Carotid IMT Definition

- IMT is an acronym often used to refer to the phrase “intima-media thickness”.
- IMT refers to the combined thickness of the intimal and medial layers of the arterial wall.
- Carotid IMT is measured from two-dimensional noninvasive B-mode ultrasound images.

Carotid IMT Definition (Cont’)

- Histological slices show the intimal and medial layers of two atherosclerotic arteries with B-mode Carotid IMT Definition (different plaque characteristics).
- The maximum IMT of each wall is indicated by the vertical yellow line.
- This thickness includes that of both the media (M) and the plaque (P). The plaques affect both the intima and the media.

Schematic diagram with lesions at the BIF and ICA

Clinical Value of Carotid IMT

- Prediction of risk for cardiovascular events using traditional risk factors, such as Framingham Risk Score (ATP-III risk assessment tool), is somewhat limited.
- Many cardiovascular events cannot be predicted from traditional risk factors (lipids, blood pressure, smoking, etc.).
Clinical Value of Carotid IMT (Cont’)

- Carotid IMT is an independent predictor of cardiovascular events in general populations after adjustment for traditional risk factors.

- Observational studies have found that for an absolute carotid IMT difference of 0.1 mm, the future risk of MI increases by 10% to 15%, and the stroke risk increases by 13% to 18%.

Adapted from Lorenz MW, et al. Circulation 2007;115

**Absolute IMT and Risk of CHD**
Atherosclerosis Risk in Communities (ARIC)

- N=12,841
- Age: 45–64 years
- ‘Healthy’, No CVD symptom
- Follow-up: 4–7 years
- Adjusted for age, center and race

Adapted from Chambless LE et al. Am J Epidemiol 1997;146

**Absolute IMT and Risk of Stroke**
Atherosclerosis Risk in Communities (ARIC)

- N=14,214
- Age: 45–64 years
- ‘Healthy’ without CVD symptom
- Follow-up: 6–9 years
- Adjusted for age, center and race

Adapted from Chambless LE et al. Am J Epidemiol 1997;146

**Absolute IMT and Risk of Stroke or MI**
Cardiovascular Health Study (CHS)

- N=4,476
- Age > 65 years
- ‘Healthy’, No CVD symptom
- Follow-up: 7 years
- After controlling for age/sex, the odds ratio of MI or stroke was 4.5 for the highest IMT quintile as compared to the lowest quintile
- The possibility of stroke or MI incidence was 4% for the lowest IMT quintile, 26% for the highest quintile
- Compared to other risk factors, IMT was the strongest predictor of stroke or MI


**Absolute IMT and Risk for Stroke**
The Rotterdam Study

- N=1,683
- Age ≥ 55 years
- Model 1- adjusted for age/sex
- Model 2- adjusted for age/sex, stroke history, BMI, smoking, SBP, TPC, HDL-C, DM
- With every 0.15 mm increase in Baseline IMT, the 10 year absolute risk for stroke increased by 4.1%

Adapted from Rots et al. Circulation 1997; 96

**Absolute IMT and Risk of Stroke**
Japanese Elderly Men

- N=1,289
- Age: 60–74 years
- ‘Healthy’ without CVD history
- Follow-up: 4.5 years

Adapted from Kitaoka A, et al. Stroke 2004;35
**Comparison with Other Risk Assessment Tools**

**Atherosclerosis Risk in Communities (ARIC)**

- Follow-up: 5.2 years (mean)

<table>
<thead>
<tr>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.69</td>
<td>2.54</td>
</tr>
<tr>
<td>2.88</td>
<td>1.95</td>
</tr>
</tbody>
</table>

Adapted from Chambers LE, et al. Am J Epidemiol 1996;146

**The Rotterdam Study**

- N=6,913
- Follow-up: 6.1 years (mean)
- Relative Risk (highest to lowest tertile) of Stroke
  - Model-1: Adjusted for age and sex
  - Model-2: adjusted for age, sex, diabetes mellitus, smoking, systolic and diastolic BP, total-C and HDL-C, history of CVD

**The Multi-Ethnic Study of Atherosclerosis (MESA)**

- N=6,698
- Age: 45–84 years
- ‘Healthy’, free of CVD
- Followed-up: 5.3 years
- Adjusted for age, sex and race

**IMT and Stroke Risk in MESA**

Figure 2. Stroke incidence Kaplan-Meier curves for the lower 3 quartiles of intima media thickness (IMT) progression (%) and upper quartile (squares).

**AstraZeneca Research**

- METEOR International Study used CIMT to assess and measure change in the carotid artery of asymptomatic subjects with early atherosclerotic disease and at low CHD risk.
- First study to show positive benefit on atherosclerosis for people with early signs of diseased arteries.
- FDA approved expanded marketing of Crestor based on CIMT data in the METEOR Study (drug halted progression of disease)
- Data showed a 0.0014 mm/yr decrease in the mean maximum carotid intima-media thickness—a marker of atherosclerotic burden, of Crestor patients, compared to a progression of 0.0131 mm/yr for those on placebo.
- The Ward A Riley Ultrasound Center was the Core Reading Laboratory and Ultrasound Training and Quality Control/Quality Assurance Center for the United States as well as an IMT Scanning site for this important pharmaceutical trial.
Summary of Research

- Absolute carotid IMT is an independent predictor of MI, TIA and stroke incidence.
- The progression of carotid IMT is associated with increased risk of MI, TIA and stroke event.
- Carotid IMT is a stronger predictor of clinical events than cholesterol and some measures of atherosclerotic burden.
- Carotid IMT progression can be significantly reduced or possibly halted in certain populations.
- Such reduced carotid IMT progression could profoundly affect the incidence of CHD or stroke over the long-term.

American Heart Association
Prevention Conference V

Carotid IMT

- Is an independent predictor of TIA, stroke, and coronary events such as MI.

Recommendation

- Can be considered for CHD risk assessment in asymptomatic persons > 45 years old in experienced labs.

Screening for Heart Attack Prevention and Education (SHAPE) Task Force

1st Guideline:

- Age: Males: 45-75 years
  Females: 55-75 years
- Apparently healthy: No known history of CHD NOT at very low risk
- Carotid IMT evaluation for CHD risk assessment

CIMT Appropriate Use Criteria

Appropriate use criteria for carotid intima media thickness testing

1. New or worsening symptoms of carotid artery disease
2. Carotid plaque or stenosis
3. Carotid artery disease as a predictor of stroke
4. Carotid artery disease as a predictor of coronary artery disease
5. Carotid artery disease as a predictor of peripheral artery disease
6. Carotid artery disease as a predictor of acute coronary syndrome
7. Carotid artery disease as a predictor of cardiac arrest
8. Carotid artery disease as a predictor of transient ischemic attacks
9. Carotid artery disease as a predictor of myocardial infarction
10. Carotid artery disease as a predictor of stroke
11. Carotid artery disease as a predictor of death from any cause

Wake Forest Baptist Health
Appropriate Use Criteria
Importance of Plaque

- Presence of plaque predicts increased risk, irrespective of IMT values
- Exact definition and cut points have varied
- Most protocols include assessment and reporting of plaque in addition to the IMT data
- Acoustic shadowing confers increased risk
- Effects seen across age, race, and gender

Prevalence of Carotid Disease and ABI in ARIC


Plaque and CVD risk in NOMAS by Max Carotid Plaque Thickness (MCPT)

Rundek et al, Neurology, 2008

Impact of Plaque by Age, Race, Ethnicity

Rundek et al, Neurology, 2008

Impact of Plaque on FRS Values

Rundek et al, Neurology, 2008

Plaque and Acoustic Shadowing

Prabhakaran et al, Atherosclerosis, 2007
Impact of Plaque w/wo Shadowing in NOMAS

![Graph showing annual incidence per 100,000 with and without plaque shadowing.]

Plaque Shadowing in NOMAS (N= 1,118)

Prabhakaran et al, Atherosclerosis, 2007

CVD Risk Assessment Using IMT

Lack of Universal Standardized Protocol:
• What to measure
• Where to measure
• How to measure

Carotid IMT Protocols

- Interrogation Angle: Circumferential, Fixed-Angle
- Arterial Site: CCA Far Wall, Multiple Sites*

(*Multiple sites: Far and Near walls of the CCA, Bulb, ICA)

Table 1: Hazard ratios and 95% CI for combined vascular outcome (stroke, MI, or vascular death)

<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
<th>Model 1*</th>
<th>Model 2*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque with AS vs no plaque</td>
<td>3.8 (1.7-8.5)</td>
<td>2.1 (1.0-4.1)</td>
<td>2.1 (1.0-4.1)</td>
</tr>
<tr>
<td>Plaque with AS vs no plaque</td>
<td>2.9 (1.3-6.2)</td>
<td>1.7 (1.0-2.8)</td>
<td>2.2 (1.0-5.0)</td>
</tr>
<tr>
<td>Plaque with AS, plaque without AS</td>
<td>1.4 (0.7-2.6)</td>
<td>1.0 (0.7-2.6)</td>
<td>1.2 (1.0-2.7)</td>
</tr>
</tbody>
</table>

Prabhakaran et al, Atherosclerosis, 2007
Carotid IMT Protocols (Cont’)

Interrogation Angle

<table>
<thead>
<tr>
<th></th>
<th>Fixed-Angle</th>
<th>Circumferential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical effort</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Measurement Error</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Reliability</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Missing the max IMT</td>
<td>↑</td>
<td>↓</td>
</tr>
</tbody>
</table>

Carotid IMT Protocols (Cont’)

Arterial Site

<table>
<thead>
<tr>
<th></th>
<th>CCA FW</th>
<th>F &amp; N W of CCA+BIF+ICA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tech effort</td>
<td>Less</td>
<td>More</td>
</tr>
<tr>
<td>Reliability</td>
<td>Best</td>
<td>Lower</td>
</tr>
<tr>
<td>Auto software</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Association with risk factors</td>
<td>Weaker</td>
<td>Stronger</td>
</tr>
<tr>
<td>IMT progression</td>
<td>Slow</td>
<td>Faster</td>
</tr>
<tr>
<td>Lesion present</td>
<td>Latest</td>
<td>BIF—I–ICA →CCA</td>
</tr>
</tbody>
</table>

Carotid IMT Protocols (Cont’)

For valid, reliable IMT measurement and CVD risk assessment, the protocol must

- Angulations: be circumferential, or have multiple defined angles
- Anatomical site(s): include the maximum IMT measurements from multiple carotid sites

Carotid IMT Measurement Precision

- Carotid IMT measurement requires very high (submillimeter) precision to permit reliable percentile classification of individuals for accurate risk assessment in a clinical setting.

<table>
<thead>
<tr>
<th>Percentile</th>
<th>Mean CIMT (mm)</th>
<th>Difference (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5th</td>
<td>0.38</td>
<td>–</td>
</tr>
<tr>
<td>10th</td>
<td>0.41</td>
<td>0.03</td>
</tr>
<tr>
<td>25th</td>
<td>0.47</td>
<td>0.06</td>
</tr>
<tr>
<td>50th</td>
<td>0.53</td>
<td>0.06</td>
</tr>
<tr>
<td>75th</td>
<td>0.61</td>
<td>0.08</td>
</tr>
<tr>
<td>90th</td>
<td>0.68</td>
<td>0.07</td>
</tr>
<tr>
<td>95th</td>
<td>0.73</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Adapted from Howard G, et al. Stroke 1993;24
Operator Related Variability (Cont’)

Frame Selection

Criteria for frame Selection
• Arterial wall is perpendicular to sound beam
• Both lumen/intima and media/adventitia interfaces are defined
• The two interfaces are moving in the same direction and at the same pace with arterial pulsation and transducer movement
• Gain/TGC settings are low enough to eliminate artifact, especially when measuring the near wall IMT

Common Errors in Carotid IMT Evaluation

• Incorrect segment identification - Key anatomical reference: Tip of the flow divider
• Ultrasound beam not perpendicular to the arterial wall - missing IMT interfaces; over estimate of IMT
• Measurement of artifact - be careful with automated and/or semi-automated software
• IMT measurement oblique – be careful with automated and/or semi-automated programs

IMT Measurement by Automated Edge Detection IMT Software

1. Sharp interfaces.
2. Correct edge detection.
3. Valid IMT measurement.

IMT Measurement by Automated Edge Detection IMT Software (Cont’)

1. False edge detection.
2. Measurement line oblique to wall.
3. Invalid IMT measurement!

Operator editing is required for a valid IMT measurement!

Carotid IMT Quality Assurance

<table>
<thead>
<tr>
<th>Error Source</th>
<th>Quality Control Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Machine</td>
<td>Standardization, Frequency, pixel size, resolution</td>
</tr>
<tr>
<td>Protocol</td>
<td>Standardization, Circumferential, multiple sites</td>
</tr>
<tr>
<td>Operator</td>
<td>Standardized training, Certification, Routine quality control Procedures</td>
</tr>
</tbody>
</table>

Wake Forest Baptist Health
Carotid IMT Screening in CVD Prevention
in Private non-University Clinical Practice

• Patients: N=209; Age=55.7±8.9 yrs
• Global risk assessment:
  • Lipids, Smoking, DM, BP, Diet, Obesity, etc.
  • Carotid IMT evaluation @ baseline and year-1
    • standardized protocols
    • standardized trained and certified CIMT sonographers
  • Treatment of multiple risk factors
  • Lifestyle modification
  • medication prescription and adjustment to control/reduce known CV risk factors

Wake Forest Baptist Health

Adapted from Bale, et al. Atherosclerosis 2006;7:161

Change of Carotid IMT after 1-year Treatment of Multiple Risk Factors

Ultrasound Screening in Asymptomatic Patients: Carotid IMT Screening

• May allow treatment or intervention years prior to a clinical event; focus on younger patients without known heart or vascular disease
• Potential role as motivational tool
• Requires careful attention to protocols, training, reading, QA/QC
• CIMT Risk Prediction Exams are becoming available
• In USA, Texas is to cover cost of IMT or CAC
• ICAVL/CAMS now accredits IMT testing

CIMT Risk Screening at WFUMS
Target Population

• Family history of premature CVD in a first-degree relative (men < 55 years old, women < 65 years old)
• Severe abnormalities in a single risk factor (e.g., genetic dyslipidemia) who otherwise would not be candidates for pharmacotherapy may be considered for screening

CIMT Risk Screening at WFUMS
Target Population

1. Individuals without established cardiovascular disease (coronary heart disease, cerebrovascular disease, peripheral arterial disease, abdominal aortic aneurysm) and with two CVD risk factors other than age (especially any combination of high blood pressure, obesity, smoking, or dyslipidemia)

Ward A. Riley Ultrasound Center
CIMT Screening Exam Report

Table 1. Far Wall IMT Measurements

<table>
<thead>
<tr>
<th>Site</th>
<th>Left Carotid</th>
<th>Right Carotid</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0.8 mm</td>
<td>2.0 mm</td>
<td>1.4 mm</td>
</tr>
<tr>
<td>Year-1</td>
<td>1.2 mm</td>
<td>2.7 mm</td>
<td>2.0 mm</td>
</tr>
</tbody>
</table>

Percentile: Percentile intervals illustrate the distribution of baseline and year-1 measurements. The given percentile (P) represents the value below which a certain percentage of the measurements fall.

Prediction Intervals: Prediction intervals describe the uncertainty in IMT measurements. They are calculated to provide a range within which 80% of new measurements will lie, within the limits of error for each individual.
Initial Overview

**Risk Assessment:**
- CHD risk for CHD is 2.17, based on average 45-year-old female patient's age, gender, and ethnicity.
- Age 45-70-year-old female patients with a CHD risk score of 2.17 or greater have an increased likelihood of developing CHD.
- Female patients are at a 2.2 times increased risk compared to male patients.

**Physician Notes:**
I have personally reviewed the CIIMT results and agree with the interpretation.

Reviewing Physician: [Signature]
Date: 3/21/2012

---

**Patient Statistics Overall**

- **Patients Scanned:**
  - Total: 763
  - Men: 251
  - Women: 474
- **Patients Average Age:**
  - Overall: 52.57
- **Patients Average Thickness:**
  - Overall: 1.63
- **Patients Average Relative Risk Value:**
  - Overall: 1.16

Overall (N=763) see 19% prevalence of plaque of 2 mm or greater.
Ongoing QA for CIMT at WARUC

Alternatives:
IMT and Coronary Artery Calcium
- Unique strengths and weaknesses
- Assess different issues along the continuum of atherosclerosis
- Different body and length of experience
- Radiation dose with CAC
- Problems with low or zero calcium score
- Good CAC association for CVD outcome (MESA), but IMT better predictor for stroke

Alternatives:
IMT and CAC
- IMT may be useful to use with FRS to identify risk when CAC score is zero (Lester SJ, et al, Mayo Clin Proc 2009)
- IMT may be useful to identify risk in those missed by traditional RF screening (Adolphe A, et al, Mayo Clin Proc 2009)
- ASE published guidelines for clinical use of IMT (Stein JH, et al, JASE 2008)

Measurement of Carotid Artery IMT Wrap-up
- Can predict risk of CHD, Stroke and other CVD
- Helps PCPs improve CVD risk assessment and make decisions on appropriate risk reduction management
- Motivates patients compliance
- Can evaluate risk reduction treatment efficacy
- Must use standardized protocols and QC procedures to ensure measurement validity and reliability for accurate risk assessment and monitoring change over time
- Level 3 CPT code at present (0126T); some insurance reimbursing in a few States. Now ICAVL/CAMS accreditation
- Potential for collaboration to perform readings and provide risk prediction reports for other labs

Thank you for your attention