flow: eg *convert turbulent flow in laminar flow*. This effect can be achieved only through the superposition of several nested layers, so-called "interlock", one upon the other so as to form a spatial structure in volume. Flow modulation is a result of the elimination of the local micro-turbulence (recirculation) by straightening the flow lines.(50)

Studies and experiments with the multilayer flow modulator validated that the optimal flow modulation through the layers is at a mean porosity of 65%.

Due to its low 3D design porosity, the MFM shows a high permeability (about 95%), similar to a monolayer with high porosity. The figure below illustrates the porosity and permeability impact with traditional monolayer, stent-grafts and a MFM.(50)

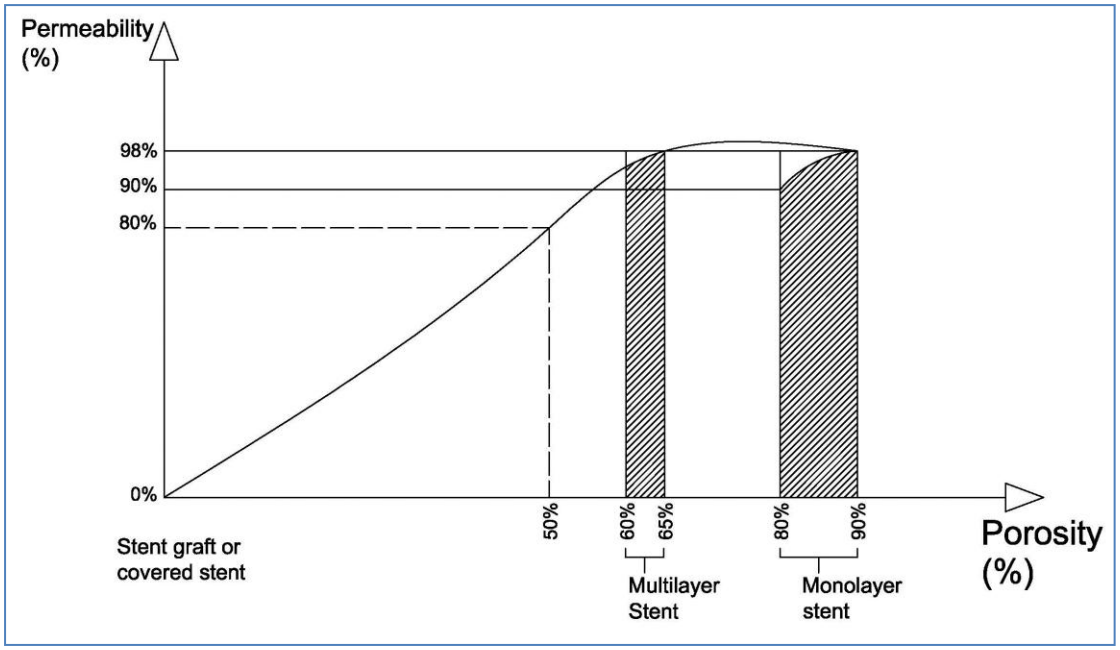


Fig.(14):different porosity of different stent types & its effect on permeability

MFM Implant Design

The 3D structure is made up of several layers braided together, creating a configuration of multiple interlocked layers, as shown in Figures 3 and 37. The technology is a platform able to produce sizes from 3 up to 50mm. The braiding configuration for different sizes depends on the number of layers, number of wires, and size of the wires.

The braiding machine, illustrated in a schematic manner hereunder, consists of 5 layers, 64 wires per layer, and is subdivided into 16 sectors. The use of all 320 wires provides a closed metal surface area with a 0 porosity (full occupation)

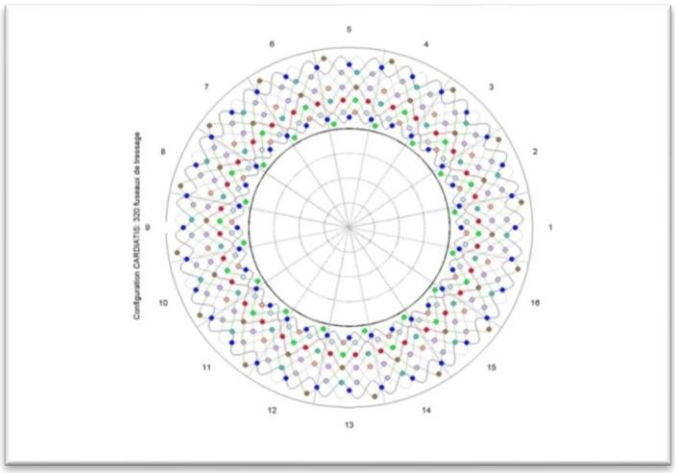


fig.(15) The schematic figure shows the full occupation and the coloured spots are the wires position

:

Therefore, to obtain a mean target porosity of 65% for each MFM size, the parameters for the number and size of wires need to be configured as shown in the example below,i.e,the braiding machine'd consist of 3 layers, 32 wires per the outer & inner layers, and interconnected by an intermediate layer of 64 wires.

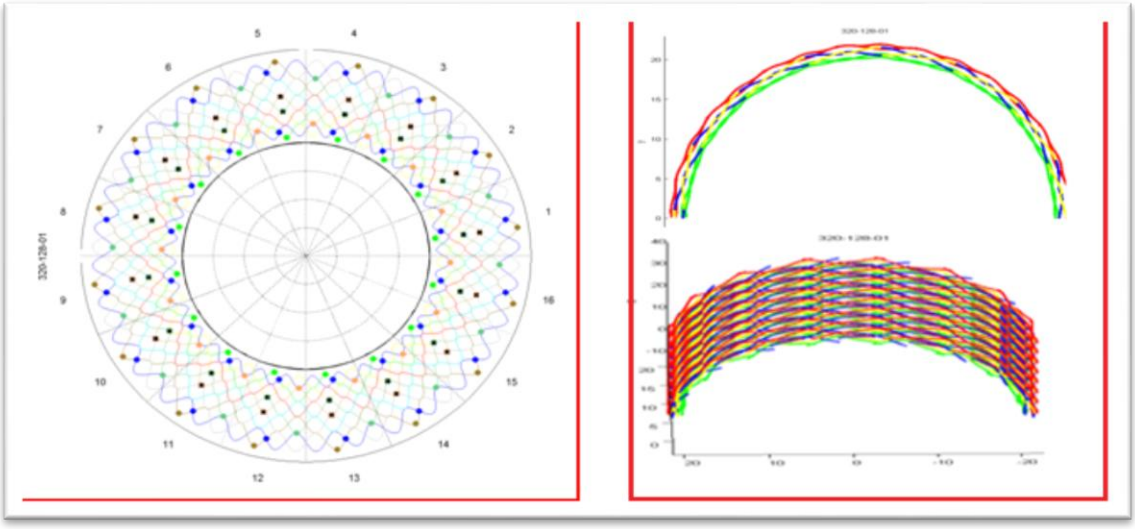


Fig.(16): An example of 128 wires for a 40 mm implant size. Two layers of 32 wires each (inner (green) & outer (red)) interconnected by an intermediate layer of 64 wires (blue and yellow)

The braiding for each configuration is characterized by a repetitive geometric pattern or base cell unit.

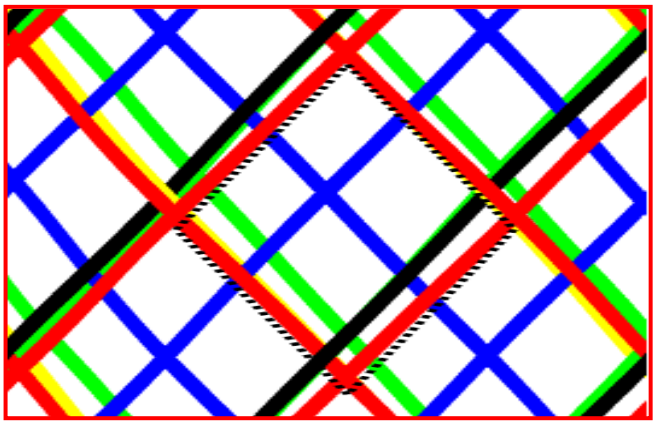


Fig.(17): An example of cell unit limited by the dotted black diamond shape

(128 wires for a 40mm implant size – schematic view)

What is the base cell unit?

This question is related to the design. Each diameter has its own pattern; in order to keep the same porosity for all used device sizes ,the number of layers and the number of wires and their sizes have to be changed and consequently the pattern of the cell unit. The cell unit is the pattern shape repeated through the mesh (like a fractional pattern).

Then, the repetitive geometric pattern or base cell unit candiffer from one diameter to another, but follow convergent geometrical series as detailed below:

$$\frac{1}{2}+\frac{1}{4}+\frac{1}{8}+\frac{1}{16}+\frac{1}{32}+\frac{1}{64}+\cdots\frac{1}{2^n}=1 \quad \text{(Full coverage, 0 porosity)}$$

This can be presented as an exponential equation:

$$Un = \left(\frac{1}{2}\right)^n$$

Where Un is a series function, which describes the number of the wires to cross each to make the cell unit. For example Un = 1/4 means 4 wires cross each other to make a cell unit. This the way in which we define the design of the device.

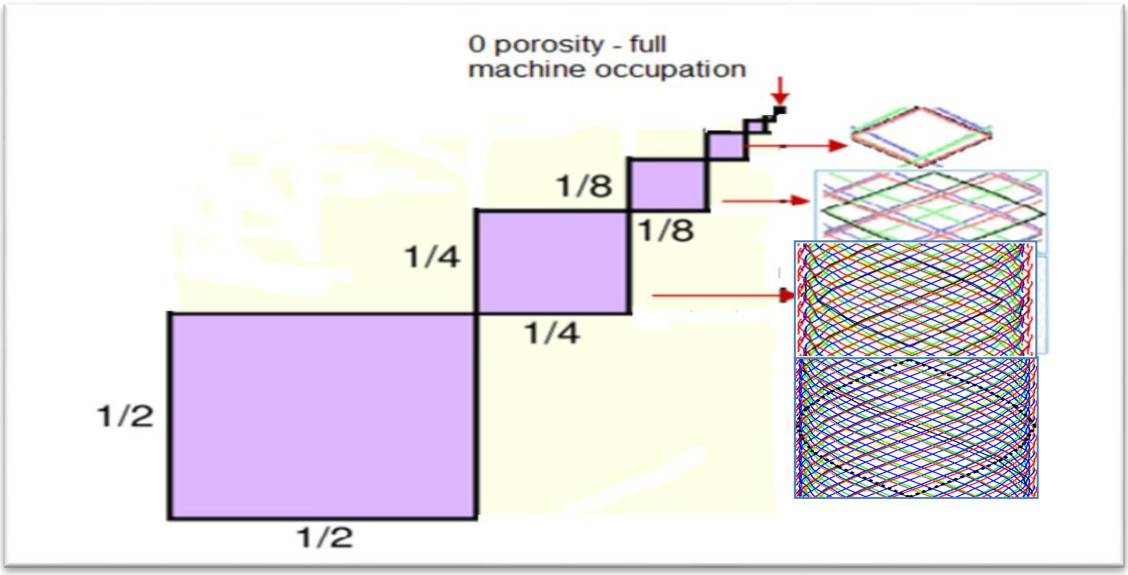


Fig.(18): The scale and distribution of cell unit for each used configuration

To obtain a MFM with an average porosity of 65%, the base cell unit is adapted for each diameter by wire size, wire number and number of layers; Only the configurations where the number of crossing wires/ unit cell is $\frac{1}{4}, \frac{1}{8}, \frac{1}{16}$ are used.

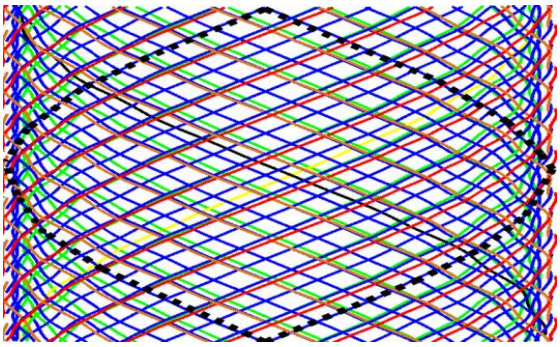
To make a braid, minimum 1 pitch is required, equivalent to a complete rotation of each wire (360 degrees) with half of the wires crossing each other.

Then, the basic cell unit can be expressed as a geometrical series with a constant ratio of ½.

$$Un = \left(\frac{1}{2}\right)^n$$

The repetitive geometric pattern (or base cell unit) of ½ number of wires crossing each other is not practical and is too large as shown as shown by the dotted black diamond shape below.

$$U1 = \left(\frac{1}{2}\right)^1 = \frac{1}{2}$$



To have a smaller and practical base cell unit, the number of crossing wires for each cell is brought to ¼:

$$U2 = \left(\frac{1}{2}\right)^2 = \frac{1}{4}$$

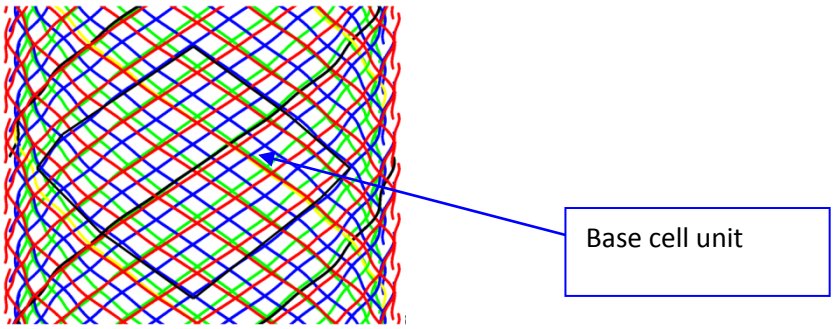
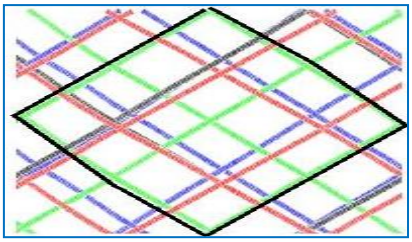


Table (1):illustrates that, in the braiding configuration for this pattern, the number of crossing wires increases with implant diameter.(Ratio Crossing Wires/Implant Diameter)

Implant Diameter (mm)	**Wire diameter (µm)**	**Number of wires**	**Number of crossing wires/ unit cell. (¼ of the wires number)**
5	**75**	**48**	**6+6=12**
6	**80**	**56**	**7+7=14**
7	**80**	**72**	**9+9=18**
8	**90**	**72**	**9+9=18**
9	**90**	**72**	**9+9=18**
10	**100**	**72**	**9+9=18**
28	**190**	**104**	**13+13=26**
32	**200**	**120**	**15+15=30**
35	**210**	**120**	**15+15=30**

In order to maintain the same porosity ratio, the configuration needs to be adapted for each size.

For n=3, 1/8 of the number of wires cross each other in the base cell unit. Then, the pattern for 1 cell unit is:

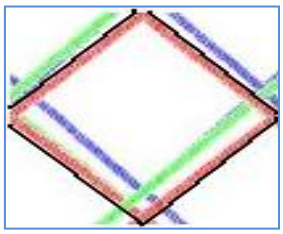


$$U3 = \left(\frac{1}{2}\right)^3 = \frac{1}{8}$$

Table(2): illustrates that, in the braiding configuration for this pattern, the number of crossing wires increases with implant diameter. The Ratio Crossing Wires/Implant Diameter

Implant Diameter (mm)	**Wire diameter (µm)**	**Number of wires**	**Number of crossing wires/ unit cell. (1/8 of the wires number)**
12	**100**	**80**	**5+5=10**
30	**200**	**112**	**7+7=14**

For the diameters in table 3, 1/16 of the total number of wires cross each other in the base cell unit, the pattern is as shown below:



$$U4 = \left(\frac{1}{2}\right)^4 = \frac{1}{16}$$

Table (3) illustrates that, in the braiding configuration for this pattern, the number of crossing wires increases with diameter size. The Ratio Crossing Wires/Implant Diameter.

Stent Diameter (mm)	Wire diameter (µm)	Number of wires	Number of crossing wires/ unit cell. (1/16 of the wires number)
14	**110**	**96**	**3+3=6**
16	**120**	**96**	**3+3=6**
18	**150**	**96**	**3+3=6**
20	**160**	**96**	**3+3=6**
22	**170**	**96**	**3+3=6**
25	**180**	**96**	**3+3=6**
40	**210**	**128**	**4+4=8**
45	**210**	**160**	**5+5=10**

For the platform (MFM diameters from 5mm to 45mm), the wire surface (for one braiding pitch) increases exponentially with the MFM diameter size

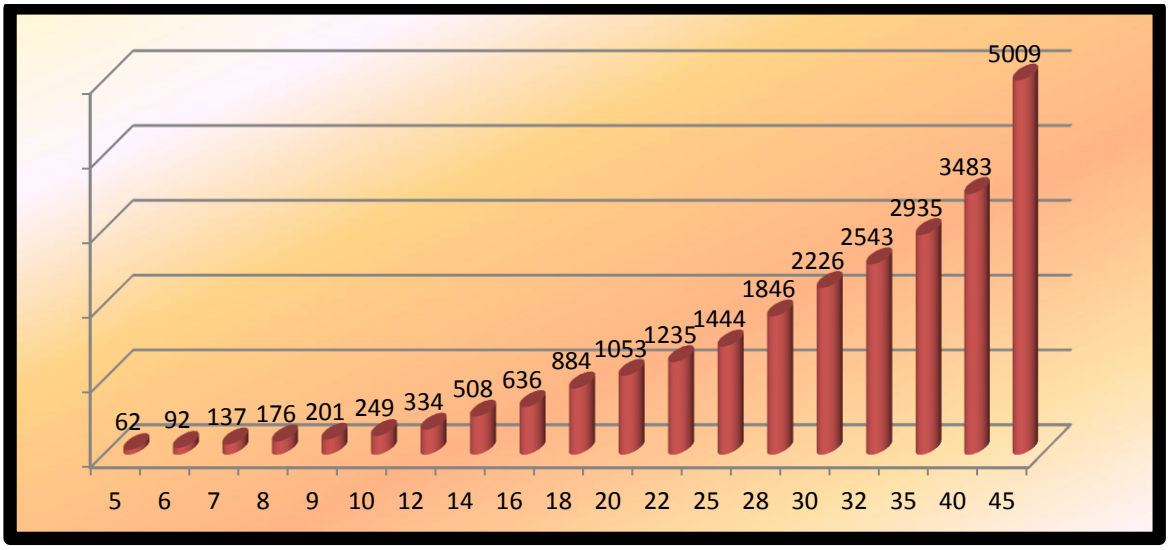


Fig.(19): Ratio MFM Diameter/Wire Surface (mm² for 1 Pitch)

To standardize the design parameters, the wire surface is divided by 1 braiding pitch: the braiding pitch length increases linearly with the MFM diameter size.

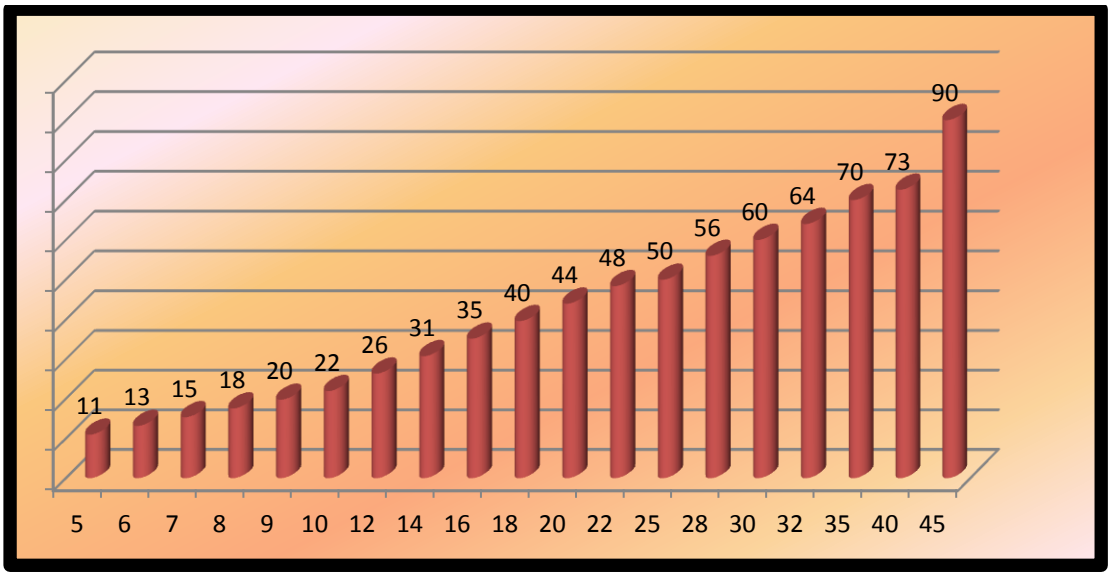


Fig.(20): Ratio MFM Diameter/Pitch Length (mm)

The porosity (MFM surface free area) remains constant for all the MFM sizes as shown below .

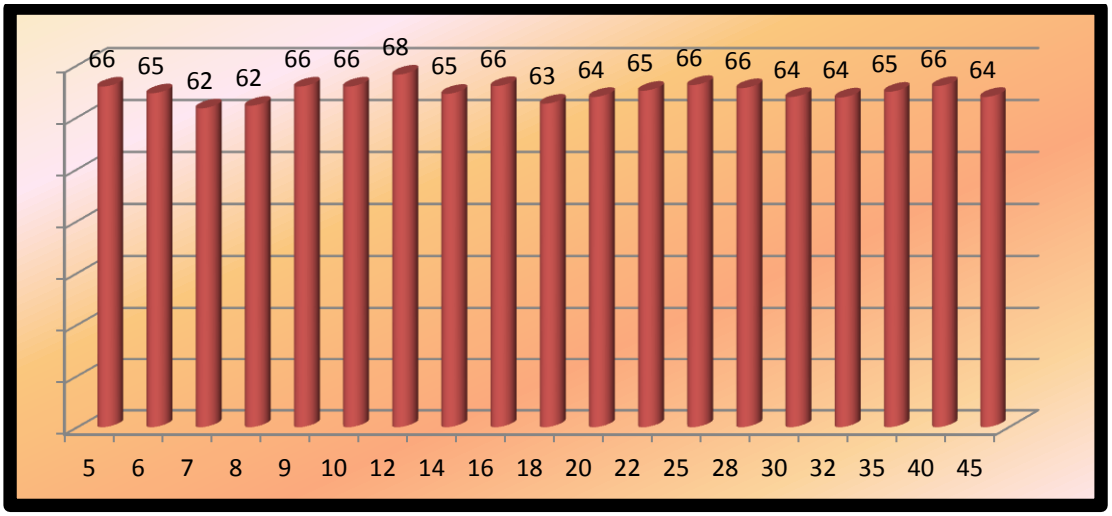


Fig.(21): Ratio MFM Diameter/Porosity (%)

Table (4) summarizes the braiding configuration parameters for the entire multilayer platform: Configuration Parameters for each multilayer flow modulator diameter

Implant Diameter (mm)	Wire Size (µm)	Nb of Wires	Nb of Wires crossing / cell unit	Wire Surface/ pitch (mm^2)	Pitch (mm)	Max compression (18-25%)	Recommen-ded compression (11-14%)	Min Compression (4-8%)
5	75	48	1/4	62	11	65.5	66.0	65.4
6	80	56	1/4	92	13.2	64.4	64.8	64.3
7	80	72	1/4	137	15.4	61.2	61.7	61.1
8	90	72	1/4	176	17.6	61.7	62,2	61.7
9	90	72	1/4	201	19.8	65.5	66.0	65.4
10	100	72	1/4	249	22.0	65.5	66.0	65.4
12	100	80	1/8	334	26.4	67.8	68.2	67.8
14	110	96	1/16	508	30.8	64.1	64.5	63.5
16	120	96	1/16	636	35.2	65.5	66.0	65.5
18	150	96	1/16	884	39.6	62.0	62.6	62.0
20	160	96	1/16	1053	44.0	63.3	63.9	63.6
22	170	96	1/16	1235	48.4	64.4	65.1	64.6
25	180	96	1/16	1444	50.0	66.1	66.2	63.5
28	190	104	1/4	1846	56.0	65.5	65.6	64.9
30	200	112	1/8	2226	60.0	63.7	63.9	63.0
32	200	120	1/4	2543	64.0	63.5	63.8	62.7
35	210	120	1/4	2935	70.0	64.8	64.9	63.9
40	210	128	1/16	3483	72.6	66.3	66.0	64.7
45	210	160	1/16	5009	90.1	63.7	63.9	62.7

Proof Of Concept (50)

I-the relation between pressure and aneurysm rupture

a-Porosity and Permeability and Functionality of the MFM

The 3D structure of MFM is made up of several layers braided together, creating a configuration of multiple interconnected layers. These configurations give a 3D low porosity design, and high permeability.

The importance of the 3D porosity is that it modulates the flow based on the geometrical environement bridged by the MFM.

For example :

- in a branch the flow its naturally turbulent, If covered by MFM then the pressure drops from 1 layer to the next whereas the speed flow is laminated.
- in a saccular aneurysm it modulates the formed the vortex by reversing its direction reducing its speed u to 90%
- in branched aneurysm it modulates the flow between the neck of the aneurysm (flow input) and the branch entry (output) and creates a negative pressure resulting in the collapse of the aneurysmal wall.
- in fusiform aneurysm it modulates the flow from turbulent vortex to laminated one
- in the vessel the shear flow is adjusted in the right range which prevents heperplasia

The conclusions reached in this study *(PR041)*and based on calculation and experimental tests show that porosity should average between 60 and 65% and permeability between 80 and 95%. This enabled the:

- Determination of the effective parameters in flow modulator design depending on vessel diameter and flow rate.
- Preservation of branch and collateral permeability, regardless of the size of the collateral.

6- Pressure Monitoring

Monitoring the pressure in an aneurysm sac using "EndoSure Wireless AAA Pressure Sensor" is developed by CardioMems. The study is carried out due to the late appearance of type I and II endoleaks in aneurysms of the abdominal aorta treated with stent grafts. A lack of sealing between the wall and the device (Endoleak Type I) and the retrograde perfusion of the collateral vessels (Endoleak type II) re-supplies (retrograde flow) and pressurise the sac.(54)

- This type of assessment was not carried out for the MFM for the following reasons:The reliability of the pressure sensors has not yet been established, especially in thoracoabdominal aneurysm which extends over a large length. This leads to the compartmentalisation of the position of the sensors position in the sac in the place where there may or may not be thrombus or branches. In addition, other questions are yet to be answered; do the sensors maintain their functionality and reliability in the long-term? Will it migrate or deteriorate over time? And so on.(55)
- Type II endoleaks no longer an issue, as branch and collateral vessels continue to be supplied (absence of retrograde flow). The MFM preferentially directs the flow towards the branch vessels, as a result the wall starts to retract because the whole aneurysmal sac is no longer under pressure (this retraction of the wall has been clinically proven in aneurysmal zones with branches.(55)
- Type I endoleaks cannot appear if the MFM is placed according to the Instructions for Use, i.e. correct over--sizing providing adequate self-fixation and a "landing zone" on the healthy part of the aorta far away from the pathological zone of the vessel for good sealing.(55)
- To date, only patients with an aneurysm or dissection who presents a high surgical risk with no other therapeutic alternative were treated by the MFM. The majority of these patients presented with acute pain obviously in relation to the aneurysm. As soon as the local anaesthetic wears off, they tell the pain has disappeared. This shows that the danger linked to the wall pressure is removed by the placement of the MFM.To date no peripheral or visceral (around 1,100 cases) or aortic (more than 100 compassionate cases) aneurysm rupture has been reported since aneurysms .Aortic Checks at 3, 6, 12 and 18 months on aortic aneurysms have shown either a retraction of the wall in the zone of the branch vessels or a reduction in the diameter of the aneurysm.(55)

c- The relation of pressure and its effect on the aneurysmal wall

In general the aneurysmal dilation of a vessel is responsible for blood flow turbulence and its recirculation within the sac. The nature of the flow, parameters such as speed, pressure, shear stress and the nature of the thrombus differ according to whether the aneurysm is fusiform or saccular. Due to their cylindrical shape, fusiform aneurysms affect the entire circumference of the vessel whereas saccular ones only affect part of the vessel.

What is meant by vortex velocity?

Hydrodynamically when a stream flow deviates from a linear flow, the fluid re-circulates and creates systematically a vortex. Here the flow deviates into the aneurysmal sac the flow is forced to rotate. In other words when the motion of the fluid swirling rapidly around a center is called a vortex. The speed and rate of rotation of the fluid in a free (irrotational) vortex are greatest at the center, and decrease progressively with distance from the center, whereas the speed of a forced (rotational) vortex is zero at the center and increases proportional to the distance from the center.

The vortex creates a constant and continues pressure against the arterial wall which leads to damage by destroying the elastin and consequently stretching and weakening the collagen

In fusiform aneurysms, the appearance of a vortex changes the field of pressure on aneurysmal zone by inducing quite a large vortex zone. The result is a local pulsatile peak in pressure ∂P acting perpendicularly and constantly on the aneurysmal zone while increasing the dilation and continuing to damage the components of the wall.

Fig(22). 3-dimensional vortical structure of the large aneurysm model flow

However in the case of saccular aneurysms the vortex runs alongside the aneurysmal wall damaging it through shear stress.

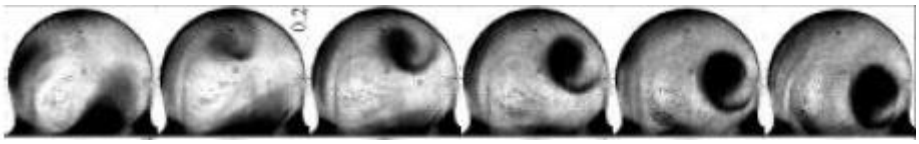


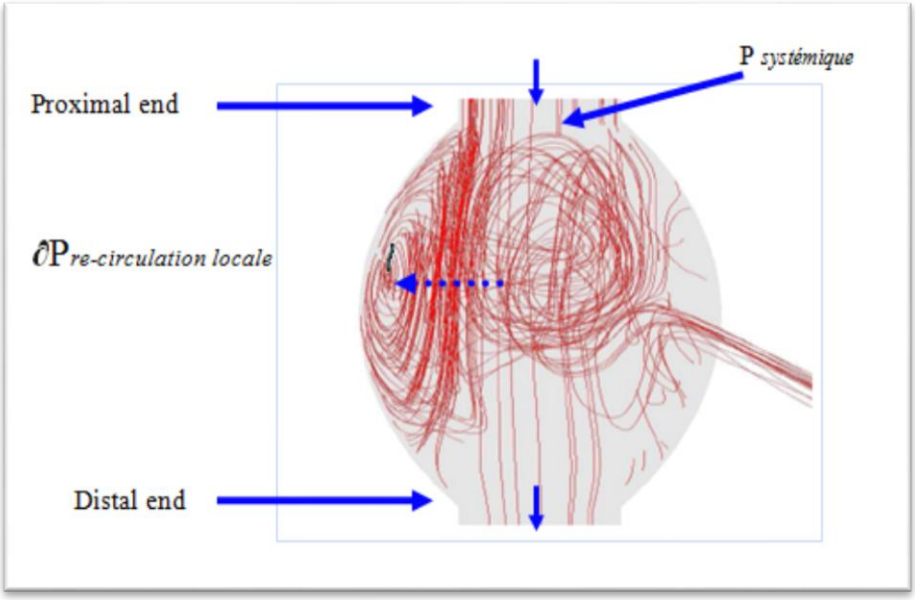
Fig.(23) Formation and whorl of the vortex exerting shear stress on the cavity of the aneurysm in the absence of a stent in saccular aneurysms

In both cases the wall is damaged, destroying its elastin, the collagen has no support and tends to stretch in a non-linear manner under the effect of the local pressure gradient ∂P .(56)

Fig(24). The image to left shows a healthy human artery with an elastin-collagen structure. To the right the elastin is destroyed and the collagen stretched. Published in the "Journal of Vascular Surgery- Volume 17, N°2 Feb.1993" This article shows the origin of the start of the aneurysmal rupture.

d-Pressure in fusiform aneurysms

In the aneurysm sac, the systemic pressure is increased by the gradient ∂P, (P *sys* + ∂P *local re-circulation*).



Fig(25). 2D model of a CFD showing the route of flow lines in a fusiform aneurysm

The wall pressure gradient ∂P is the result of the force which is acting perpendicularly on the arterial wall. In other words, the definition of pressure is the normal force at the surface on which it is exerted. As for systemic pressure, this is parallel to the wall and is therefore not responsible for the rupture.

This explanation is supported by White J et al., ***w***ho shows that the risk of rupture is produced in the zone where the elastin is most damaged and where the collagen is at its thinnest, Therefore only a very weak wall pressure gradient is needed to start the fissuring.(57)
The recirculation produces a thrombus which maintains and transmits this transmural pressure into the aneurysm pouch. (58)
This thrombus is soft and rubbery, non homogenous, does not stick to the wall and does not strengthen the aneurysmal wall.(59)
This thrombus is unstable and unorganised and that all the mediators that appear are cleaned away by the flow stream. As the thrombus grows, the platelets stick less and less. Because of its structure, this type of thrombus transmits wall pressure.(59)
The placement of the MFM prevents the recirculation or vortex, from forming while bringing the flow circulating at the entrance to the aneurysm. As a result the flow lines are laminated along the wall and the wall pressure force is no longer exerted.(60)

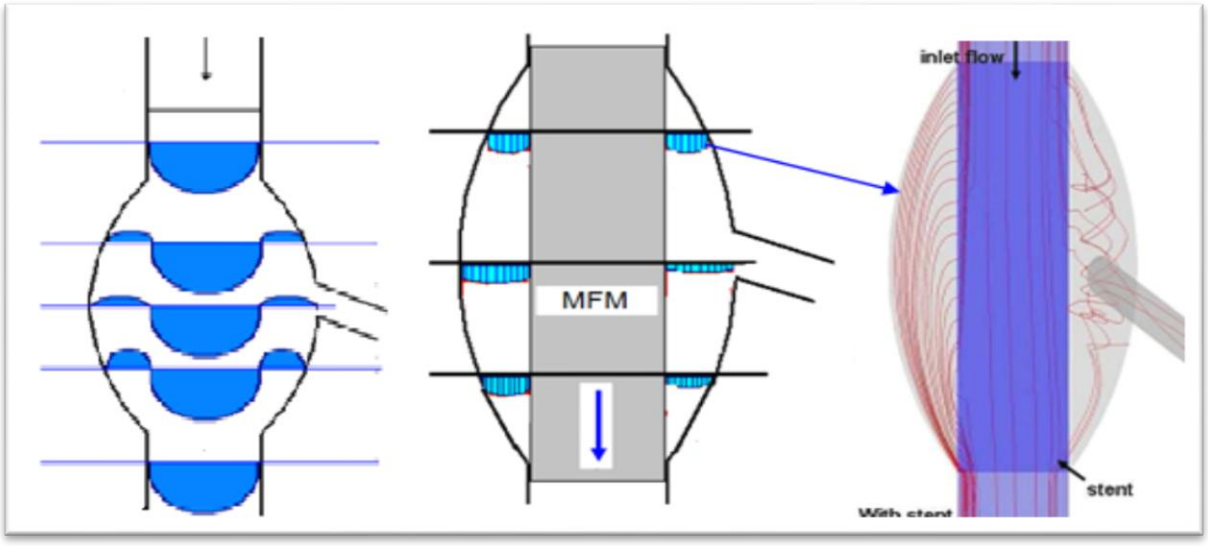


Fig.(26)2D model of a CFD showing the velocity profile before (left) and after (centre) the placement of the MFM. The flow lines are represented on the right.

It was shown through CFD that the difference in the average pressure on the wall with or without the MFM is quite small. This small difference is none other than the ∂P created through the recirculation which appears as a localized peak of pressure.(60)

The wall distribution of the average pressure exerted along the aneurysmal wall is constant on account of the lamination.(60)

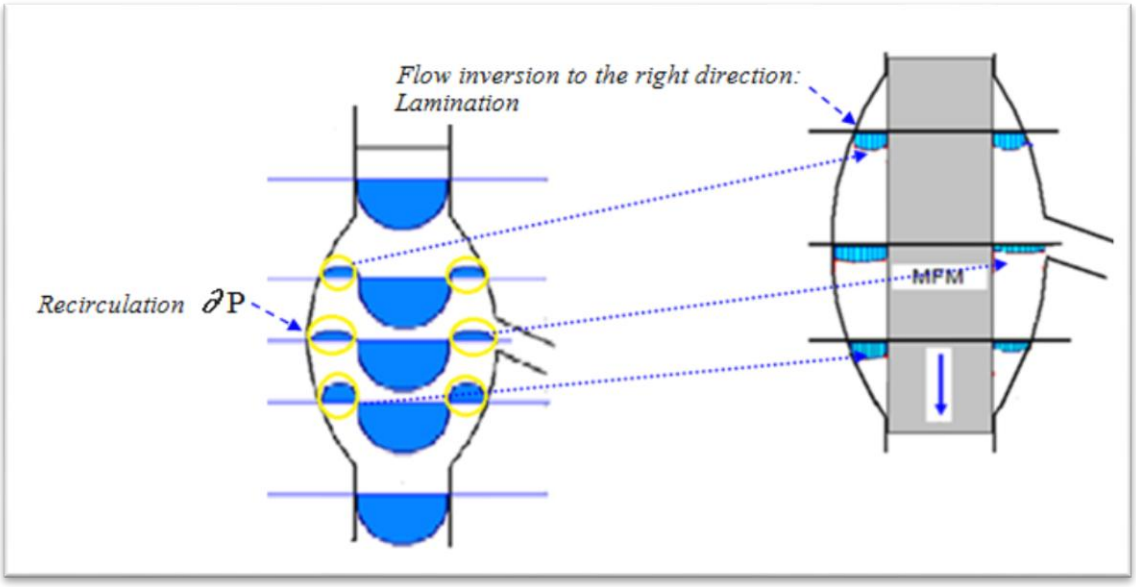


Fig.(27) 2D model of a CFD showing the change in direction of the velocity flows along the wall in the same direction as the systemic pressure flow direction (blue arrow on the right).

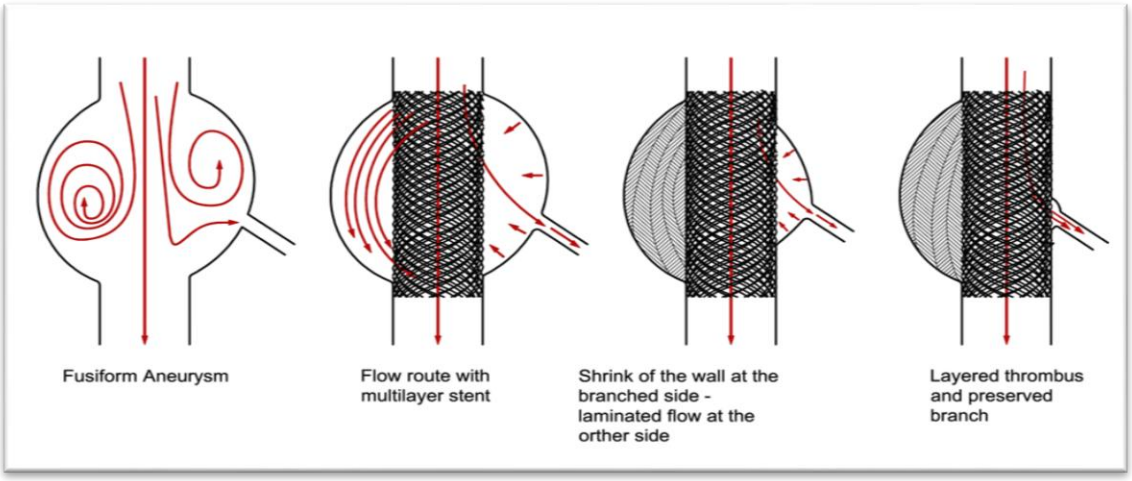


Fig.(28): Principle of hemodynamics in a fusiform aneurysm without a stent (left) and with a MFM (right)

The MFM transforms the recirculation flow into a laminated flow. Lamination generates fine fibrin layers, which gradually become stratified and ultimately thromboses.(60)

e- Pressure in saccular aneurysms

The Fig.(29) shows that at each systolic phase, an amount of flow enters the sac, where it forms a vortex which exerts shear stress. As it advances along the wall, its strength increases and its residence time (in the aneurysm) decreases.

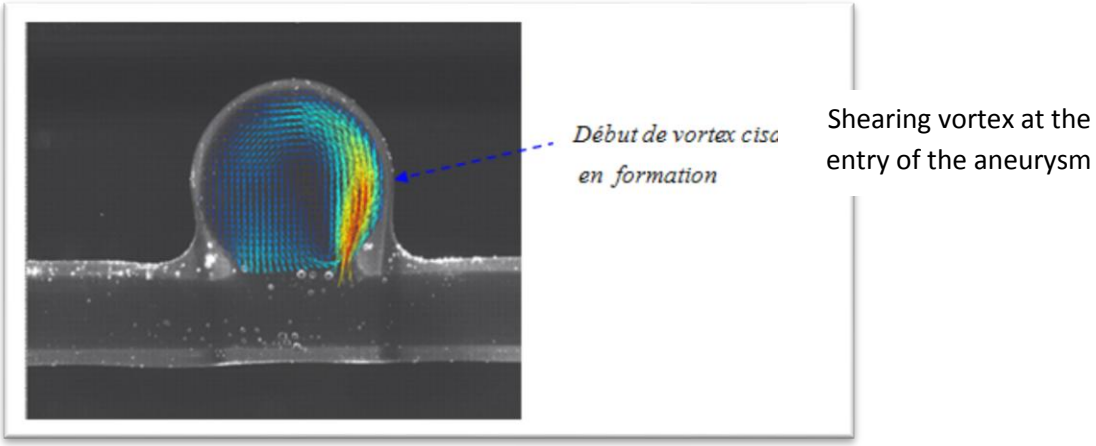
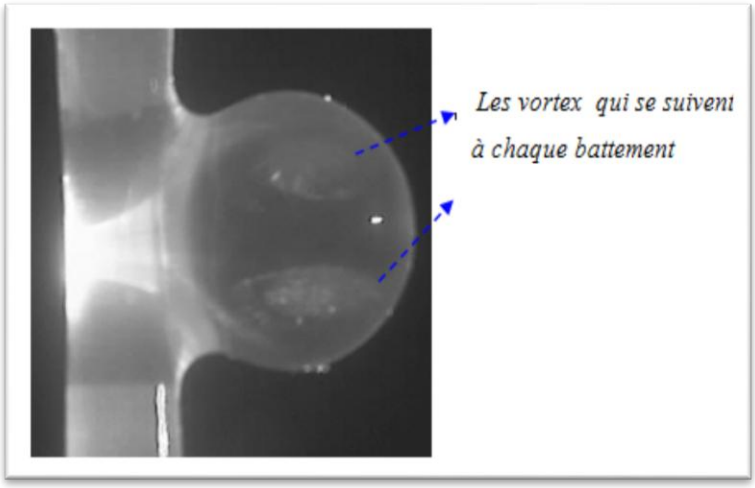


Fig.(29)2D model of a CFD showing the change in direction of the velocity flows along the wall

This cyclic movement damages the wall and creates tension at the entrance to the aneurysm (i.e. at the neck) which results in the wall being stretched and thinned until it ruptures.



Vortices between each systolic phase

Fig.(30): In vitro model showing the vortex formed between 2 systolic beats

In saccular aneurysms, the MFM affects the haemodynamics by modifying the overall flow in the aneurysmal sac. This has the effect of decelerating the vortex and weakening its strength by inverting its trajectory. The time of residence in the aneurysm is longer which has the effect of slowing the vortex which aligns itself and creates a sort of obstruction which results in a thrombosis layer.

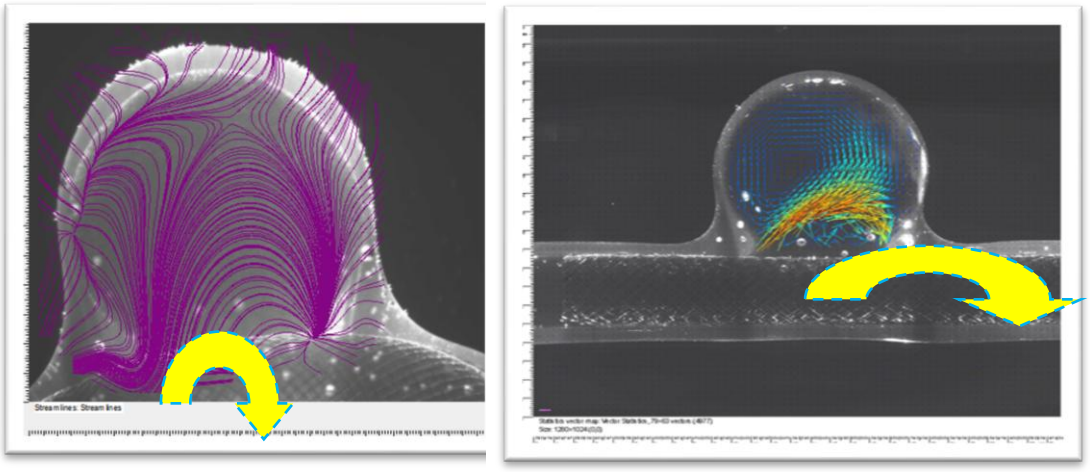


Fig.(31): In vitro model of 2 different experiences showing the haemodynamic change created by the MFM (flow inversion)

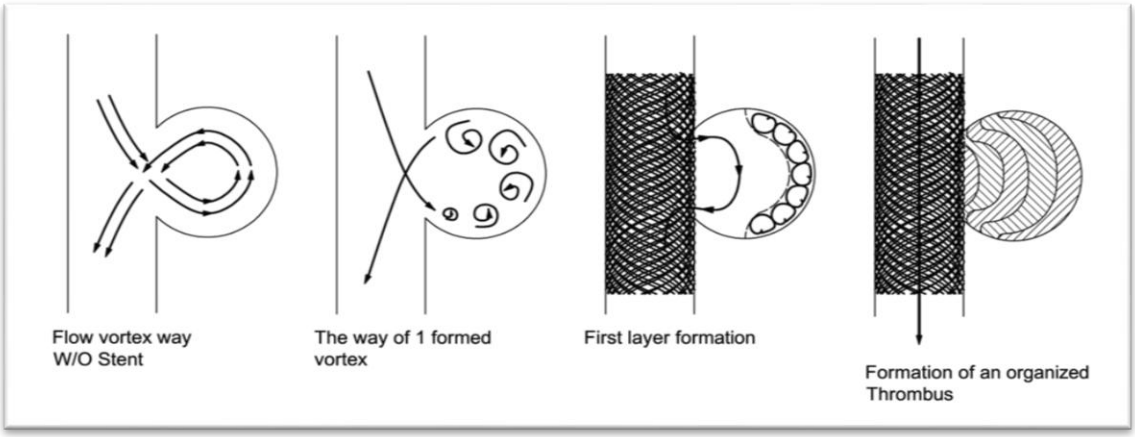


Fig.(32):Principle of vortex hemodynamics in a saccular aneurysm and layer formation with and without a stent

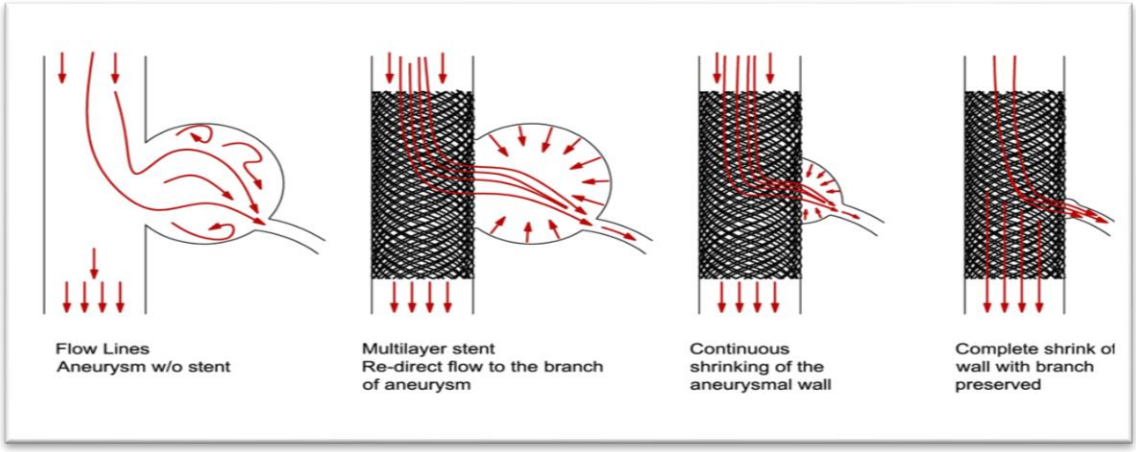


Fig.(33): Principle of hemodynamics in a saccular aneurysm with branch,without a multilayer stent (left) and with a multilayer stent (right)

f.Organized thrombus induced by the MFM and pressure

The thrombus architecture formed after the placement of the MFM appears in the form of several stratified layers. These layers are stratified like peel and are defined by lines called lines of Zahn.(59)

The platelet layers appear whitish, and are sandwiched between the red fibrin layers where the red corpuscles are trapped, the thrombus is said to be organized.

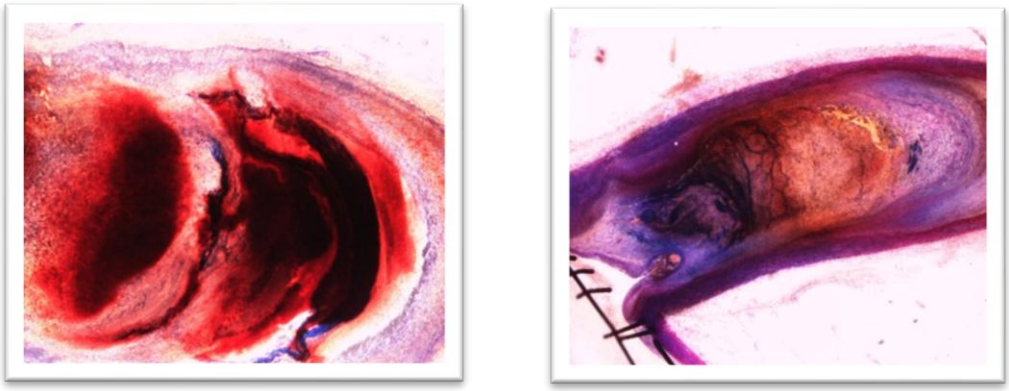


Fig.(34)Two stratified thrombus sections, post MFM, in elastase-induced aneurysms in rabbits

The German pathologist Ludwig Aschoff, who has studied the formation mechanism of Zahn layers, shows that the layers' mechanism is a haemodynamic phenomenon resulting from the interaction between the platelet physiology and the blood flow.(59)
These explanations support the results of the study, by Cardiatis, on elastase-induced aneurysms in rabbits. The endothelialization of the MFM isolates the aneurysm from the aortic flow while preserving the branch and collateral vessels.

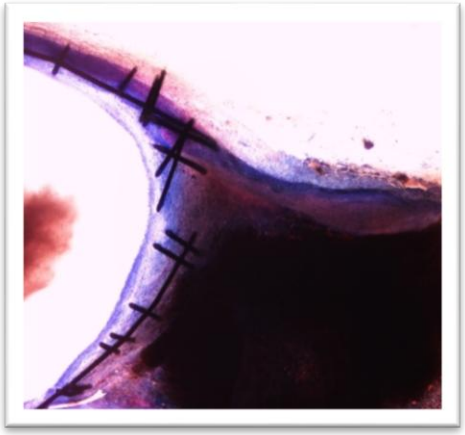


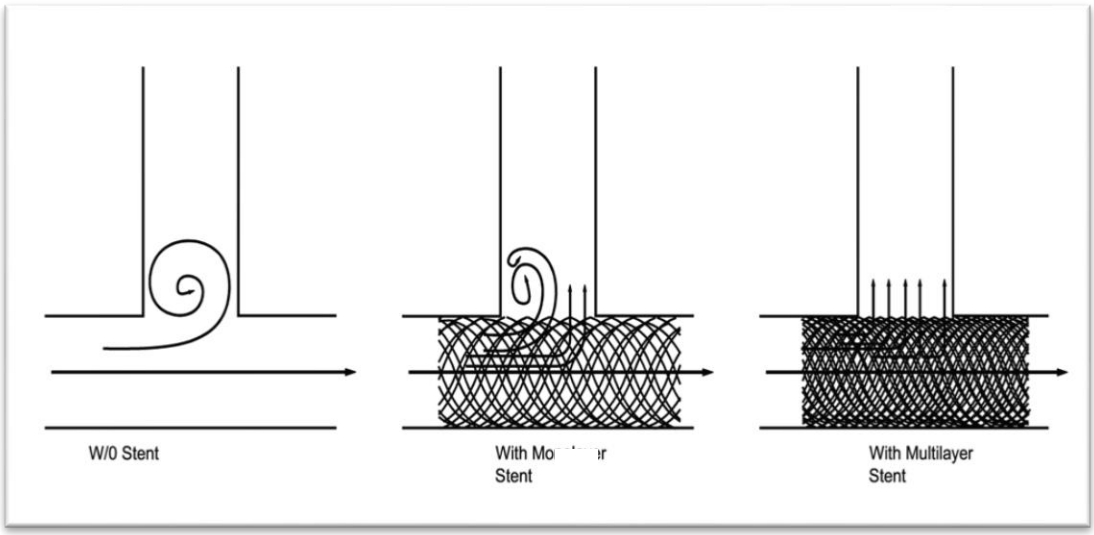
Fig.(35): Aneurysm isolated from the lumen by endothelium

In conclusion the MFM eliminates the harmful effects of wall pressure on the aneurysmal wall, creates a stable organised thrombus in the aneurysms with no branch vessels, retracts the aneurysmal wall where there are branch vessels and isolates the aneurysm from the blood flow by endothelialization.

II- BRANCH AND COLLATERAL PATENCY (50)

i) Principle – Concept

Without a stent, the flow entering a collateral branch is turbulent and a recirculation vortex is created.
Given the 3D meshing of the multilayer stent and the directional flow by the branch, the flow entering the branch covered by the multilayer stent is aligned and accelerated, thus ensuring excellent permeability.



Figs.(36) Principle of hemodynamics at the inlet of a branch without device (left), with monolayer stent (centre) and with a multilayer device (right)

The multilayer stent laminates the flow in branches. The collaterals remain patent regardless of size. This phenomenon is due to weaker pressure from one layer to the next whereas the speed is increasing. This causes flow alignment on entry into the branch, This lamination flow prevents cells from adhering to the part of the stent that covers the branch.

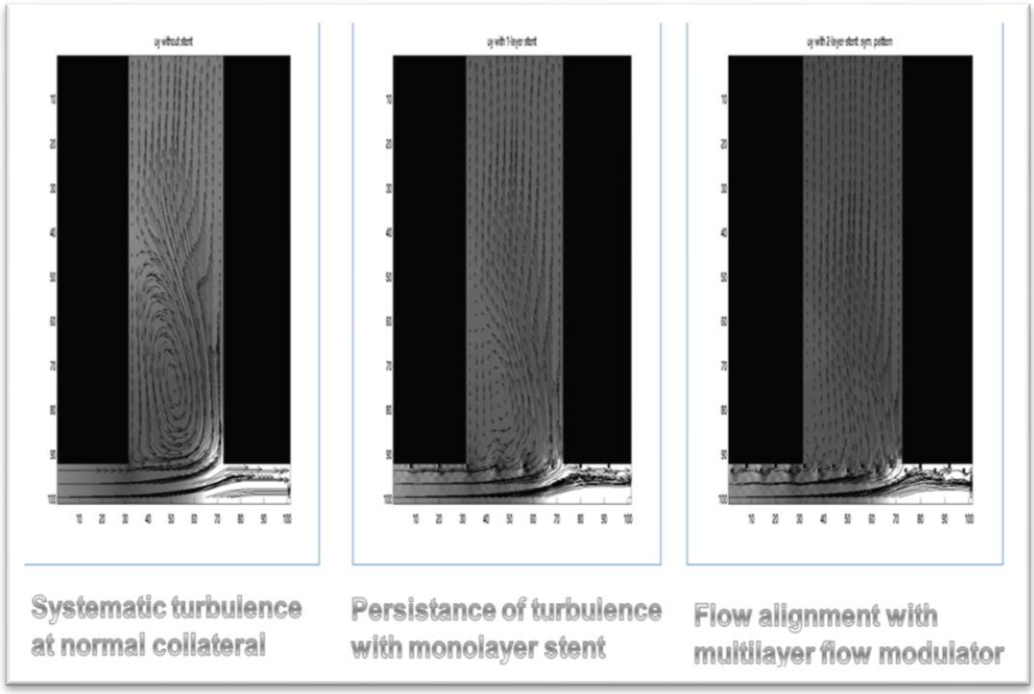


Fig.(37):Flow lines on entering a collateral branch without a stent (left), with a single-layer stent (centre) and with a multilayer flow modulator (right)

The histological study of MFM explanted in the abdominal aortas of 2 pigs after 10 days and 1 month, respectively, shows the perfect permeability of the branches covered by the multilayer flow modulator. The endothelialized neointimal tissue stops at the entrance to the branch.

Figs.(38) MEB photos of a multilayer flow modulator explanted in a porcine abdominal aorta in front of the lumbar aorta. Perfect patency of the branches.

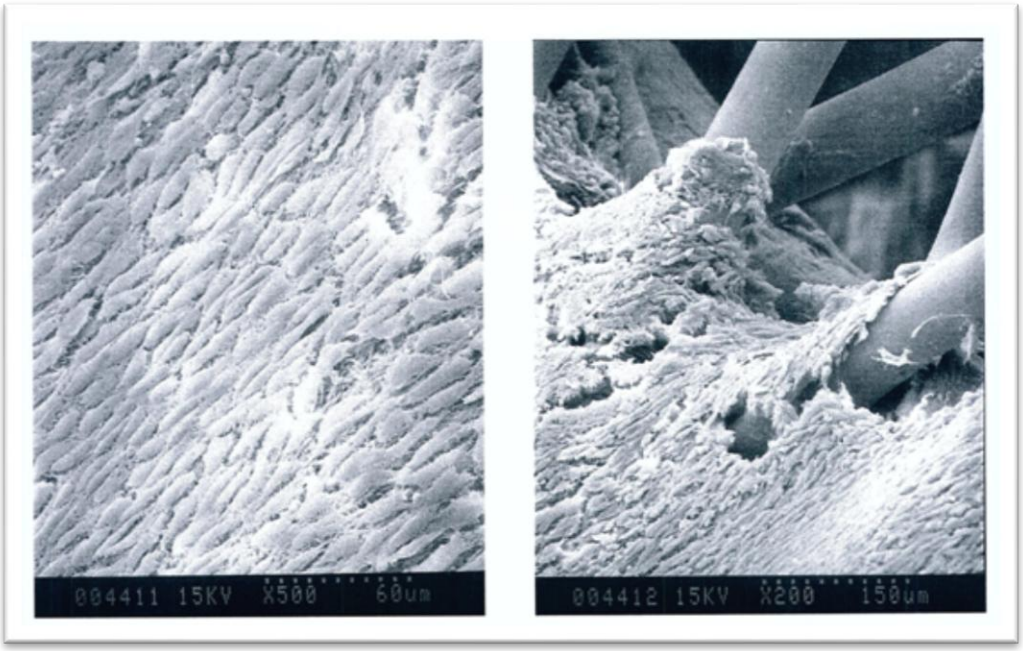


Fig.(39) Magnified MEB photos of the above stent: to the left: a carpet of endothelial cells on the stent in the artery. To the right: endothelialised neo-intimal tissue stops at the entrance to the branch.

ii) ENDOTHELIALIZATION

Given the micro-spacing between the layers, the multilayer stent creates a biological barrier between the interior layer of the stent and the artery wall, potentially capable of reducing the volume of neo-intimal hyperplasia.

The CFD study showed that, along the arterial vessel wall, the multilayer stent increases the shear, creates a non-recirculation zone along the wall redirecting the flow towards the centre of the artery and increasing the speed of the central flow in the artery, accounting for the formation of fine, stable, neo-intimal tissue.

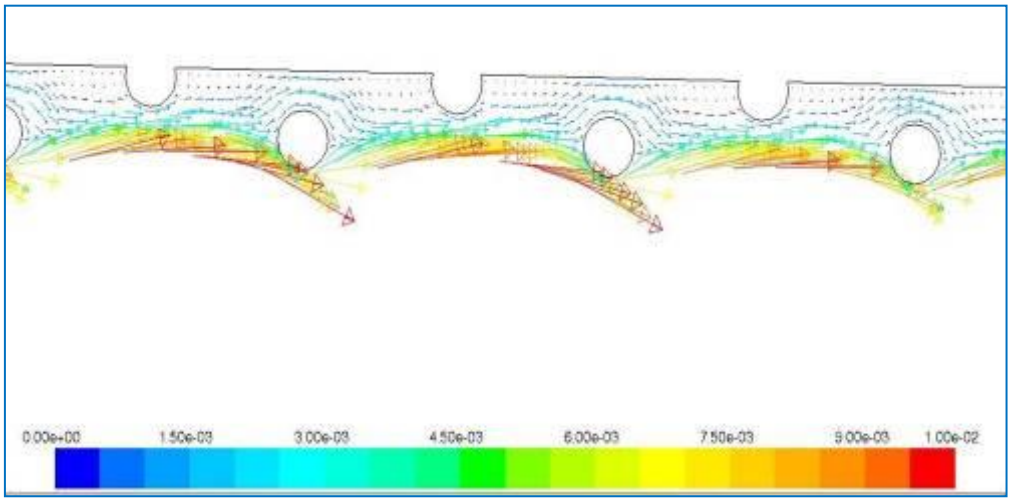


Fig.(40):Flow lines in an artery stented with a MFM

With the multilayer flow modulator, there is no flow along the external layer (along the wall). However, the flow is sheared along the internal wall and the shear rate is thus within the range of values that does not disturb the endothelium.
The histology report showed that the multilayer flow modulator causes a fibrous layer to appear between the smooth muscle cells and the endothelium. This fibrous layer forms a 'biological barrier' that is potentially capable of reducing the volume of neointimal hyperplasia and thrombosis in the stented artery.
It seems that the deposited flow of circulating progenitor cells subsequently differentiate themselves into pseudo-endothelial cells.

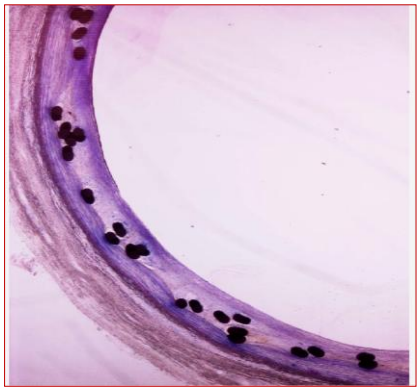


Fig.(41): Histological section of a multilayer stent explanted from a pig after 1 month's

Results of the studies showed:

- Perfectly normal intra-stent stenosis in the short, mid and long-term compared to the implantation sites studied,
- The permeability of all the collateral branches
- A correlation between the number of wires and neo-intimal thickening. Fine, stable neo-intimal tissue has appeared in arteries with a slightly higher number of wires.

This allowed to determine the stent design parameters according to the size of the vessel and the flow within the vessel whilst maintaining permeability in all types of collateral branches.
The technological platform has enabled to produce flow modulators of different configurations and different sizes ranging from 2 to 50 mm.

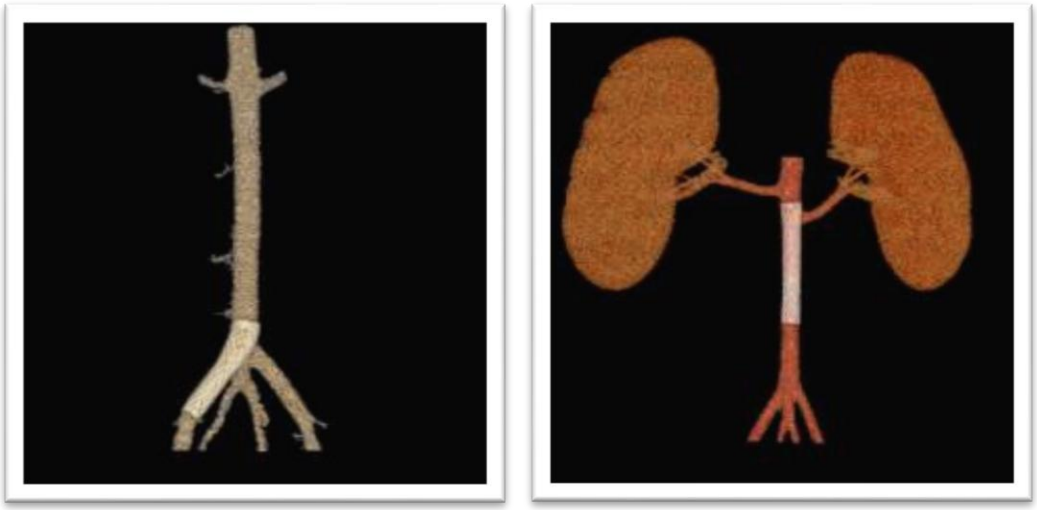


Fig.(42)CT scan of a MFM implanted in the aorta and right iliac covering the left iliac (to the left) and implanted in the abdominal aorta in front of the left renal artery (to the right). Both branches are entirely permeable.

The Multilayer Flow Modulator comprises the following key principles:

1. Reduction of the vortex velocity in saccular aneurysm up to 90%;
    - ***Physiological thrombosis with a gradual reduction in the aneurysm***
2. Reduction of the vortex velocity and flow lamination along the wall in fusiform aneurysms;
    - ***Physiological wall thrombosis***
3. Channeling flow to the branch in branching aneurysms, with wall shrinking (back to the normal wall);
    - ***Retraction of the aneurismal sac and preservation of the branch***
4. Flow lamination in the branches ensuring branch patency;
    - ***Branch preservation***
5. Shear stress flow acceleration (good shear range) in the parent vessel which induces endothelialization
    - ***Preservation of intimal hyperplasia***

STRATO TRIAL

STRATO Trial

The French prospective multicenter study STRATO enrolled a total of 23 patients in 10 centers. Twenty two (22) patients were followed up to 12 months; one patient was lost at discharge.

Patients were enrolled from April 7th, 2010 to February 9th, 2011 and examined by CT or MRI imaging at 30-days, 3-months (optional), 6-months and one year.

Patient Characteristics

All Patients were high risk for surgery, with no alternative for treatment and had at least one of the following risk factors:

- Age ≥80
- ASA≥3
- history of thoracic or abdominal aorta surgery
- coronary artery disease (history of myocardial infarct or angina) with positive functional tests and coronary lesions for which revascularisation is impossible or not indicated
- cardiac insufficiency with clear clinical manifestations
- inoperable aortic stenosis
- LVEF < 40 %
- chronic respiratory insufficiency objectified by one of the following criteria:
    - FEV1 < 1.2 l/sec;
    - VC < 50 % of the predicted value according to age, sex and weight;
    - arterial blood gas analysis in the absence of oxygen:$PaCO^2$>45 mm Hg or PaO^2<60 mmHg;
    - oxygen therapy.
- renal insufficiency if creatinine > 200 micromol/l before injection of contrast product
- hostile abdomen, including presence of ascites or other signs of portal hypertension
- obesity

The population enrolled 23 patients (4 female (19%) / 19 male (83%)), mean age 73 years old (range 57-91 years-old) with the history details below:

	Yes	No	Unknown
Smoker	**15**	**8**	**0**
Coronary artery disease	**6**	**14**	**3**
Cardiac insufficiency	**1**	**21**	**1**
MI	**2**	**20**	**1**
Hypertension	**20**	**2**	**1**
Hyperlipidemia	**13**	**8**	**2**
Diabetes	**2**	**21**	**0**
Stroke	**4**	**19**	**0**
Renal Insufficiency	**7**	**16**	**0**
PAD	**13**	**10**	**0**
Aortic Disease	**14**	**8**	**1**

		Yes	No	Unknown
Aortic Interventions (All types)		**15**	**7**	**1**
	Endovascular	**1**		
	Surgery	**14**		

Twenty two (22) patients (96%) had a fusiform aneurysm and 1 patient (4%) had a saccular aneurysm. Nineteen (19) patients (83%) had branches within the aneurysm, 11 patients (48%) had branches at the landing zone covered by the MFM.

Classification of thoracoabdominal aorta aneurysm is as follow:

Aneurysm Classification	Number of Patients (%)
Crawford Type II	**9 (39%)**
Crawford Type III	**14 (61%)**

The aneurysm had an average of maximal diameter of 65mm (46-85mm) and an average length of 177mm (55-408mm), on pre CT-imaging.

Device Characteristics

The total number of devices implanted is 58 (mean 2,5/patient) and allocated as follow:

Number of Patients	Number of Devices
7	**1**
5	**2**
6	**3**
3	**4**
1	**5**
1	**6**
Mean Nb Devices/Patient	**2,5 (± 1,4)**

MFM Diameter	Number of implanted devices
25	2
28	1
30	7
32	3
35	21
40	15
45	9

MFM Lengths	Number of implanted devices
80	5
100	16
120	17
150	20

The procedures were performed either by percutaneous approach (7 (30%) or by cut down approach 16 (70%)).

Safety Outcomes

Mortality (aneurysm-related, all-cause)

i-Aneurysm-related Mortality Definition

Aneurysm-related mortality is defined as a death of any cause within 30 days of the initial procedure or a death caused by an aneurysm rupture, a conversion to open surgery or any other secondary endovascular procedure as evidenced by CT, angiography of direct observation at surgery or autopsy. The aneurysm involved must be located in the vascular segment treated by the MFM.

No aneurysm-related death was reported at the time of data snapshot.

ii-All-cause Mortality

The primary safety hypothesis was based on 30-day and 12-month all-cause mortality. Patients who received the MFM experienced an all-cause mortality rate of 0% at 30 days, 0% at 6 months and 4,5% at 12 months (1 patient died at 11 months at home, reason not reported).

Mortality	**30 days**	**6 months**	**12 months**	**Cumulative Mortality**
All-cause	**0**	**0**	**1**	**1**

Major Adverse Events

Definition:

A major adverse event (MAE) was defined as the occurrence of any of the following:

- Cardiac events (MI, CHF, arrhythmia requiring intervention or new treatment, cardiac ischemia requiring intervention, refractory hypertension, cardiac event involving arrest)
- Pulmonary events (ventilation > 24h, re-intubation, pneumonia requiring antibiotics, chronic obstructive pulmonary disease, pleural effusion requiring treatment, pulmonary embolism, pulmonary edema requiring treatment, pneumothorax, hemothorax)
- Renal events (urinary tract infection requiring treatment, renal failure requiring dialysis, renal insufficiency, permanent dialysis, hemofiltration)
- Gastrointestinal events (bowel/mesenteric ischemia, gastrointestinal infection requiring treatment, gastrointestinal bleeding requiring treatment, paralytic ileus > 4 days, bowel resection)
- Neurological events (CVA, TIA/RIND, carotid artery embolization/occlusion, SCI, paraparesis, paraplegia)
- Vascular events (vascular injury, aneurysm rupture, aneurysm or vessel leak requiring re-intervention, pseudoaneurysm requiring repair, aneurysm expansion requiring re-intervention, fistula, arterial thrombosis, embolization resulting in tissue loss or requiring intervention, deep vein thrombosis, hematoma requiring surgical repair, coagulopathy requiring surgery, post-procedure transfusion)

- Wound events (wound infection requiring treatment, incisional hernia, lymph fistula, wound breakdown requiring debridement, seroma requiring treatment, wound complication requiring treatment)

Major Adverse Events	30 days	6 months	12 months	Cumulative MAE
Cardiac	**1 (hypotension)** [1]	**0**	**0**	**1**
Pulmonary	**0**	**0**	**0**	
Renal	**0**	**0**	**0**	
Gastrointestinal	**1 (infarcts)** [2]	**0**	**0**	**1**
Neurological	**0**	**1 (stroke)** [3]	**0**	**1**
Vascular	**1 (iliac rupture)** [4]	**2 (expansion)** [5]	**0**	**3**
Wound	**0**	**0**	**0**	
Any MAE	**3**	**3**	**0**	**6**

[1] Hypotension due to inappropriate medication

[2] Mesenteric and Splenic infarctus due to distal emboli. The reason is not clearly identified; It believed to be related to Disseminated Intravascular Coagulation (DIC) or non compliance to medication protocol.

[3] Stroke post endovascular secondary intervention, patient has permanent atrial fibrillation

[4] One (1) iliac rupture when retrieving the introducer sheath.

[5] One (1) aneurysm expansion related to misplacement inducing proximal type I endoleak – One (1) aneurysm expansion related to type III endoleak (mis-overlapping due to short neck of previous bifurcated graft)

No major adverse event related to spine cord ischemia (SCI) has been reported

Effectiveness & Functionality Device Outcomes

Clinical success

Definition:

Clinical success is defined by the exclusion of the aneurysm with preservation of collateral branches patency at 6 months and 12 months, post to MFM implantation. Aneurysm exclusion is characterized by the increase of the thrombus and decrease of circulating flow inside the aneurysm. However, in the part of the aorta , close to the visceral branches, remains a residual flow which preserves branch patency.

Clinical Success	1-3 months	6 months	12 months
Aneurysm Exclusion	**Not assessed**	**65% (13/20)**	**75% (15/20)**
Aorta and MFM Patency	**100% (22/22)**	**100% (20/20)**	**100% (20/20)**
Branch Patency* **(nb patients)**	**97% (63/65)** **(n=22)**	**100% (58/58)[1]** **(n=20)**	**97% (56/58)** **(n=20)**
Secondary Patency*	**100% (65/65)** **(n=22)**	**100% (58/58)** **(n=20)**	**100% (58/58)** **(n=20)**

* n/m with n = number of branches patent and m = number of covered branches (patent at Pre-imaging)

[1] Patient with re-intervention for occluded branches did not show up at 6 months, but showed up at 12 months.

Aneurysm Exclusion, Aorta and MFM Patency:

At 6 months and 12 months follow-up time frames, 65% (13/20) and 75% (15/20) of patients, respectively, showed aneurysm exclusion. Endoleaks were identified in the five (5) remaining patients, which were associated to the persistent flow inside the aneurysm. One patient underwent a secondary procedure with additional MFM, 12 months later.

All MFMs and main vessels are patent at 12 months.

Branch Patency:

In total, sixty nine (69) visceral branches were covered by the MFM in the whole STRATO cohort.

During the procedure, the decision has been made by the physicians not to cover the visceral branches for 4 patients.

Two (2) occluded branches were detected in 1 patient at 15 days. Distal thrombus were identified in the mesenteric artery and the common hepatic artery due likely to DIC (Disseminated Intravascular Coagulation) or non compliance to dual antiplatelet therapy. This induced mesenteric and splenic infarcts. This patient underwent surgical repair: thrombectomy with complete recovery of both branches patency. Nevertheless, aorto-mesenteric and aorto-hepatic bypasses were performed.

Branch Patency	12 months
Number of patients	n=20
Celiac Trunk Patency	92,9% (13/14)
Secondary Patency	100% (14/14)
Superior Mesenteric Artery Patency	93,8% (15/16)
Secondary Patency	100% (16/16)
Left Renal artery Patency	100% (13/13)
Right Renal Artery	100% (15/15)

Technical success

Definition:

Technical success is outlined with the adequate deployment of the device within the target location with main vessel and branch patency at the end of the procedure.

Technical success was achieved in all patients (23/23 (100%)).. Four (4) minor events were recorded related to device deployment with friction (1), inability to deploy a device (replaced) (1) and inadequate evaluation of the positioning requiring additional device (2).

Migration

Definition:

In the protocol, there was no specific definition for MFM migration used by the sites. Therefore, migration is commonly defined as proximal or distal movement of the device (≥10mm) relative to fixed anatomic landmarks. When available, the pre-discharge CT scan was used as the baseline (if not available, the 1-month CT scan was used).

No significant migration was reported for any of treated patient (i.e. migration resulting in endoleak, growth, or requiring secondary intervention).

Migration	1-3 months	6 months	12 months
Migration	0% (0/21)	0% (0/20)	0% (0/20)

A maximum of movement was measured within ~8mm.

Endoleak

Definition:

Only Type I (proximal and distal peri-stent endoleak, incomplete sealing) and III (inadequate overlapping of devices) endoleaks are taken in consideration with the multilayer flow modulator. Type II and IV endoleaks are not applicable to this device.

Endoleaks	Discharge-3 months	6 months	12 months
All Endoleaks (any and persistent)	**30,3% (7/23)**	**30% (6/20)**	**20% (4/20)**
Type I (Proximal)	**21,7% (5/23)[1]**	**20% (4/20)**	**20% (4/20)**
Type I (Distal)	**4,3% (1/23)[2]**	**5% (1/20)**	**0% (0/20)**
Type III (Mis-overlapping)	**4,3% (1/23)[3]**	**5% (1/20)**	**0% (0/20)**

All the endoleaks (n=7 in total) were identified between hospital discharge and 3 months.

[1] The five (5) **proximal type I endoleaks** are related to inadequate positioning of the device at the proximal critical landing zone of the arch as the protocol does allow strictly to deploy the device below the subclavian. The 2 patients underwent a secondary endovascular repair: first patient at 97 days (cuff stent-graft extension) and at 200 days (subclavian artery embolization) and second patient at 474 days (after 12 month follow up) with recovery. Secondary procedure is required, preventively, for the other three (3) asymptomatic patients.

[2] For the (1) patient with **distal type I endoleak**, positioning was technically complex because of previous bifurcated aorto-iliac graft with short neck. The distal positioning into the graft was not possible due to the acute angulation at the anastomosis between the graft and the abdominal aorta. At 96 days, a secondary procedure with additional MFM extension was not correctly overlapped.

[3] Short overlapping resulted in **Type III endoleak** for one (1) patient. Secondary endovascular procedure with additional MFM was performed at 350 days.

*Device Integrity**Definition:*

Device integrity is defined as any loss of device functionality, fracture or kinking

Device Integrity	1-3 months	6 months	12 months
Fracture	**0% (0/22)**	**0% (0/20)**	**0% (0/20)**
Kinking	**0% (0/22)**	**0% (0/20)**	**0% (0/20)**
All Device integrity findings	**0% (0/22)**	**0% (0/20)**	**0% (0/20)**

Change in aneurysm size

Definition:

Change in aneurysm size is defined as a variation in average maximum aneurysm diameter (>10mm/year at 6 months (>5mm) and 12 months (>10mm) follow-up and is based on discharge imaging. When discharge imaging was not available, 1-month imaging was used as baseline (in the absence of, pre imaging).

Additionally, the total volume, thrombus and flow volume were measured using evolution of the ratio Aneurysmal Flow Volume / Total Volume and the ratio Thrombus Volume / Total Volume as indicators.

Change in Size	**Baseline**	**6 months**	**12 months**
Maximal Diameter[1] (mean (range) (nb patients))	**6,8mm (5,3 – 8,1mm) (N=21)**	**7,0mm (4,9 – 9,0mm) (N=19)**	**7,2mm (5,4 – 9,0mm) (N=20)**
Increase (>10mm/year)	**-**	**21% (4/19)**	**10% (2/20)[2]**
Stable (<10mm/year)	**-**	**74% (14/19)**	**90% (18/20)**
Decrease (>10mm/year)	**-**	**5% (1/19)**	**0% (0/20)**
Aneurysmal Flow Volume / Total Volume (% / range (nb patients)[1]	**16,3% (2,2 - 42,9%) (N=19)**	**12,1% (0 - 31,1%) (N=18)**	**10,1% (0 - 31,7%) (N=17)**
Thrombus Volume / Total Volume (% (range) (nb patients))[1]	**43,9% (17,1 - 80%) (N=19)**	**53,2% (39,9 - 78,4%) (N=18)**	**55,2% (37,9 - 79,4%) (N=17)**

[1] Using Osirix software, the Total volume of the aneurysmal zone is measured at each follow-up time point. The maximum diameter is calculated based on the maximum surface which is computed from the volume.

The total flow volume and the MFM volume are also measured. Thrombus volume is calculated by subtracting the Flow volume to the Total Volume. Aneurismal Flow Volume is calculated by subtracting the MFM volume to the Flow volume.

[2] Aneurysm diameter expansion reported at 12 months represents (10%, 2/20 patients). Both patients with aneurysm enlargement had proximal type I endoleaks; one patient underwent a secondary endovascular procedure after 12 month follow-up (474 days). None was converted

to surgery. The remaining patient with aneurysm expansion was not treated and had no directly attributable outcomes during their time in the trial.[2]

Aneurysm Rupture

No aneurysm rupture was reported within the 12 months follow-up timeframe as shown

Rupture	1 month	6 months	12 months
Aneurysm Rupture	0% (0/22)	0% (0/22)	0% (0/21)

Re-interventions (Endovascular / Surgery)

Five (5) patients underwent at least one re-intervention within 12 months subsequent to the initial aneurysm repair with the MFM: Five (5) were secondary endovascular interventions and one (1) was surgical.

Re-intervention	1 month	6 months	12 months
Endoleak Type I	**0% (0/22)**	**10% (2/20)[1]**	**10% (2/20)[2]**
Endoleak Type III	**0% (0/22)**	**0% (0/20)**	**5% (1/20)[3]**
Total Endovascular re-intervention	**0% (0/22)**	**10% (2/20)**	**15% (3/20)**
Conversion to Surgery:	**4,5% (1/22)**	**0% (0/20)**	**0% (0/21)**
Branch Occlusion	**4,5% (1/22)[4]**	**0% (0/20)**	**0% (0/21)**

[1] One patient underwent stent-graft extension (97 days). The other patient underwent secondary procedure with MFM (96 days).

[2] The patient with the stent-graft extension (see [1]) had persistent type I endoleak and underwent subclavian embolization (200 days) to fully treat the endoleak. The other patient had successful secondary endovascular procedure with MFM (474 days).

[3] due to short overlapping; the patient was successfully treated with deployment of additional MFM bridging the mesh lacking (350 days).

[4] Due to distal thrombi in SMA and common hepatic artery; the patient underwent thrombectomy with complete recovery of SMA and common hepatic artery patency. However, aorto-mesenteric and aorto-hepatic bypass was also performed.

Supplemental Acute Procedural Data

The acute procedural data for STRATO subjects and comparison with data from *the Report of HAS ("Haute Autorité de la Santé" – Health High Authority in France) for Fenestrated/multibranched endoprothesis in the treatment of complex aortic aneurysms (October 2008)*.

Acute Procedural Data	**STRATO**	**HAS Report** **(Fenestrated endoprosthesis)**
Average Deployment time (min)	**5 min**	**-**
Duration of Procedure (min) (mean (range))	**< 84 min** **(45-125min - n=19)**	**237 min** **(85-600, 6 studies)**
Duration of Fluoroscopy (min) (mean (range))	**14 min** **(5-30min, n=21)**	**60 mn** **(5-117min, 7 studies)**
Contrast Volume (ml) (mean (range))	**129 ml** **(50-300ml, n=21)**	**199 ml** **(9-400ml, 9 studies)**
Overall Hospital Stay (days) (mean (range))	**8 days**[1] **(2-23 days, n=23)**	**7 days** **(2-90 days, 6 studies)**

[1] The overall hospital stay was about 8 days as recommended by the protocol because patients were all high risk for their previous medical history and the device is new for this indication. Only 3 patients stayed at the hospital for complications (1 iliac rupture, 1 hypotension, 1 with coagulation complication).

The treatment of aneurysm with the MFM requires local anesthesia. The average hospitalization stay is 3 days.

CASES SERIES

Cases series

A series of 5 patients were operated on in HIS (HOPITEAU IRIS AU SUD) at Bruxelles starting the beginning of this year

Demographic data

	Case 1	Case2	Case3	Case4	Case5
AGE	**70 years**	**71 years**	**64 years**	**76 years**	**62 years**
GENDER	**female**	**male**	**male**	**male**	**male**
SMOKING	**NO**	**YES**	**NO**	**NO**	**YES**
CAD	**NO**	**NO**	**NO**	**NO**	**NO**
CHF	**NO**	**NO**	**NO**	**NO**	**NO**
MI	**NO**	**NO**	**NO**	**NO**	**NO**
HYPERTENSION	**NO**	**NO**	**YES**	**NO**	**NO**
HYPERLIPIDEMIA	**NO**	**NO**	**YES**	**NO**	**NO**
DM	**NO**	**NO**	**NO**	**NO**	**NO**
CVS	**NO**	**NO**	**NO**	**NO**	**NO**
RENAL INSUFFICENCY	**YES**	**NO**	**NO**	**NO**	**NO**
PAD	**NO**	**NO**	**NO**	**NO**	**NO**

Aneurysm morphology

	Case 1	Case2	Case3	Case4	Case5
classification	**Crawford I**	**Crawford IV**	**DTAA type A**	**Crawford IV**	**Crawford IV**
type	**fusiform**	**fusiform**	**saccular**	**fusiform**	**saccular**
Maximal diameter	**53.5mm**	**53.5mm**	**60mm**	**59mm**	**70mm**
Diameter 2 cm above aneurysm	**44.7mm**	**23 mm**	**29.7mm**	**33mm**	**25mm**
Diameter 2 cm below aneurysm	**38.5mm**	**35mm**	**NA**	**24mm**	**22mm**
Diameter of RT CIA	**7mm**	**7.7mm**	**8mm**	**7.7mm**	**9.2mm**
Diameter of LT CIA	**7mm**	**7.5mm**	**9mm**	**7.8mm**	**9mm**

Branch patency	Case1	Case 2	Case 3	Case 4	Case5
Brachiocephalic trunk	PATENT	PATENT	PATENT	PATENT	PATENT
Left carotid artery	PATENT	PATENT	PATENT	PATENT	PATENT
Left subclavian artery	PATENT	PATENT	PATENT	PATENT	PATENT
Intercostals branches	PATENT	PATENT	PATENT	PATENT	PATENT
Celiac trunk	PATENT	PATENT	PATENT	PATENT	PATENT
Renal arteries	PATENT	PATENT	PATENT	PATENT	PATENT
SMA	PATENT	PATENT	PATENT	PATENT	>70% STENOSIS
IMA	PATENT	PATENT	PATENT	PATENT	PATENT
Rt CIA	PATENT	PATENT	PATENT	PATENT	PATENT
Lt CIA	PATENT	PATENT	PATENT	PATENT	PATENT
BRANCH TREATMENT	NO	NO	NO	NO	YES

IN CASE 5 ,PTA & STENTING WAS DONE 25 DAYS PRIOR TO AORTIC TREATMENT.

INTRA-OPERATIVE OUTCOMES

Item	Case 1	Case 2	Case3	Case4	Case5
Fluoroscopic exposure	**20 min**	**15min**	**15min**	**13min**	**10min**
Contrast used	**125ml**	**180ml**	**150ml**	**120ml**	**150ml**
Estimated blood loss	**100ml**	**100ml**	**150ml**	**150ml**	**100ml**
Anaesthesia	**GA**	**GA**	**GA**	**GA**	**GA**
Arterial access	**Cutdown Rt femoral artery**	**Cutdown Rt iliac artery**	**Cutdown Rt femoral artery**	**Cutdown both femoral arteries**	**Cutdown Rt iliac artery**
Landing zone	**suitable**	**Suitable**	**suitable**	**suitable**	**suitable**

Device deployment details

Deployment duration per single device MFM lasts 2.5-3.5 min

	Case1	Case2	Case3	Case4	Case5
MFM deployed	**1**	**1**	**1**	**2**	**2**
Injury to access vessel	**no**	**No**	**no**	**no**	**no**
Successful deployment	**yes**	**yes**	**yes**	**yes**	**yes**
Post deployment dilatation	**no**	**yes**	**no**	**yes**	**yes**
Post deployment aneurismal flow	**No change**	**Less flow**	**No flow at all**	**No change**	**Less flow**
Branches within target landing zone	**intercostals**	**Celiac trunk,SMA,IMA, Renals,iliacs**	**Lt subclavian, coliac trunk**	**Celiac trunk, SMA,IMA, RENALS**	**Celiac trunk, SMA,RENALS**
Device in target location	**yes**	**yes**	**yes**	**yes**	**yes**
Twisting,kinking	**no**	**No**	**no**	**no**	**no**
Integrity loss	**no**	**No**	**no**	**no**	**no**
Wall apposition	**complete**	**complete**	**complete**	**complete**	**complete**
Access closure	**sutures**	**sutures**	**sutures**	**sutures**	**sutures**

Discharge and follow up

Cases were discharged in a period of 7-11 days postoperatively on plavix 75 mg

Till now available a 3 months follow up showing no complications,complete branch patency,and no change in aneurysms diameters was observed

Case1

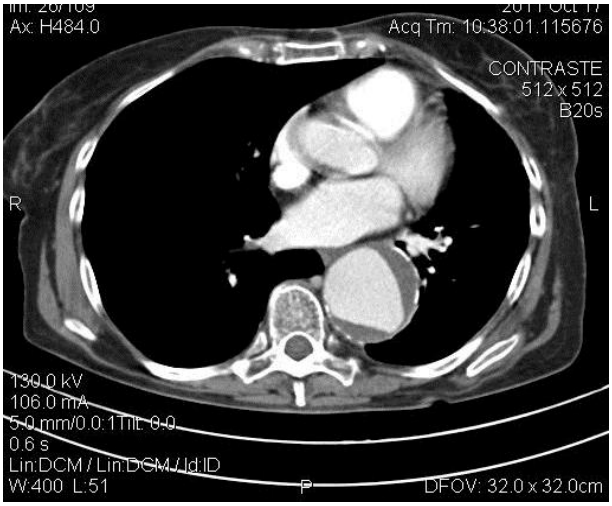


fig.(43) TAAA Crawford I pre-stenting

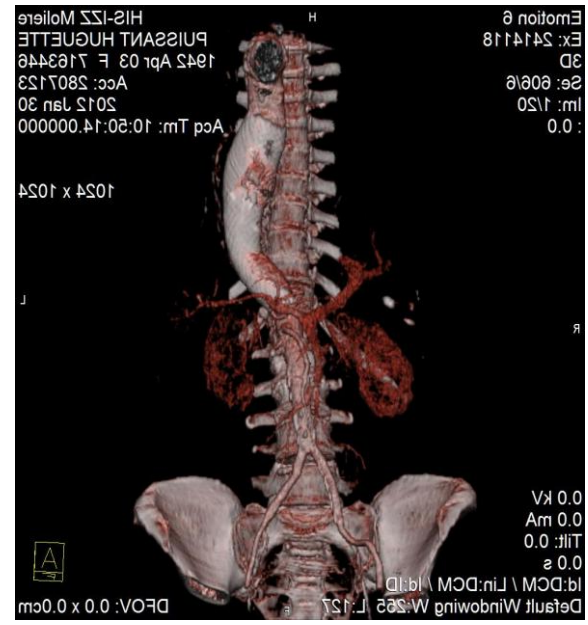


fig.(44) TAAA Crawford I POST-STENTING (3D RECONSTRUCTION)

Case 2

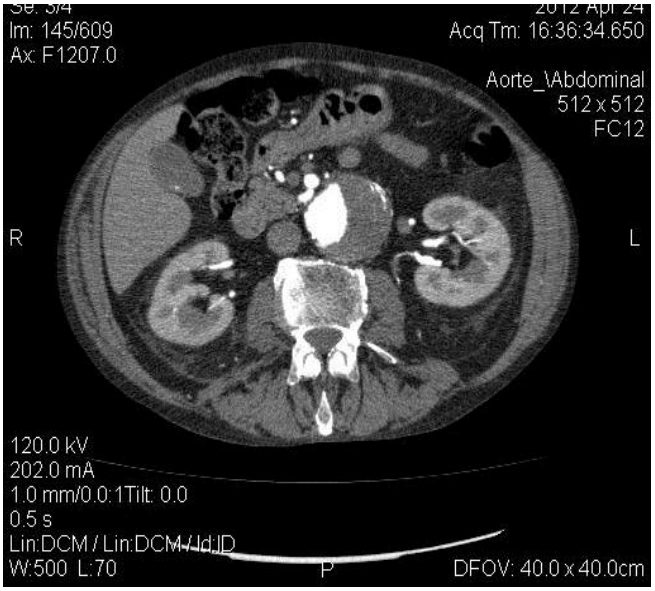


fig.(45) TAAA Crawford IV pre-stenting

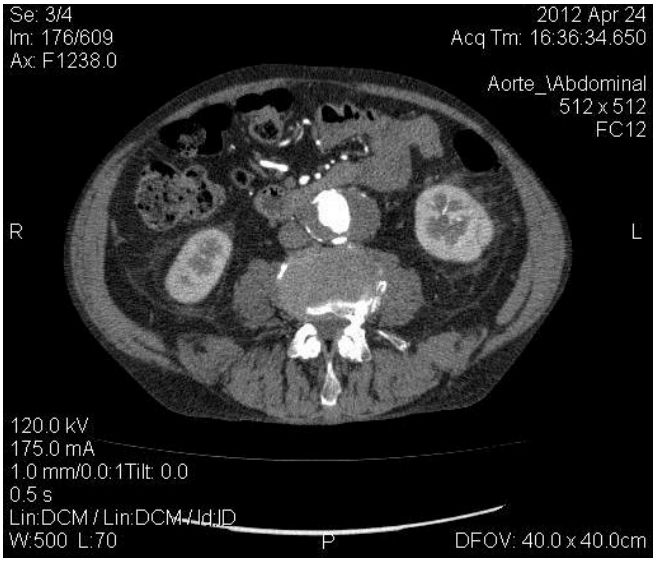


fig.(46) TAAA Crawford IV pre-stenting & PATENT SMA

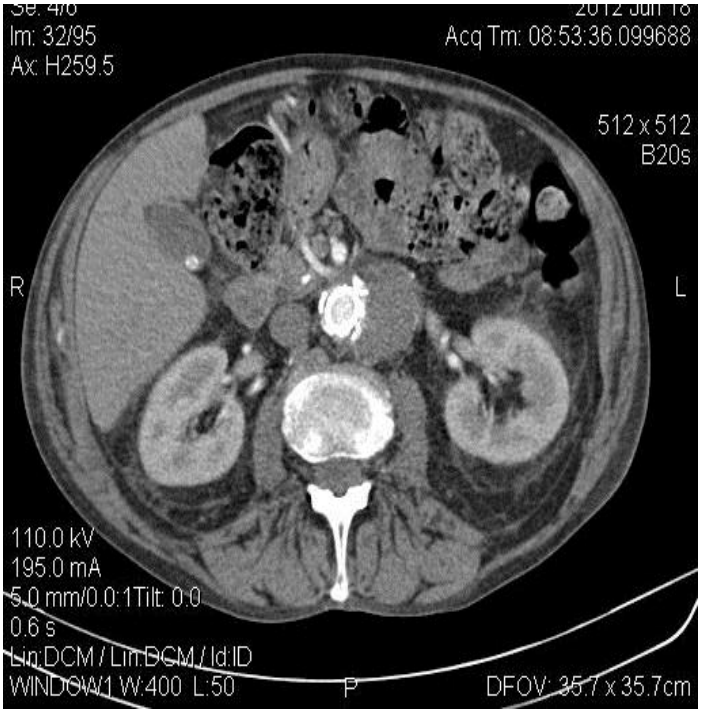


fig.(47) TAAA Crawford IV POST-STENTING & PATENT SMA

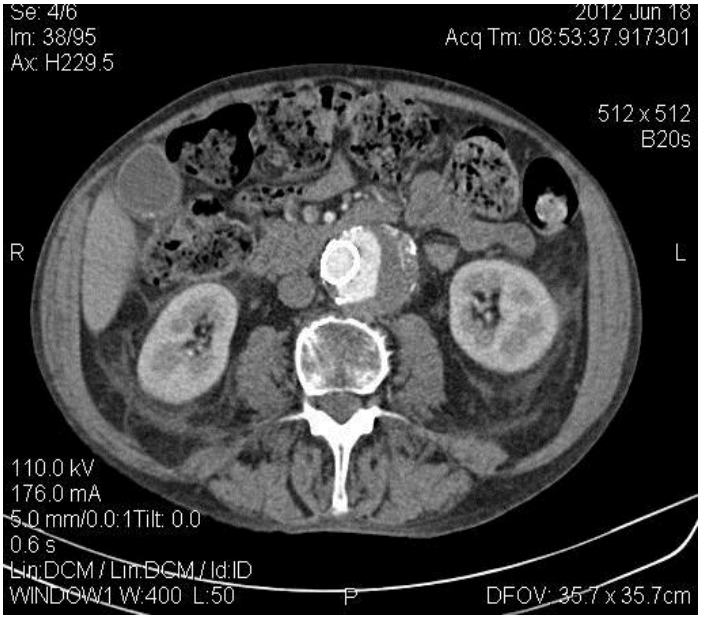


fig.(48) TAAA Crawford IV POST-STENTING & PATENT SMA

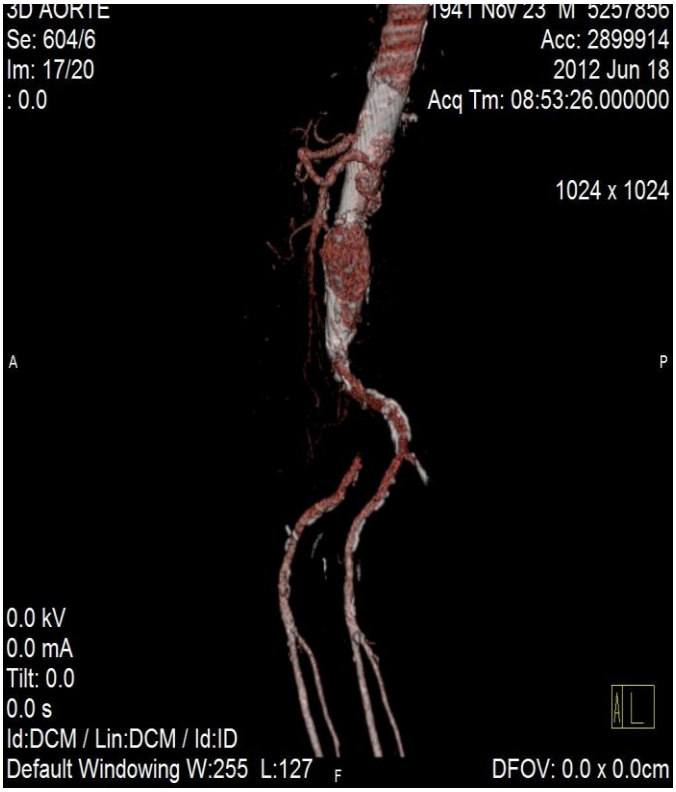
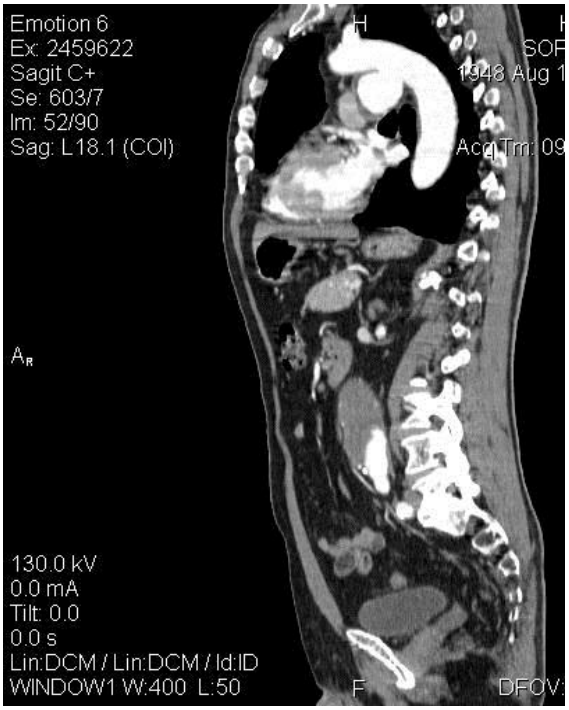
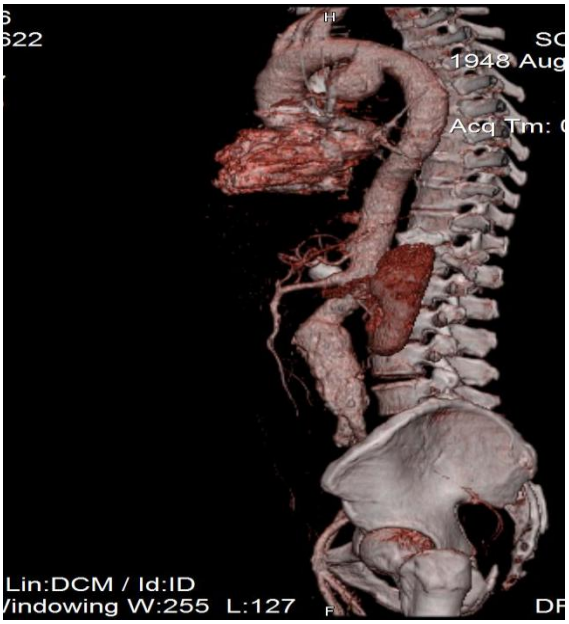


fig.(49) TAAA Crawford IV POST-STENTING & PATENT SMA (3D RECONSTRUCTION)

Case 3



Fig(50) DTAA PRE-STENTING



Fig(51) DTAA PRE-STENTING (3D RECONSTRUCTION)

Case 4

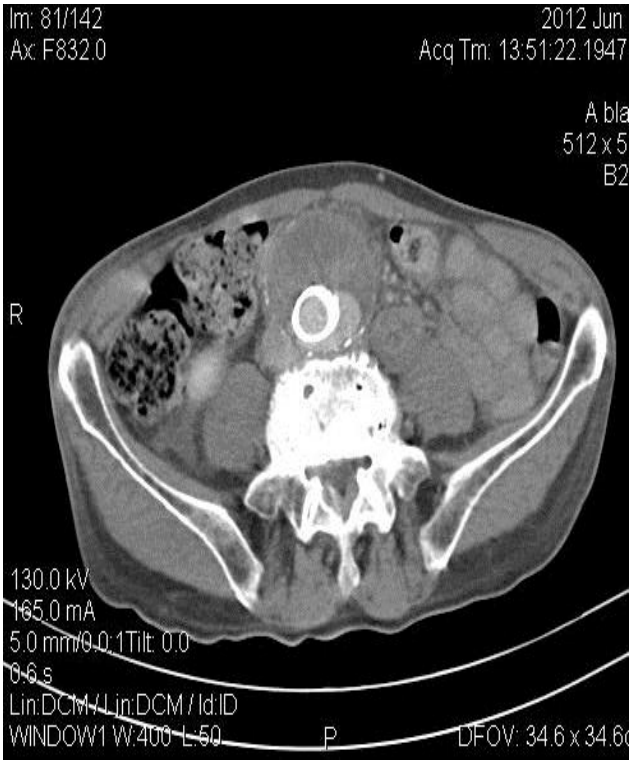


Fig.(52)TAAA Crawford IV POST-STENTING

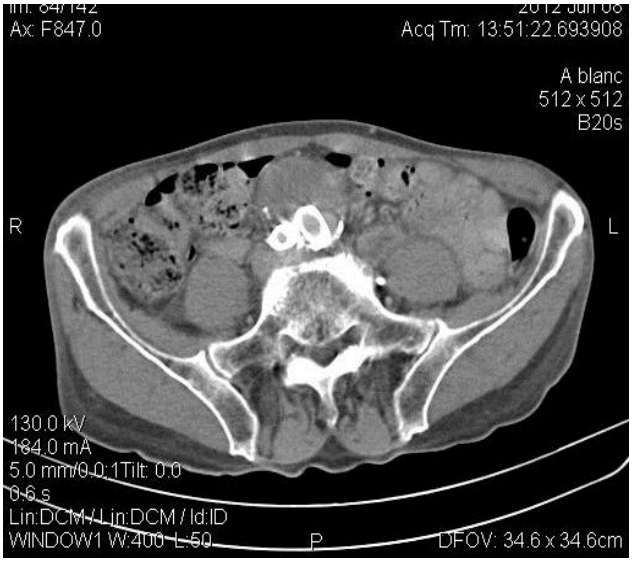


Fig.(53)TAAA Crawford IV POST-STENTING & THE STENT IS EXTENDING INTO ILIAC BIFURCATION

Case 5

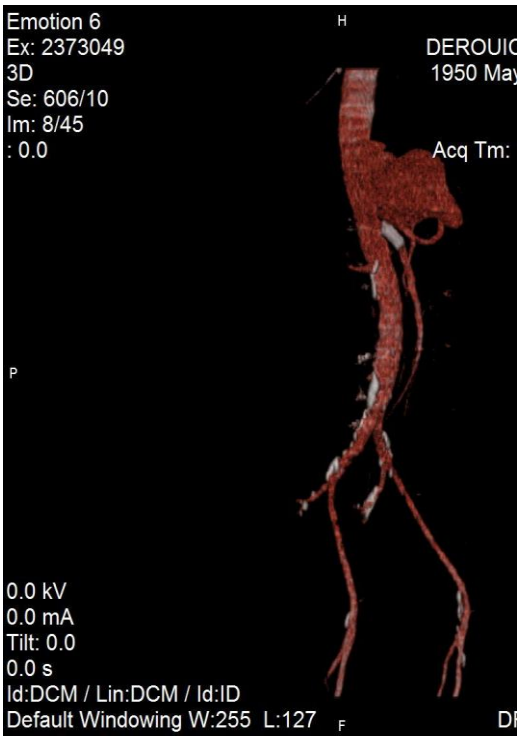


Fig.(54) TAAA Crawford IV AND STENTED SMA PRIOR TO AORTIC INTERVENTION (3D RECONSTRUCTION)

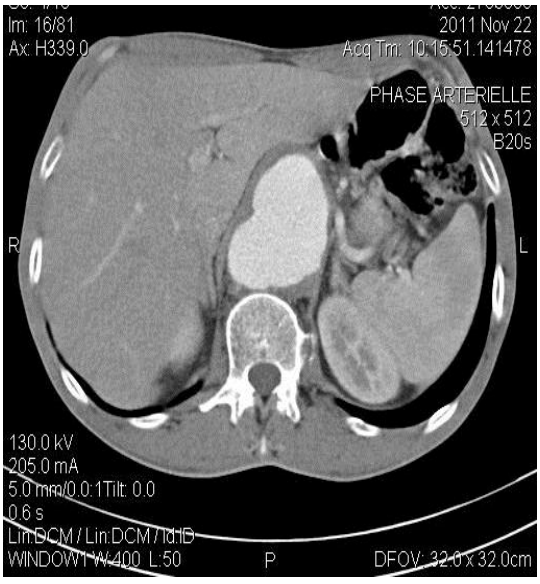


Fig.(55) TAAA Crawford IV PRIOR TO AORTIC INTERVENTION

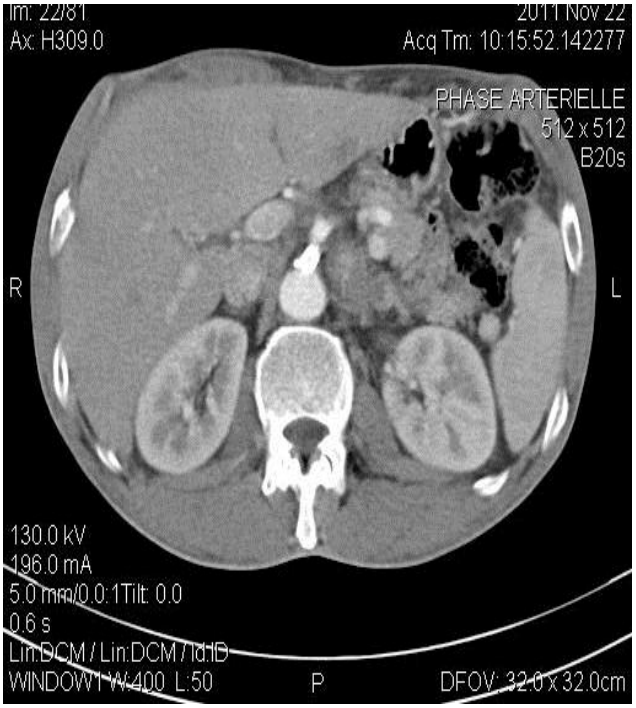


Fig.(56) TAAA Crawford IV AND STENTED SMA PRIOR TO AORTIC INTERVENTION

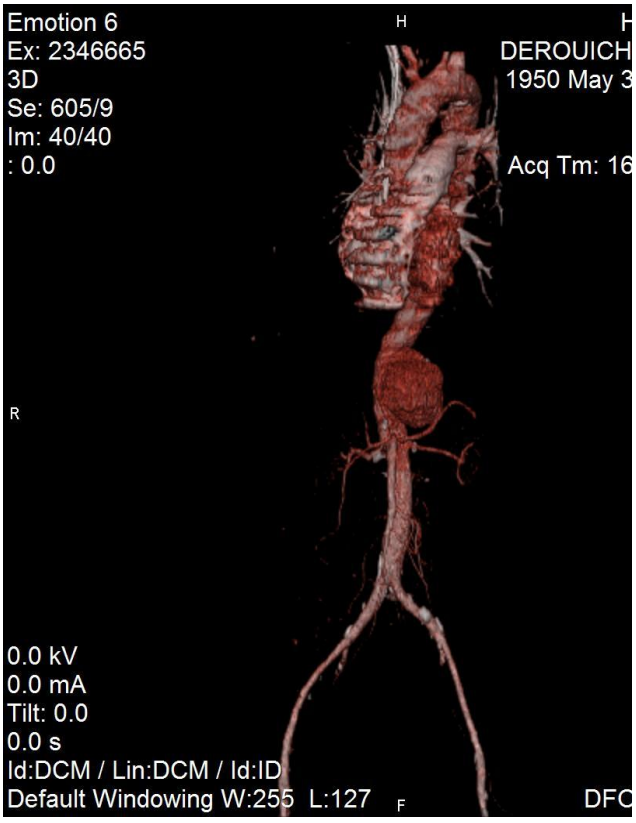


fig.(57) TAAA Crawford IV PRIOR TO AORTIC INTERVENTION (3D RECONSTRUCTION)

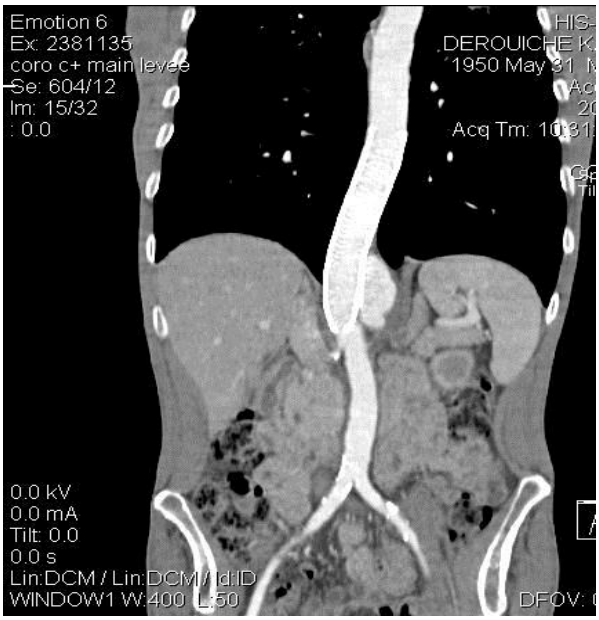


Fig.(58) TAAA Crawford IV POST AORTIC INTERVENTION (STENTING)

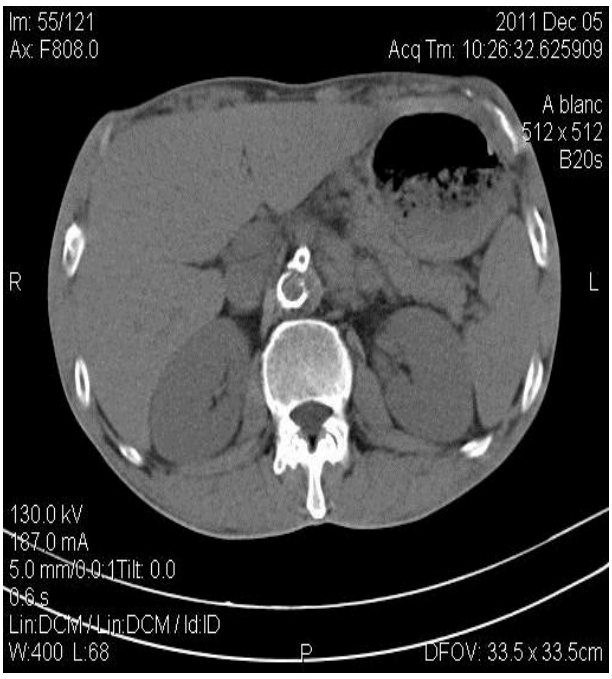


Fig.(59) TAAA Crawford IV POST AORTIC INTERVENTION (STENTING) & PATENT STENTED SMA

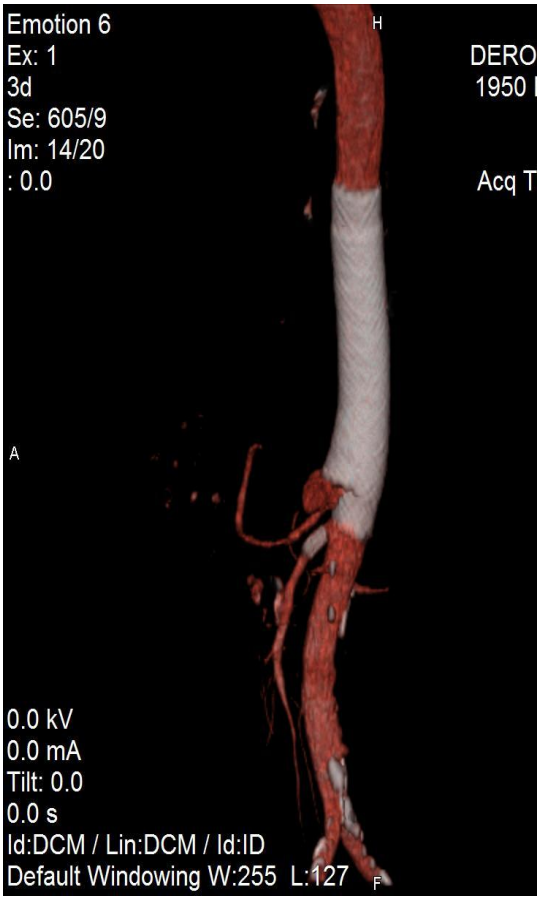


Fig.(60) TAAA Crawford IV POST AORTIC INTERVENTION (STENTING) & PATENT STENTED SMA (3D RECONSTRUCTION)

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