NUFFIELD DEPARTMENT OF SURGICAL SCIENCES

UNIVERSITY OF OXFORD

PROGRESS THROUGH PARTNERSHIP

OxAAA

Oxford Abdominal Aortic Aneurysm Study

Multi-modal approach to predict AAA growth

~ Towards Precision Management of Abdominal Aortic Aneurysms~

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Conflict of Interest Declaration: Regent Lee is an academic co-founder and chief medical officer of AiSentia Limited.

OxAAA team

Co-PI: Professor Ashok Handa

Nicholas Killough, Felicity Woodgate, Ismail Cassimjee, Pierfrancesco Lapolla, Anirudh Chandrashekar, Kirthi Bellamkonda, Matthew Williams, Amy Jones, Joel Ward

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Oxford Regional Vascular Services Unit

Target Discovery Institute, University of Oxford

Institute of Biomedical Engineering, University of Oxford

University of Oxford MEDICAL SCIENCES DIVISION

The Academy of Medical Sciences

NHS National Institute for Health Research Oxford Biomedical Research Centre

Heart Research UK

UK Research and Innovation

Discrepancies in the management of ‘small’ AAAs between geographical regions

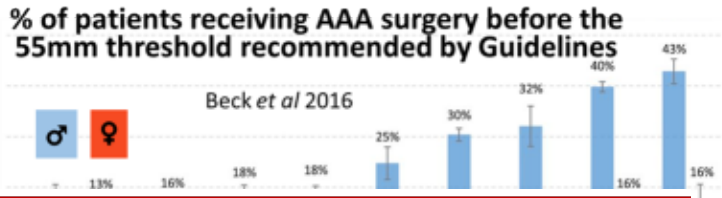
Surveillance Interval

SVS, ESVS, AHA, EHJ guidelines:

- 3.5-4.4cm – yearly scan
- 4.5-5.5cm – **biannual** scan

N

Surgical threshold



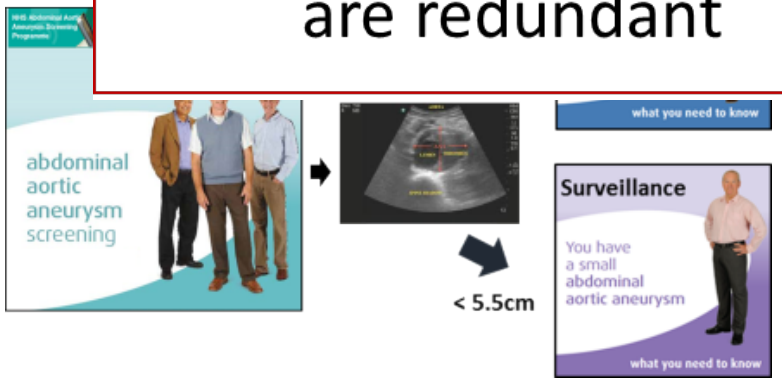
In real life

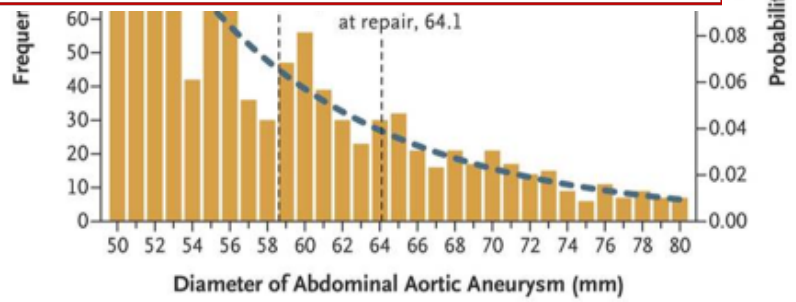
Problem 1

Many scans are redundant

Problem 2

Many operations are unnecessary





Karthikesalingam et al NEJM 2016

methods for the prediction of AAA growth can impact on these aspects of clinical practice

AAA Growth Prediction Method

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OxAAA

Oxford Abdominal Aortic Aneurysm Study

Prediction of growth in AAA patients – OxAAA study

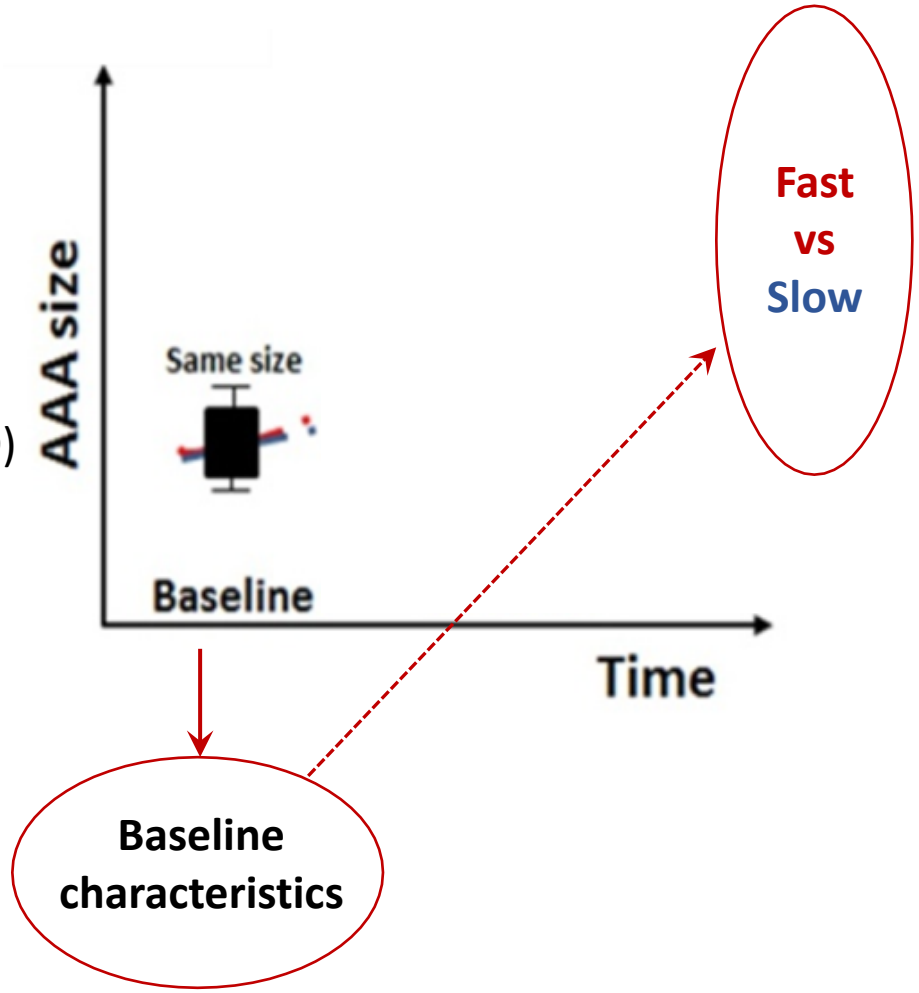
Oxford Abdominal Aortic Aneurysm Study

Methods:

- Prospective cohort study of AAA patients undergoing NHS surveillance pathway
- Individual consent (IRB: SC/0250/13)
- Recruitment: since Nov 2013
- At baseline:
  - AAA size by U/S – max AP diameter (APD)
  - Measurement of FMD
    - Marker of endothelial dysfunction
  - Collection of plasma samples
    - EDTA, **platelet poor plasma**
- Future growth rate calculation :

$$\frac{(\Delta APD/APD \text{ at baseline})}{(\text{number-of-days-lapsed}/365\text{days})}$$

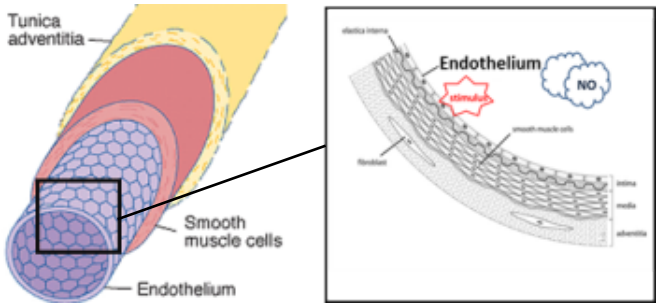
- For patient receiving AAA surveillance:
  - repeat sampling yearly follow up
- For patients undergoing AAA surgery:
  - Repeat sampling before and after Surgery
  - Intra-operative tissue biopsy

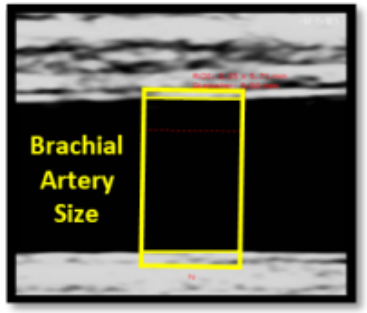


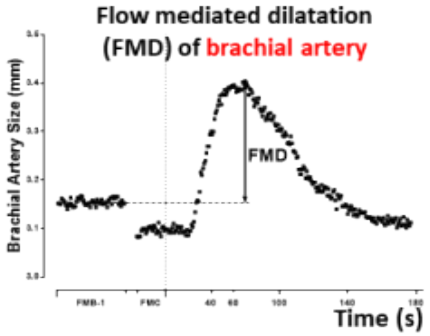
Aim:
Using baseline features
To predict future growth rate

Flow Mediated Dilatation (FMD) as a biomarker of AAA growth

Flow mediated dilatation (FMD) of brachial artery is physiological index of endothelial function (ie 'healthiness' of the artery)





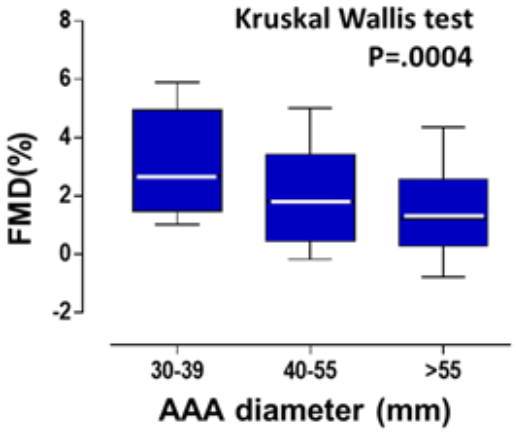


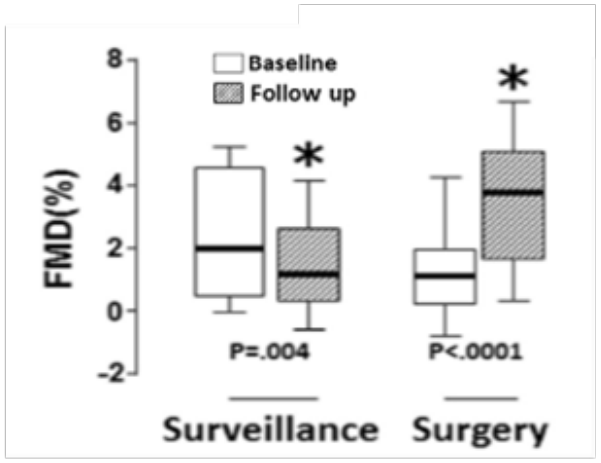
Flow Mediated Dilatation and Progression of Abdominal Aortic Aneurysms

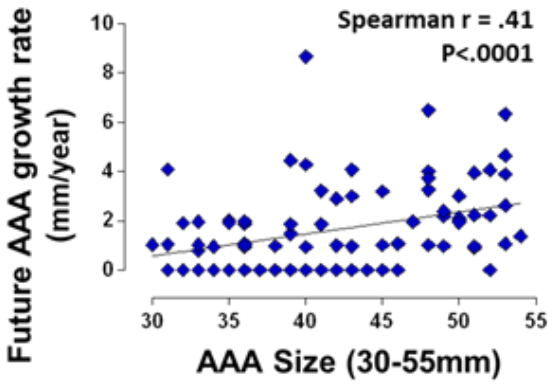
R. Lee *, K. Bellamkonda, A. Jones, N. Killough, F. Woodgate, M. Williams, I. Cassimjee, A. Handa, on Behalf of the Oxford Abdominal Aortic Aneurysm Study

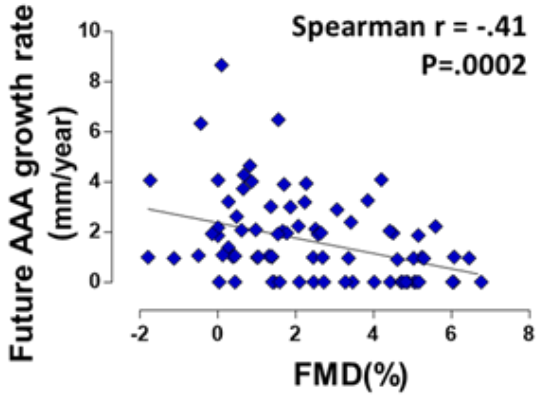
Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK

R. Lee et al EJVES 2017 Jun;53(6):820-829







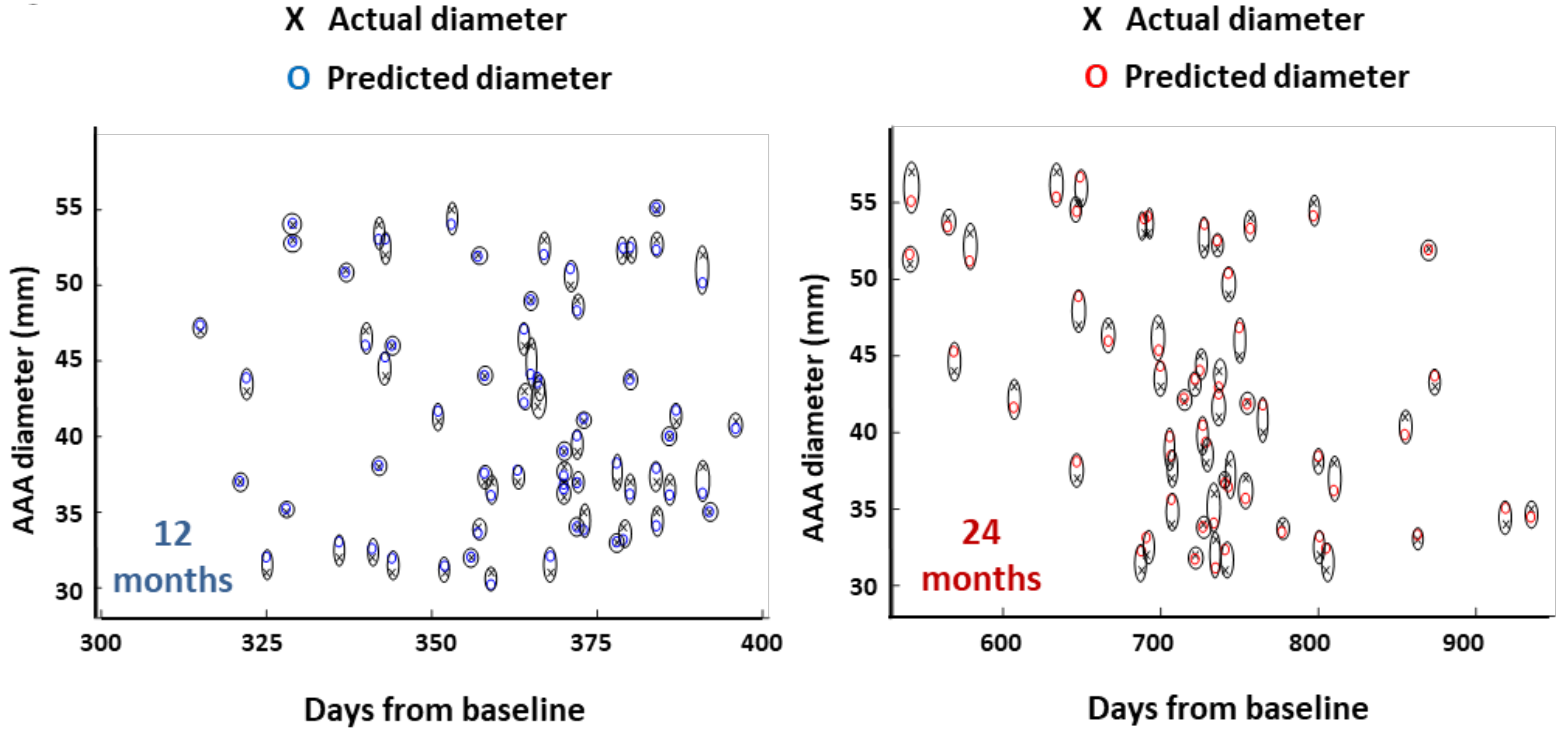


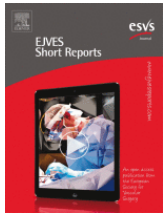
Mode 1: prediction of AAA growth using physiological parameter

Bench mark Machine Learning techniques:

- Two input features (FMD, AAA diameter),
- nonlinear support vector machine regression (SVR) with Kernel tricks
- hyper-parameter optimisation with nested 5-fold cross-validations
- Allowed 2mm margin of size prediction (accepted technical variation between U/S scans)

Successful prediction of growth: At **12 months** - **85%**; at **24 months** - **71%**



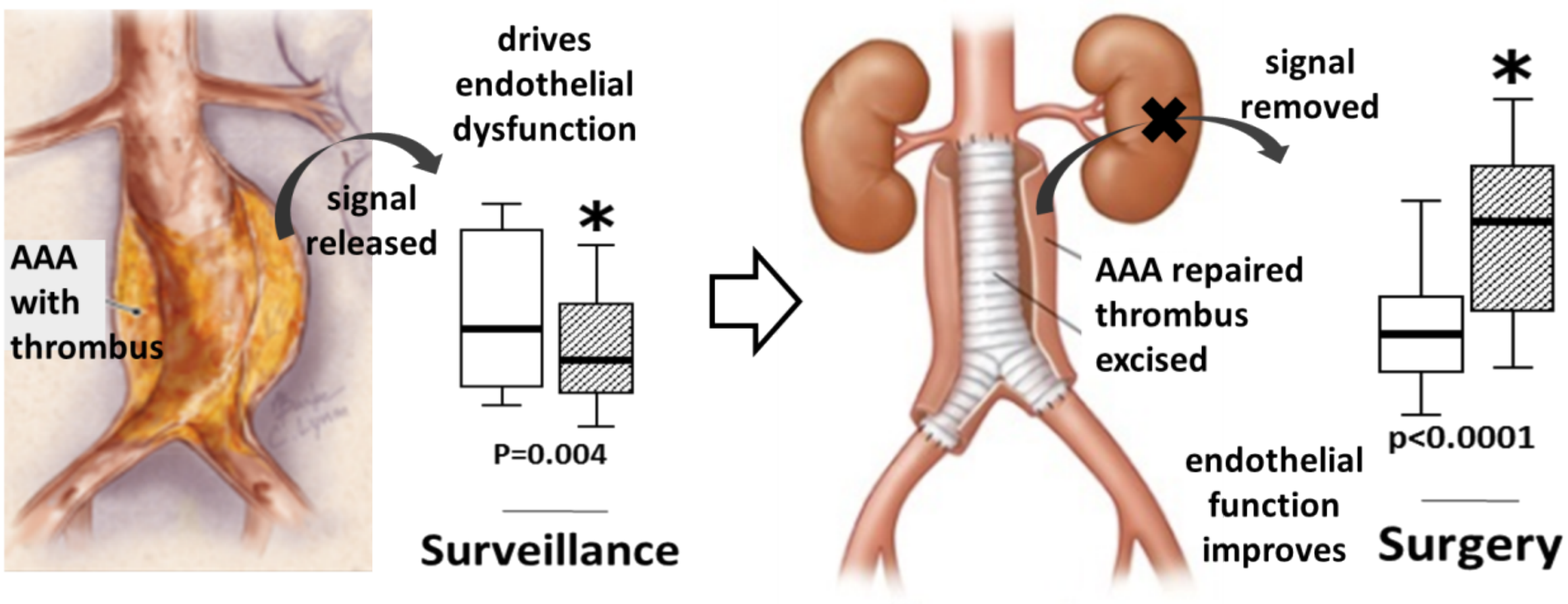


EJVES Short Rep. 2018 May 1;39:24-28. doi: 10.1016/j.ejvssr.2018.03.004. eCollection 2018.

Applied Machine Learning for the Prediction of Growth of Abdominal Aortic Aneurysm in Humans.

Lee R[1], Jarchi D[2], Perera R[3], Jones A[1], Cassimjee I[1], Handa A[1], Clifton DA[3]; Oxford Abdominal Aortic Aneurysm Study and; Oxford Regional Vascular Service.

AAA "complex" as the source of mediators for systemic biological manifestations



Hypothesis:

The aneurysm complex is the source of mediators that drives systemic biological effects in AAA patients

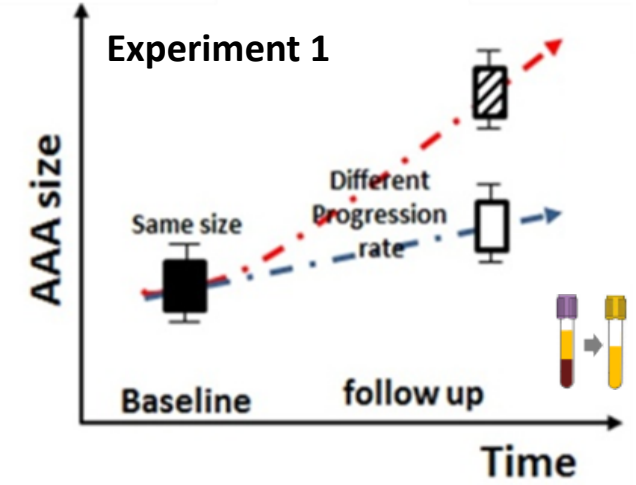
Integrated Plasma and Tissue Proteomics Reveals Attractin Release by Intraluminal Thrombus of Abdominal Aortic Aneurysms

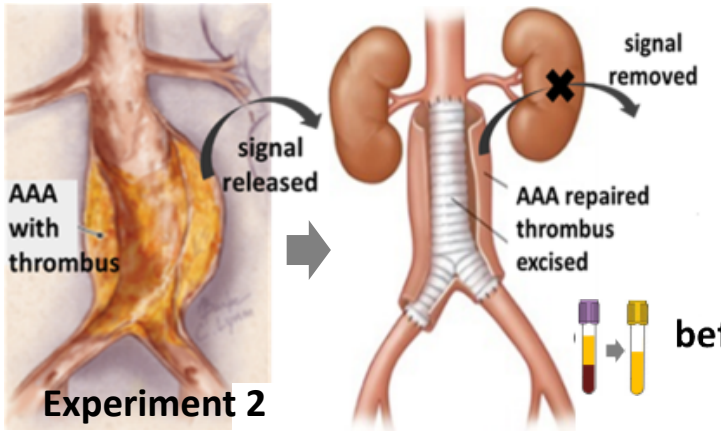
Experiment 1: plasma samples of fast vs slow growth patients

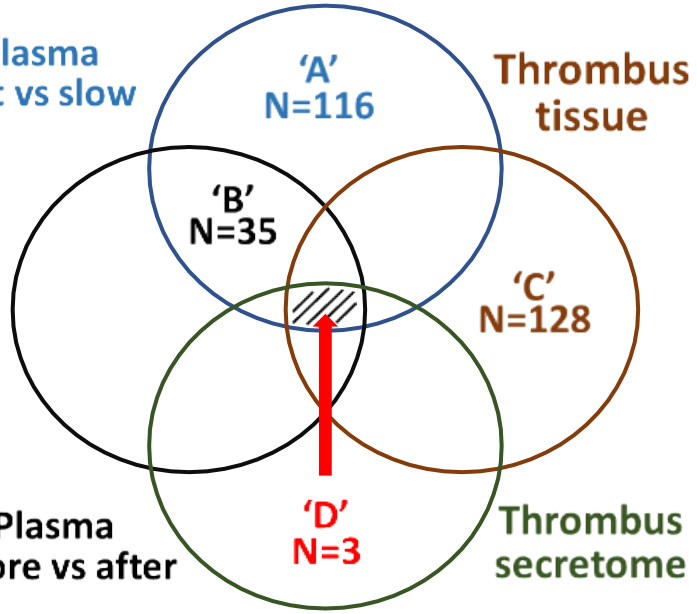
Experiment 2: plasma samples from same patient before vs after surgery

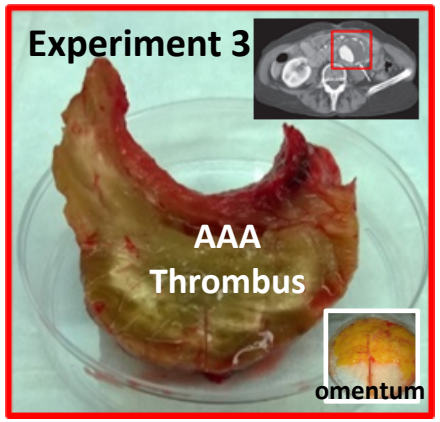
Experiment 3: Analysis of ILT protein content

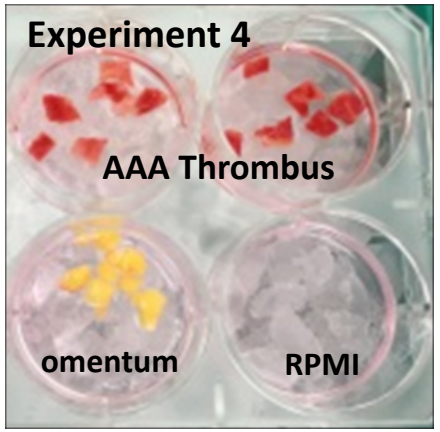
Experiment 4: Analysis of ILT protein 'secretome'





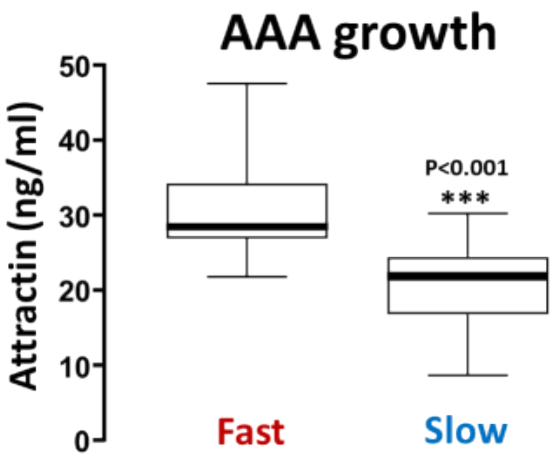


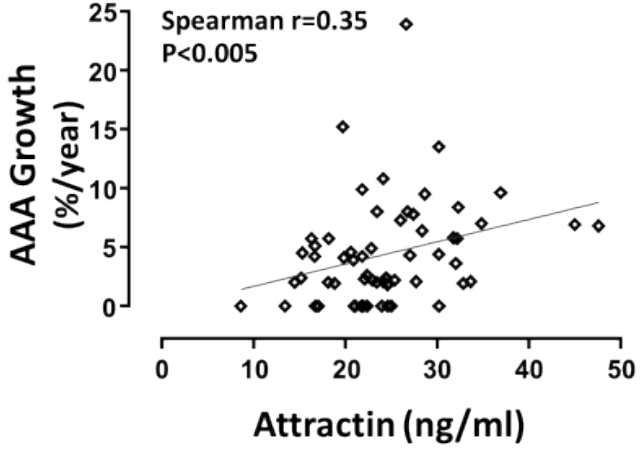




We found 3 proteins that: (1) higher in patients with fast growing AAA, **(2)** reduced in systemic circulation after AAA repair, **(3)** highly abundant in AAA ILT, **(4)** released from ILT: **Attractin,** Complement C8, HSPAA5P

Technical validation of the LC-MS/MS data by ELISA





AI enables high throughput characterization of arterial morphology with or without contrast

ANNALS OF SURGERY

Annals of Surgery: November 23, 2020

Articles & Issues | COVID-19 | Social Justice | Videos | For Authors | Journal Info

ORIGINAL ARTICLE: PDF ONLY

A Deep Learning Pipeline to Automate High-Resolution Arterial Segmentation with or without Intravenous Contrast

Chandrashekar, Anirudh BE*; Handa, Ashok MBBS FRCS MA*; Shivakumar, Natesh MBBS*; Lapolla, Pierfrancesco*; Uberoi, Raman BMSc MBBchir MRCP*; Grau, Vicente PhD†; Lee, Regent MBBS MS(Vasc Surg) DPhil (Oxon) FRCS (Vasc Surg)* Author Information

Anirudh Chandrashekar
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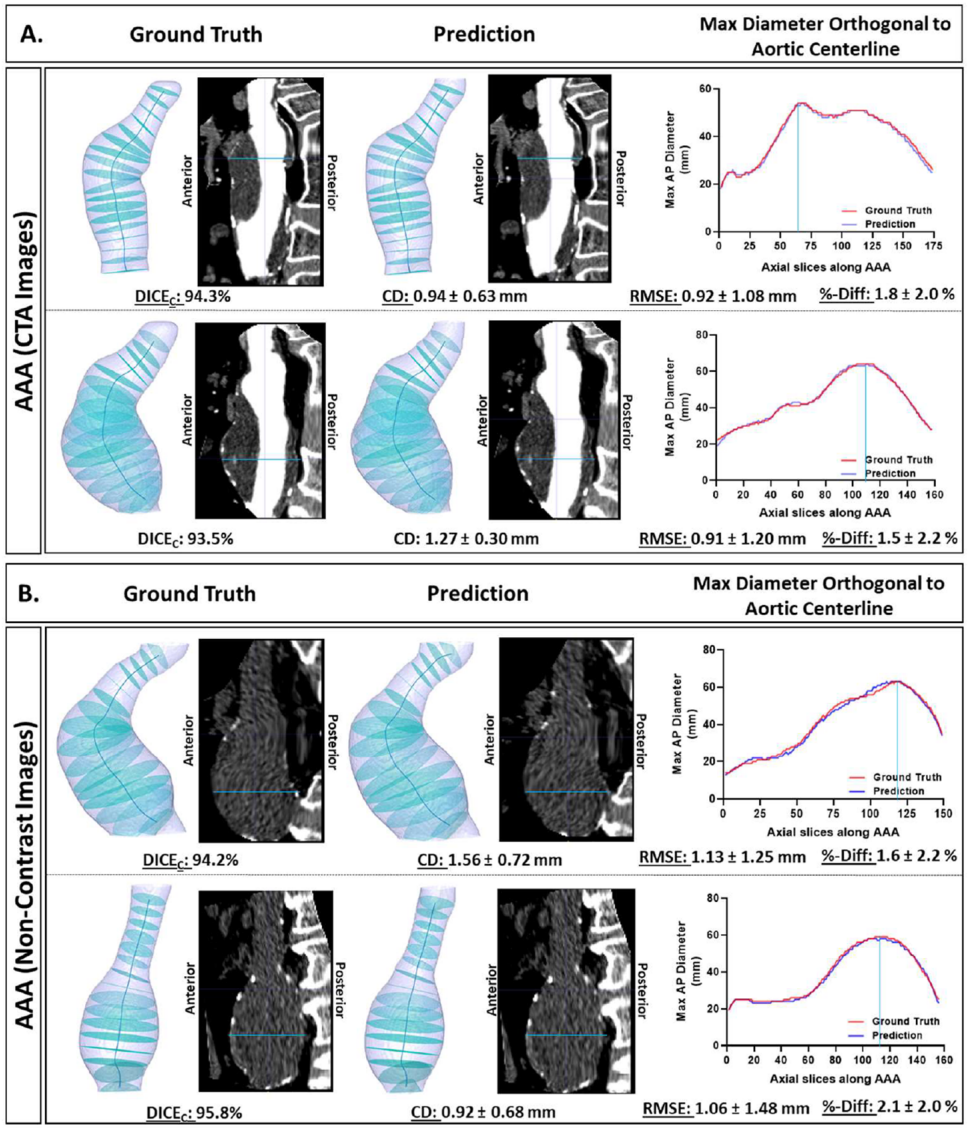

Fig 6: Maximum AAA Diameter profiles along planes orthogonal to AAA centerline. Profiles were generated from ground truth and model predictions of AAA volumes derived from contrast-enhanced (**A**) and non-contrast (**B**) CT images. The perpendicular planes were used to generate the re-aligned or straightened views of AAA. Corresponding DICE scores, average Euclidean distance deviations between centerlines, RMSE and %-difference of diameter profiles are indicated.

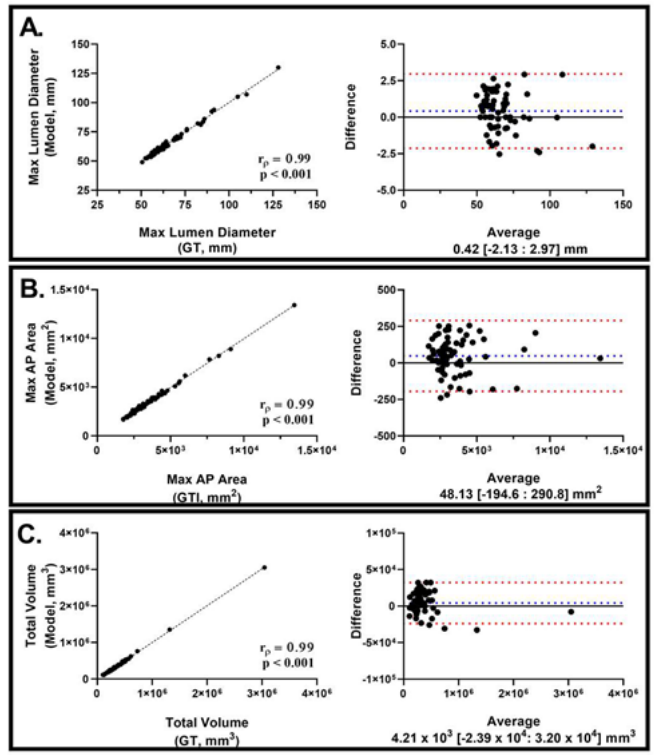

Fig 7: Bland-Altman plots and correlation-coefficient analysis comparing the 1-D (Max AP Diameter of AAA - **A**), 2-D (Max axial area of AAA - **B**), and 3-D (Total volume of AAA - **C**) measurements from model predictions compared against those derived from GT. This analysis was limited to volumes extracted from non-contrast CT images. Spearman correlation coefficients (r_p) and p-values are indicated on the graphs.

Geometric features and AAA growth: radius of curvature and undulation index

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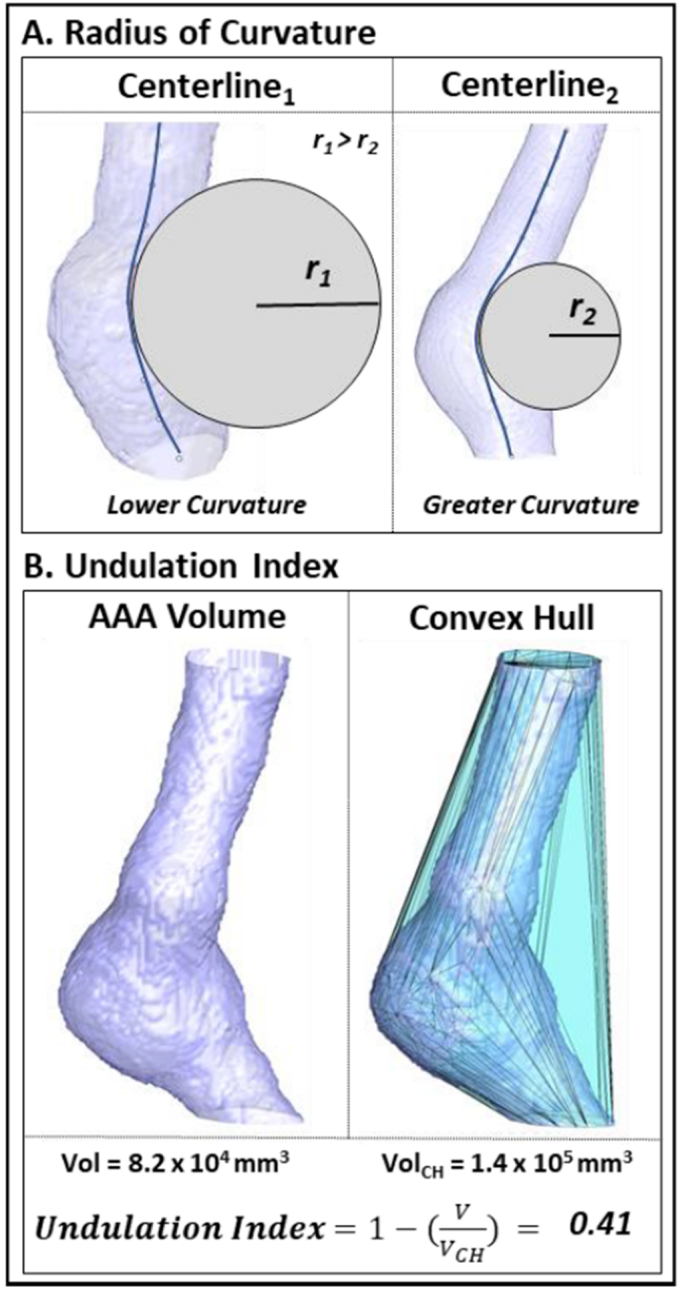
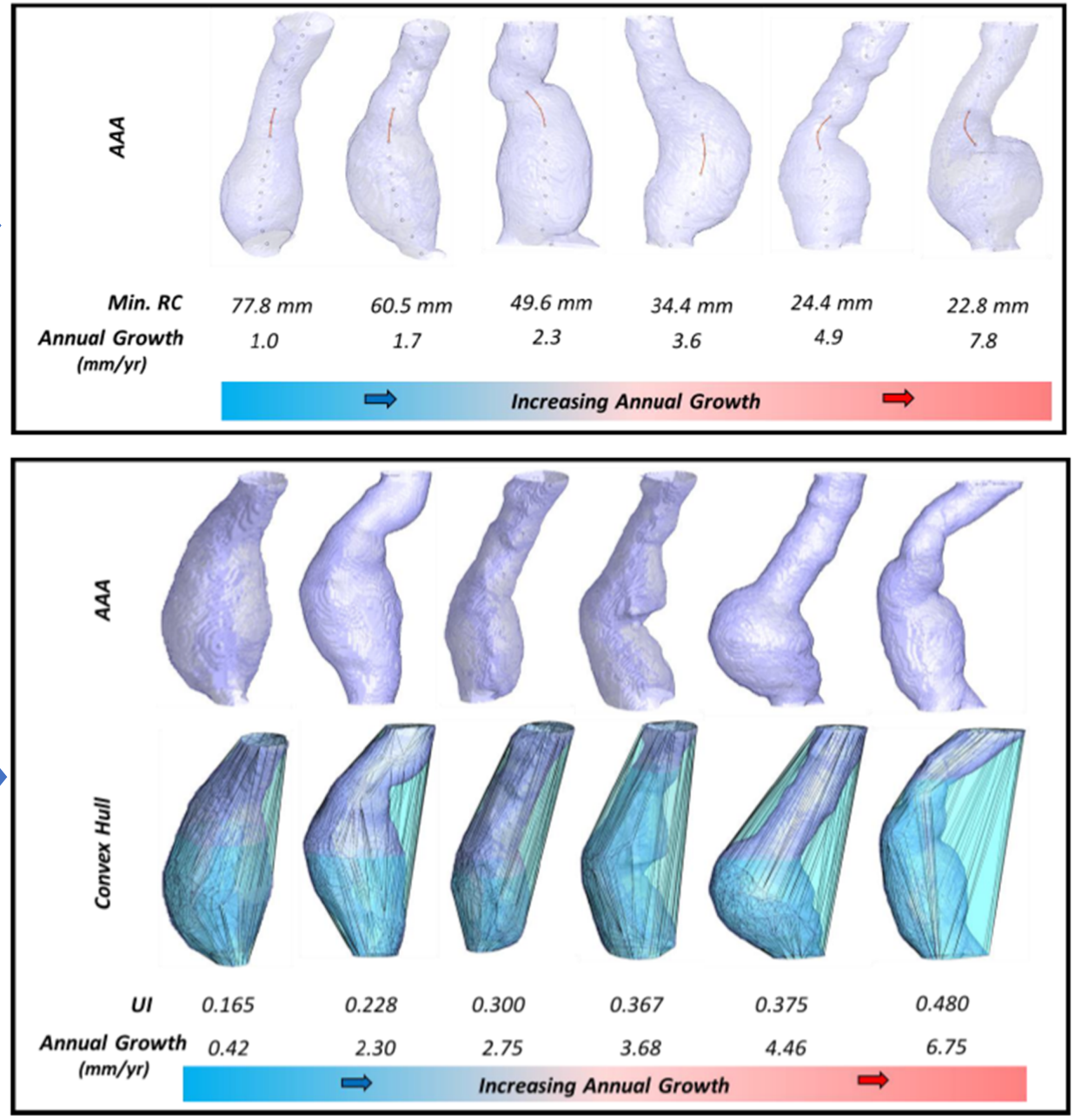
Prediction of Abdominal Aortic Aneurysm Growth Using Geometric Assessment of Computerised Tomography Images Acquired During the Aneurysm Surveillance Period

Chandrashekar, Anirudh*†‡; Handa, Ashok*; Lapolla, Pierfrancesco*; Shivakumar, Natesh*; Ngetich, Elisha*; Grau, Vicente†; Lee, Regent* Author Information

Annals of Surgery: December 29, 2020 - Volume Publish Ahead of Print - Issue -
doi: 10.1097/SLA.0000000000004711

Chandrashekar A et al, Annals of Surgery, 2021





Radius of Curvature and Undulation Index are independent of demographic traits

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Prediction of Abdominal Aortic Aneurysm Growth Using Geometric Assessment of Computerised Tomography Images Acquired During the Aneurysm Surveillance Period

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TABLE 1. Summary of Participant Demographics at the Pre-surgical Assessment and Significance of Spearman Correlation With Extracted Geometric Parameters

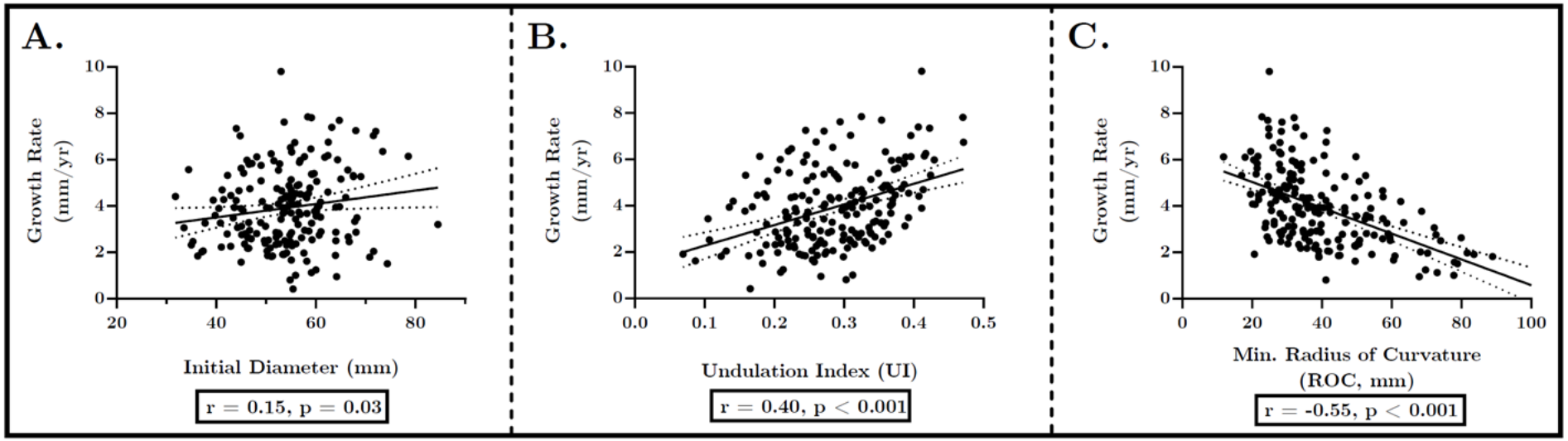
		Significance of Spearman Correlation Coefficient		
	All Participants (n = 102)	Diam.	UI	RC
Male (%)	99 (97)	0.35	0.36	0.09
Age at consent (median/IQR)	72 (67–79)	0.12	0.83	0.70
Height (±SD)	1.75 ± 0.08	0.07	0.45	0.06
Weight (Median/IQR)	81.9 (74–90.2)	0.17	0.15	0.07
BMI (Median/IQR)	26.8 (24.3–28.7)	0.61	0.35	0.18
MAP (±SD)	102.2 ± 12.8	0.13	0.70	0.20
Current smoker (%)	24 (24)	0.57	0.99	0.09
Past smoking Hx (%)	68 (67)	0.97	0.48	0.59
Never smoked (%)	13 (13)	0.65	0.34	0.44
CAD Hx (%)	33 (32)	0.25	0.15	0.56
Coronary intervention (%)	26 (25)	0.63	0.41	0.88
PAOD History (%)	16 (16)	0.85	0.59	0.22
Cerebral art. disease (%)	12 (12)	0.10	0.16	0.34
HTN history (%)	74 (73)	0.53	0.77	1.00
Hypercholesterolemia (%)	61 (60)	0.61	0.67	0.75
Tot. cholesterol (median/IQR)	3.8 (3.2–4.6)	0.23	0.76	0.63
HDL (median/IQR)	1.1 (0.9–1.3)	0.47	0.41	0.06
LDL (median/IQR)	1.5 (0–2.5)	0.26	0.92	0.37
TG (median/IQR)	1.2 (0.8–1.6)	0.49	0.65	0.66
Diabetes (%)	16 (16)	0.88	0.26	0.78
HbA1C (median/IQR)	5.6 (5.4–5.9)	0.19	0.81	0.41
Diabetes - oral/insulin (%)	12 (12)	0.19	0.22	0.17
CKD - eGFR <60 (%)	28 (27)	0.15	1.00	0.96
Creatinine (median/IQR)	86.5 (73.3–101.3)	0.19	0.07	0.74
Beta-blockers (%)	32 (31)	0.68	0.30	0.49
ACEI/ARB (%)	56 (55)	0.27	0.77	0.97
Aspirin (%)	47 (46)	0.83	0.89	1.00
Thienopyridine (%)	9 (9)	0.55	0.17	0.44
Ticragrelor (%)	3 (3)	0.81	0.64	0.72
Anticoagulant (%)	12 (12)	0.93	0.46	0.21
CCBs (%)	43 (42)	0.13	0.64	0.34
Diuretics (%)	22 (22)	0.47	0.38	0.58
Gastro-restraint (%)	31 (30)	0.57	0.68	0.32
Steroids (%)	7 (7)	0.36	0.97	0.15
Statins (%)	74 (73)	0.57	0.76	0.24
AAA Diam (Median/IQR)	63 (58–72.5)			
UI (±SD)	0.23 ± 0.08			
RC (Median/IQR)	35.9 (29.7–46.9)			

Participant demographics were collected at the pre-surgical assessment and were correlated against the extracted geometric parameters of AAA diameter, undulation index, and radius of curvature. Characteristics that follow a Gaussian/Normal Distribution are indicated with a +. For such variables, mean ± SD are presented, and cohort differences are compared using a Student *t*-test. For variables that do not follow a Gaussian distribution, median and inter-quartile range (IQR) are presented and cohort differences are compared using a Mann-Whitney test.

ACEI indicates angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blocker; BMI, body mass index; CAD, coronary artery disease; CCB, calcium channel blockers; CKD, chronic kidney disease; HDL, high density lipoprotein; HTN, arterial hypertension; Hx, history of; IQR, Interquartile range; LDL, low density lipoprotein; MAP, mean arterial pressure; PAD, peripheral arterial occlusive disease; PAOD, peripheral arterial occlusive disease; RC, radius of curvature; SD, standard deviation; TG, triglyceride; UI, undulation index.

Diameter, UI and RC correlates with future AAA growth Independently observed in two cohorts

Oxford Cohort (n=192)



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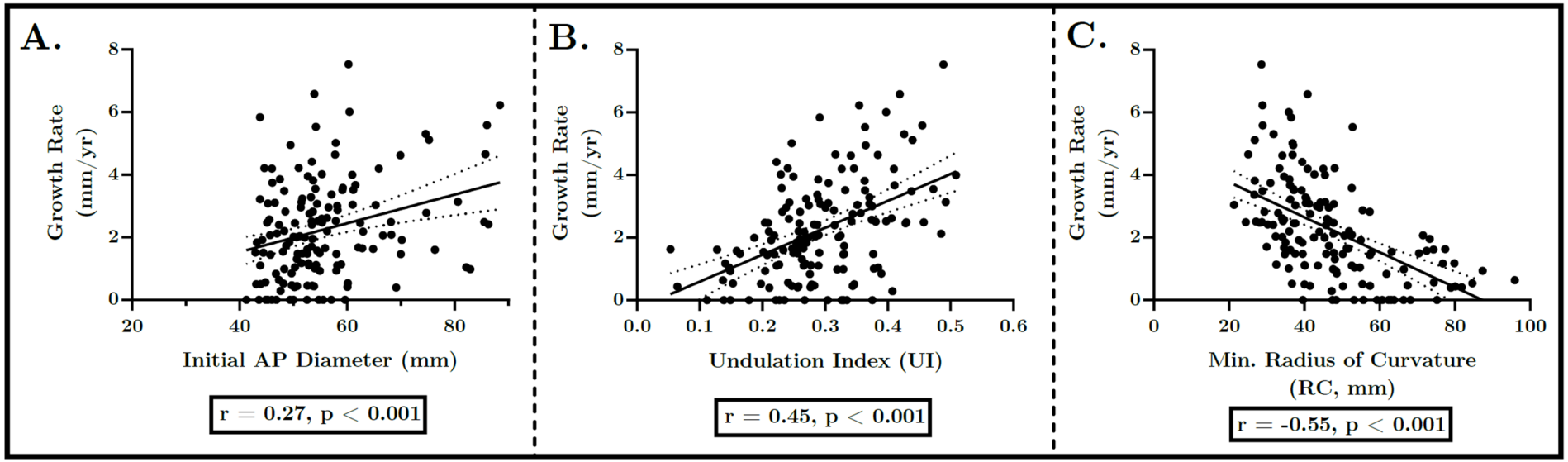
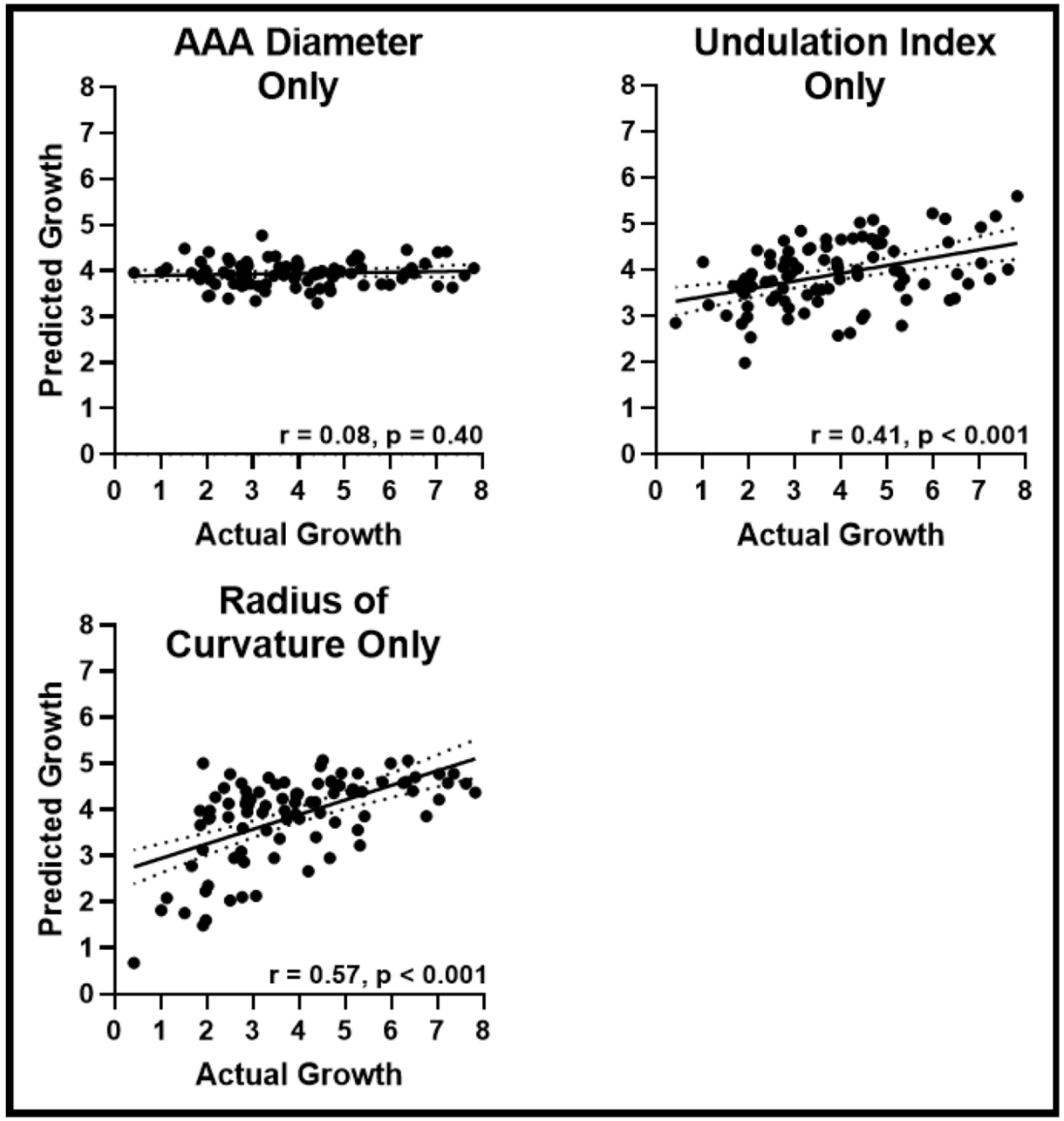
MA3RS Cohort (n=148)

Newby et al. (Edinburgh)



Mode 3: Prediction of AAA growth using Geometric Features on CT scans

Oxford Cohort



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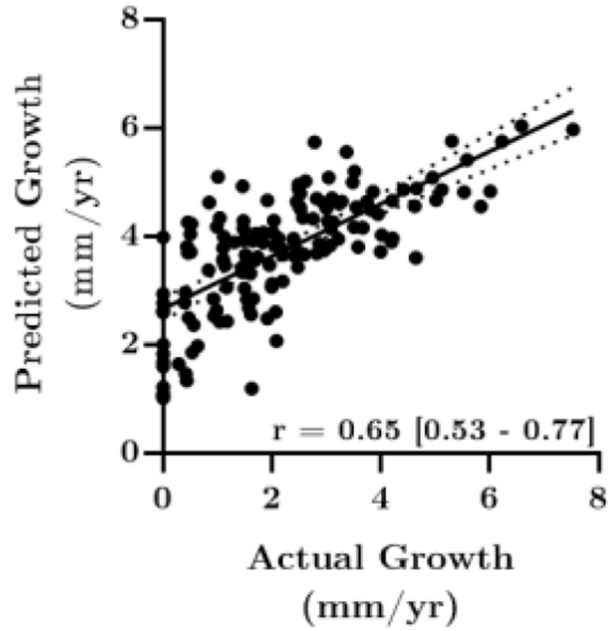
Linear regression model, trained and optimised using 10 fold cross validation to predict AAA growth as a continuous variable

The optimised prediction model was tested in the independent **MAR3S cohort**



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ABSTRACT ONLY | VOLUME 74, ISSUE 4, E362-E363, OCTOBER 01, 2021

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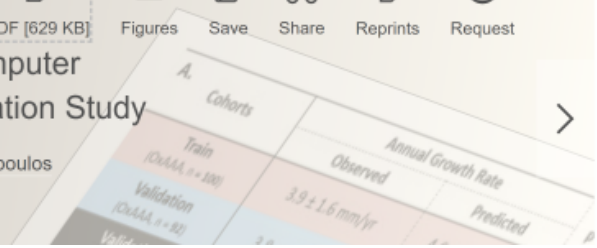
Abdominal Aortic Aneurysm Growth Prediction Using Computer Vision-Based Geometric Assessment—An External Validation Study

James Kaan • Anirudh Chandrashekar • Nicos Labropoulos • Regent Lee • Apostolos Tassiopoulos

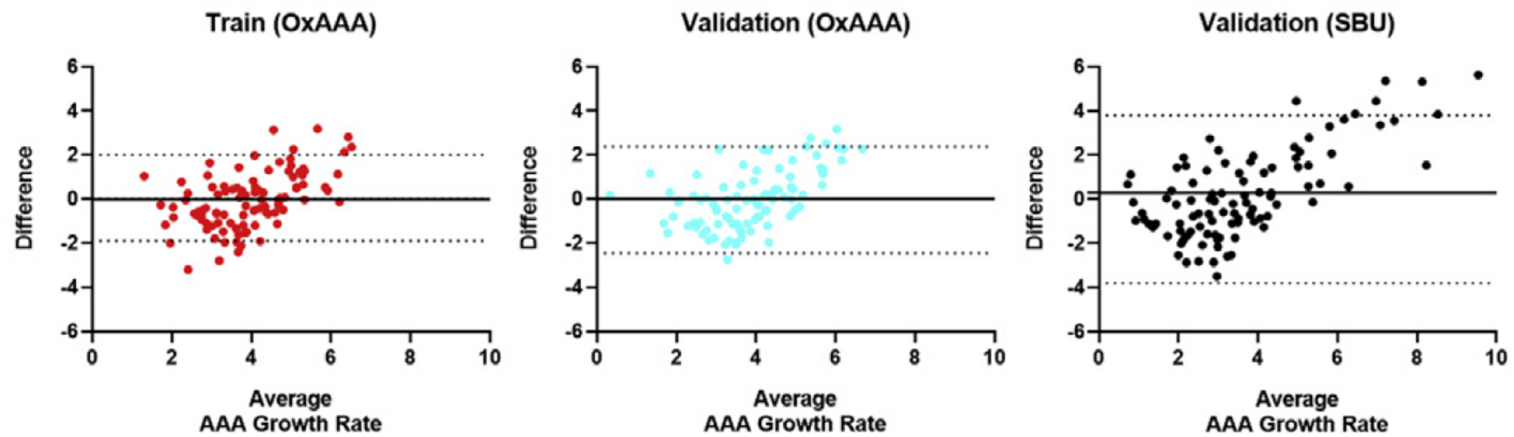
DOI: https://doi.org/10.1016/j.jvs.2021.07.055 • Check for updates



A.

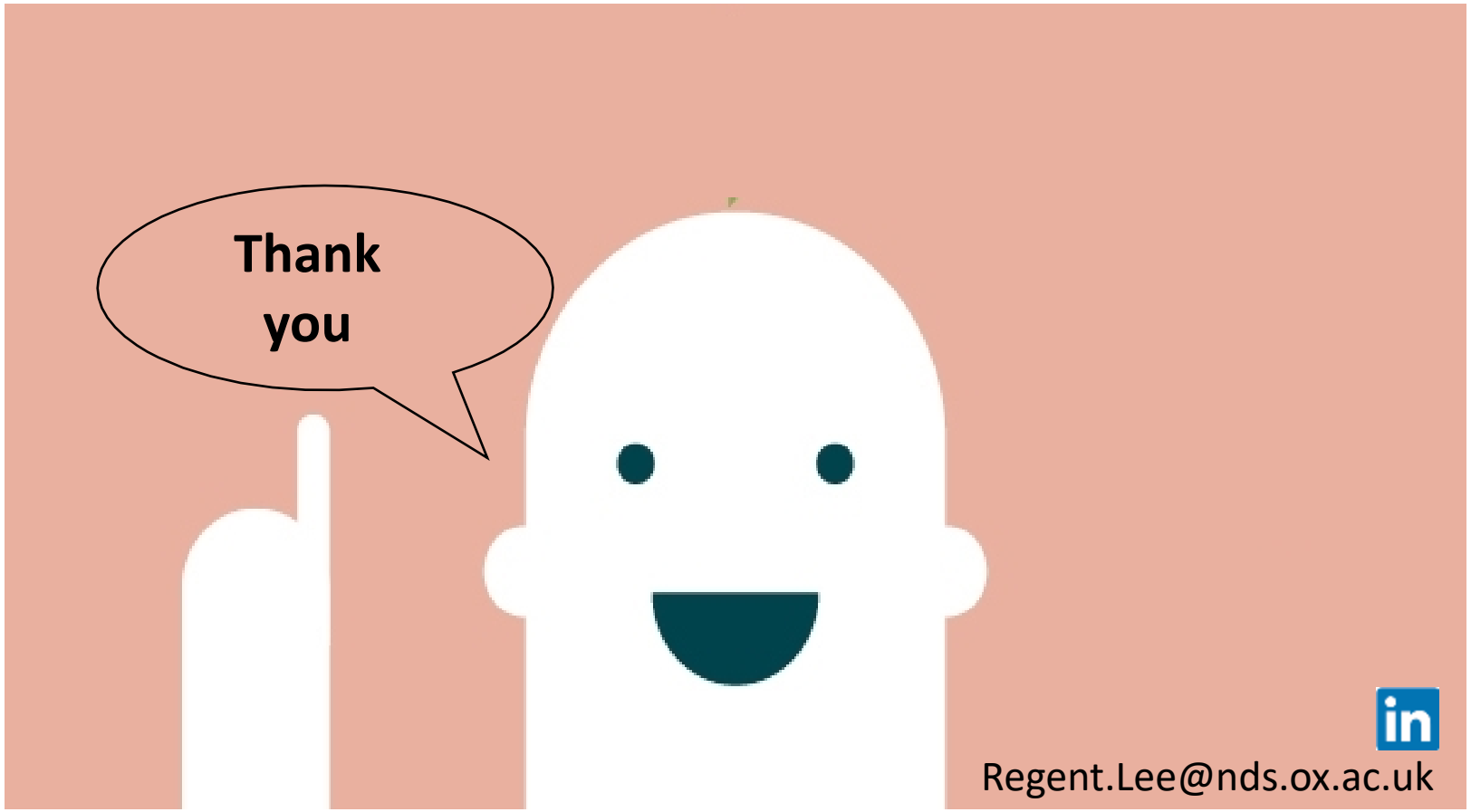
Cohorts	Annual Growth Rate		p	Correlation (ρ)
	Observed	Predicted		
Train (OxAAA, n = **100**)	3.9 ± 1.6 mm/yr	4.0 ± 1.0 mm/yr	0.41	**0.59**
Validation (OxAAA, n = **92**)	3.8 ± 1.7 mm/yr	3.9 ± 1.1 mm/yr	0.32	**0.61**
Validation (SBU, n = **100**)	3.8 ± 2.7 mm/yr	3.6 ± 1.4 mm/yr	0.34	**0.60**

B.



Prediction of individual AAA growth is feasible

Seeking Collaborators for further validation studies



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