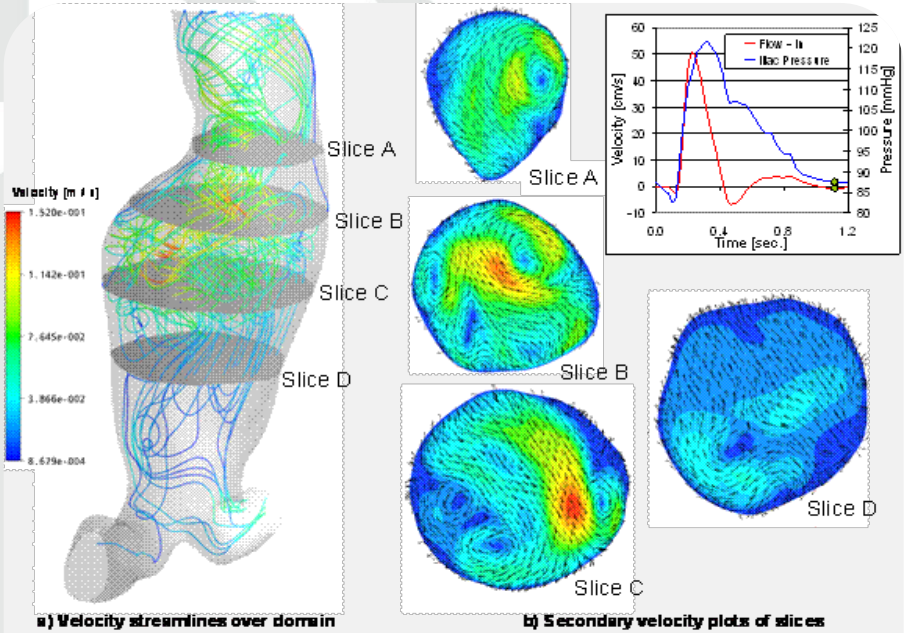
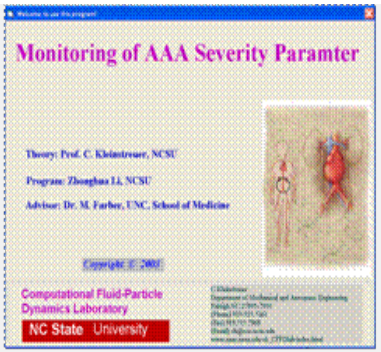
Wall stress and Rupture risk predictor

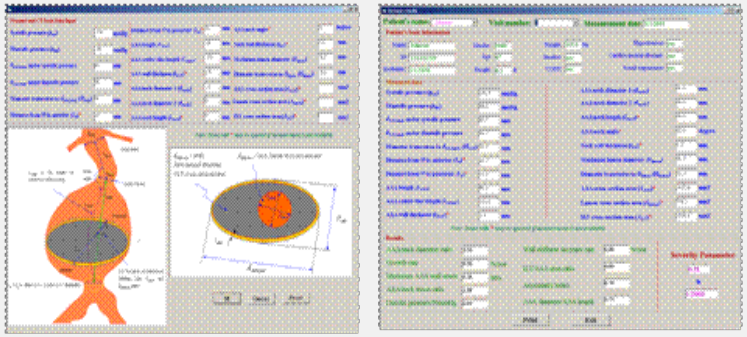


Hemodynamics of patient-specific abdominal aortic aneurysm

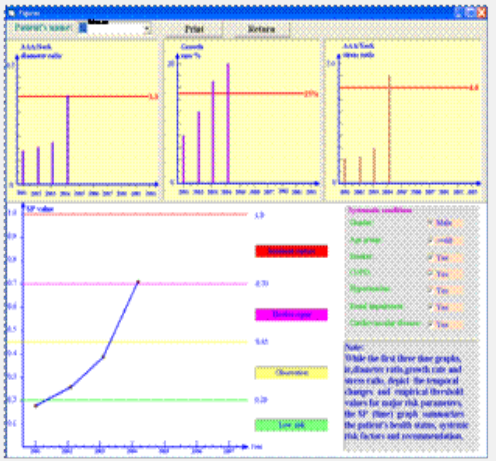
A. Santago, NCSU



⇩ *Enter patient's specific pathology*

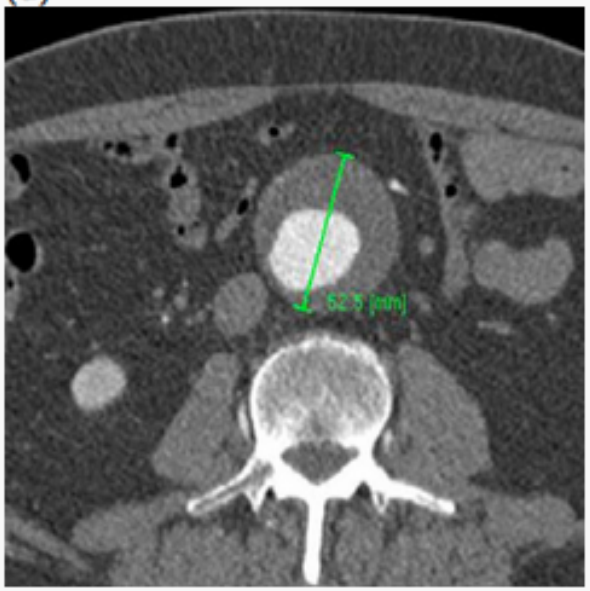


⇩ *Rupture-risk assessment*

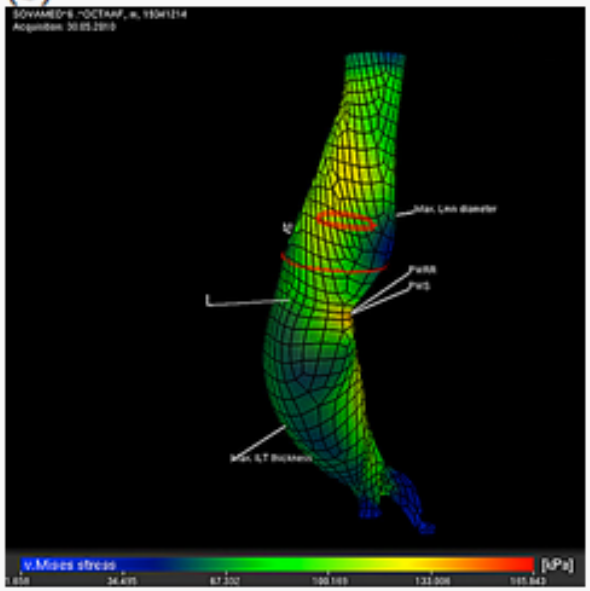


Screenshots of severity parameter program [5]

(a)



(b)



(c)

Patient details	
Name	Clinical case I
Patient ID	Anonymus
Acquisition date	2009/11/02
Age	80
Gender	M
Arterial pressure	140/80 [mmHg]
Mean arterial pressure	100 [mm Hg]
Smoking	N
AAA family history	N

A4clinics Geometrical Analysis	
Outer diameter of the infrarenal aorta	22.2 [mm]
Max. outer AAA centerline (slice) diameter	52.3 (50.8) [mm]
Max. luminal AAA centerline (slice) diameter	30.9 (28.1) [mm]
Max. ILT thickness	12.3 [mm]
Tot. vessel volume	163.9 [ml]
Tot. lumen volume	63.2 [ml]
Tot. ILT volume	79.9 [ml]

A4clinics FE Analysis	
Max. stress in the AAA wall	147.7 [kPa]
Max. rupture risk in the AAA wall - A4PWRR	0.31
Max. stress in the ILT	30.5 [kPa]
Max. rupture risk in the ILT	0.52

(d)

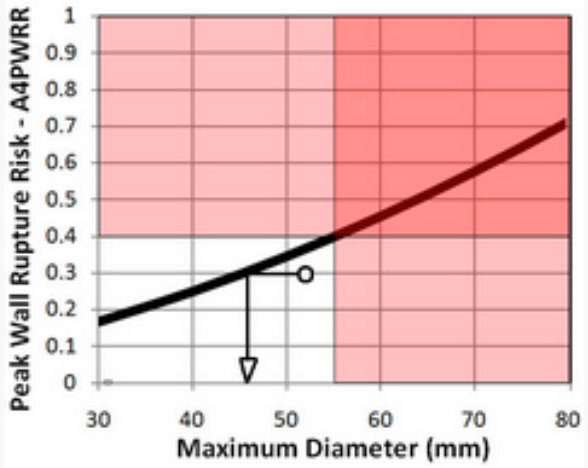
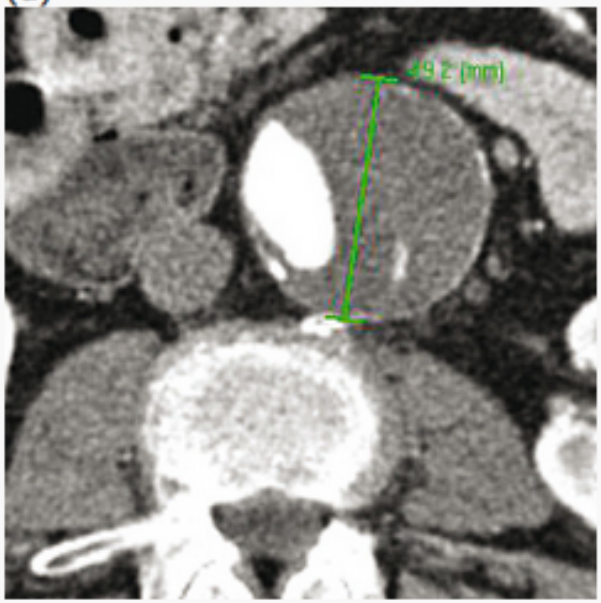
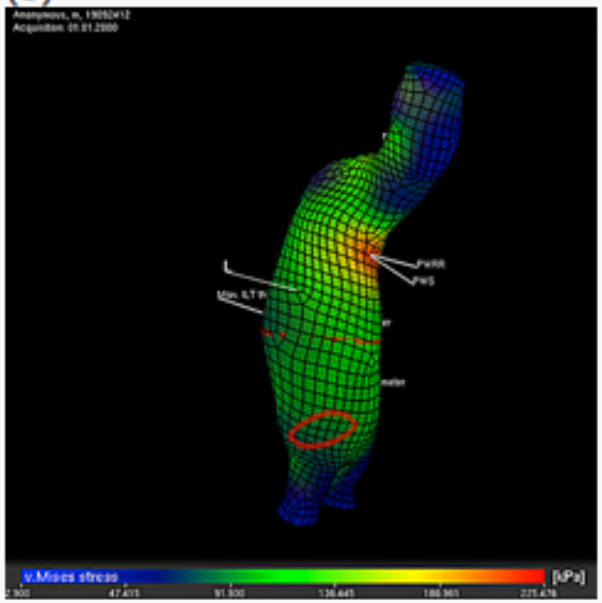


Figure 1: Clinical case I. (a) CT slice at the largest diameter of 5.2cm. (b) Wall stress distribution. (c) A4clinics summary with highlighted A4PWRR. (d) Rupture risk equivalent diameter of 4.6 cm.

(a)



(b)



VASCOPS
Vascular Diagnostics

(c)

Patient details	
Name	Clinical case II
Patient ID	Anonymus
Acquisition date	2010/05/30
Age	76
Gender	M
Arterial pressure	140/80 [mmHg]
Mean arterial pressure	100 [mm Hg]
Smoking	N
AAA family history	N

A4clinics Geometrical Analysis	
Outer diameter of the infrarenal aorta	22.1 [mm]
Max. outer AAA centerline (slice) diameter	49.5 (45.3) [mm]
Max. luminal AAA centerline (slice) diameter	28.9 (26.5) [mm]
Max. ILT thickness	31.2 [mm]
Tot. vessel volume	223.8 [ml]
Tot. lumen volume	68.7 [ml]
Tot. ILT volume	135.8 [ml]

A4clinics FE Analysis	
Max. stress in the AAA wall	217.5 [kPa]
Max. rupture risk in the AAA wall - A4PWRR	0.42
Max. stress in the ILT	39.7 [kPa]
Max. rupture risk in the ILT	0.65

(d)

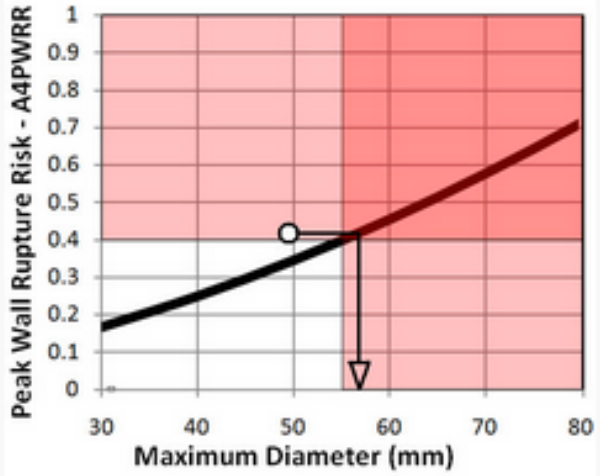
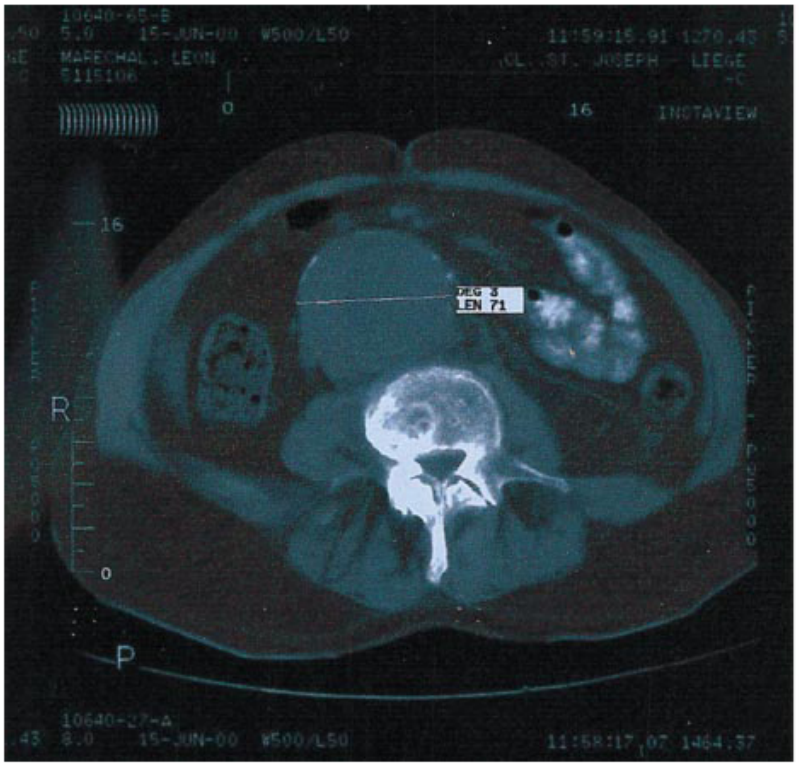


Figure 2: Clinical case II. (a) CT slice at the largest diameter of 4.9 cm. (b) Wall stress distribution. (c) A4clinics

PET -18F-fluorodeoxyglucose



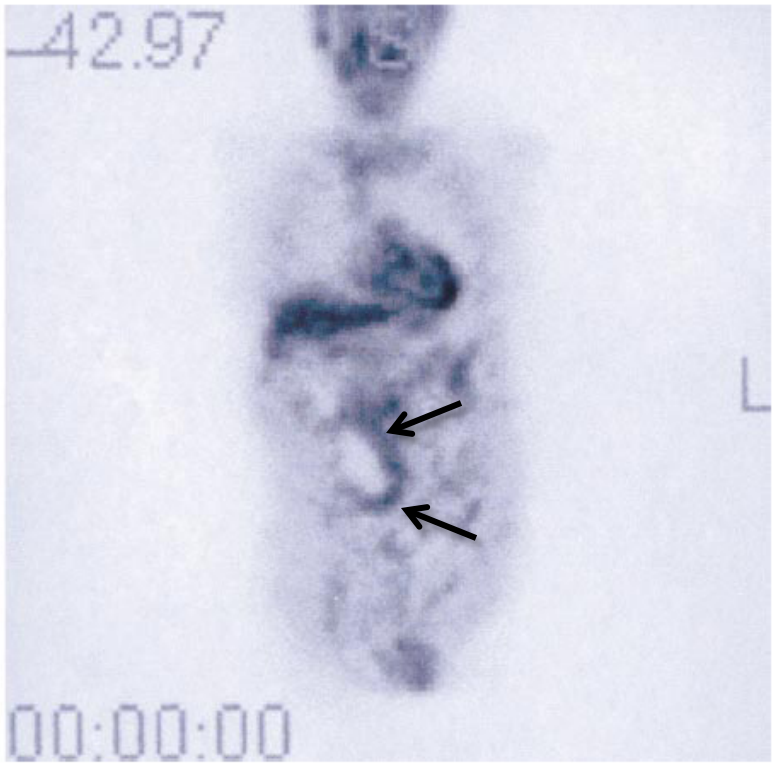


Fig. 2. This painful rapidly expanding aneurysm of 70 mm displays 18-FDG uptake at the level of the aneurysmal wall.

N. Sakalihasan et a. Eur J Vasc Endovasc Surg 2002

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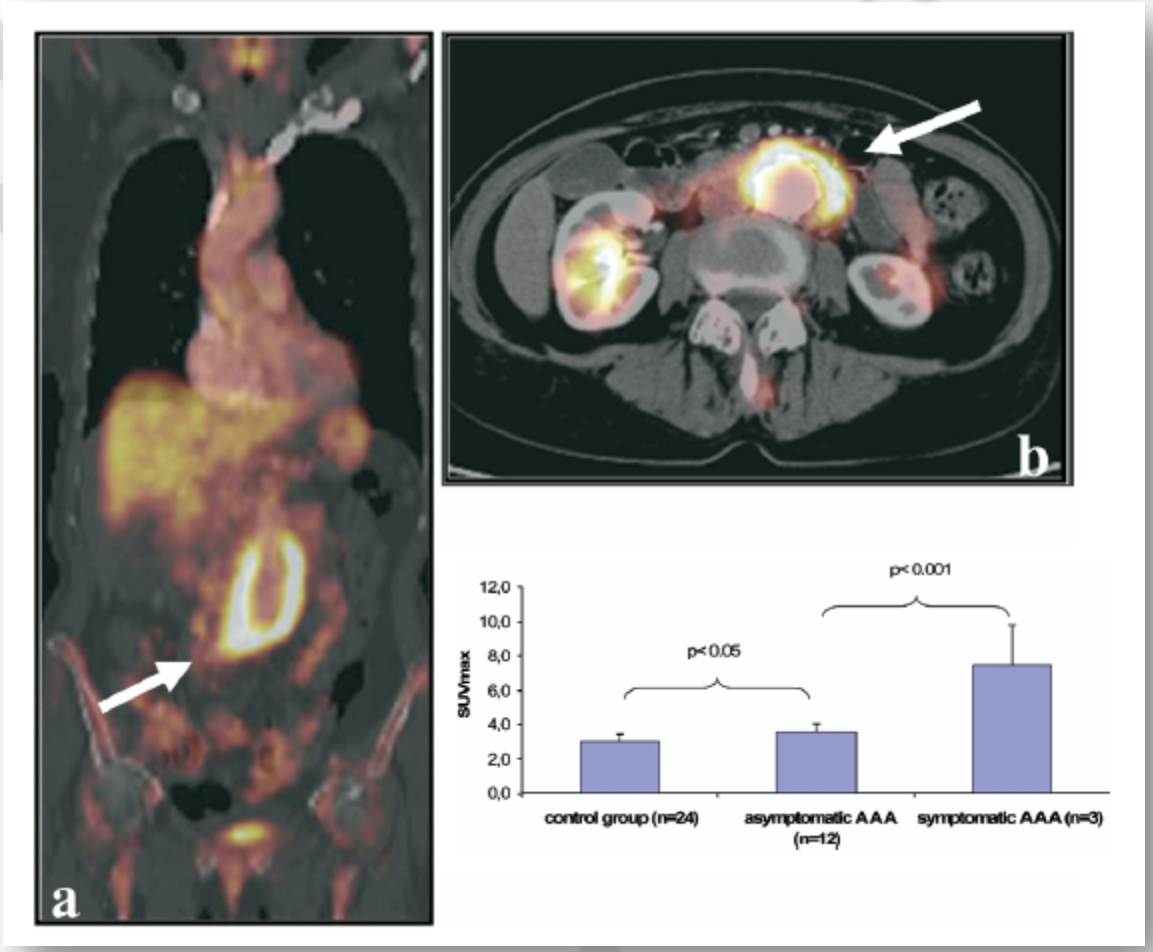
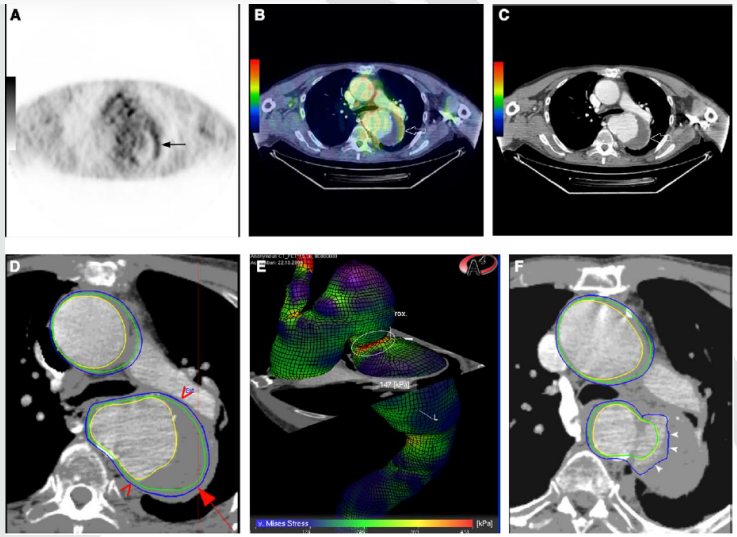
PET -18F-fluorodeoxyglucose

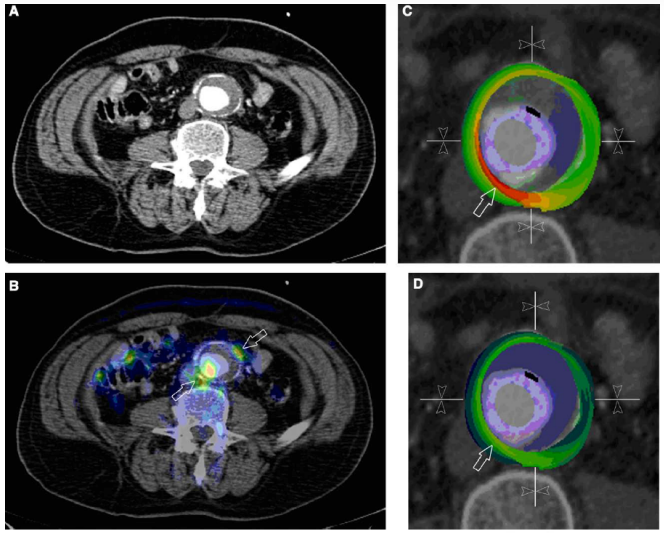


C Reeps et al. J Vasc Surg 2008

Multifactorial Relationship Between ^{18}F-Fluoro-Deoxy-Glucose Positron Emission Tomography Signaling and Biomechanical Properties in Unruptured Aortic Aneurysms

Alain Nchimi, MD; Jean-Paul Cheramy-Bien, MLT; T. Christian Gasser, PhD; Gauthier Namur, MD; Pierre Gomez, MD; Laurence Seidel, MSc; Adelin Albert, PhD; Jean-Olivier Defraigne, MD, PhD; Nicos Labropoulos, MD, PhD; Natzi Sakalihasan, MD, PhD





Conclusions—Increased ^{18}F-FDG positron emission tomographic uptake in aortic aneurysms is strongly related to aneurysm location, wall stress as derived by finite element simulations, and patient risk factors such as acquired and inherited susceptibilities. **(*Circ Cardiovasc Imaging*. 2014;7:82-91.)**

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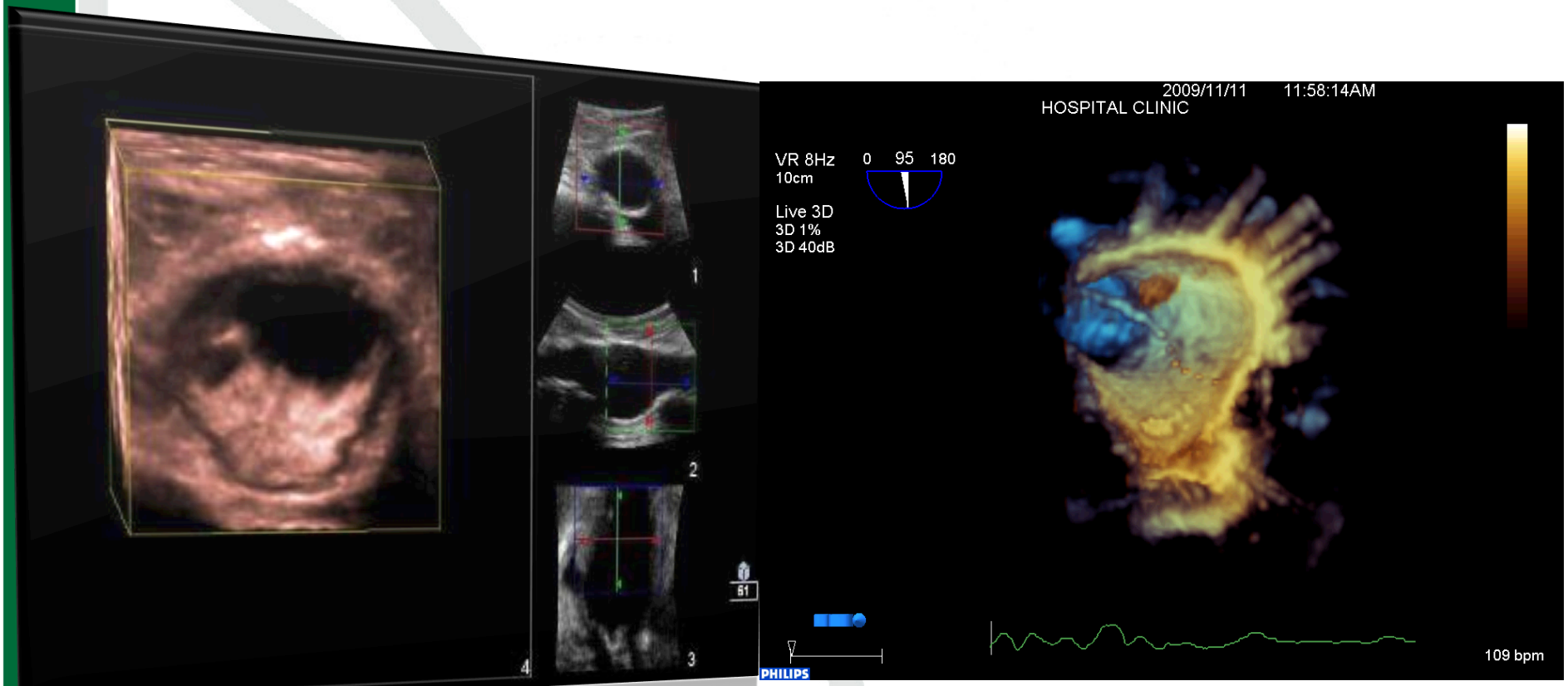
3D Ultrasonography



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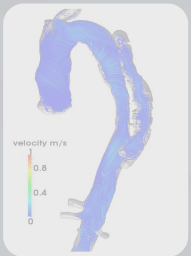
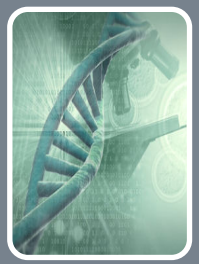
Diagnostic elements for the future

Index



Functional imaging



Genomics

Biomarkers

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ELSEVIER

European Journal of Cardio thoracic Surgery xxx (2009) xxx xxx

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

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Review

Inherited diseases and syndromes leading to aortic aneurysms and dissections

Ahmet Okay Caglayan [a,*], Munis Dundar [b]

Table 1
Genes responsible for non syndromic aortic aneurysm and dissection.

	Locus name (gene cards)	Gene symbol	Chromosomal localization	Protein name
Affected genes	TAAD1 (AAT2)	Unknown	5q13 14	Unknown
	FAA1 (AAT1)	Unknown	11q23.3 24	Unknown
	TAAD2 (AAT3)	TGFBR2	3p24 25	TGF beta receptor type 2
	MYH11	MYH11	16p13.13 p13.12	Myosin 11
Positional candidate genes	FBLN2	FBLN2	3p25.1	Fibulin 2
	TIMP4	TIMP4	3p25	Tissue inhibitor of metalloproteinases 4
Candidate genes	MMP3	MMP3	11q22.3	Matrix metalloprotease 3
	COL1A1	COL1A1	17q21.3 q22	Collagen alpha 1(I) chain
	COL1A2	COL1A2	7q22.1	Collagen alpha 2(I) chain

Table 2
Genes responsible for aortic aneurysm and dissection in frequent syndromes.

Syndrome (inheritance)	Gene symbol	Chromosome localization	Protein name	Gene function	Affected aortic segments
Marfan (autosomal dominant)	*FBN1*	15q21.1	Fibrillin 1	*FBN1* encodes fibrillin 1, a large glycoprotein that is a component of extracellular matrix structures called microfibrils	Dilatation of the ascending aorta involving the sinuses of Valsalva; dissection of the ascending aorta
	TGFβR2[a]	3p24 25	Transforming growth factor beta receptor type II	TGF signaling plays an important role in cellular proliferation, differentiation and extracellular matrix production	Predominantly ascending aortic disease; however, significant descending aortic disease and aneurysms of other vessels also occurred in affected family members
Ehlers Danlos syndrome type IV (autosomal dominant)	*COL3A1*	2q31	Collagen alpha 1 (III) chain	The *COL3A1* gene encodes the chains of type III procollagen, a major structural component of skin, blood vessels, and hollow organs	Proximal branches of the aortic arch, the descending thoracic aorta and the abdominal aorta. The distal branches of the aorta, especially the renal, mesenteric, iliac and femoral arteries, are also particularly affected [102]
Turner syndrome (chromosomal)		45X			Aortic root dilatation with or without dissection has been incidentally noted in 6% 9% of patients with Turner syndrome [103,104]
Noonan syndrome (autosomal dominant)	*PTPN11*	12q24.1	Tyrosine protein phosphatase non receptor type 11 (SHP 2)	The protein is expressed throughout the body and it is an important player in cellular response to growth factors, hormones, cytokines and cell adhesion molecules	Coarctation of aorta
	KRAS	12p12.1	GTPase KRas	Their proteins regulate cell fates and they are key regulators of the RAS RAF MEK ERK pathway, which is important for proliferation, growth and death of cells	
	RAF1	3p25	RAF proto oncogene serine/ threonine protein kinase		
	SOS1	2p22 p21	Son of sevenless homolog 1		

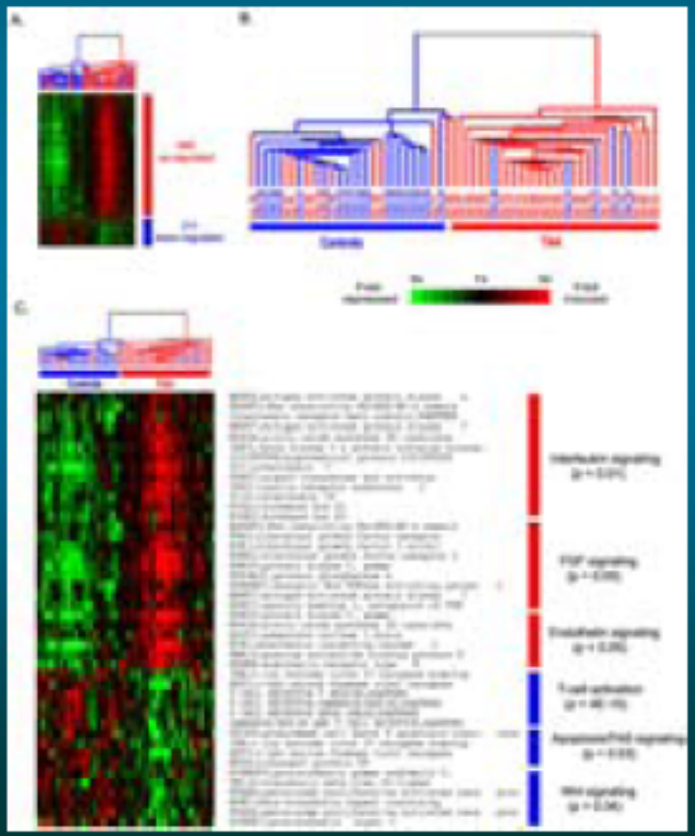
Table 2
Genes responsible for aortic aneurysm and dissection in frequent syndromes.

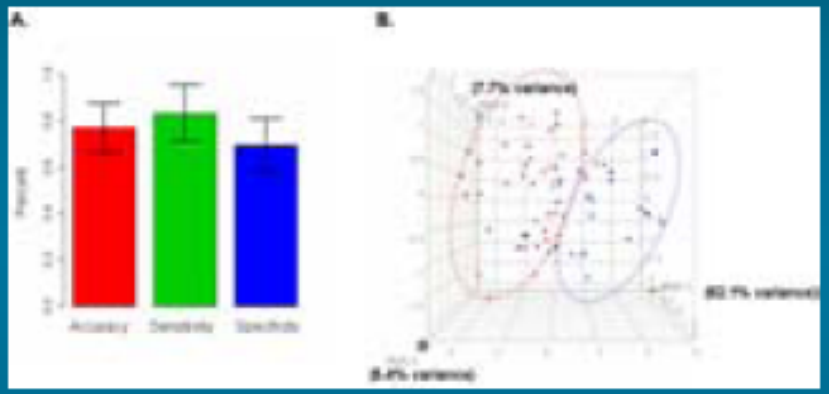
Syndrome (inheritance)	Gene symbol	Chromosome localization	Protein name	Gene function	Affected aortic segments
Osteogenesis imperfecta (autosomal dominant)	*COL1A1*	17q21.3 q22	Collagen alpha 1(I) chain	They encode the chains of type I procollagen, the major protein in bone and most other connective tissues	Ascending aorta
	COL1A2	7q22.1	Collagen alpha 2(I) chain		
Homocystinuria (autosomal recessive)	*CBS*	21q22.3	Cystathionine beta synthase	CBS is a pyridoxal 50 phosphate (PLP) dependent enzyme and condenses homocysteine and serine to cystathionine, an irreversible step in transsulfuration	Abdominal aorta (especially elderly patients)
Autosomal dominant polycystic kidney disease (autosomal dominant)	*PKD1*	16p13.3	Polycystin 1	Cell cycle regulation and intracellular calcium transport	Thoracic aortic aneurysms
	PKD2	4q21 q22	Polycystin 2	Member of the family of voltage activated calcium channels	
Pseudo xanthoma elasticum (autosomal recessive)	*ABCC6 (MRP6)*	16p13.1	ATP binding cassette transporter C6 (multidrug resistance associated protein 6)	Cellular transport protein	Especially abdominal, sometimes arch and thoracic aortic aneurysms
Hurler syndrome (autosomal recessive)	IDUA	4p16.3	Alpha L iduronidase	Lysosomal degradation of glycosaminoglycans (heparan and dermatan sulphate)	Coarctation of aorta
Loeys Dietz syndrome (autosomal dominant)	*TGFBR1* and *TGFBR2*	9q33 q34 and 3p24 p25	Transforming growth factor β receptors 1 and 2	TGF signaling plays an important role in cellular proliferation, differentiation and extracellular matrix production	Affected patients have a high risk of aortic dissection or rupture at an early age and at aortic diameters that ordinarily would not be predictive of these events

[a] Germline *TGFBR2* mutations are responsible for the inherited predisposition to familial TAAD in 5% of these cases.

Gene Expression Signature in Peripheral Blood Detects Thoracic Aortic Aneurysm

Yulei Wang, Catalin C. Barbacioru, Dov Shiffman, Sriram Balasubramanian, Olga Iakoubova, Maryann Tranquilli, Gonzalo Abomoz, Julie Blake, Necip N. Mehmet, Dewi Ngadimo, Karen Poulter, Frances Chan, Raymond R. Sarraha, and John A. Elefteriades





- 94 samples
- Significance analysis of microarray
- 41 classifier genes identified

PLoS ONE. 2007; 2(10): e1050.

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Ann Vasc Surg. 2011 April ; 25(3): 388–412. doi:10.1016/j.avsg.2010.09.004.

Genes and Abdominal Aortic Aneurysm

Irene Hinterseher, **Gerard Tromp**, and **Helena Kuivaniemi**
The Sigfried and Janet Weis Center for Research, Geisinger Health System, Danville, PA, USA

Abstract

Abdominal aortic aneurysm (AAA) is a multifactorial disease with a strong genetic component. Since first candidate gene studies were published 20 years ago, nearly 100 genetic association studies using single nucleotide polymorphisms (SNPs) in biologically relevant genes have been reported on AAA. The studies invest
cardiovascular system, the immune s
enough to draw firm conclusions and
The more recent unbiased approache
genetic association studies, which ha
appropriately powered and well-char
AAA have already been identified in
was of a variant in a gene called *CN*
studies, however, could not replicate
chromosome 9p21 and 9q33 were re
supporting evidence of contribution
known as *ANRIL*, which encodes an
dependent kinase inhibitors CDKN2
cell growth and survival. Functional
these genes contribute to AAA pathc

Contents lists available at SciVerse ScienceDirect

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esvs Journal

Review

Low Density Lipoprotein Receptor Related Protein 1 and Abdominal Aortic Aneurysms

J.B. Wild*, P.W. Stather, N. Sylvius, E. Choke, R.D. Sayers, M.J. Bown

Department of Cardiovascular Sciences, Vascular Surgery Group, University of Leicester, Leicester LE2 7LX, UK

WHAT THIS PAPER ADDS

- A recent genome wide association study has demonstrated a highly significant association between abdominal aortic aneurysm (AAA) and the LRP1 (low density lipoprotein receptor related protein 1) gene. This review outlines how this cell surface transport molecule may influence the establishment and propagation of aneurysmal disease, essentially introducing LRP1 as a new potential candidate gene for AAA.

Diagnostic elements for the future

Index

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Biomarkers in AAA diagnostic and AAA expansion

Thrombosis Research xxx (2009) xxx–xxx

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Regular Article

D-dimer

Haemostatic markers in patients with abdominal aortic aneurysm and the impact of aneurysm size

Jonas Wallinder [a], David Bergqvist [c], Anders E. Henriksson [b,c,*]

Eur J Vasc Endovasc Surg (2008) 36, 273–280

serum elastin peptides (SEP) and plasmin-antiplasmin (PAP) complexes; metalloproteinase 9 (MMP9) and interferon-gamma (IFN-gamma)…

REVIEW

Potential Circulating Biomarkers for Abdominal Aortic Aneurysm Expansion and Rupture - a Systematic Review

S. Urbonavicius [a,b,*], G. Urbonaviciene [a], B. Honoré [b], E.W. Henneberg [a], H. Vorum [b], J.S. Lindholt [a]

Identification of microRNAs associated with abdominal aort aneurysms and peripheral arterial disease

P. W. Stather[1], N. Sylvius[2], D. A. Sidloff[1], N. Dattani[1], A. Verissimo[1], J. B. Wild[1], H. Z. Butt[1], E. Choke[1], R. D. Sayers[1] and M. J. Bown[1,3*]

Departments of [1]Cardiovascular Sciences and [2]Genetics and [3]National Institute for Health Research, University of Leicester, Leicester, UK
Correspondence to: Mr P. W. Stather, Department of Cardiovascular Sciences, University of Leicester, Leicester LE2 7LX, UK
(e-mail: philstather@doctors.org.uk)

Br J Surg. 2015

Background: MicroRNAs are crucial in the regulation of cardiovascular disease and represent potential therapeutic targets to decrease abdominal aortic aneurysm (AAA) expansion. The aim of this study was to identify circulating microRNAs associated with AAA.

Methods: Some 754 microRNAs in whole-blood samples from 15 men with an AAA and ten control subjects were quantified using quantitative reverse transcriptase–PCR. MicroRNAs demonstrating a significant association with AAA were validated in peripheral blood and plasma samples of men in the following groups (40 in each): healthy controls, controls with peripheral arterial disease (PAD), men with a small AAA (30–54 mm), those with a large AAA (over 54 mm), and those following AAA repair. MicroRNA expression was also assessed in aortic tissue.

Results: Twenty-nine differentially expressed microRNAs were identified in the discovery study. Validation study revealed that let-7e (fold change (FC) −1·80; $P = 0·001$), miR-15a (FC −2·24; $P < 0·001$) and miR-196b (FC −2·26; $P < 0·001$) were downregulated in peripheral blood from patients with an AAA, and miR-411 was upregulated (FC 5·90; $P = 0·001$). miR-196b was also downregulated in plasma from the same individuals (FC −3·75; $P = 0·029$). The same miRNAs were similarly expressed differentially in patients with PAD compared with healthy controls. Validated and predicted microRNA targets identified through miRWalk revealed that these miRNAs were all regulators of AAA-related genes (vascular cell adhesion molecule 1, intercellular cell adhesion molecule 1, DAB2 interacting protein, α1-antitrypsin, C-reactive protein, interleukin 6, osteoprotegerin, methylenetetrahydrofolate reductase, tumour necrosis factor α).

Conclusion: In this study, circulating levels of let-7e, miR-15a, miR-196b and miR-411 were differentially expressed in men with an AAA compared with healthy controls, but also differentially expressed in men with PAD. Modulation of these miRNAs and their target genes may represent a new therapeutic pathway to affect the progression of AAA and atherosclerosis.

Summary

- New elements, besides the diameter, should be added in the AAA detection and decision making process for intervention
- Functional imaging, genomics and biomarkers would be developed and applied for the oncoming clinical decision equation

“There is no disease more conductive to clinical humility than aneurysm of the aorta”

Sir William Osler

1849-1919

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