# Blood Flow in Distal End-to-side Anastomoses with PTFE, Numerical and experimental study of blood flow through a patient-specific arteriovenous fistula, Computer aided design and fabrication of models for in vitro studies &Research

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**Abstract-Background: Experimental modeling of arteriovenous hemodialysis fistula (AVF) hemodynamics is challenging. Mathematical modeling struggles to accurately represent the capillary bed and venous circulation. In vivo animal models are expensive and labor intensive. We hypothesized that an in vitro, physiologic model of the extremity arteriovenous circulation with provisions for AVF and distal revascularization and interval ligation (DRIL) configurations could be created as a platform for hemodynamic modeling and testing. non-physiological flow behaviour plays a significant role in the development of distal anastomotic intimal hyperplasia. To investigate flow patterns in four anastomotic types of femoral end-to-side distal bypass graft anastomoses, a flow visualisation study was performed. Arteriovenous fistula (AVF) pathologies related to blood flow necessitate valid calculation tools for local velocity and wall shear stress determination to overcome the clinical diagnostic limits. To illustrate this issue, a reconstructed patient-specific AVF was investigated, using computational fluid dynamics (CFDs) and particle image velocimetry (PIV). The aim of this study was to validate the methodology from medical images to numerical simulations of an AVF by comparing numerical and experimental dataAn integrated computer aided design/computer aided manufacture system has been used to model the complex geometry of blood vessel anastomoses. Computer models are first constructed with key dimensions derived from radiological images of bypass grafts, and from casts of actual blood vessel anastomoses. Physical models are then fabricated in one of two ways: the surface geometry data can be used to control the movement of a three-axis milling machine; alternatively, the same data can be exported in a form that can be interpreted by a stereolithography apparatus. Simulation allows surgical trainees to acquire surgical skills in a safe environment. With the aim of reducing the use of animal experimentation, different alternative nonliving models have been pursued. However, one of the main disadvantages of these nonliving models has been the absence of arterial flow, pulsation, and the ability to integrate both during a procedure on a blood vessel. In the present report, we have introduced a microvascular surgery simulation training model that uses a fiscally responsible and replicable pulsatile flow system.**

## 1. INTRODUCTION

As arteriovenous fistulas (AVFs) have become the preferred modality for hemodialysis access, the understanding of the hemodynamics that underlie their encompassing problems lacks clarity. From a fluid dynamics perspective, little is known as to why AVF creation is successful for some patients, while others require additional procedures. In particular, the understanding of the hemodynamics associated with access-related ischemia is incompletely understood. Distalrevascularization and interval ligation (DRIL)is among one of the corrective procedures improving distal ischemia; however, its underlying hemodynamics are unclear. Our goal was to create an in vitro model because of its advantages over expensive, not easily reproducible animal models.(1)In the last 25 years of vascular graft research, it has beenwidely confirmed that local haemodynamics play a significant role in the development of intimal hyperplasia. In mostlocations, the blood flow in thearteries is laminar. However, when there is anabruptchange in the vessel diameter and angle, as at distalend-to-side anastomosis, flow separation, recirculationand flow stagnation occur. In these areas thehaemodynamic forces are thought to be correlated with the development of intimal hyperplasia, which is an important cause of late graft failure. Furthermore, the geometrical shape of the bypass configuration may play a role in the development and progression of the disease process intimal hyperplasia isreported to occur mainly at the heel and the toe of the anastomosis, on the floor of the artery and at the suture lines.(2)End Stage Renal Disease (ESRD) corresponds to the ultimate loss of the kidneys' ability to perform their main functions, i.e. to eliminate excess fluid and waste material from the blood. The most common treatment (about 1.3 million patients worldwide) is hemodialysis, which purifies the blood through an extracorporeal artificial kidney (dialyzer), with a mean flow rate of at least 300 ml min-1. The puncture and reinjection sites are located on a peripheral vein that is surgically connected to an artery. This arteriovenous fistula (AVF) is usually located in the arm . After creating the AVF, blood flow rate slowly progresses and reaches an average of 1200 ml min−1 after maturation(3) With advances in computer aided design/computer aided manufacture (CAD/CAM ) and rapid prototyping techniques, the design and fabrication of complex vascular models can be more easily and reliably accomplished. For example, Friedman et al. Described the fabrication of a scaled model of an aortic bifurcation from magnetic resonance imaging (MRI) scans. Because of the ease with which the geometrical parameters can be controlled reliably and accurately, consistent models canbe produced for parametric studies. The teaching of microsurgical procedures represents a key step in several surgical specialty training programs. Practical learning of such procedures becomesdifficult if kept only within the scope of the operating room.1-7 This is especially true in the treatment of vascular disease, because, owing to the development of new technologies for endovascular therapy, a clear trend toward the use of endovascular therapy has emerged worldwide. This increasing trend has resulted in a scenario in which open surgical procedures are performed less frequently and, in general, have been confined to patients with severe cerebrovascular disease who require surgery by experienced neurosurgeons. This has drastically reduced the possibility of interns or surgery trainees to acquire the necessary skills for the neurosurgical treatment of vascular disease. Therefore future complex surgical procedures that require open techniques will have fewer surgeons qualified to perform them. One possible solution to ameliorate this issue is to train interns using microvascular surgery simulators. Different types of simulators are available, each with its own advantages and disadvantages. The most suitable model forsurgical simulation suggested by the reported data has been the in vivo model(5)

## MATERIALS AND METHODS

Material properties. For the consideration of the materials of the physical model of the arm vasculature, the resistance and compliance of the vessels needs to be takeninto consideration. To capture the equivalent resistance of the vessels, Poiseuille's law was applied. The resistance, R, for laminar, steady-state flow through a tube: R ¼ 128mLp/D4 , where m is the viscosity of the fluid, L is the length of an isolated diameter, D, of tubing.6 By examining Poiseuille's law, which represents vascular resistance in its simplest form, we extract physical parameters that potentially have the largest impact on vascular resistance. Therefore, it was important to emulate the equivalent length and diameter (the governing parameter to laminar resistance), by matching these values to average anatomic values found through a literature search.(1)

Transparent polyester replicas of distal end-to-side graft anastomoses created by conventional techniques, In the described setting, reproducible flow patterns Miller-cuff, Taylor- and Linton-patch werefabricated for each type of anastomosis could be obtained. Conusing geometry data obtained from vascular grafts ventional, Linton- and Taylor-patch (CL&T), showed implanted into the femoral arteries of sheep. The ori-similar flow patterns, whereas the pattern in the Millerginal anastomoses were cast with polymer (Technovit ⍰ cuff show considerable differences. 7143) under arterial pressure. From this cast a silicon During the acceleration phase of early systole lamreplica (Wacker Elastosil⍰ M4440) wasmade and filled inar flow was observed along the hood of all graft with wax (NestlerParaffin 52). From this wax model anastomoses, with the main flow guided by the dea polyester cast was made to obtain the transparent clining anastomotic hood. Fig. 2 shows the situation replica for visualisation (Voss Chemie GTS, polyester atthe systolic maximum in the Miller-cuff (Re=100). casting resin). The model was then carefully cleaned Figs 3a to 3c show examples for different Reynolds and polished.(2)

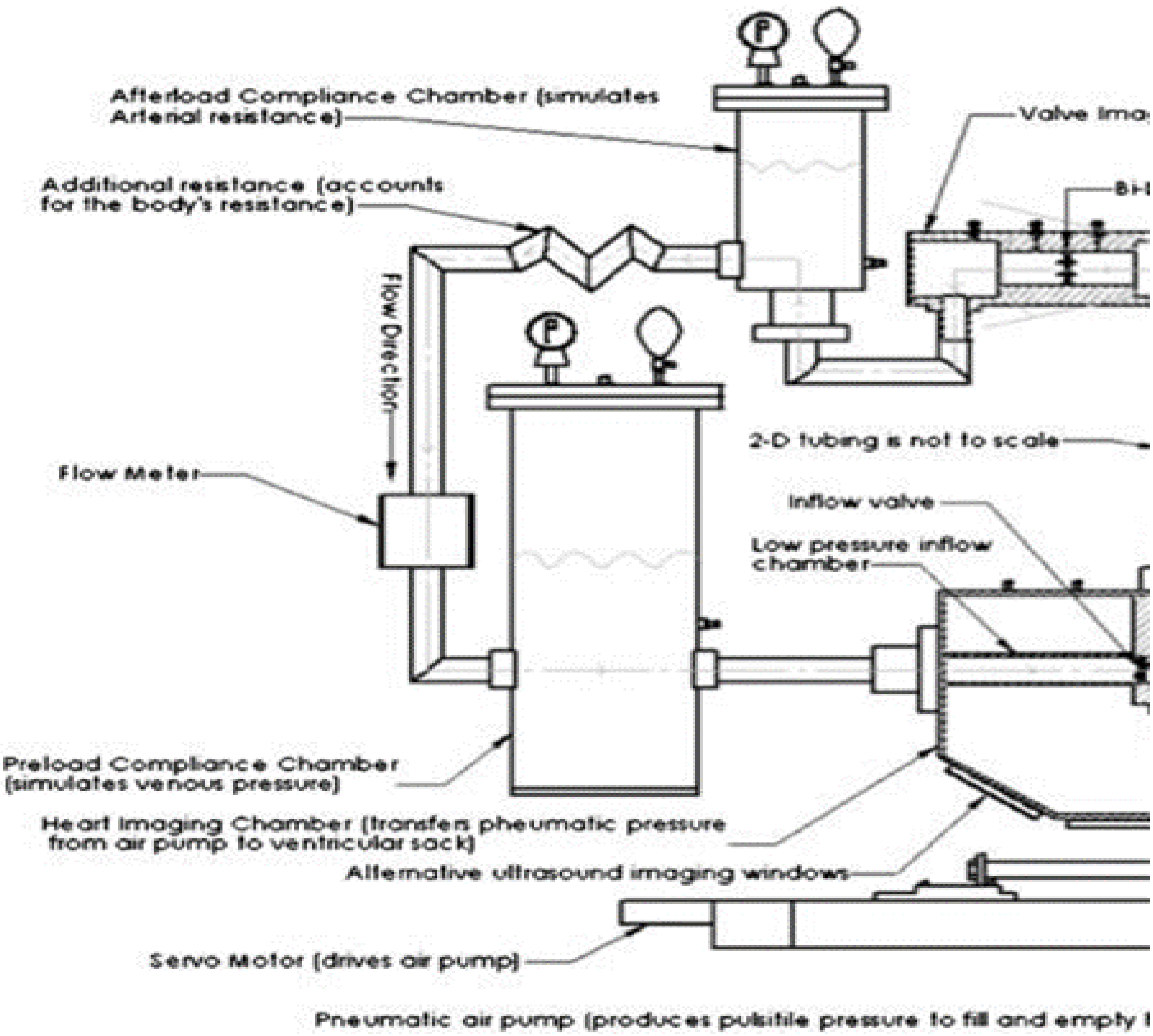
Relevant geometrical and physiological data The functional brachio-cephalic AVF geometry originates from a previous work by [18], where image acquisition, segmentation and reconstruction procedures were justified and detailed (Fig. 1). Our approach here is to compare the PIVvelocity vector results with two distinct numerical models. The same AVF geometry was thus transferred to CAD software (Solidworks®, version 2003, SP03) in order to produce the mold for the PIV experimentation. The physiological velocity waveform at the brachial artery was measured using colorflow Doppler ultrasound (CDU, Fig. 2). The velocity signal followed neither the classical waveform nor the magnitude found in arteries. This is commonly observed in AVF due to vein enlargement.(3)

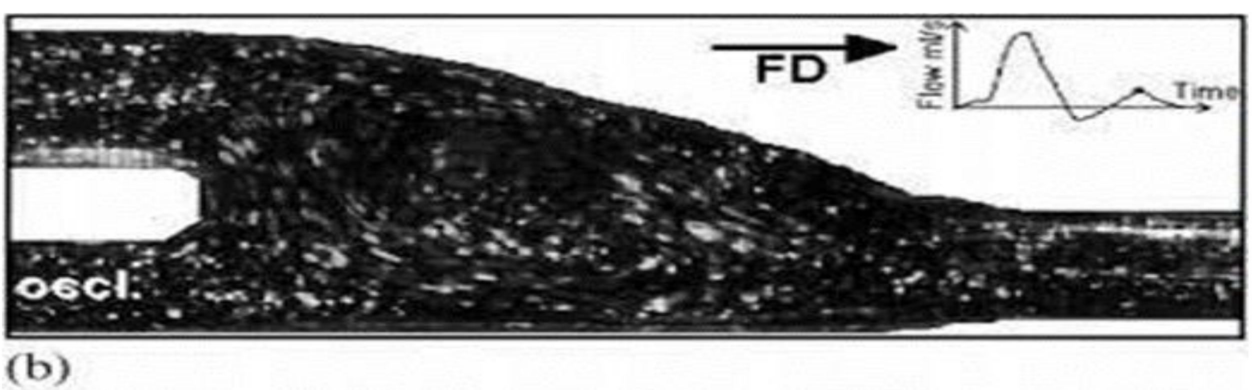
Computer aided design (CAD):-An integrated CAD/CAM system (DUCT5.3, DelcamInternational, Birmingham, UK ) is used to define the complex surface geometry of a range of vascular anastomosis models. As an aid to the modelling process, computer models can be manipulated interactively on the graphics screen and viewed from different perspectives. In addition, the surface of eachmodel can be rendered to help with visualization. Here, the surface geometry is defined by a network of rectangular or triangular ‘patches’. The software interpolates between the patch boundaries to produce a surface having the desired shape and geometry. The surface geometry of a complete model can be exported in the form of a triangle file to CAM or rapid prototyping systems where the information can be processed into a physical model.(4)

We included 30 placentas in the present study. Of the 30 placentas, 15 were used foraneurysm simulation and 15 for anastomosis simulation.19 The simulations in the present study were performed by neurosurgery senior residents with experience in cerebrovascular surgery, and the results were evaluated by 2 qualified vascular neurosurgeons. To create a replica of the microflow system, a 5e12-V submersible minipump was used. The pump was connected to a power electronic module (MOSFET [metal oxide silicon field effect transistor or metal oxide semiconductor field effect transistor] 30Aprogrammable time cycle delay trigger switch drive module) with a 5e36-V operating range. This module allowed forautomatic control of the active and inactive

keeping the water and glycerin in solution power cycles ranging from milliseconds to minutes. Also, it could be set to power on and off for 0.5 second and for unlimited cycles. Hence, the minipump could generate a pulsatilemicroflow. A 12e220-V power transformer was used as the power supply to allow for safe performance (Figure 1). A standard intravenous tube was adjusted to the pump outlet.(5)

Fluid viscosity. As stated in Poisuelle’s law and most other analytical models of fluidic resistance (such as Womersley’s Impedance Method), viscosity (m) is directly proportional to resistance. For an accurate analytical model to be produced, the viscosity of fluid in the system must match that of blood. There is substantial variation in physiological viscosities, but a glycerin/water mixture of an approximate40/60 ratio yields a viscosity of 3.5 centipoise (cp). Blood is a non-Newtonian fluid at high shear stresses due to its composition of erythrocytes, monocytes, platelets, and plasma; however, at low shear stress, the viscosity of blood can be approximated as 3.5 cp.12,13 The fluid mixture is composed of 2 liters of 99.9%vegetable-based glycerin and 3 liters of distilled water. The mixture was tested withcalibrated Cannon Size 50 and Size 100 viscometers, and it was found to yield a 3.43 cp mixture with 1.5% confidence interval. Prior to filling the model, the solution was agitated and the system was allowed to run for several minutes prior to collecting data to facility Schematic of Hemodynamic Simulator Pump (image credited to Matthew DeCapua; published with permission).(1)




(b)

Miller-cuff end-to-side anastomosis: Flow pattern at maximum systole at mean Re=100; V: vorte artery input of the fistula. The maximum velocity at the systole is 0.56 m s−1 and the minimum is 0.42 m s−1.
Pulse
x; FD: flow direction

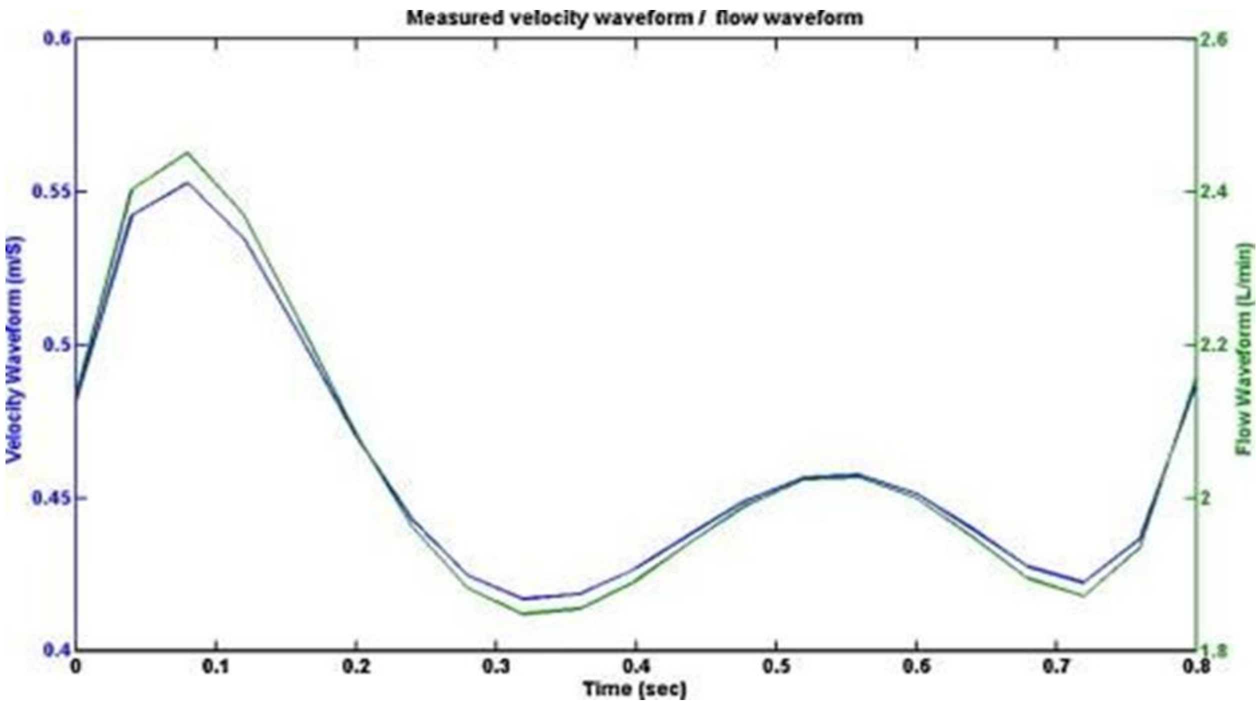



Fig:-The physiological mean velocity waveform measured with CDU at the radial frequency is 75 beats/min; radial artery diameter at this location is 8.73 mm. (b) Thecalculated input flow waveform.

MEASUREMENTS

Instantaneous flow rate was measured upstream and downstream of the fistula with electromagnetic flow meters (Gould Statham SP2202; accuracy within 10%). The same flow rate as the patient's flow rate was investigated. The period was equal to 0.8 s so that the frequency parameters ⸲ = r/ were Equal to 7.45 is the kinematic viscosity of the fluid and ω the angular frequency ω = 2/T, where T is the period and r is the radius of the tube. PIV measurements were carried out in two different planes (Fig. 3(b)) at the level of fistula using a double-pulsed mini Yag laser (NewWave, 120mJ) and a CCD camera PIV- CAM 10-30 (1000 × 1016 pixel resolution) from TSI Inc (Shoreview, MN, USA). The flow was seeded with 15–20 m nylon particles with the same density as the working fluid. The flow was illuminated by a 1 mm thick sheet of laser light. The PIV system was triggered by the pump signal. The measurements were carried out at 20 instants during the cycle and the time that elapsed between two successive instants was equal to 40 ms. The time that elapsed between two laser pulses was 100 s for the horizontal plane and 200 s for the vertical plane. Cross-correlation was performed to determine the displacement of the particles within a 50% overlapping interrogation window, 32 × 32 pixels in size, giving a spatial resolution of 2.28 mm × 2.28 mm and 2.53 mm × 2.53 mm for the horizontal and vertical planes, respectively. No post- processing smoothing function was required. To obtain good statistical convergence, 100 pairs of images were recorded at each moment. The average standard deviation was equal to 1.10% at all the instants investigated.

Numerical model(3)

Mesh generation As described in [18], AVF geometry was meshed using a Cooper algorithm implemented in Gambit® 2.3 with hexahedron cells and a boundary layer at the wall. We followed a methodological refinement approach, with respect to the artery, anastomosis and venous diameters. For the present study, we generated a large choice of grids, of which two are presented here (HEX-I with 80,000 cells) and (HEX-II with 350,000 cells). The first was defined according to the arterial cross-sectional inlet and the second according to thevenous cross-sectional outlet. The longitudinal edge node number was also increased from 90 to 120 along the venous side for HEXII. Finally, the internal distance of the first mesh adjacent to the boundary wall was 256 m for HEX-I and 175 m for HEX-II. Total average cell size dropped from 7.6

× 10−10 to 4.4 × 10−10 m3 for HEX-I and HEX-II, respectively.

CFD model The Navier–Stokes equations (momentum and continuity) are non-linear and time dependent. The Fluent package (6.2.16, Fluent Inc., Lebanon, NH, USA) solves these governing equations using the finite volume method, with classical schemes described in the Fluent Theory Manual. The solution obtained under steady conditions was used as an initialization for the unsteady simulations. Periodic steady state solutions were reached at the fifth period with a time step oft = 0.04 s (error within 0.6% compared to the fourth period). They are reported below. The blood was assumed to be a Newtonian fluid with characteristics identical to those used in the PIV experiments. This assumption is largely employed in the literature under these flow conditions. The vessel wall was considered to be rigid. The physiological velocity waveform was implemented at the artery inlet. The calculated physiological velocity waveform for an equivalent arterial diameter of 0.85 cm was also plotted (Fig. 2) for further use in mesh refinement studies. A straight cylindrical tube was extruded from the real venous outlet to avoid upstream perturbations. Its length was 10 times the hydraulic diameter of the venous outlet and a free outflow was set as a boundarycondition.

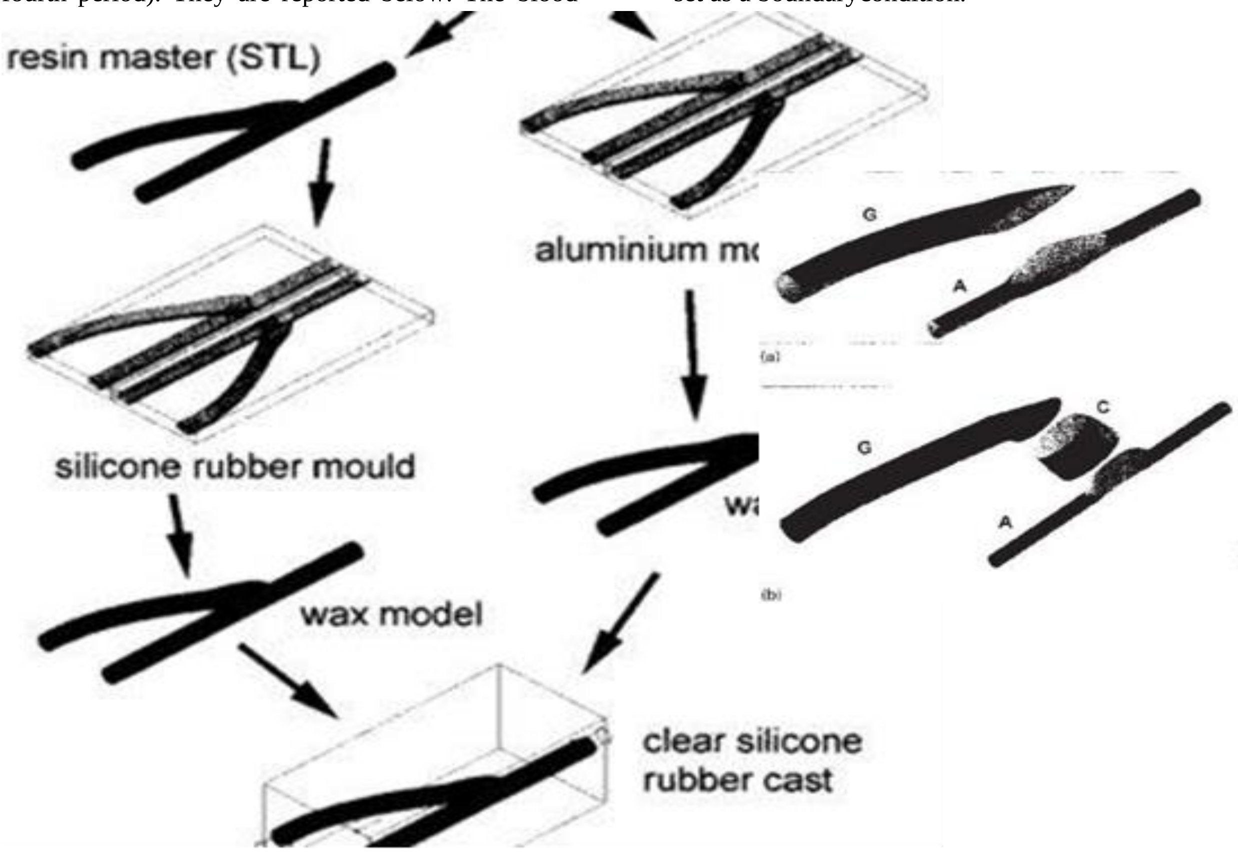



Fig:-Schematic diagram of vascular modelsproductionusing CAD/CAM techniques

Fig:-(a) Surface-rendered anastomosis model of 30° angle. The end section of the cylindrical graft G is modified to conform to the arteriotomy of the host artery A(b) Surface-rendered anastomosis model with a cuff C, using CAD/CAM techniques the graft G and the artery A

## DISCUSSION

In this study, we focused on the flow pattern in four types of currently used anastomoses. To obtain as natural geometrical conditions as possible, replicas of only a few used natural models with their inherent irregularities, and none compared all 4 types presented here Bassiounyet al.2 investigated an idealised model of a conventional end-to-side anastomosis. Like their experiments, our results of this graft type showed the vortex forming in early systole, its axial shift during the cardiac cycle and its breakdown in the diastolic phase. In another study of flow visualisation, da Silva et al.25 investigated the flow behaviour at the end-toside of the Miller-cuff anastomosis configuration using a flow pattern with a rather exponential decay during diastole. Despite this difference, the flow behaviour, the vortex forming in the middle of the anastomosis,its motion during the cardiac cycle, and even the duration in which the vortex remains standing between the diastolic phase and the early systole of the next wave pulse coincide with our findings.(2)as match-up criteria, we compared qualitatively the velocity vectors and quantitatively the velocity profiles acquired by both PIV and CFD. Since exact geometry was used in both, the challenges were to reproduce exact mold geometry, control the boundary condition set-up and correctlyregister the corresponding planes and lines. The PIV/CFD comparison allowed us to set- up an adequate numerical model. The complex flow characteristics were closely observed. This comparison increased the confidence levels of the consecutive physiopathological analysis. In the previous sections we particularized complex non-uniform hemodynamic flow in the AVF. Velocity vector cartography in both planes demonstrated a number of axial separation flows. They were of particular importance since they affected physical processes such as pressure and energy loss. Further analysis of their effect on AVF is now required on other fistula cases.(3)ACAD/CAM approach has been adopted in the fabrication of vascular models mainly because of the relative ease with which these techniques can produce a series of complex models precisely and consistently with dimensions that are within known tolerances. CAD model scan also be readily imported into other numerical analysis packages that model themechanical properties of the vessel wall, or computational fluid dynamics packages, for example, thus allowing comparison to bemade between experimental studies and numerical simulations the same anatomical model It has been proved that the road to expertise requires the deliberate practice ofa skill or task.20,21 Therefore, the main at required to learn, acquire, and maintain the necessary skills to perform microsurgeryis not natural talent but continuous training.3,22 However, unlike other skills and medical techniques, microsurgery can only be learned in a microsurgery laboratory. The use of a microsurgery laboratory is required for both operational and ethical reasons. Learning microsurgery should not result from mistakes made performing surgery in humans. However, learning without making mistakes is not possible in any discipline or field.3,17,23-25 Thus, simulators were developed as a potential solution to provide basic training in diverse skills, without risking the life of patients, by presenting situations similar to those that can occur in real life to allow for the management and reduction of mistakes. This artificial environment of simulation allows trainees to acquire critical experience without additional risk and allows trained surgeons to perform continuous training to maintain and refine their skills.(5)

## CONCLUSIONS

Through the construction and validation of an in vitro, pulsatile arteriovenous model, the intricate hemodynamics of AVF and treatments for ischemic steal can be studied. The findings of the AVF as a pressure sink and the relative role of IL with DR bypass has allowed this model to provide hemodynamic insight difficult or impossible to obtain in animal or human models. We observed: (1) the DR with or without IL maintains AVF flow rates unchanged from the native state; and (2) the DR bypass can be performed without IL to promote a higher flow rate through the bypass at a smaller sacrifice to distal flow and pressure. Further study of these phenomena with this model should allow for more effective AVF placement and maturation while personalizing treatment for associated ischemic steal.(1)vements of the stagnation point on the floor of the artery of similar magnitude and growth and collapse of the washout vortex within every cardiac cycle. Because of its wider cavity, the Miller-cuff shows lower shift of the bottom stagnation point, but a persistent wash out of the anastomotic cavity. These findings support the good clinical performance reported for this unconventionally shaped anastomosis type, which we therefore use for below-knee reconstructions, if adequate autologous venous grafts are not available.(2)In this study, as match-up criteria, we compared qualitatively the velocity vectors and quantitatively the velocity profiles acquired by both PIV and CFD. Since exact geometry was used in both, the challenges were to reproduce exact mold geometry, control the boundary condition set-up and correctlyregister the corresponding planes and lines. The PIV/CFD comparison allowed us to set- up an adequate numerical model. The complex flow characteristics were closely observed. This comparison increased the confidence levels of the consecutive physiopathological analysis. In the previous sections we particularized complex non-uniform hemodynamic flow in the AVF. Velocity vector cartography in both planes demonstrated a number of axial separation flows. They were of particular importance since they affected physical processes such as pressure and energy loss. Further analysis of their effect on AVF is now required on other fistula cases During a hemodialysis session, blood is pumped fromthe venous side of the AVF at a relatively high flow rate (350–500 ml min−1) to the dialyzer via an access needle, and then returns to the vessel using a second adjacent needle placed distally (3–5 cm). Frequently, a second needle is placed in a recirculation zone: some portion of the cleaned blood flow leaving the dialyzer outlet goes back to the dialyzer inlet without picking up toxins from the blood stream. This phenomenon is called access recirculation. The impact of access recirculation on the adequacy of dialysis has to do with the resulting decrease in efficiency of the hemodialysis session (i.e. the cumulative amount of toxins removed from the blood is dramatically lower than the expected values). This event cannot be immediately detected by nurses and several sessions may be completed under circumstances that could lead to life- threatening problems. As an immediatetreatment the needle will be blindly relocated. If clinicians were provided in advance with the recirculation zones they could avoid them and thus reduce the number of needle stick injuries in patients (3) CAD/CAM techniques can be used to reproduce the complex geometry of anastomoses for vascular studies. When coupled with studies in which had verse biological responses are monitored under equally well controlled flow conditions in vivo, physical modelling techniques may well reveal what improvements should be made to current designs of vascularprosthesis and may help vascular surgeons decide what anastomosis configurations should be adopted for a particular arterialbypass procedure.(4)We have provided a step-by-step guide for the assembly of a replicable and inexpensive pulsatile flow system and its use in placentas for the simulation of, and training in, different types of anastomoses and intracranial aneurysms surgery.(5)

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## REFERENCES

In vitro hemodynamic model of the armarteriovenous circulation to study hemodynamics of native arteriovenous fistula and the distal revascularization and interval ligation procedure NicoleVarble, MS,a Steven Day, PhD,a Daniel Phillips, PhD,b Doran Mix, BS,c Karl Schwarz, MD,d Karl A. Illig, MD,e and Ankur Chandra, MD,c Rochester, NY; and Tampa, Fla

1) Blood Flow in Distal End-to-side Anastomoses with PTFE and a Venous Patch: Results of an in vitro Flow Visualisation Study∗ N. Noori1, R. Scherer1, K. Perktold2, M. Czerny1, G. Karner2, W. Trubel†1, P. Polterauer1 and H. Schima1
2) Numerical and experimental study of blood flow

through a patient-specific arteriovenous fistula used for hemodialysis ZaherKharboutlya, Valerie Deplano b, Eric Bertrandb, Cecile Legallais

3) Computer aided design and fabrication of models for in vitro studies of vascularfluid dynamics C K Chong, C S Rowe, S Sivanesan, A Rattray, R A Black, A P Shortland and T V How* Department of Clinical Engineering, University ofLiverpool, UK
4) Novel Simulation Model with Pulsatile Flow System for Microvascular Training,Research, and Improving Patient Surgical Outcomes Federico Carlos Gallardo1, Jorge Luis Bustamante1,2, Clara Martin1, Cristian Marcelo Orellana1, Mauricio Rojas Caviglia1, Guillermo Garcia Oriola3, Agustin Ignacio Diaz1, Pablo Augusto Rubino1, VicentQuilis Quesada3.