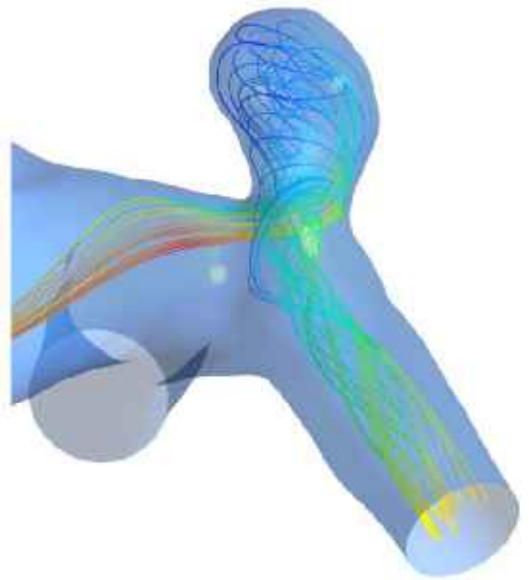
aneurIST
Integrated biomedical informatics for the management of cerebral aneurysms

IDAC



Computer Modelling of Flow, Shape and Tissue Stress/Strain in Intracranial Aneurysm

Alberto Marzo, Derek Sweeney, Martin Murphy

Demonstration layout

- IDAC company background
- IAs clinical background
- role of haemodynamics in IAs
- @neurIST technology
- demonstration of unstented case
- demonstration of stented case
- SBNS study
- what next

IDAC company background

- CAE Consultants, established in 1997
- 5 Employees
  - Derek Sweeney
  - Dr. Paul Fanning
  - Bob Moore
  - Barbara Leichtenstern
  - Dr Alberto Marzo
- In collaboration with partners in 3 successful European projects, we have developed a range of web-enabled simulation applications aimed at Medical Device Manufacturers and Clinical Researchers
- @neurIST (European Project) finished in March 2010. We are now trying to market the tools developed.
- We supported Martin Murphy in his Research work (**poster won a best in section prize at the SBNS meeting**)
- Purpose of this meeting is to show you what can be done and then explore possibility of Research projects etc

@neurIST

Members of the consortium

- Multidisciplinary European initiative funded by the EU*
- 4-year project, budget 17 million €
- Neurosurgeons, neuroradiologists, epidemiologists, engineers, biologists and computer scientists from 32 EU institutions
- Industrial, academic and medical institutions
- Aim: improve current management of intracranial aneurysms

Clinical background

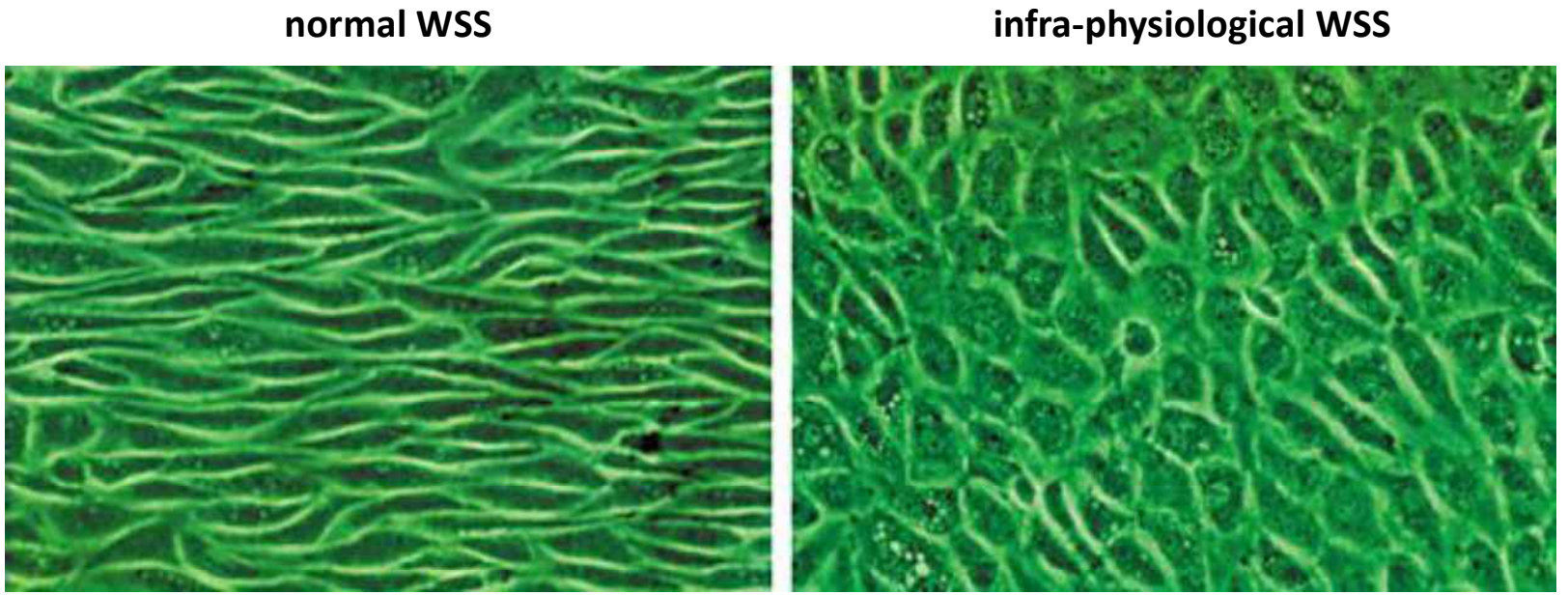
- Aneurysmal SAH major cause of morbidity and mortality with high rates of case fatality (40-50%) [1,2]
- Management of unruptured IAs remains controversial topic in Neurosurgery
- Most aneurysms do not rupture [2], etiological/pathological factors responsible for rupture remain poorly understood
- Morbidity and mortality from operative/endovascular treatment, prompts need for better management protocol
- Evidence from literature suggests an emerging role of haemodynamics, shape and tissue stress/strain in aneurysmal pathogenesis [3,4]

(1) Inagawa Stroke 2001, (2) ISUIA N Eng J Med 1998, (3) Sekhar et al. Neurosurgery 1981, (4) Ujiie et al. Neurosurgery 1999

Role of haemodynamics

Wall Shear Stress (WSS)

- WSS definition: frictional tangential force exerted by blood flow on endothelial layer
- Supra- and infra-physiological values of WSS have been associated to endothelial damage, aneurysm formation and rupture [1]



(1) Malek et al JAMA 1999

Role of haemodynamics

Hemodynamic factors	Intracranial Aneurysm			Proposed mechanism(s)	References
	Initiation	Growth	Rupture		
Dynamic					
Wall Shear Stress (WSS)	High	Low	Low	Increased WSS increases the production of MMP-13 which in turn leads to vessel wall damage Decreased WSS increases iNOS synthesis-NO induced damage to vessel wall Low WSS increases endothelial proliferation and apoptosis	Gao et al (2008), Fukuda et al (2000), Meng et al (2007), Shojima et al (2004), Jou et al (2008), Malek et al (1999), Ujie et al (1999), Boussel et al (2008),
Oscillatory Shear Index (OSI)	High/Low	High	High	Degenerative changes in endothelium	Mantha et al (2006), Glor et al (2004), Goubergrits et al (2008)
Jet of Blood Stream	Impingement	Impingement	Impingement	Localized endothelial cell injury	Foutrakis et al (1999), Cebral et al (2005), Cebral et al (2008)
Flow Pattern	-	-	Complex	Statistical association	Cebral et al (2005), Cebral et al (2008)
Hydrostatic					
Pressure	High	High	High	Passive yield/ water hammer effect	Inci and Spetzler (2000), Morimoto et al (2002), Steiger et al (1989)

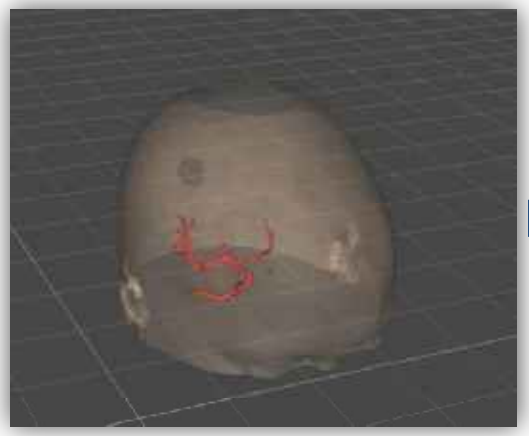
NB: WSS; wall shear stress, MMP-13; matrixmetalloproteneases-13, iNOS; inducible-nitric oxide synthase, NO; nitric oxide, OSI; oscillatory shear index

Singh PK, Marzo A et al Comput Intell Neurosci 2009

@neurIST technology

medical image

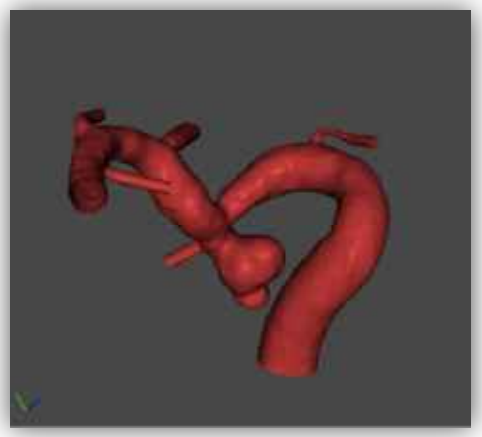
surface reconstruction 1



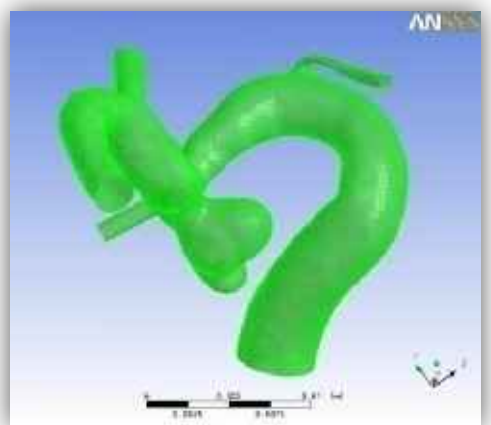
surface reconstruction 2

Click Here for Video

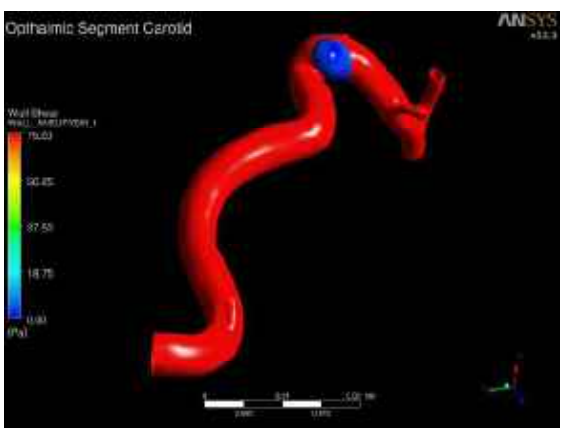
surface reconstruction 3



computer model



flow prediction

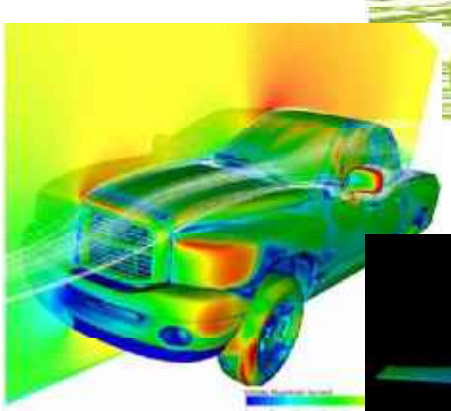


Click Here for Video

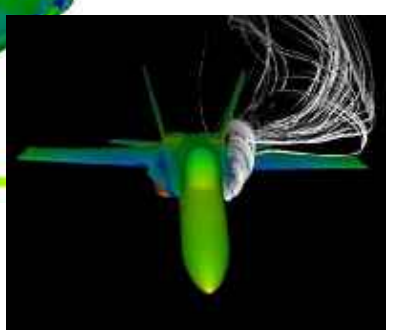
@neurIST technology: CFD

- Detailed in-vivo measurements of relevant flow variables in regions affected are currently impossible
- Motivated by its success in other disciplines scientists started using CFD to predict blood flows in IAs

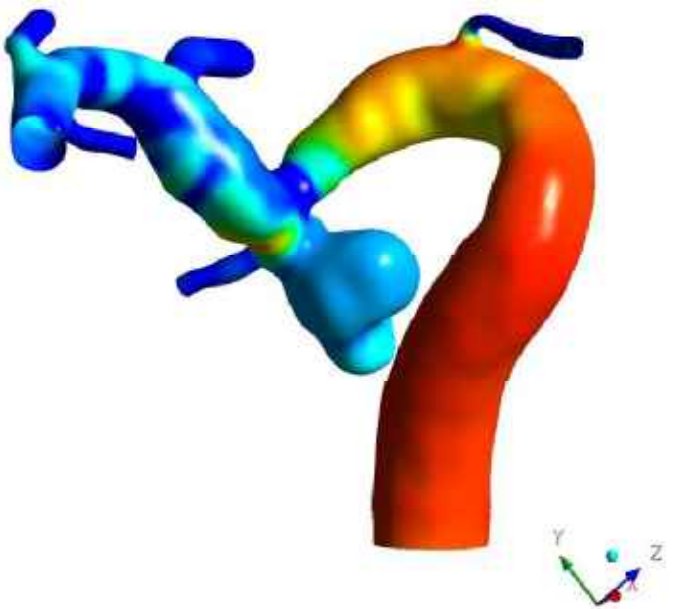
Sports Engineering



Automotive

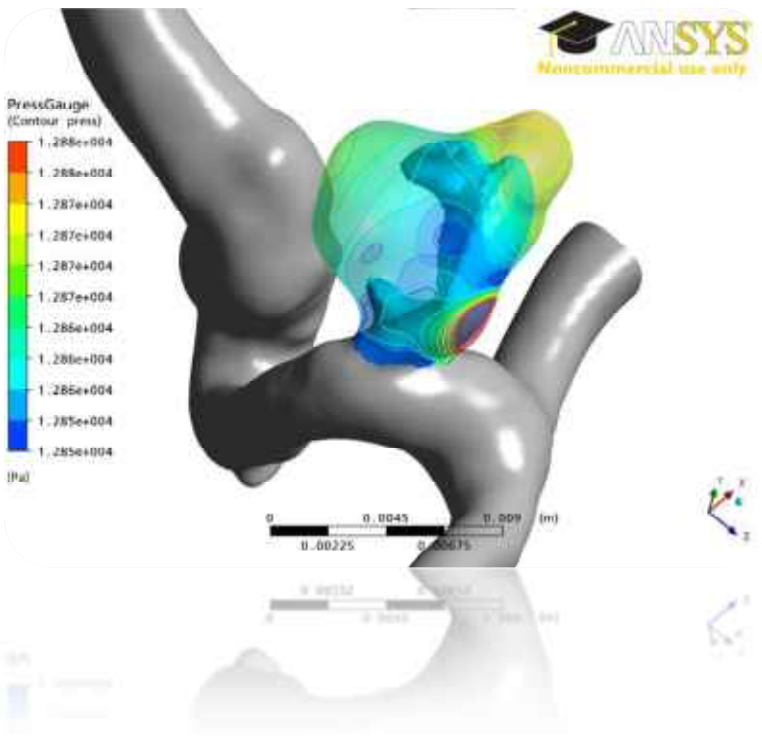


Aerospace



@neurIST technology:
haemodynamic predictions

inflow jet and pressure

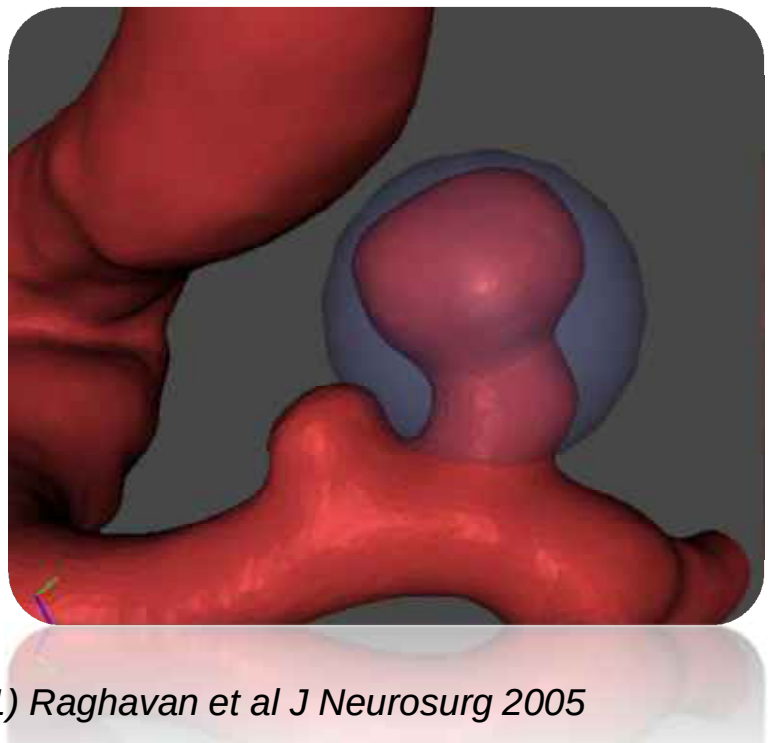


wall shear stress

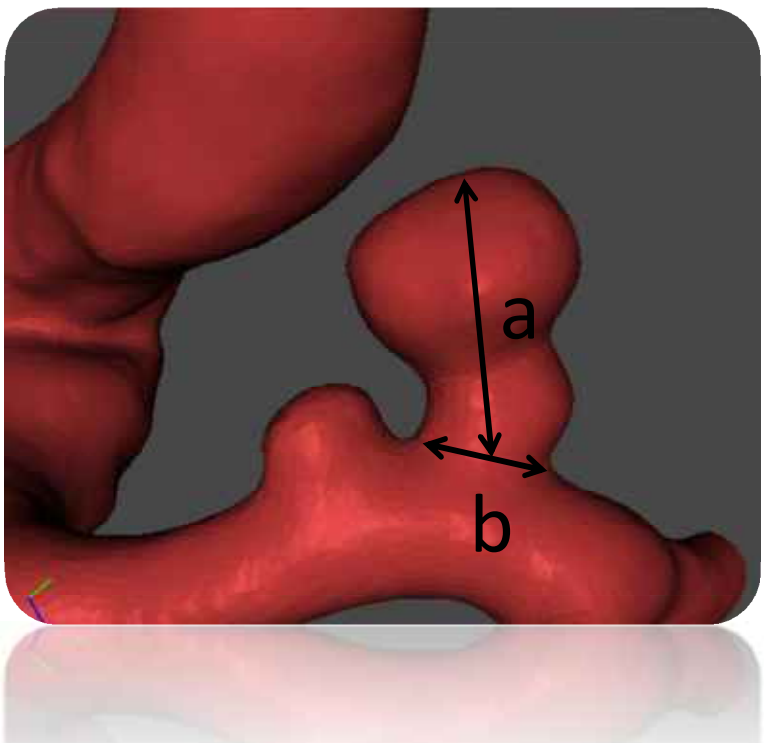
@neurIST technology:
shape measurements

- non-sphericity-index (NSI): quantifies difference between aneurysm shape and a perfect circumscribed sphere
- Aspect ratio: ratio between aneurysm depth and neck max width. It has been correlated with aneurysm rupture [1]

non-sphericity-index



aspect ratio

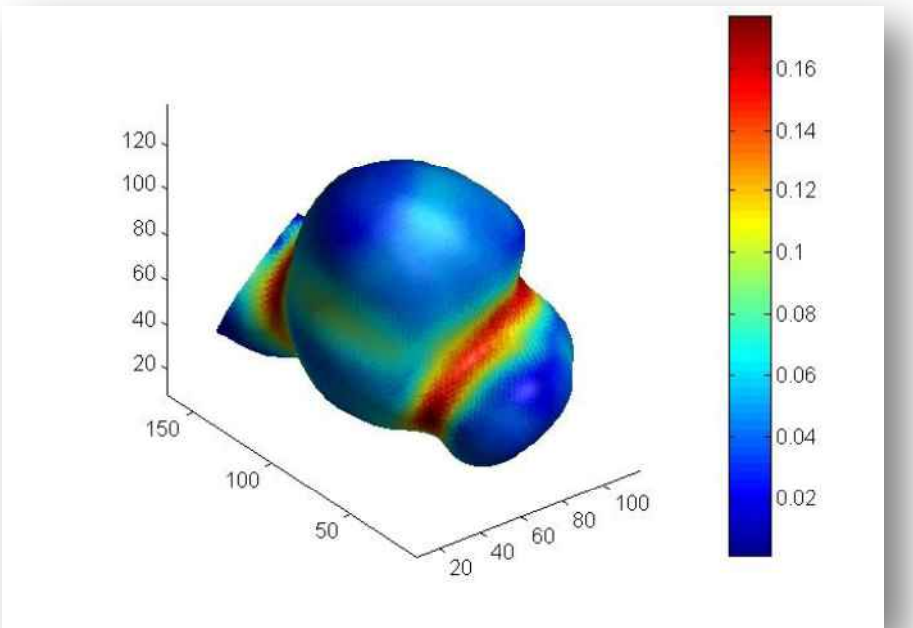


(1) Raghavan et al J Neurosurg 2005

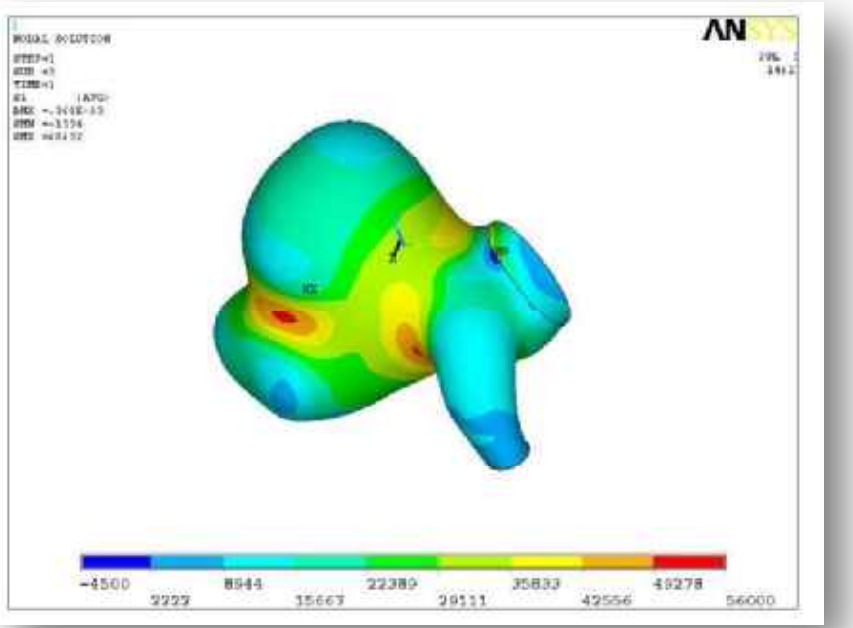
@neurIST technology:
stress/strain predictions

- it is likely that the event of rupture occurs when the tissue stress or strain exceeds some sustainable level

tissue stress



tissue strain



Live Demo
Unstented Case

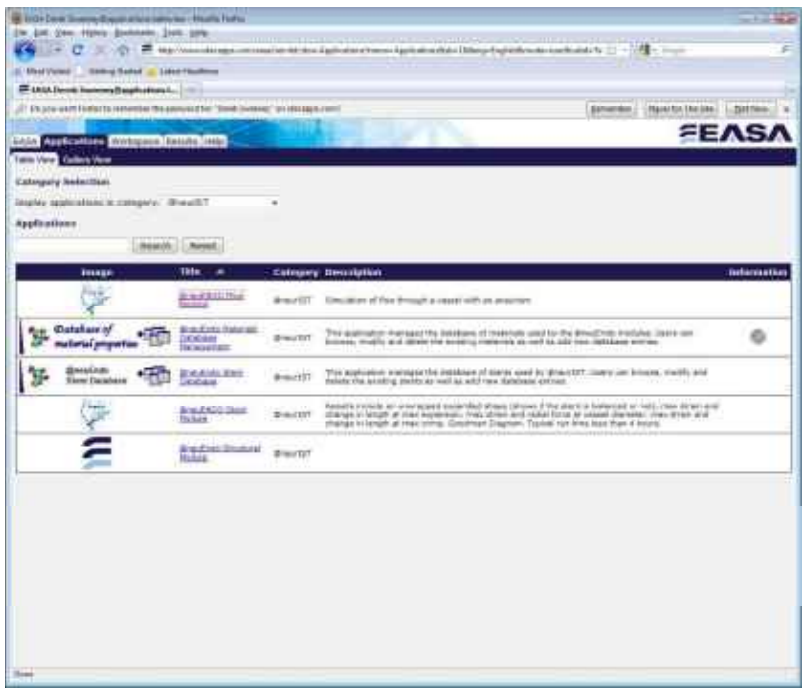
Click Above for Demo

Analysis computation

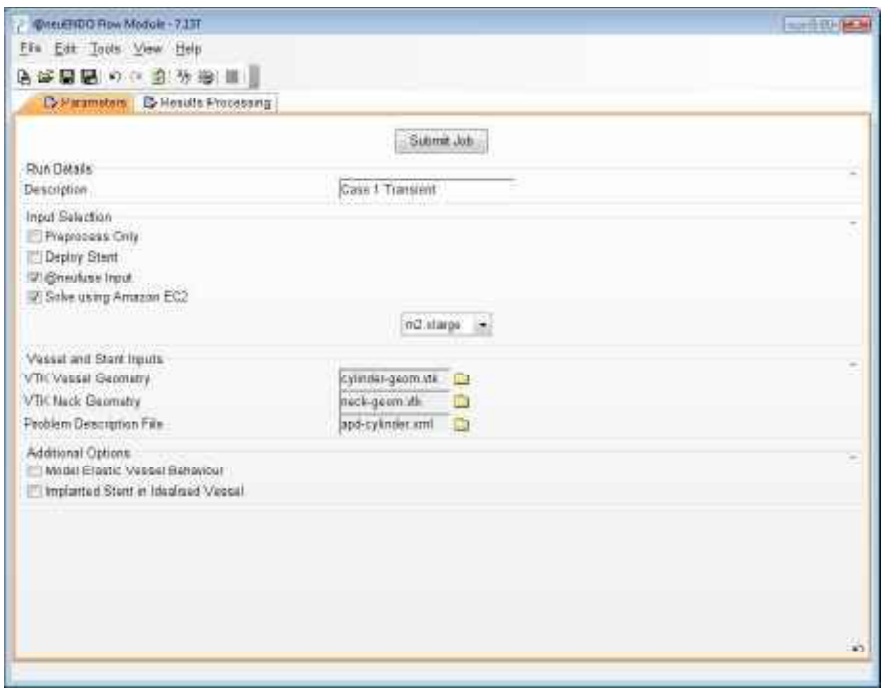
IDAC EASA web-based computing power

- @neuFuse files can be uploaded on the web to run analyses using web-based computing power (IDAC EASA)

user interface



file uploading

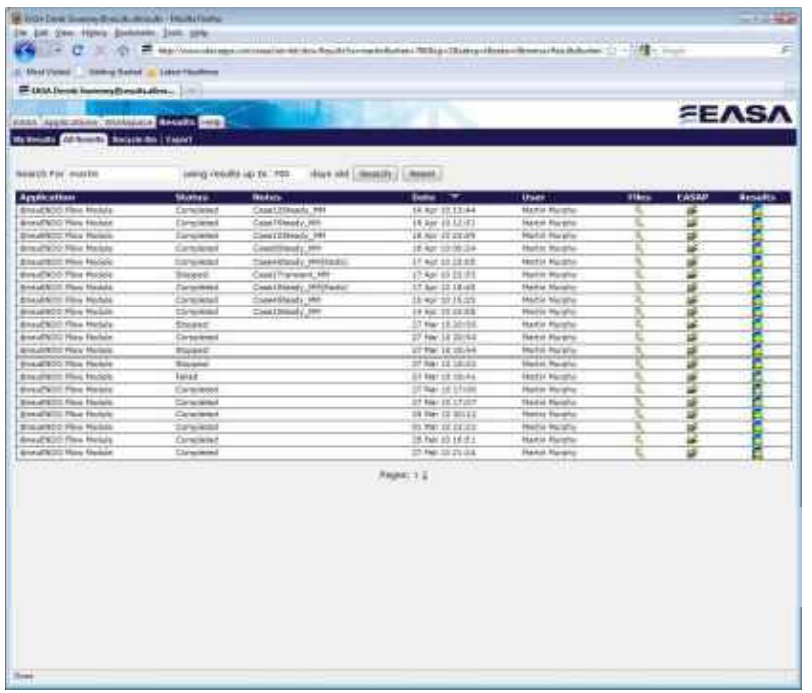


Analysis computation

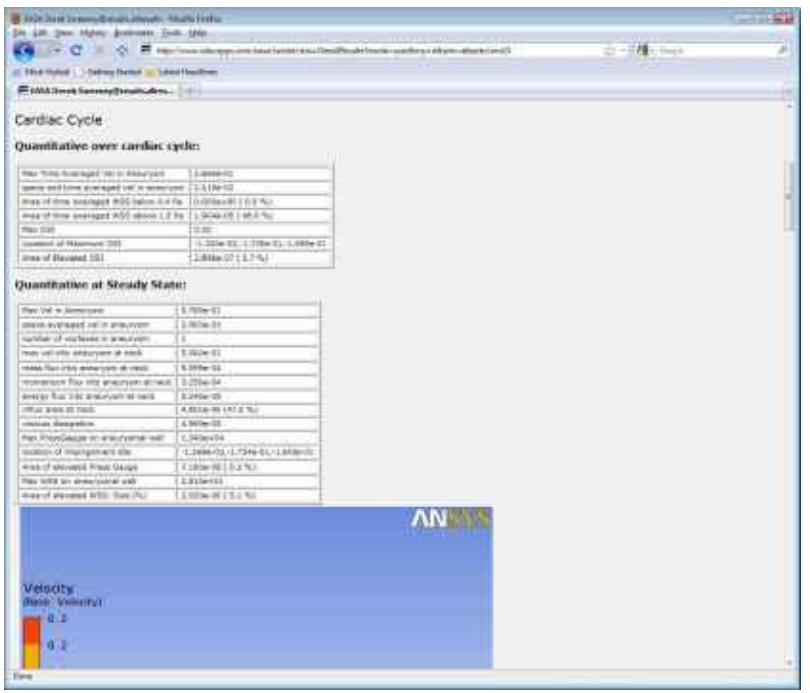
IDAC EASA web-based computing power

- Analysis status can be monitored and results (e.g. tabulated indices, WSS plots) accessed once analyses are completed

analysis status



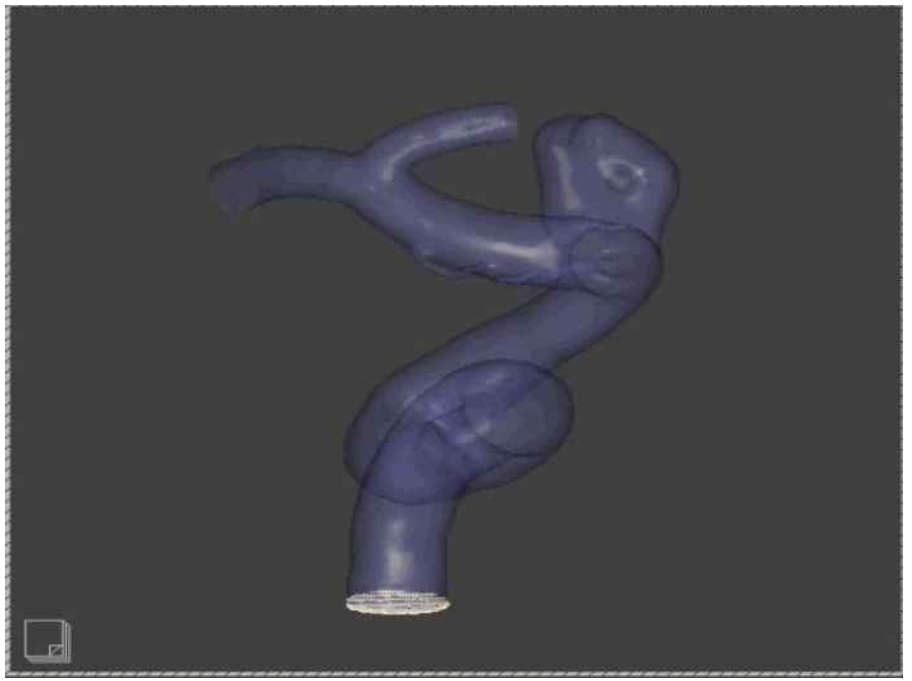
results post-processing



Validation

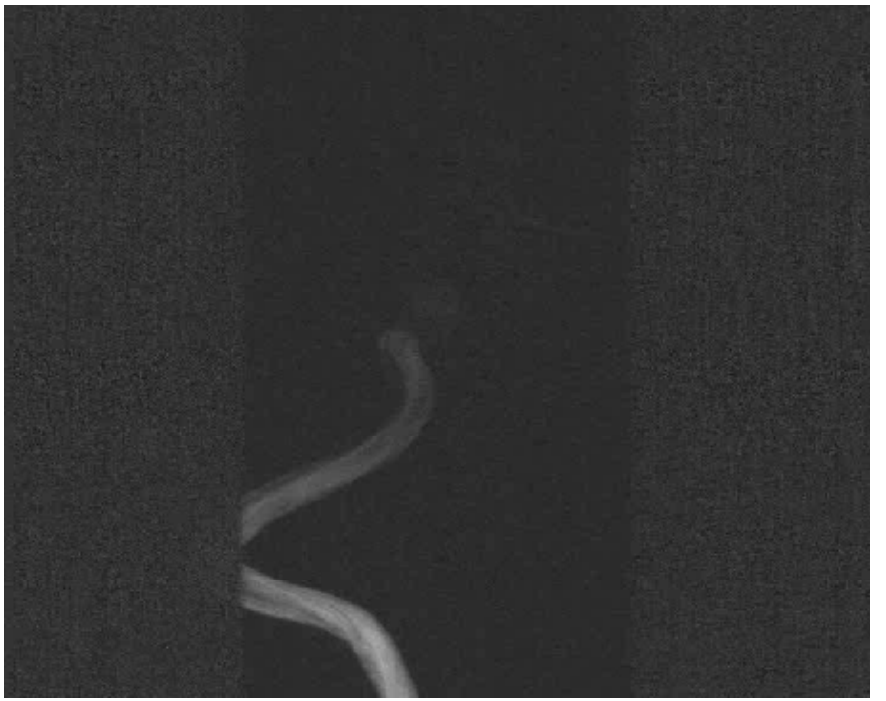
- it is likely that the event of rupture occurs when the tissue stress or strain exceeds some sustainable level

Virtual Angio



Click Here for Video

Real Angio



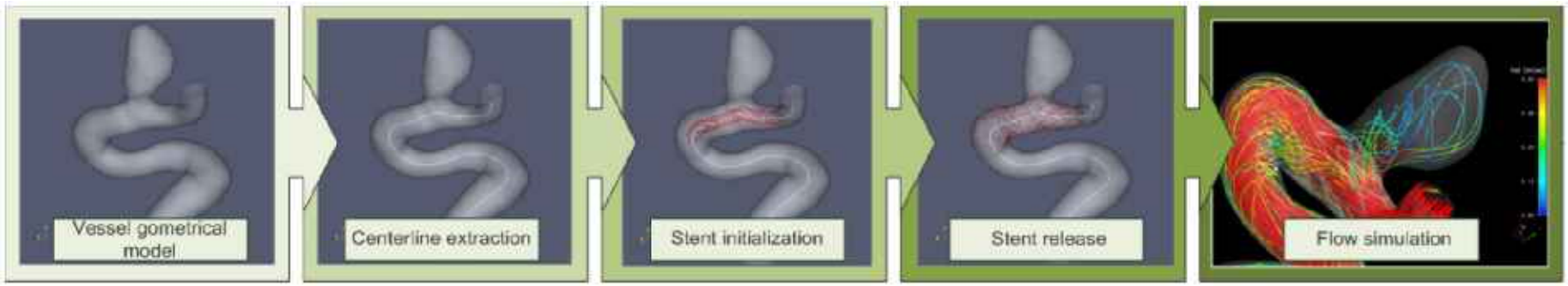
Click Here for Video

Stented Case

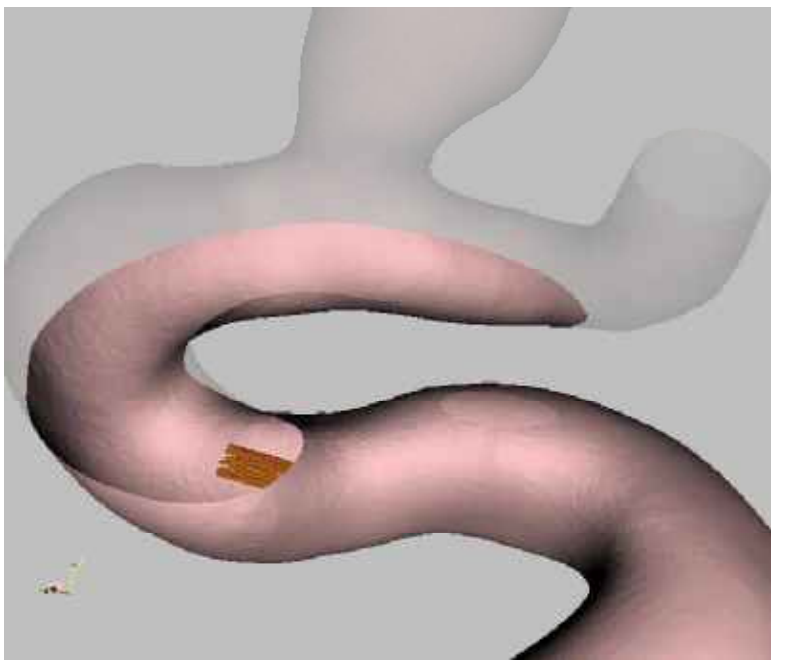
Click Above for Demo

@neurEndo

Virtual Endovascular Treatment

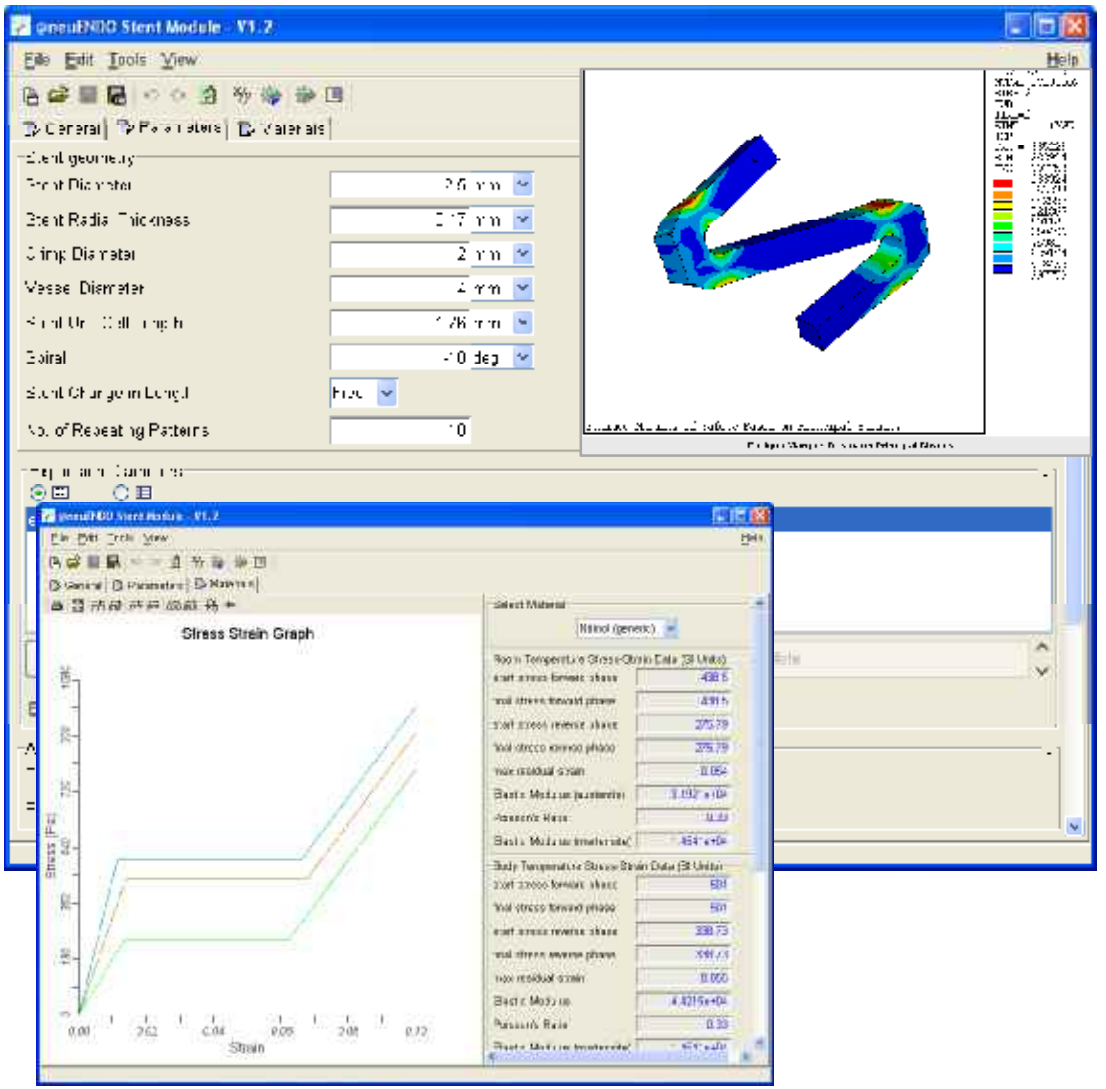


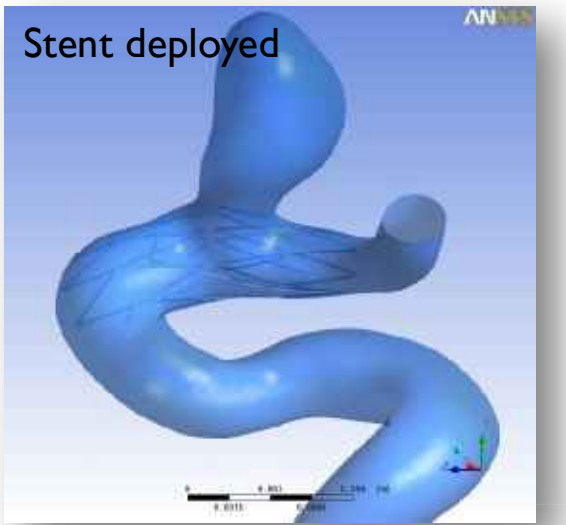
- The stent is represented by a deformable model expanding into the vascular lumen
- The stent deformation is constrained with information on the stent design (strut length, angle between struts)
- Time consumption: approximately 1 minute

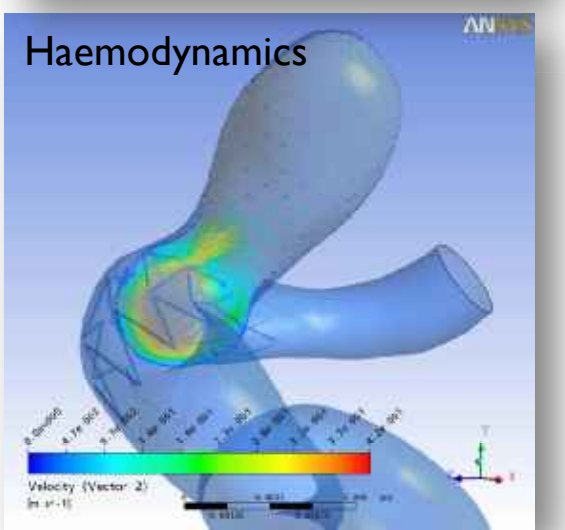


@neurEndo

Virtual Endovascular Treatment







Physical Characterisation of Cerebral Aneurysms and Identification of Factors Suggestive of Imminent Rupture

TM Murphy[1,3], A Marzo[2], DR Rawluk[1], C Bolger[1,4]

1 Department of Neurosurgery, Beaumont Hospital, Dublin.
2 Department of Cardiovascular Engineering, Royal Hallamshire Hospital, Sheffield
3 Department of Vascular Research Engineering, University College Dublin
4 Department of Neurosciences, Royal College of Surgeons of Ireland, Dublin

Updated ISUIA (2003)

	< 7	< 7	7-12	13-24	≥25
	Group 1	Group 2			
Cavernous carotid	0	0	0	3%	6.4%
AC/MC/IC	0	1.5%	2.6%	14.5%	40%
Post-P comm	2.5%	3.4%	14.5%	18.4 %	50%

Wiebers DO et al. Lancet 2003

Materials and methods

- Retrospective pilot study investigating role of haemodynamic indices in subarachnoid haemorrhage
- 10 patients from Beaumont Hospital recruited
- Ethical approval
- 3D rotational acquisitions (3DRA) images were processed with @neuFuse

Case	Age	Urgency?	Location	Size
1	59	Elective	Basilar	4
2	59	SAH	R P Comm	3
3	53	SAH	R P Comm	2
4	35	Elective	R P Comm	3
5	42	SAH	Basilar	10
6	35	SAH	R ICA	3
7	66	SAH	L P Comm	10
8	67	SAH	L P Comm	6
9	57	SAH	R P Comm	10
10	60	Elective	L P Comm	7

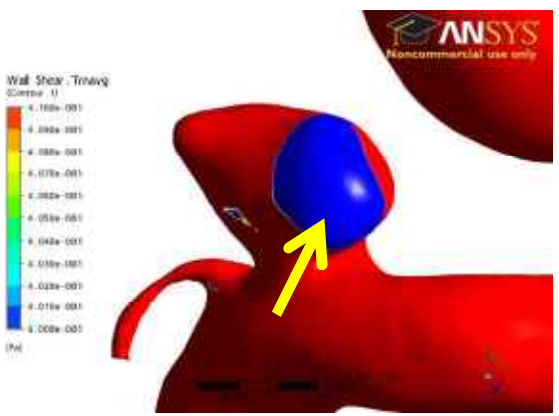
Haemodynamic Results

Infra-physiological time-ave Wall Shear Stress (<0.4 Pa)

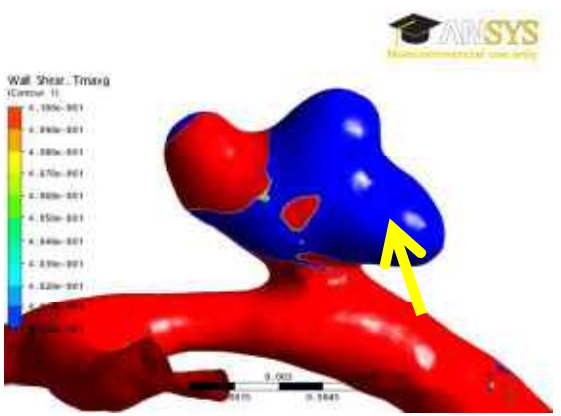
Case Number	Age	Ruptured?	Location	Size	Area WSS<0.4Pa (mm^2)	% WSS<0.4Pa
1	59	Elective	Basilar	4	0	0
2	59	SAH	R P Comm	3	7.5	11.4
3	53	SAH	R P Comm	2	0	0
4	35	Elective	R P Comm	3	0	0
5	42	SAH	Basilar	10	76.6	59.4
6	35	SAH	R ICA	3	0	0
7	66	SAH	L P Comm	10	16.9	7.4
8	67	SAH	L P Comm	6	4.7	5.6
9	57	SAH	R P Comm	10	0	0
10	60	Elective	L P Comm	7	0	0

WSS<0.4 Pa

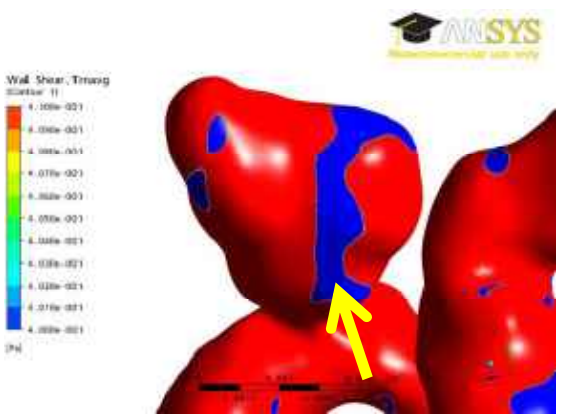
Aneurysm 2



Aneurysm 5



Aneurysm 7



Haemodynamic Results

Jet impingement at peak systole

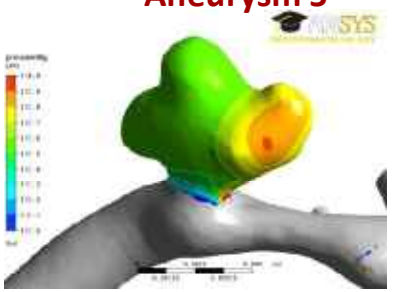
Case Number	Age	Ruptured/Elective	Location	Size (mm)	Maximum Pressure (mmHg)	Area Pressure Elevated (%)
1	59	Elective	Basilar	4	100.8	0.2
2	59	SAH	R P Comm	3	110.5	0.6
3	53	SAH	R P Comm	2	114.3	3.2
4	35	Elective	R P Comm	3	118	16.5
5	42	SAH	Basilar	10	119.5	0.2
6	35	SAH	R ICA	3	109	8
7	66	SAH	L P Comm	10	103	2.6
8	67	SAH	L P Comm	6	106	6.4
9	57	SAH	R P Comm	10	141	3
10	60	Elective	L P Comm	7	110.5	52

Aneurysm 4

Aneurysm 5

pressure

jet



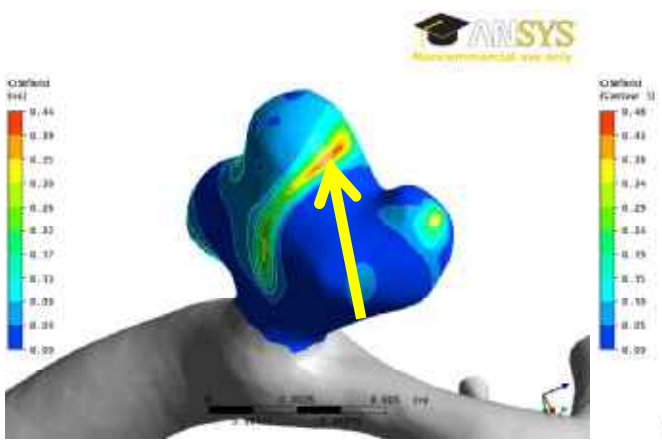
Haemodynamic Results

Oscillatory Shear Index

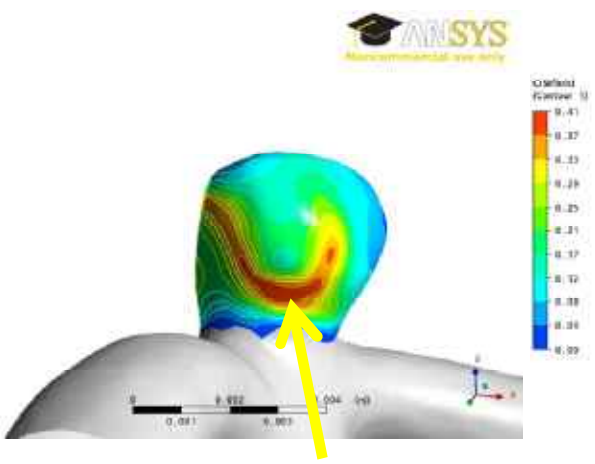
Case Number	Age	Ruptured/Elective	Location	Size	Maximum OSI	Area Elevated OSI (%)
1	59	Elective	Basilar	4	0.32	0.7
2	59	SAH	R P Comm	3	0.47	7.7
3	53	SAH	R P Comm	2	0.38	4.5
4	35	Elective	R P Comm	3	0.28	0.9
5	42	SAH	Basilar	10	0.44	4
6	35	SAH	R ICA	3	0.48	24.1
7	66	SAH	L P Comm	10	0.41	3.4
8	67	SAH	L P Comm	6	0.42	1.2
9	57	SAH	R P Comm	10	0.44	3.0
10	60	Elective	L P Comm	7	0.38	8.9

OSI

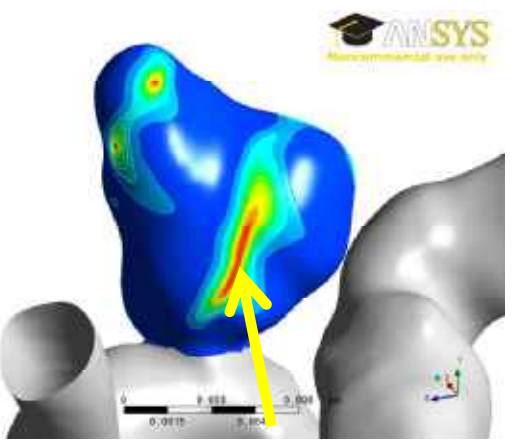
Aneurysm 5



Aneurysm 6



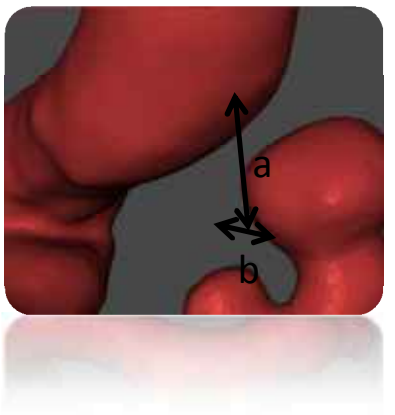
Aneurysm 7



Morphological Results

Shape indices automatically extracted from @neuFuse

Case Number	Age	Ruptured/Elective	Location	Size	Aspect Ratio	Non-sphericity index	Size ratio
1	59	Elective	Basilar	4	0.92	0.09	1.5
2	59	SAH	R P Comm	3	1.38	0.2	1.71
3	53	SAH	R P Comm	2	0.81	0.12	0.86
4	35	Elective	R P Comm	3	0.92	0.09	1.63
5	42	SAH	Basilar	10	2.09	0.29	2.36
6	35	SAH	R ICA	3	1.27	0.15	1.25
7	66	SAH	L P Comm	10	2.59	0.26	2.49
8	67	SAH	L P Comm	6	1.83	0.25	1.81
9	57	SAH	R P Comm	10	1.88	0.29	3.09
10	60	Elective	L P Comm	7	0.87	0.21	0.83



Aneurysm 1

Aneurysm 2

Aneurysm 3

Aneurysm 4

Aneurysm 5

Aneurysm 6

Aneurysm 7

Aneurysm 8

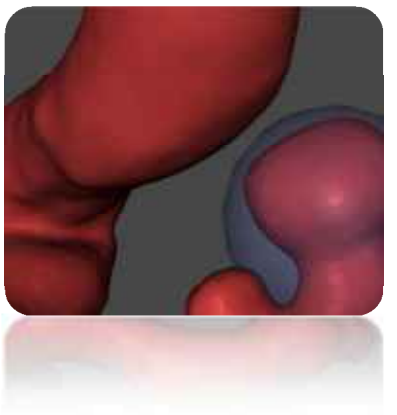
Aneurysm 9

Aneurysm 10

Morphological Results

Shape indices automatically extracted from @neuFuse

Case Number	Age	Ruptured/Elective	Location	Size	Aspect Ratio	Non-sphericity index	Size ratio
1	59	Elective	Basilar	4	0.92	0.09	1.5
2	59	SAH	R P Comm	3	1.38	0.2	1.71
3	53	SAH	R P Comm	2	0.81	0.12	0.86
4	35	Elective	R P Comm	3	0.92	0.09	1.63
5	42	SAH	Basilar	10	2.09	0.29	2.36
6	35	SAH	R ICA	3	1.27	0.15	1.25
7	66	SAH	L P Comm	10	2.59	0.26	2.49
8	67	SAH	L P Comm	6	1.83	0.25	1.81
9	57	SAH	R P Comm	10	1.88	0.29	3.09
10	60	Elective	L P Comm	7	0.87	0.21	0.83



Aneurysm 1

Aneurysm 2

Aneurysm 3

Aneurysm 4

Aneurysm 5

Aneurysm 6

Aneurysm 7

Aneurysm 8

Aneurysm 9

Aneurysm 10

Qualitative comparison

case 1 – wall shear stress

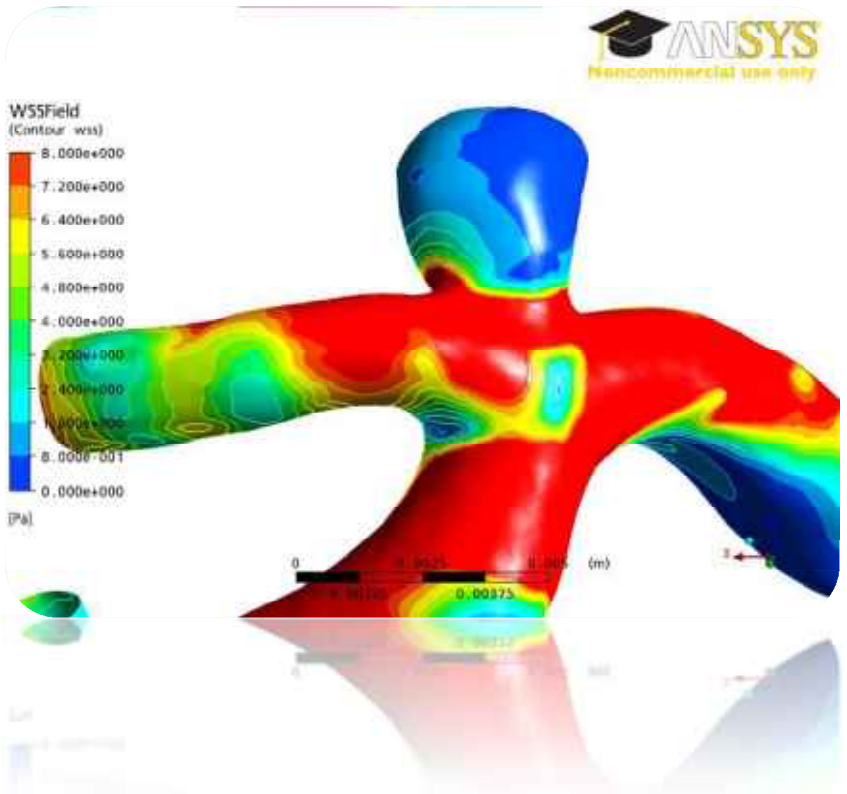
Martin

Alberto

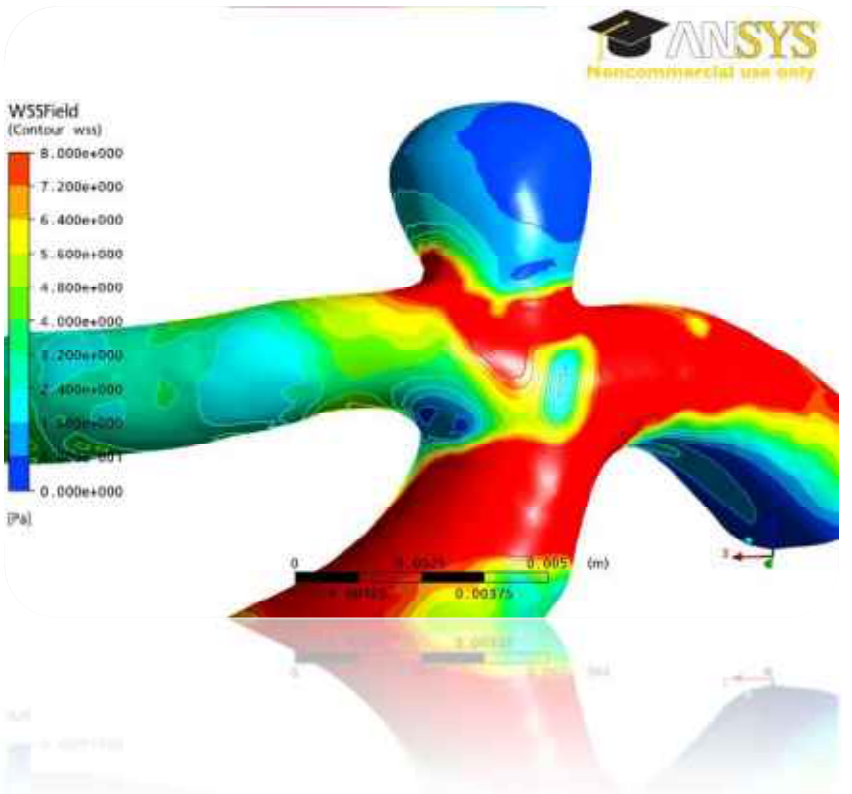
Qualitative comparison

case 8 – wall shear stress

Martin



Alberto



Results Summary

	Predicted the SAH patients?
Accepted "wisdom"	
Size matters (7mm)	3/7
Proposed indices	
Aspect ratio (1.6)	5/7
Size ratio (3)	1/7
WSS	4/7
Oscillatory shear index (0.40)	6/7
Non-sphericity index (0.183)	6/7

- The software is easy to use by clinicians
- Results were interchangeable with Dr Marzo's within 5 cases.
- 45 minutes clinician time + 2-3 hours computation

Conclusions

- Size is not the best predictor of aneurysm's rupture potential
- Haemodynamic and shape indices may have greater influence on rupture potential
- Strongest correlations found for Oscillatory Shear Index and Non-sphericity index

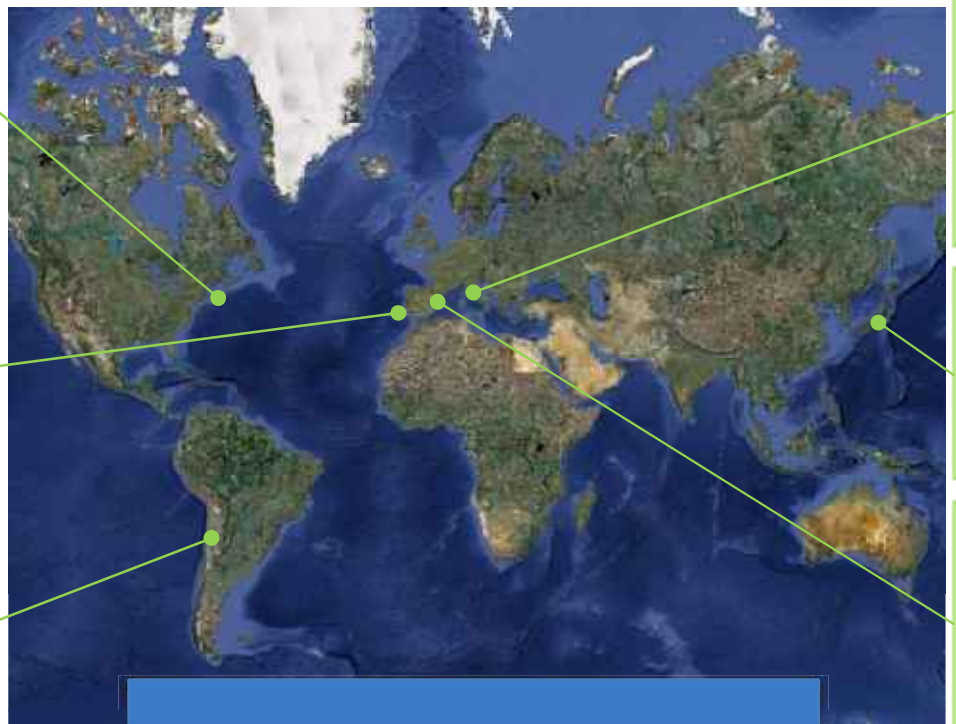
Dissemination

- The software has been exposed and used by clinicians at several venues with positive feedback
- Feedback was collected and used to improve the software

Location: Boston, USA
Conference: WFNS 2009
Exposure: Workshop
Participants: 38 neurosurgeons
Feedback: Overall impression positive, audience showed great interest @neurIST

Location: Lisbon, Portugal
Conference: ESMINT 2008
Exposure: Workshop
Participants: 36 neuroradiologists, neurosurgeons, engineers
Feedback: Very positive

Location: Santiago, Chile
Conference: SILK-Workshop 2009
Exposure: Workshop
Participants: 22 Endovascular Neuroradiologists
Feedback: Very positive, GUI needs improvement



Location: Bertinoro, Italy
Conference: ICCB 2009
Exposure: Workshop
Participants: 13 biomedical engineers
Feedback: Engineering community showed great interest and positive feedback

Location: Nagoya, Japan
Conference: ICCVS 2009
Exposure: Presentation
Participants: 50+ neurosurgeons
Feedback: Audience showed great enthusiasm

Location: Barcelona, Spain
Conference: ESMINT 2009
Exposure: Workshop
Participants: 104 neuroradiologists, epidemiologists, engineers, neurosurgeons
Feedback: Positive

Published in *Computational Intelligence and Neuroscience 2009*

What next?

- We can offer tools and services to support the following activities:
  - Research into cerebral aneurysms
  - Research into other vascular diseases
  - Patient specific CFD study*

- Typical cost for a 100 Case Research Project would be €10,000. This includes
  - Initial training in use of software and interpretation of results
  - Tailoring of report and output data
  - Ongoing support and training
  - Use of @neuFuse and @neuEndo software

- Typical cost for a single patient CFD study would be € 400. This includes
  - Transient CFD study
  - Interactive discussion with clinician on results
  - Presentation of results in summary report

- Open Forum
  - Feedback
  - Interest in further collaboration
  - Can we identify a funded research project?

APPENDIX Computational Fluid Dynamics - What is it?

- CFD is the science of predicting **fluid flow**, **heat** and **mass transfer** and it's based on the **physical principles** that govern any fluid flow:
  - Conservation of Mass
  - Conservation of Momentum (Newton's Second Law)
  - Conservation of Energy (First Law of Thermodynamics)

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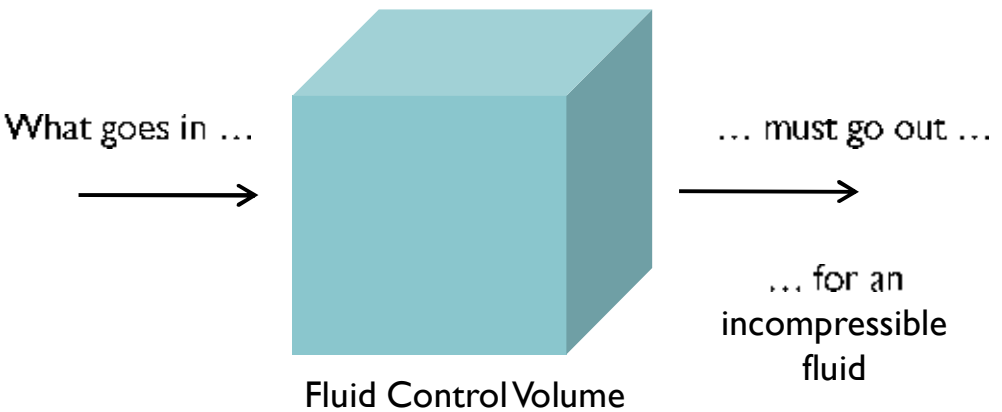

$$\nabla \cdot \boldsymbol{u} = 0$$

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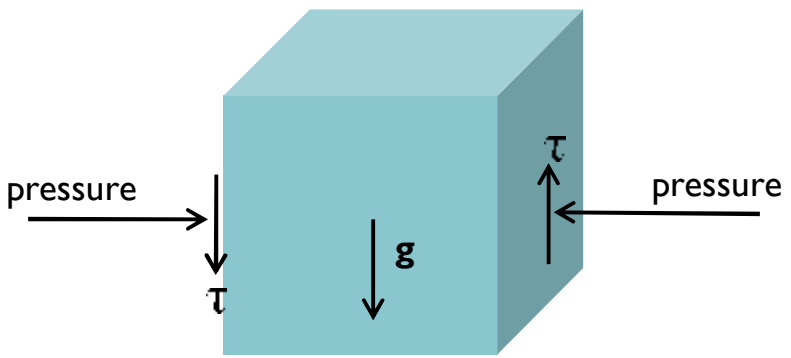

Fluid Control Volume

$$\rho\left(\frac{\partial \boldsymbol{u}}{\partial t}+\boldsymbol{u}\cdot\nabla\boldsymbol{u}\right)=-\nabla p+\nabla\cdot\boldsymbol{T}+\boldsymbol{f}$$

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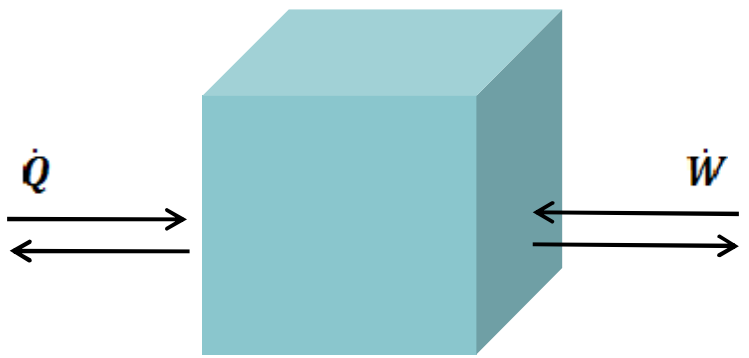


Fluid Control Volume

$$\rho\left(\frac{\partial e}{\partial t}+\boldsymbol{u}\cdot\nabla\boldsymbol{e}\right)-\nabla\cdot(\mathrm{K_H}\nabla T)+p\nabla\cdot\boldsymbol{u}=0$$

APPENDIX Computational Fluid Dynamics - Navier-Stokes Equations

$$\nabla \cdot \boldsymbol{u} = 0$$

$$\rho\left(\frac{\partial \boldsymbol{u}}{\partial t} + \boldsymbol{u} \cdot \nabla \boldsymbol{u}\right) = -\nabla p + \nabla \cdot \boldsymbol{T} + \boldsymbol{f}$$

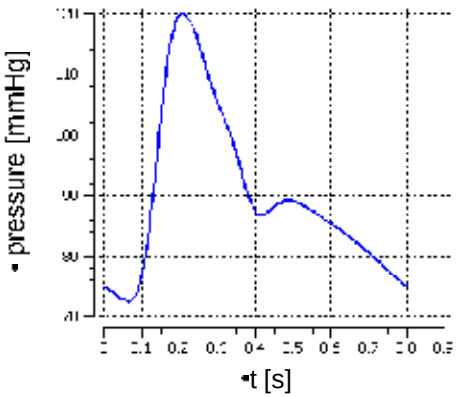
$$\rho\left(\frac{\partial \boldsymbol{e}}{\partial t} + \boldsymbol{u} \cdot \nabla \boldsymbol{e}\right) - \nabla \cdot (\mathrm{K_H} \nabla T) + p \nabla \cdot \boldsymbol{u} = 0$$

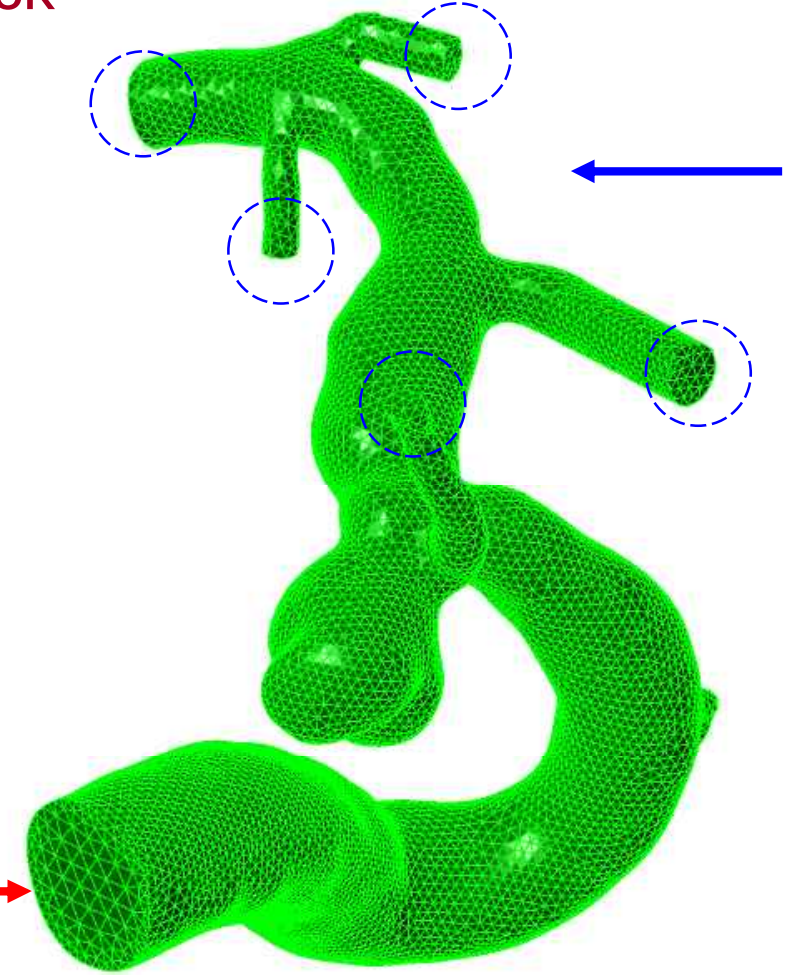
Analytical or closed solution currently impossible for complex physical problems

Designated as Millenium Problem by Clay Mathematics Institute in Cambridge, MA, USA. Solution worth 1M $

APPENDIX Computational Fluid Dynamics –
The engineering trick

•pressure waveform





•flowrate waveform