Imaging biomarker or surrogate end point: How do assess arterial stiffness as independent predictor for mortality and physical aging in population-based studies?

Ronny Westerman Phd
Competence- Center Mortality-Follow, NAKO Health Study at Federal Institute for Population Research
Background

• Imaging biomarker OR Surrogate end point?

• Assessment and Measurement Techniques of Biomarkers for Early Stage of Atherosclerosis

• Results of SHIP (STUDY OF HEALTH IN POMERANIA)
  THANKS TO: Dr. Roberto Lorbeer, Institute of Clinical Radiology, LMU Munich
  Institute for Community Medicine, Section SHIP-KEF University Medicine Greifswald,
  Institute of Diagnostic Radiology and Neuroradiology University Medicine Greifswald,
  Centre for Cardiovascular Research, Christian Albrechts University, Kiel
Short Facts to Arterial Stiffness

- Definition: Arterial Stiffness
- Degenerative changes in the walls of large elastic arteries
  - Increased stiffening over time
- Mechanical fraying of lamellar elastin structures
- Increases in content of arterial collagen proteins
- Compensatory mechanism against the loss of arterial elastin and partially due to fibrosis
- Crosslinks of adjacent collagen fibers by Advanced Glycation Endproducts (AGEs)
Short Facts to Arterial Stiffness

- Why should we consider Arterial Stiffness as Biomarker?

- Cardiac organ damage (cTOD), caused by measures of left ventricular (LV) hypertrophy and dysfunction and is associated with future CV events, but problematically can not assessed in asymptomatic individuals

- Detection of vascular dysfunction before clinical manifestation of cTOD

- Premature Risk of cTOD to prevent further damage

- Noninvasive biomarker of subclinical cTOD

Source: Vitamink2.org
Short Facts to Arterial Stiffness

- Carotid-femoral pulse wave velocity (cfPWV)
- Results from a Meta-Analysis (Laurent et al. 2013, Vlachopoulos et al. 2010)
- 17 longitudinal studies (with 15877 subjects)
- 1 SD increase in PWV
  - RR 1.47 (1.31-1.64) for total mortality
  - RR 1.47 (1.29-1.66) for CV mortality
  - RR 1.42 (1.29-1.58) for all cause mortality
Assessing of Atherosclerosis: A practical Problem I

• The time of onset: Atherosclerosis begins with childhood and remains subclinical over decades

• The Biomarker Vessel luminal diameter is minimal affected by early plaque development

• Vessel lumen often narrow at end stage diagnosis of stenoses

• The absence of stenoses in early stages of atherosclerosis,
• As a consequence CVD also subclinical for decades
Assessing of Atherosclerosis: A practical Problem II

• Different measurement techniques:
• Median Aortic Diameter ultrasonography in fetuses with intrauterine growth restriction (IUGR) and in appropriate for gestational age (AGA) fetuses (Cosmi et al. 2009)
• Aortic Wall Thickness (AWT) (Li et al 2004 in Multiethnic Study of Atherosclerosis, Mensel et al 2013 in SHIP)
• Pulse wave velocity (PWV)- primary method of arterial stiffness (Wentland et al. 2014)
• PWV- a very strong early biomarker of atherosclerosis – arterial stiffness first increases without vascular geometry
• Glagov phenomen:

• 1. Early plagues grow outwardly into the vessel wall via a compensatory mechanism that preserves the luminal area of a vessel

• 2. Vessel luminal diameter does not decrease in early atherosclerosis

• 3. Early changes can not be imaged with angiography

• 4. During late stage of atherosclerosis: the compensatory mechanism fail to overcome the tendency for plaques to narrow the vessel lumen
Glagov phenomenon showing plaque development over time in vessel cross-sections and along the length of the vessel. Compared to a normal vessel (A), early plaque development (B) causes outward remodeling of the vessel wall, which leads to either no change in vessel diameter or slight dilatation. Over time the compensatory dilatation of the vessel fails and the plaque begins to encroach upon the vessel lumen (C,D). Arrow heads identify the region from where the cross-sectional depictions are taken from the length-wise view of the vessels.

Wentland et al. 2014
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Transcatheter Echocardiography</th>
<th>Transesophageal Echocardiography</th>
<th>CT</th>
<th>MR Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spatial resolution</strong></td>
<td>Very good: Pixel sizes can be 1–2 mm, depending on technical parameters.</td>
<td>Excellent: Pixel sizes can be 0.5–1.0 mm, depending on technical parameters.</td>
<td>Excellent: Pixel sizes range from 0.6 to 0.75 mm.</td>
<td>Good: In-plane resolution approaches that at CT and echocardiography, but through-plane resolution is usually 6–8 mm.</td>
</tr>
<tr>
<td><strong>Temporal resolution</strong></td>
<td>Excellent: Real-time image acquisitions can be performed at a rate of 30–60 frames per second.</td>
<td>Excellent: Real-time image acquisitions can be performed at a rate of 30–60 frames per second.</td>
<td>Depends on scanner technology: Even with gantry rotation time of 83 msec, inability to obtain a sufficient number of images per heartbeat limits cine reconstruction; when ECG gating is applied, 10–20 frames per beat are typically reconstructed.</td>
<td>Depends on pulse sequence and heart rate: Acquisition time per image may be as short as 5–10 msec, but multiple beats typically are required to generate a cine image; when ECG gating is applied, 20–30 frames per beat are typically reconstructed.</td>
</tr>
<tr>
<td><strong>Flow velocity and volume measurements</strong></td>
<td>Excellent: Use of Doppler US is well established for flow measurements.</td>
<td>Excellent: Use of Doppler US is well established for flow measurements.</td>
<td>Poor: There is no current clinical method for measuring flow velocity or flow volume at CT.</td>
<td>Good: Cine phase-contrast imaging allows flow velocity and flow volume measurements, but these are not as widely used or standardized as Doppler flow measurements.</td>
</tr>
<tr>
<td><strong>Patient-specific limitations</strong></td>
<td>Poor acoustic windows limit assessment in some patients.</td>
<td>This technique is somewhat invasive and requires sedation.</td>
<td>Images are easily acquired in many patients, but the need for radiation and contrast material injection may limit use.</td>
<td>It cannot be performed in patients with pacemakers or internal defibrillators; claustrophobia may limit its use in some patients.</td>
</tr>
<tr>
<td><strong>Ancillary information</strong></td>
<td>Good: Left ventricular dimensions and volumes can be measured, though less precisely than with CT or MR imaging.</td>
<td>Good: Left ventricular dimensions and volumes can be measured, though less precisely than with CT or MR imaging.</td>
<td>Excellent: It allows quantitative measurement of left ventricular dimensions and volumes; aortic disease can be imaged at the same time.</td>
<td>Superior: It allows quantitative measurement of left ventricular dimensions and volumes and assessment of myocardial fibrosis; aortic disease can be imaged at the same time.</td>
</tr>
</tbody>
</table>
Quantitative Techniques: Measurement of Calcification

- Aortic valve calcification can be measured on the CT images comparative to coronary calcium scores.

- Agatsson Score (amount of valvular calcification) correlates with severity of aortic stenosis and provide a prognostic information (Cueff et al., 2011, Messika-Zeitoun et al., 2004).

- An early risk stratification as patients with a high Agatston score (>160) have an increased risk for a major adverse cardiac event (MACE).

- It does not allow for the assessment of soft non-calcified plaques.
Planimetric Measurements with CT or MRI and estimates on Aortic Valve correspond with more invasive techniques eg. Transthoracic Echocardiography or cardiac cathereization.

Radiologic imaging techniques yield on overestimates concerning measurement can be derived from velocity and pressure relationship.

Can be explained with discrepancy of the size of the functional stenotic valve orifice (smaller than) to anatomic cross-sectional problem (Feuchtner et al. 2007, Pouler et al. 2007a,b, Reant et al. 2006)
Quantitative Techniques: Ventricular Volume and Mass

• Ventricular volume and mass important of aortic valve diseases

• Decreased left ventricular ejection fraction and increased left ventricular mass correspond with poor of aortic stenosis in asymptomatic patients

• Ventricular volumes can be measured on MR images obtained with SSFP sequences by measuring the area of the ventricular cavity on end-systolic and end-diastolic images and then summing the measurements to yield end-systolic and end-diastolic volumes.

• The ventricular stroke volume and ejection fraction can be calculated.
• MR imaging is widely accepted as the reference standard for quantifying these parameters
Study of Health in Pomerania
Arterial Stiffness in SHIP

- **Baseline recruitment of the first cohort (SHIP-0)** between 1997 and 2001 (including 4,308 subjects, age range, 20–79 y)
- **SHIP-2** is the second follow-up of the first cohort and between 2008 and 2012
- 2008 and 2012 (including 2,333 subjects).
- **(SHIP-TREND)** between 2008 and 2012 (including 4,420 subjects, age 20–79 y)
- During the period from 2008 to 2012, 1,507 subjects from **(SHIP-2 and SHIP-TREND)** were examined by cardiovascular MR imaging.
  
  - Exclusion of subjects with insufficient imaging quality (n = 281) and with implausible values for calculated AWT (n = 9). Exclusion of subjects with a history of stroke (n = 18), myocardial infarction (n = 15), and missing data for potential cardiovascular risk factors (n = 8)
  - The final study sample comprised 747 subjects (308 women) 21–81 years old for SHIP-TREND and 429 subjects (215 women) 31–83 years old for SHIP-2.
Arterial Stiffness in SHIP

- Risk Factor Measurements

- Standardized interviews:
  - Smoking status (categorized as never smoker, ex-smoker, or current smoker),
  - history of stroke, myocardial infarction, and diabetes.
  - Current diabetes, a self-reported physician’s diagnosis or hemoglobin A1c (HbA1c) value \( \geq 6.5\%

- Waist circumference
- Systolic and diastolic blood pressures
- Blood samples
- LDL-C, HDL-C, and triglyceride levels
Arterial Stiffness in SHIP

• MR IMAGING

• MR imaging was performed on a 1.5-tesla scanner (MAGNETOM Avanto; Siemens) Healthcare,

• Integrated coil elements and phased-array surface coils were used for data acquisition.

• AWT values were measured by two observers independently at the level of the right pulmonary artery using OsiriX software (version 3.6.1; Pixmeo Sarl, Bernex, Switzerland).

• A two-dimensional cine steady-state free precession sequence (field of view, 360mm × 293 mm; matrix, 208 × 256; slice thickness, 6mm; repetition time/echo time, 5.62/1.18; flip angle, 68°) was used for AWT calculations.

• To ensure better comparability and to reduce motion artifacts of the aorta, the image with a trigger time closest to 600ms was chosen.

• For optimal reading image zoom (200%–300%), contrast and brightness were adjusted. Two regions of interest were placed manually including the internal and external aortic wall of the ascending aorta.

• The radius of each area was calculated, assuming that all areas are circular.

• AWT was calculated as the difference in the radii of the external and internal aortic area.
# Arterial Stiffness in SHIP

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SHIP-TREND</th>
<th>SHIP-2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Men</strong> n = 439</td>
<td><strong>Women</strong> n = 308</td>
</tr>
<tr>
<td>Age (y)</td>
<td>51 (41; 62)</td>
<td>52 (42; 59)</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>141 (32%)</td>
<td>150 (49%)</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>192 (44%)</td>
<td>88 (29%)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>106 (24%)</td>
<td>70 (23%)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.8 (25.6; 30.5)</td>
<td>26.9 (23.6; 30.7)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>95 (88; 104)</td>
<td>82 (76; 92)</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>134 (125; 143)</td>
<td>118 (109; 129)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>80 (75; 87)</td>
<td>75 (69; 81)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>216 (49%)</td>
<td>110 (36%)</td>
</tr>
<tr>
<td>Use of antihypertensive medication</td>
<td>113 (26%)</td>
<td>87 (28%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>37 (8%)</td>
<td>18 (6%)</td>
</tr>
<tr>
<td>HbA₁c (%)</td>
<td>5.3 (4.9; 5.7)</td>
<td>5.2 (4.8; 5.5)</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>1.27 (1.09; 1.48)</td>
<td>1.60 (1.35; 1.85)</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>3.47 (2.90; 4.00)</td>
<td>3.44 (2.79; 4.09)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.4 (4.7; 6.1)</td>
<td>5.6 (5.1; 6.3)</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.35 (0.96; 2.02)</td>
<td>1.21 (0.89; 1.63)</td>
</tr>
<tr>
<td>Wall thickness of ascending aorta (mm)</td>
<td>1.56 (1.40; 1.73)</td>
<td>1.45 (1.32; 1.63)</td>
</tr>
<tr>
<td>Wall thickness of descending aorta (mm)</td>
<td>1.35 (1.23; 1.50)</td>
<td>1.26 (1.13; 1.38)</td>
</tr>
</tbody>
</table>

Note: Data are given as number (percentage) or median (25th; 75th percentile).

BMI = body mass index, HbA₁c = hemoglobin A₁c, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, SHIP = Study of Health in Pomerania.

Lorbeer, et al. 2015
### Table 2. Cardiovascular Risk Factor Model for Wall Thickness of the Ascending Aorta

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>SHIP-TREND</th>
<th>SHIP-2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Partial $R^2$</td>
<td>$\beta$</td>
</tr>
<tr>
<td>Men</td>
<td>0.0260</td>
<td>0.086</td>
</tr>
<tr>
<td>Age</td>
<td>0.1109</td>
<td>0.066</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>0.0006</td>
<td>0.011</td>
</tr>
<tr>
<td>Current smoker</td>
<td>0.0026</td>
<td>0.029</td>
</tr>
<tr>
<td>BMI</td>
<td>0.0505</td>
<td>0.013</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.0005</td>
<td>−0.0004</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>0.0018</td>
<td>0.0013</td>
</tr>
<tr>
<td>HbA$_{1c}$</td>
<td>0.0032</td>
<td>0.018</td>
</tr>
<tr>
<td>HDL-C</td>
<td>0.0035</td>
<td>0.043</td>
</tr>
<tr>
<td>LDL-C</td>
<td>0.0102</td>
<td>−0.024</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.0031</td>
<td>0.013</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Adjusted $R^2$</th>
<th></th>
<th>Adjusted $R^2$</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>0.2403</td>
<td>&lt; .001</td>
<td>0.1461</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

Note: $\beta$ parameters are from linear regression.

BMI = body mass index; CI = confidence interval; HbA$_{1c}$ = hemoglobin $A_{1c}$; HDL-C = high-density-lipoprotein cholesterol; LDL-C = low-density-lipoprotein cholesterol; SHIP = Study of Health in Pomerania.
### Table 3. Cardiovascular Risk Factor Model for Wall Thickness of the Descending Aorta

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>SHIP-TREND</th>
<th></th>
<th></th>
<th>SHIP-2</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Partial $R^2$</td>
<td>$\beta$</td>
<td>(95% CI)</td>
<td>$P$</td>
<td>Partial $R^2$</td>
<td>$\beta$</td>
</tr>
<tr>
<td>Men</td>
<td>0.0571</td>
<td>0.105</td>
<td>(0.074–0.135)</td>
<td>&lt; .001</td>
<td>0.2312</td>
<td>0.186</td>
</tr>
<tr>
<td>Age</td>
<td>0.1582</td>
<td>0.006</td>
<td>(0.005–0.007)</td>
<td>&lt; .001</td>
<td>0.0179</td>
<td>0.002</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>0.0033</td>
<td>0.023</td>
<td>(−0.006 to 0.051)</td>
<td>.119</td>
<td>0.0006</td>
<td>−0.009</td>
</tr>
<tr>
<td>Current smoker</td>
<td>0.0091</td>
<td>0.044</td>
<td>(0.011–0.077)</td>
<td>.010</td>
<td>0.0039</td>
<td>−0.027</td>
</tr>
<tr>
<td>BMI</td>
<td>0.0705</td>
<td>0.013</td>
<td>(0.010–0.016)</td>
<td>&lt; .001</td>
<td>0.0203</td>
<td>0.006</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.0004</td>
<td>−0.0003</td>
<td>(−0.0015 to 0.0008)</td>
<td>.591</td>
<td>0.0019</td>
<td>0.0006</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>0.0002</td>
<td>0.0003</td>
<td>(−0.0015 to 0.0021)</td>
<td>.726</td>
<td>0.001</td>
<td>0.0003</td>
</tr>
<tr>
<td>HbA1c</td>
<td>0.0034</td>
<td>0.015</td>
<td>(−0.004 to 0.034)</td>
<td>.114</td>
<td>0.0042</td>
<td>−0.012</td>
</tr>
<tr>
<td>HDL-C</td>
<td>0.0095</td>
<td>0.057</td>
<td>(0.015–0.099)</td>
<td>.008</td>
<td>0.0001</td>
<td>−0.006</td>
</tr>
<tr>
<td>LDL-C</td>
<td>0.0089</td>
<td>−0.018</td>
<td>(−0.032 to −0.004)</td>
<td>.010</td>
<td>0.0004</td>
<td>0.003</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.0041</td>
<td>0.012</td>
<td>(−0.002 to 0.026)</td>
<td>.083</td>
<td>0.0002</td>
<td>0.002</td>
</tr>
</tbody>
</table>

**Note:** $\beta$ parameters are from linear regression.

BMI = body mass index, CI = confidence interval, HbA1c = hemoglobin $A_{1c}$, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, SHIP = Study of Health in Pomerania.

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Lorbeer, et al. 2015
Figure 1. Association of BMI with wall thickness of the ascending aorta at different ages adjusted for sex, smoking, systolic and diastolic blood pressure, HbA$_{1c}$, HDL-C, LDL-C, and triglycerides (P value for BMI × age interaction effect = .048) in SHIP-TREND.
Figure 2. Association of BMI with wall thickness of the descending aorta for never smokers, ex-smokers, and current smokers adjusted for sex, age, systolic and diastolic blood pressure, HbA1c, HDL-C, LDL-C, and triglycerides (P value for BMI \times smoking status interaction effect = .056) in SHIP-TREND.
Conclusion:

- Age, gender, BMI, and LDL-C associated with the AWT of the ascending and descending aorta

- The AWT of the descending aorta associated with smoking status and HDL-C

- Older age, male gender, higher BMI, current smoking status, higher HDL-C level, and lower LDL-C level associated with increasing AWT

- No associations of systolic and diastolic blood pressure, HbA1c, and triglyceride levels with AWT

- Results consistent with the population-based Multi-ethnic Study of Atherosclerosis also revealed increasing thoracic AWT with advancing age and for men compared with women.
Arterial Stiffness in Other Population-Based Studies

- Multi-ethnic Study of Atherosclerosis (MESA)
- A total of 6814 subjects (men and women aged 45 to 84 years)
- B-mode ultrasound of both common carotid arteries

Hazard Ratios and Confidence Intervals for each 10% increase in Reflection Magnitude and Death in Unadjusted and Adjusted Models.

<table>
<thead>
<tr>
<th>Model</th>
<th>All-Cause Mortality (617 deaths)</th>
<th>Cardiovascular Mortality (134 deaths)</th>
<th>Non-Cardiovascular Mortality (460 deaths)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>CI</td>
<td>P</td>
</tr>
<tr>
<td>Model 1*</td>
<td>1.31</td>
<td>1.11–1.55</td>
<td>0.001</td>
</tr>
<tr>
<td>Model 2†</td>
<td>1.32</td>
<td>1.12–1.56</td>
<td>0.001</td>
</tr>
<tr>
<td>Model 3‡</td>
<td>1.18</td>
<td>0.97–1.44</td>
<td>0.09</td>
</tr>
<tr>
<td>Model 4§</td>
<td>1.23</td>
<td>1.01–1.51</td>
<td>0.04</td>
</tr>
<tr>
<td>Model 5</td>
<td></td>
<td></td>
<td>1.22</td>
</tr>
</tbody>
</table>

Zamani et al. 2014
Arterial Stiffness in Other Population-Based Studies

- Northern Manhattan Study (NOMAS)
- A total of 3298 subjects (between 1993-2001)
- Transthoracic echocardiogramms in 2085 subjects

Sahisha et al. 2010
MR Imaging in Other Study-Based Population

• **Dallas Heart Study** *(Rosero et al. 2009)*
  - Multiethnic population-based study of 6,101 adults from Dallas County
  - 3,072 individuals completed Visit 3 dual-energy x-ray absorptiometry (DXA), MRI and electron beam computed tomography

• **Baltimore Longitudinal Study of Aging** *(Wang et al. 2014)*
  - Spatio-temporal brain imaging with MRI to capture longitudinal brain changes

• **NAKO Health Study** *(German National Cohort Consortium (GNC), 2014)*
  - MRI Body Scan for 30,000 individuals at 5 sites
Arterial Stiffness as Surrogate Endpoint

- **Phase 1:** Proof of Concept — Do Novel Marker Levels differ Between Subjects with and without Outcome? — **YES**

- **Phase 2:** Prospective Validation - Does the Novel Marker Predict Development of Future Outcomes in a Prospective Cohort or Nested Case-Cohort Study? — **YES**

- **Phase 3:** Incremental Value - Does the Novel Marker Add Predictive Information to Established, Standard Risk Markers? — **YES**

- **Phase 4:** Clinical Use - Does the Novel Risk Marker Change Predicted Risk Sufficiently to change Recommended Therapy? — **YES**

- **Phase 5:** The Clinical Outcomes - Does Use of the Novel Risk Marker Improve Clinical Outcomes, Especially When Tested in a Randomized Clinical Trail? — **NOT CLEAR**

- **PHASE 6:** Cost-Effectiveness - Does use of the Novel Risk Marker improve Clinical Outcomes sufficiently to justify the additional costs? — **NOT CLEAR**
NEXT STEPS:

• LEVEL-III Project in NAKO HEALTH STUDY

• Advanced Glycation Endproducts (AGEs) associated with Artial Stiffness

• Identification as predictor for aging and longevity (in Longitudinal Perspectives)

• Predictors for all-cause mortality, cardiovascular mortality, etc.
THANK YOU FOR YOUR ATTENTION!!!!!!

Ronny Westerman, PhD
Contact: ronny.westerman@bib.bund.de or nako@bib.bund.de
References

Laurent S et al. (2013) Arterial Stiffness as an Imaging Biomarker are All Pathway Equal? Hypertension 62:10-12.
Spartano NL et al. (2014) Arterial stiffness as a noninvasive tissue biomarker of cardiac target organ damage. Current Biomarker findings 4:4 23-34.
Announcement

CONFERENCE THEME: DEMOGRAPHIC CHANGE AND POLICY IMPLICATIONS
31st AUG. – 3rd SEPT. 2016 | MAINZ, GERMANY

REGISTER NOW
Announcement: 1st European meeting of the Biomarker Network

When: Wednesday, March 31, 2016, 8:30-16:00 hrs.
Where: Johannes Gutenberg University Mainz, Germany

Topics:

- biomarkers of environmental burden
- genetic markers for longevity and disability
- cardiovascular risk factors, metabolic syndrome, dementia and other chronic diseases
- markers of epigenetic effects
- micro biome and nutrition
- new measurements and methods

Submissions on other biomarkers will also be considered. In any case, however, a relation to demographic research has to be demonstrated.
Announcement: 1st European meeting of the Biomarker Network

The abstract should clarify the material to be presented: research question, data, methods, results, discussion.

Abstracts should not exceed 300 words, and should be sent to the address

Eurobiomarker@bib.bund.de

The deadline for submitting abstracts is May 15th 2016. Successful candidates will be notified until June 15th 2016.

Please join us for the opportunity to listen to recent updates on research, share ideas and new findings with colleagues, and network with experts to advance biomarker discovery and development.

Best regards

2016 European Biomarker Network Committee
Ulrich Mueller, Andrea Werdecker, Ronny Westerman