SCAPIS

Swedish **CA**rdio**P**ulmonary Bio**I**mage **S**tudy

one of the largest cardiopulmonary research programs in Sweden

VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

GÖTEBORGS UNIVERSITET

Gothia Forum
FÖR KLINISK FORSKNING

Hjärt Lungfonden

The rationale for a new population study

CVD and COPD are on decline, but…

… they are still major killers

… risk factor patterns are changing

Cholesterol/smoking → Obesity/diabetes

… unresolved issues

- Case fatality outside hospital is still high
- Large impact of socioeconomy on CVD/COPD
- Better phenotyping of COPD → better treatment of COPD
- Patients with COPD suffers from CVD

The rationale for a new population study

Technical advances

- Genetics, proteomics, lipidomics, metabolomics
- New imaging allows direct visualization of disease
- Low dose of radiation from CT
- Image analysis

SCAPIS outline

Identification of vulnerable plaques
- ✓ CTA
- ✓ Ultrasound (carotid artery)
- ✓ MRI (carotid artery)

Visceral adipose tissue, epicardial and liver fat
- ✓ CT

Structural changes in lung tissue
- ✓ CT

Baseline survey includes:
- ✓ Blood tests
- ✓ Anthropometry
- ✓ Blood pressure, ankle-arm index
- ✓ Sleep apnea
- ✓ Fitness test, activity measurement
- ✓ Lung function tests (spirometry and CT)
- ✓ Three-dimensional ECG (VCG)
- ✓ Detailed questionaire - Environmental and socioeconomic factors

Local and central biobank for blood and urine analyses

Follow-up via national registries
- ✓ Morbidity
- ✓ Mortality

Research centers at six universities

30,000 men and women aged 50 to 65 years

Other large imaging studies

	MESA	Dallas Heart Study	BioImaging	SCAPIS
Start **Completion**	2000 2002	2002 2004	2008 2009	2013 2016
Age group (years)	45-84	30-65	M >55-80 W >60-80	50-65
Sample size	N=6814 (F 53%)	N=3072 (F 55%)	N=6104 (F 55%)	N=30 000 (F 50%)
Exclusion criteria	Known CVD, cancer.	NA	Claims for CVD, cancer etc	None
Population	Stratified for ethnicity	Probability sampling (postal addresses) Stratified for ethnicity	Members of Humana Health Plan, Stratified for ethnicity	Random population sample
Participation rate (%)	7%	40%	NA	Pilot data
Carotid plaque (US)	6814	-	6104	30 000
Carotid plaque (MRI)	-	-	525	3000
Calcified coronaries (CACS)	6814	2971	6104	30 000
Coronary plaque (CTA)	-	-	-	30 000
Pumonary imaging (CT)	-	-	-	30 000
Metabolic imaging (liver)	-	2971	-	30 000
Metabolic imaging (fat)	-	2971	-	30 000
Publications (March 2012)	N=443	N=110	N=2	-

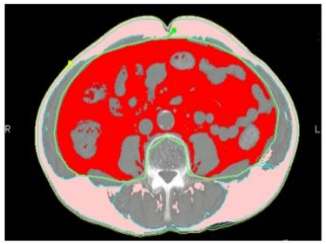
Imaging in cardiopulmonary disease development

Obesity
COPD

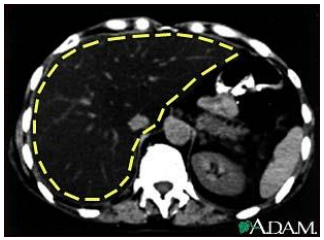
Dyslipidemia
Diabetes
Hypertension

Atherosclerosis

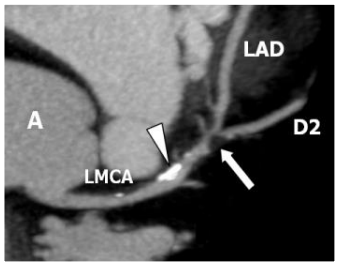
MI
Stroke



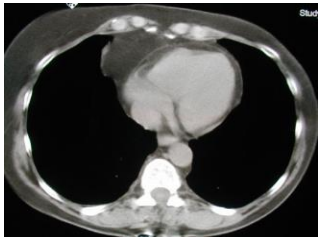
Visceral obesity (CT)



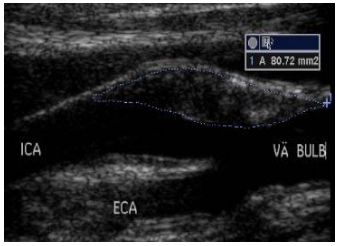
Liver steatosis (CT, US)



Coronary atherosclerosis (CT)



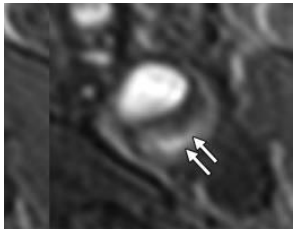
Pericardial fat



Carotid atherosclerosis (US)

Carotid plaques
>2,5 mm (≈5-10%)

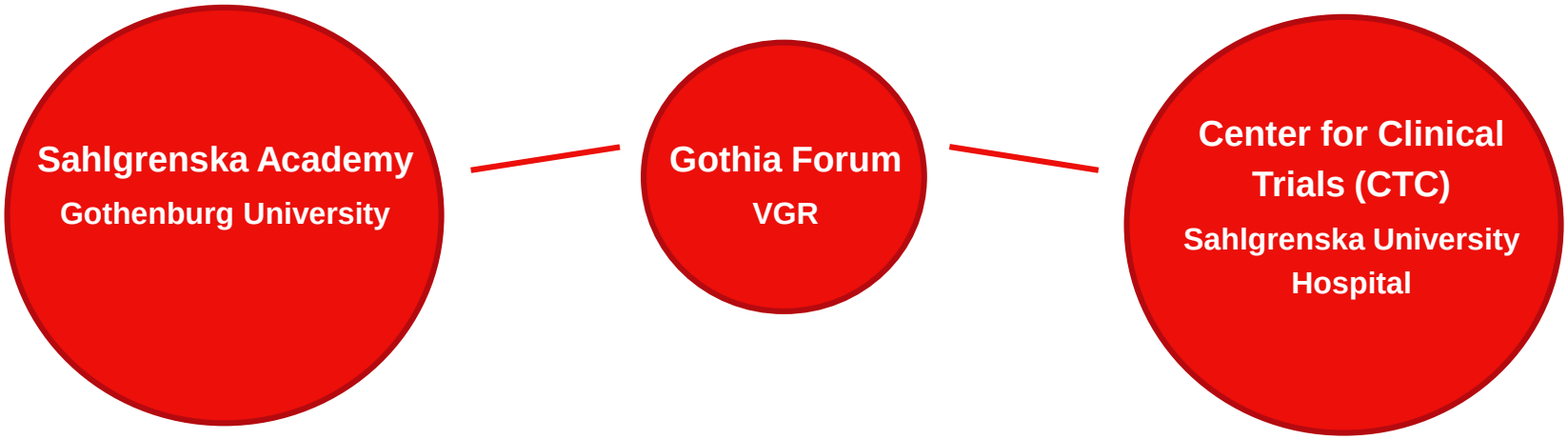
Emphysema



Carotid plaque morphology
(MR), n=3.000)

The SCAPIS pilot study

Gothenburg - Local organization for the pilot



After international expert review of the applications (3 reviewers), the HLF board chose to run the project at Sahlgrenska University Hospital, Sahlgrenska Academy and Gothia Forum

Primary aims of the pilot study

- To investigate the impact of non-participation bias on representativity
- To examine the reasons for non-participation in the study
- To investigate the feasibility of the study procedures
- To estimate the ethical and health care consequences of identifying disease states

Examinations in the SCAPIS pilot

Recruitment

Letter of invitation

Phone call (minimum x3)
New letter if no contact

Schedule visit

Local activities in recruitment area
Advertising in local news papers

Day 1

Informed consent

Blood sampling (mouth swab*)

Breakfast

Questionnaire

Spirometry with box*

Fitness test*

Sleep apnea and accelerometer*

Day 2

p-Glucose if needed

Standard breakfast

Antropometry, BP, AAI

ECG (VCG*)

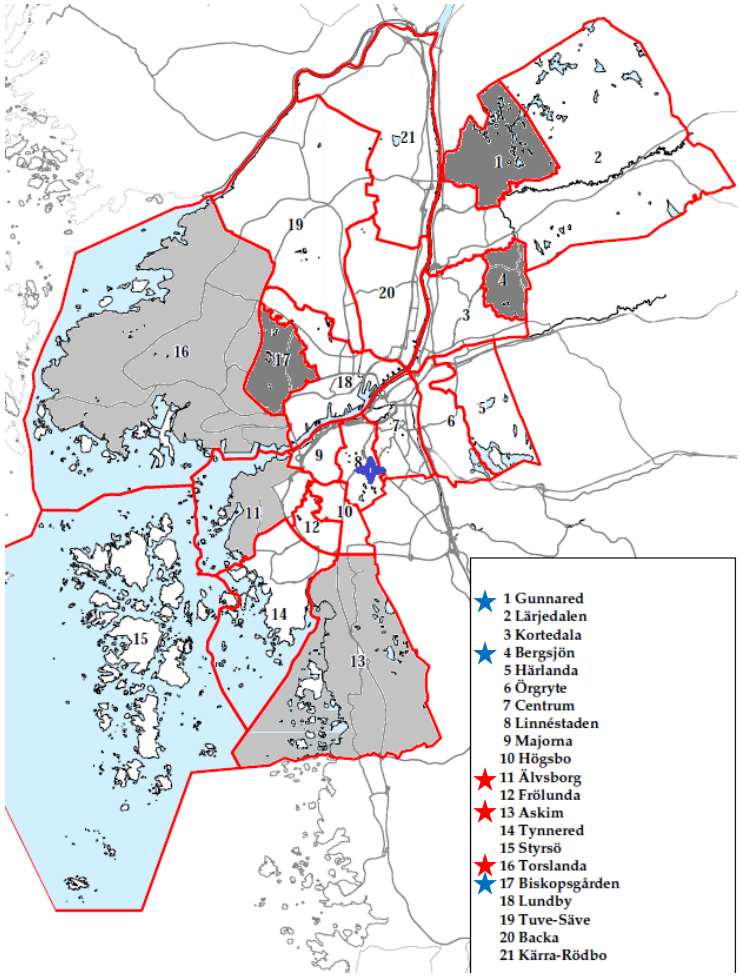
Liver ultrasound*

Carotid ultrasound

CT-examination

Serious incidental clinical findings are followed-up within 2 weeks
*added examinations tested for feasibility in pilot

Catchment areas for the SCAPIS-Pilot

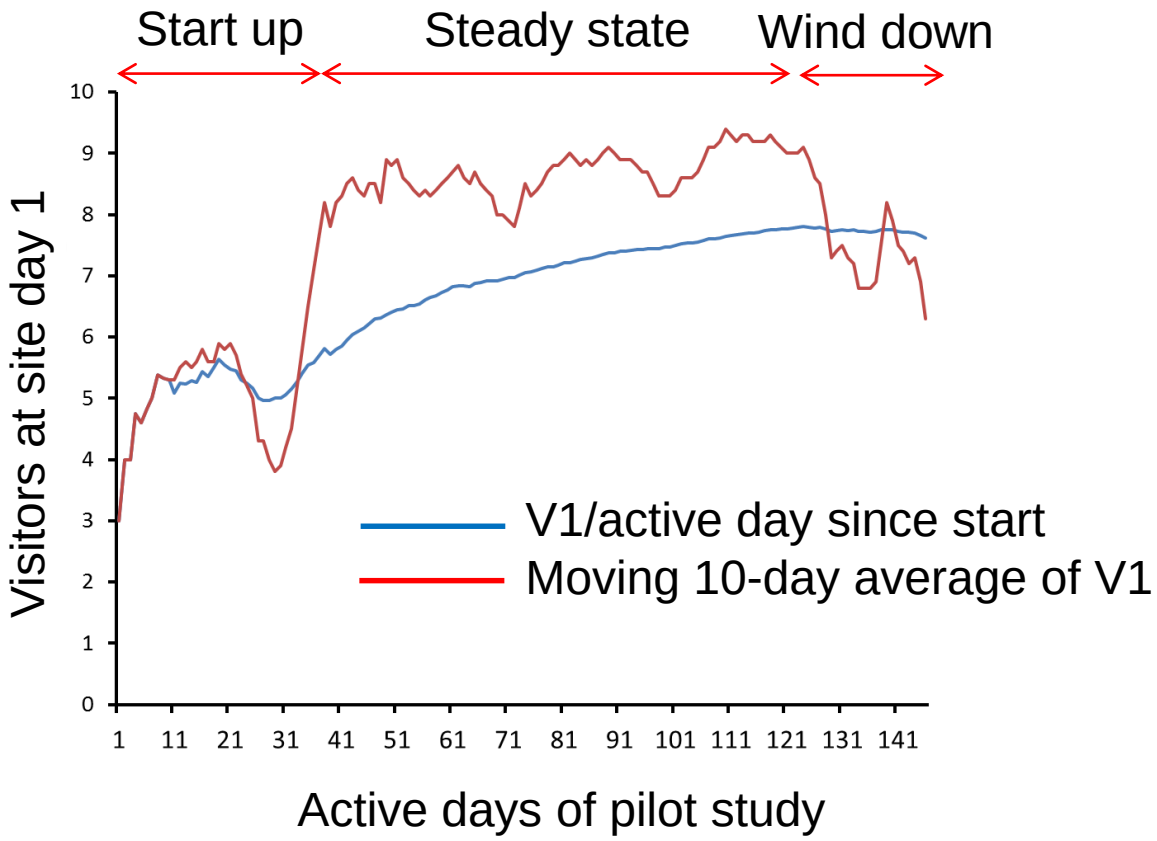


	Low SES districts			High SES districts		
	4	1	17	13	16	11
Inhabitants in ages 50-65 years (n)	4 715	3 987	3 462	4 715	4 190	4 176
Gender distribution in ages 50-65 years (% women)	51	48	49	51	48	50
Low education (%)[a]	29.6	26.4	26.2	6.7	10.6	6.8
Low income (%)[b]	54.5	41.8	38.5	18.4	13.5	19.3
Unemployment (%)[c]	53.3	43.1	38.0	16.6	11.9	16.8
Welfare support (%)[d]	23.2	15.6	12.6	1.3	1.0	1.9
Immigrant descent (%)[e]	73.4	67.2	54.4	12.6	9.7	11.8
Life expectancy in years (men/women)	73.9/ 79.8	74.1/ 79.9	76.1/ 80.7	81.8/ 84.8	80.4/ 84.0	82.7/ 84.8
Self reported BMI (kg/m^2)	28,4	27,7	28,3	26,0	26,5	25,3

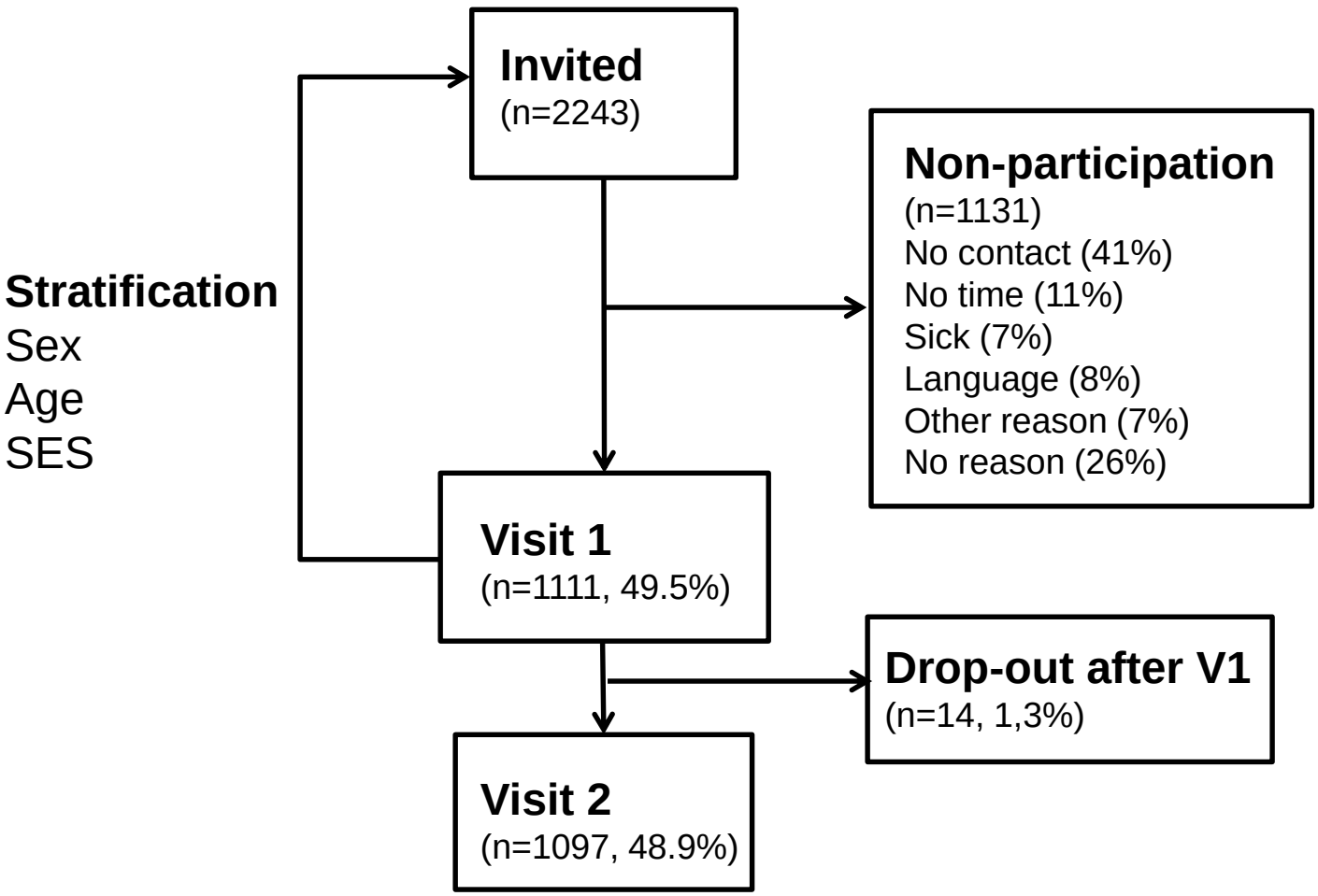
High SES n=11286
Low SES n=11702
∑ n=22988

- All eligable subjects identified in ”Västfolket” and entered in database
- Random number serie
- Database updated each month from register

Efficient recruitment and booking is feasible



Recruitment in the SCAPIS pilot



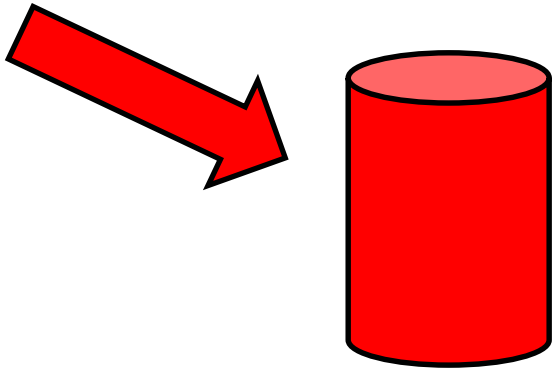
Preliminary data – SCAPIS pilot

Blood sampling

Sample type	Number of tubes	From number of individuals
Whole blood	2137 (297)	1074 (149)
LiHep plasma	1098 (0)	1098 (0)
Serum	25686 (3497)	1070 (150)
EDTA plasma	25241 (3521)	1053 (151)
LiHep plasma	16849 (2353)	1078 (150)
Citrate plasma	8572 (1162)	1050 (150)
Urine	17574 (2416)	1086 (152)
Total	**97157 (13246)**	**1105 (152)**

…nearly 100 000 aliquotes stored

On-line blood chemistry
Hb, Hct, WBC (incl. diff)
p-glucose, HbA1c
s-TG, s-cholesterol, LDL, HDL
Apo A1, Apo B
Creatinine, hsCRP
(18 ml of blood)



Sahlgrenska Biobank/BBMRI.se

Questionnaire

Annika Rosengren
Bo Hedblad, Malmö
Stefan Söderberg, Umeå

Food questionnaire evaluated
Heléne Bertéus-Forslund
Anna Winqvist
Ingrid Larsson
Dept. of Clinical Nutrition
GU

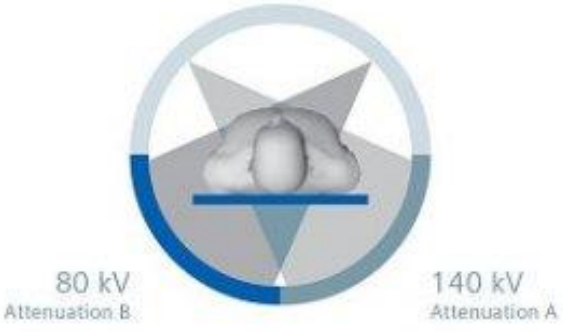
Item	Number of question
Residency	7
Education and occupation	14
Exposure to occupational noise and stress	32
Self-reported disease	22
Heredity	13
Medication	3
Womens health	7
Tobaco use	13
Alcohol use	16
Self-reported health	41
Psychosocial factors	19
Social network	13
Physical activity	21
Sleep	20
Air-way symptoms	16
Allergy	8
Total	**265**

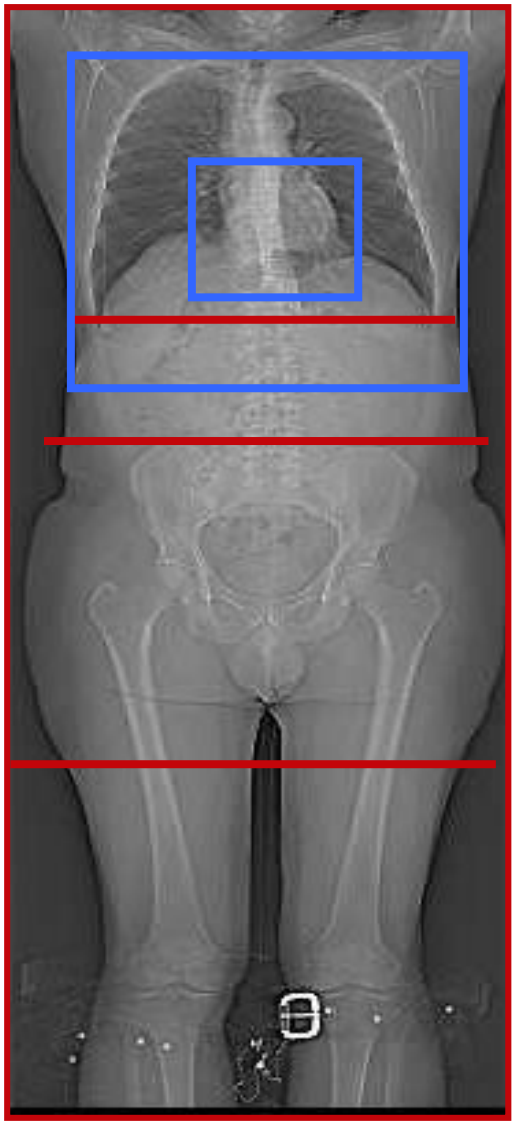
Computer tomography (CT)

Development
Time-resolution
Radiation
Double energy

Limitations
Radiation
Contrast
Calcifications

SCAPIS chose the Siemens SOMATOM Definition Flash for the pilot study

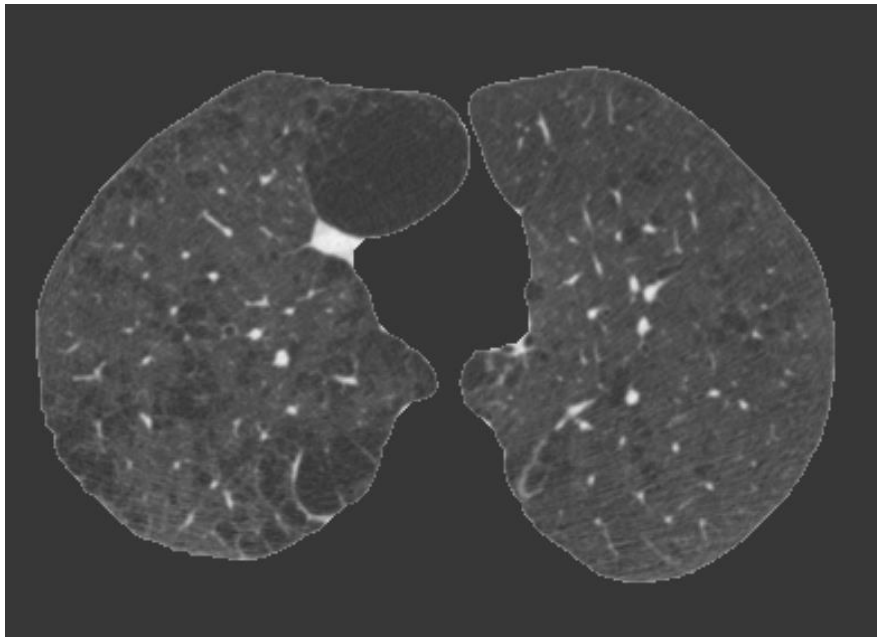


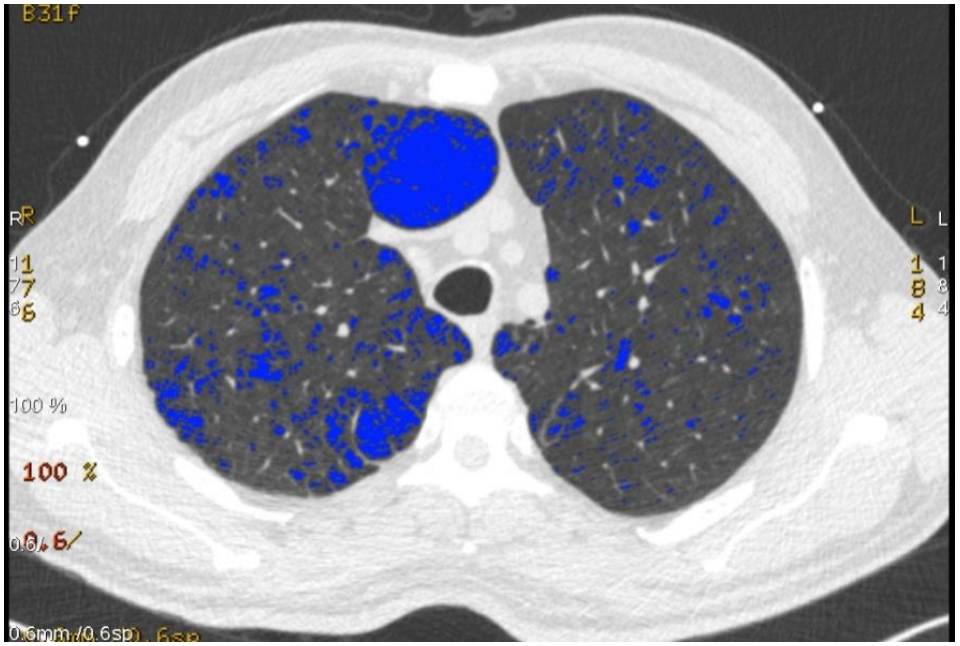


Overview

Computer tomography of the lung

Emphysema





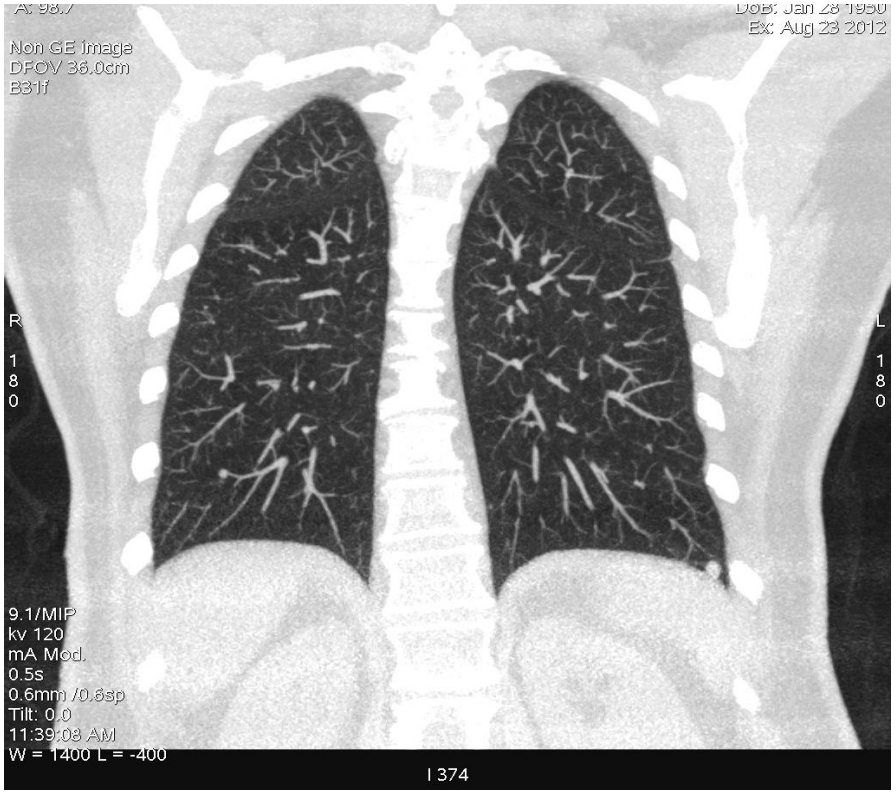
Assessing degree of emphysema, bronchiectasis and other lung abnormalities by CT

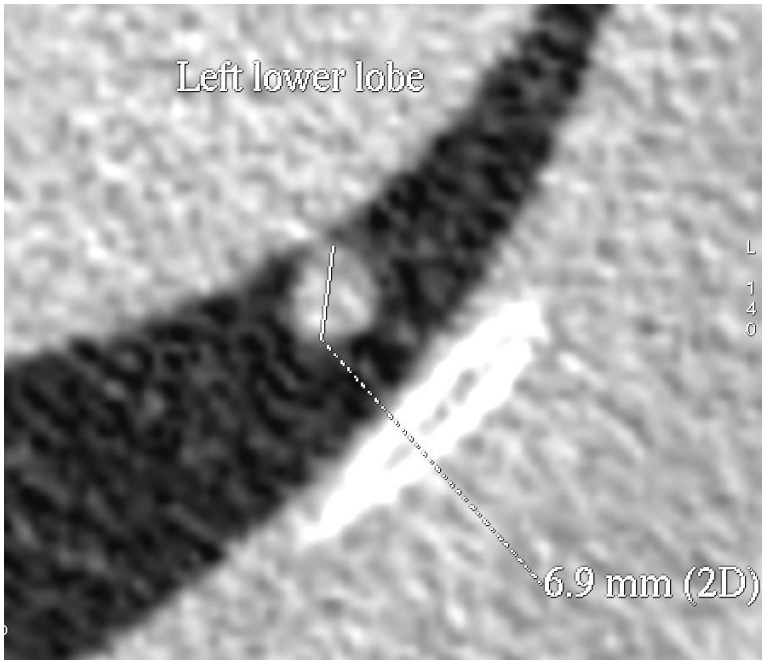
Lars Wigström, AZ

Jenny Vikgren
Radiology Sahlgrenska University Hospital

Incidental finding - Noduli

65 % of all subjects have noduli
15% is >4 mm and need follow-up





Jenny Vikgren
Radiology Sahlgrenska
University Hospital

Lung function

- Spirometry with recording of FEV1, FVC, SVC, CO diffusion capacity (DLCO) and lung volume measurements in body plethysmograph
- Recording done before and after bronchodilation

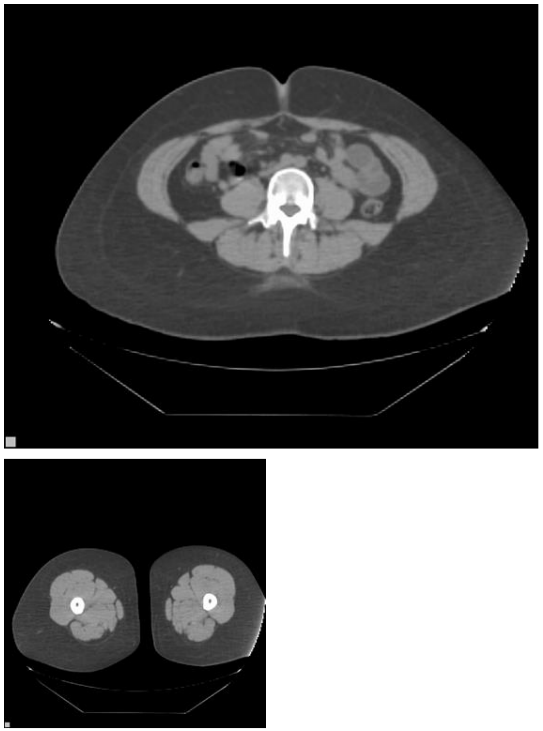
Pre- and post-bronchodilator spirometry to assess COPD

DLCO to assess degree of emphysema and other lung tissue damage

Lung volume in body plethysmograph to give further evidence for emphysema and hyperinflation in COPD

Body composition – metabolic imaging

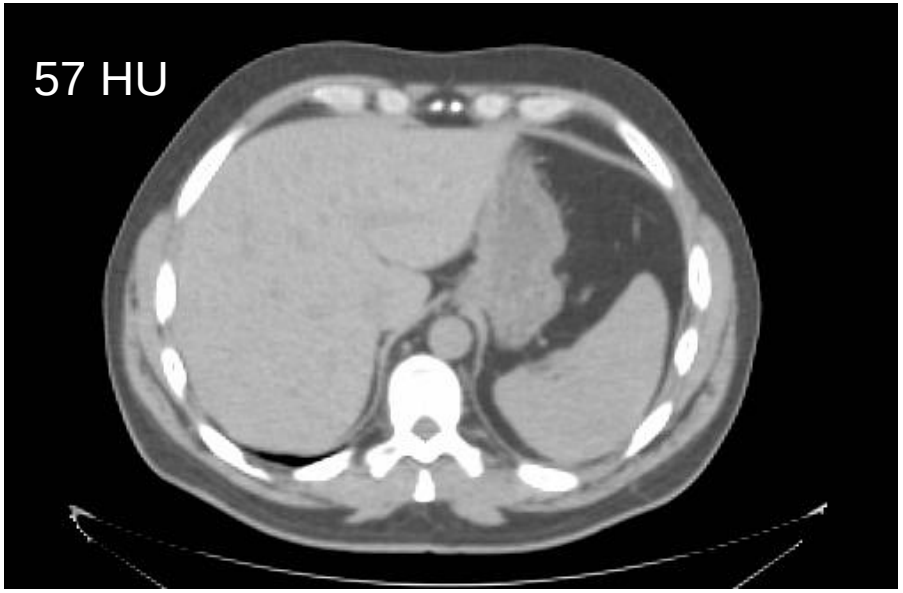
BMI 33



BMI 33

John Brandberg
Radiology Sahlgrenska
University Hospital

Liver steatosis



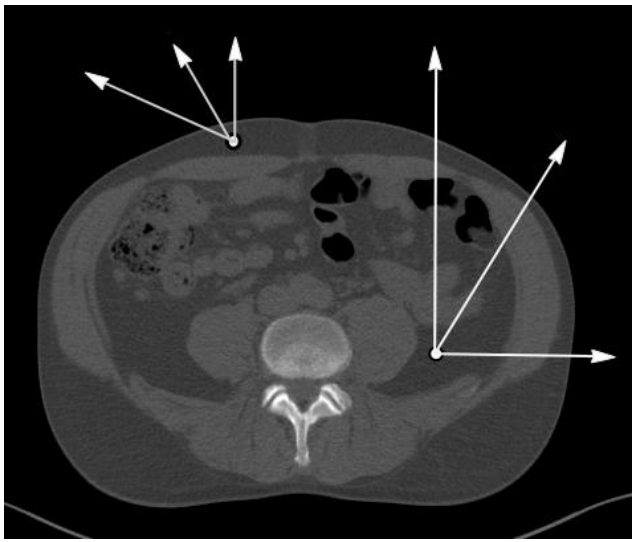
Normal

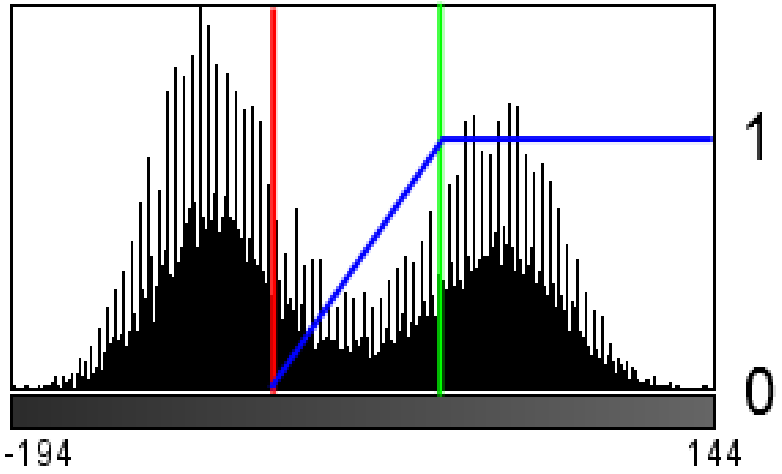
Steatosis

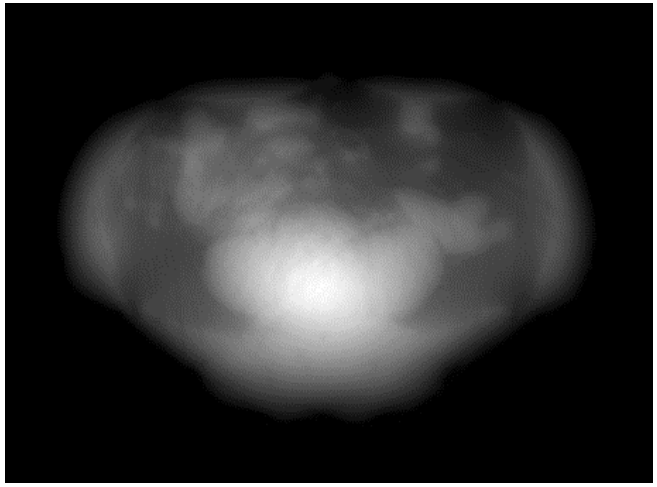
John Brandberg
Radiology Sahlgrenska
University Hospital

Validated technique for automatic segmentation of fat depots from CT images

(Joel Kullberg, Lars Johansson, Uppsala University)





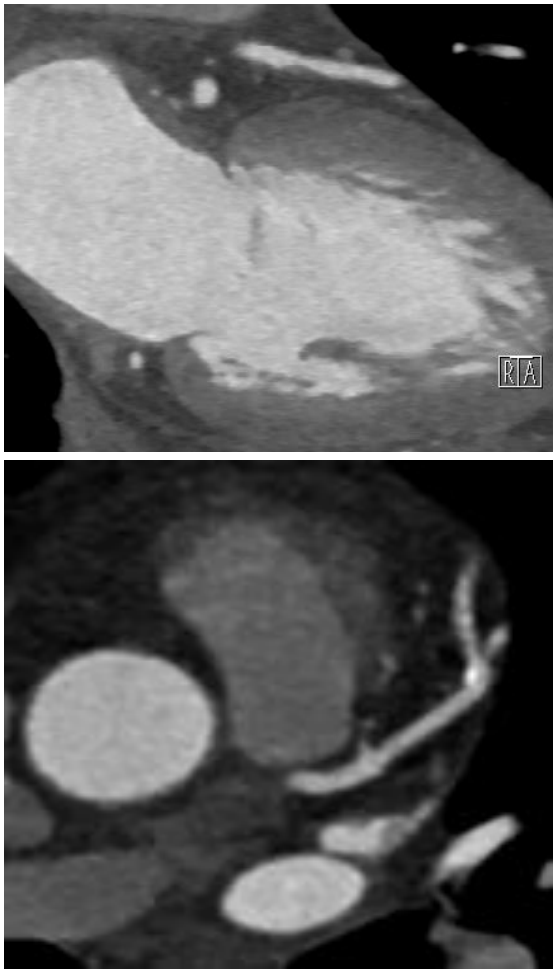


Coronary CT Angiography (CTA)

- Coronary calcium score (CS)
- Plaque burden
- Maximum stenosis
- Remodeling
- Plaque phenotype

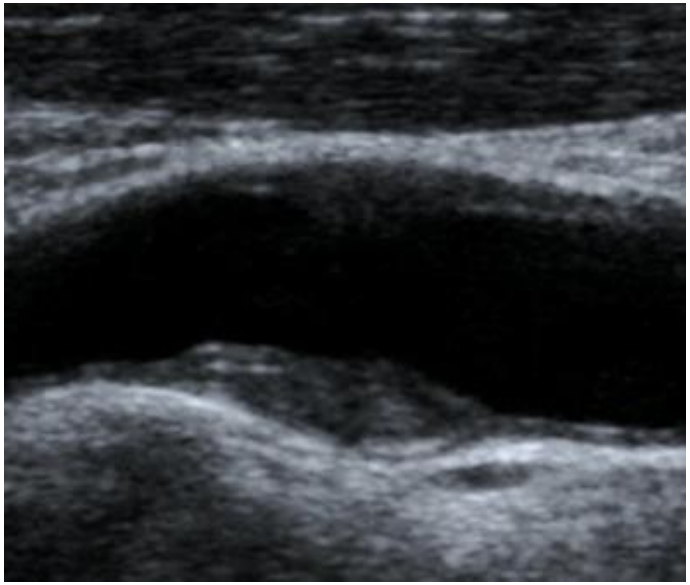
  - non-calcified, calcified, mixed

  - raw data saved for future analysis



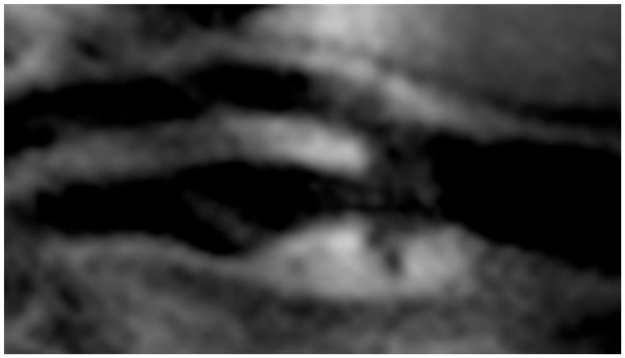
Agneta Flinck
Radiology Sahlgrenska
University Hospital

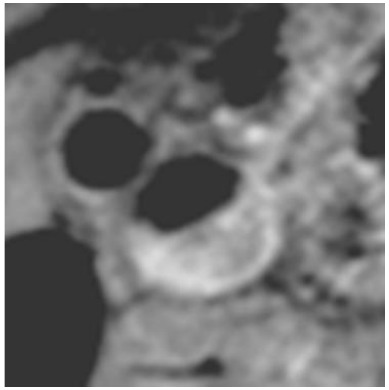
Ultrasound – carotid - liver



SCAPIS chose the Siemens S2000 for the pilot study

Magnetic Resonance Imaging (MRI) of large carotid plaques (6-7%)



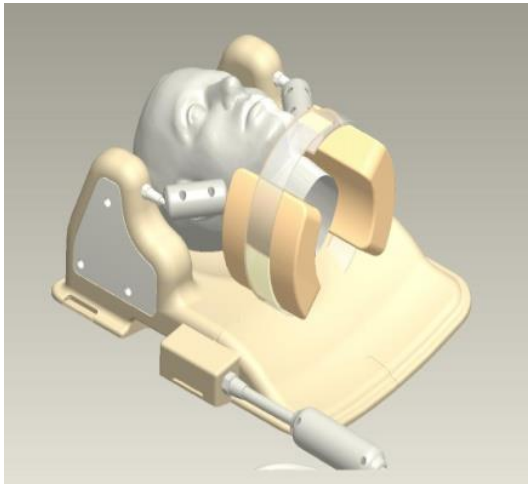


Cap thickness

Lipid rich necrotic core

Intra plaque hemorrhage (IPH)

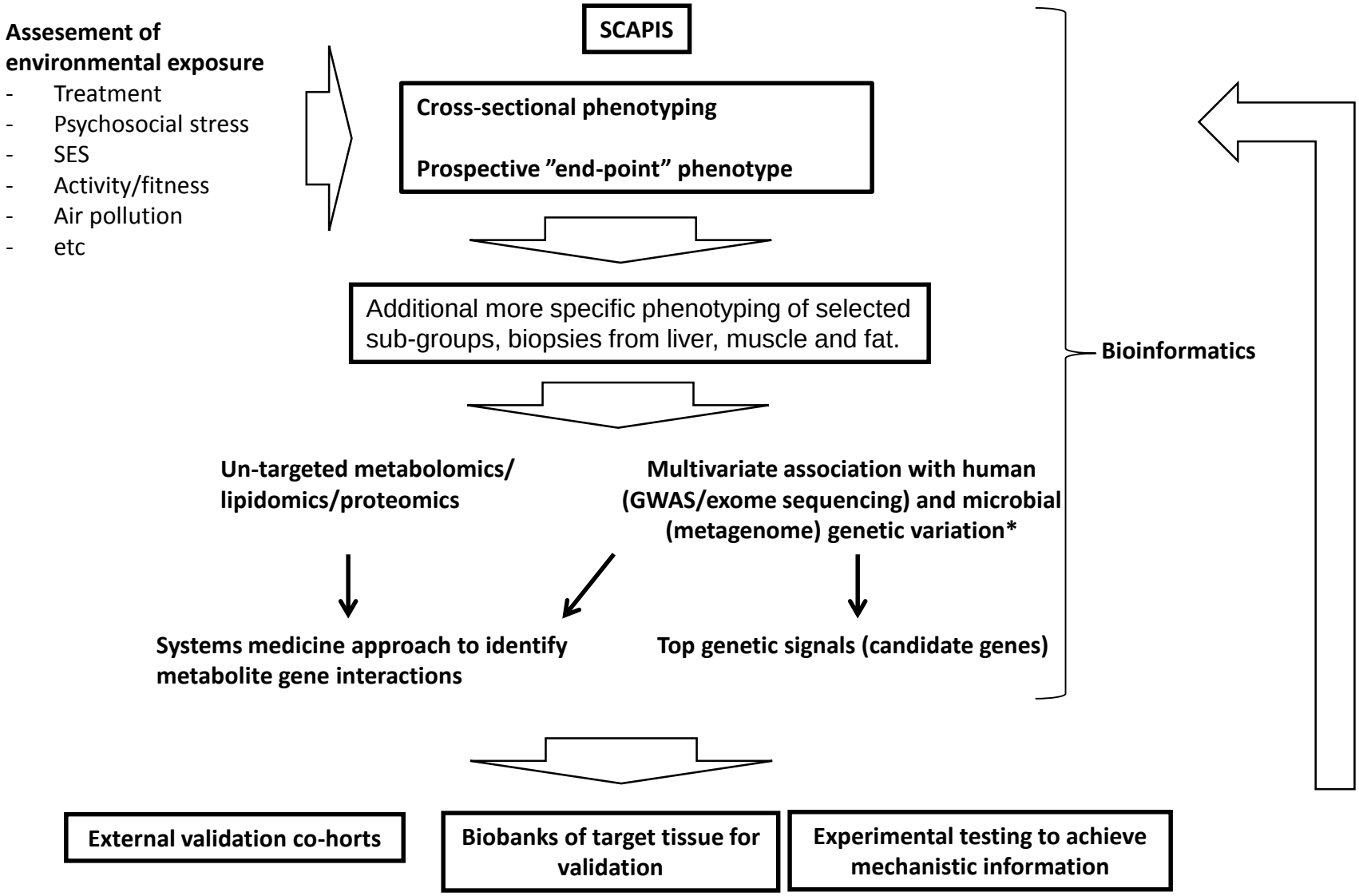
Calcifications



Dedicated carotid coil
Philips Achieva 3.0T

Water content
Magnetic field
RF-signals

Water permeability
Contrast


Assesement of environmental exposure
- Treatment
- Psychosocial stress
- SES
- Activity/fitness
- Air pollution
- etc
SCAPIS
Cross-sectional phenotyping
Prospective ”end-point” phenotype
Additional more specific phenotyping of selected sub-groups, biopsies from liver, muscle and fat.
Bioinformatics
Un-targeted metabolomics/ lipidomics/proteomics
Multivariate association with human (GWAS/exome sequencing) and microbial (metagenome) genetic variation*
Systems medicine approach to identify metabolite gene interactions
Top genetic signals (candidate genes)
External validation co-horts
Biobanks of target tissue for validation
Experimental testing to achieve mechanistic information

Organization chart for SCAPIS

National steering group
PI's from all study centers
- Imaging group
- Clinical Epidemiology
- Genetics and biomarkers
- Publication and presentation group

Scientific Advisory Board
- *National experts*
- *International experts*
- *Sponsors (H&L, VINNOVA)*

Local steering groups
- PI
- Representatives from
  - Cardiology
  - Pulmonary medicine
  - Radiology
  - Imaging
  - Clinical Trial Center

Reference group
- Dean of medical shool
- Director of research at hospital
- Director of research in region

Time-schedule

Idea	Eastern 2007 √
Application for pilot	March 25, 2011 √
HLF decision on pilot in GBG	June 15, 2011√
Start pilot	February 14, 2012 √
Finnish pilot	December 4, 2012 √
Report H&L and Sahlgrenska	March 1, 2013
Decision on final design of SCAPIS	April 27, 2013
Start SCAPIS	August 14, 2013
Finnish SCAPIS	June, 2016-2018