**THE TEST OVERVIEW**

**OVERVIEW:** The AngioDefender™ system conducts an operator-independent analysis of the brachial artery’s dilation response to increased blood flow in under 20 minutes. It can be administered in either an office or hospital setting. First, a standard blood pressure cuff is secured on the arm above the patient’s elbow. After a resting period of ten minutes, the operator presses the “Start Test” button and the system begins five automated phases described in Figure 1 below. After the test is completed, a report is instantly generated.

**INDICATION:** The AngioDefender™ System is a CE-marked, non-invasive device for the diagnostic of percentage flow-mediated dilation (%FMD) of the brachial artery.

**VALIDATION STUDIES: EQUIVALENCE TO BRACHIAL ARTERY ULTRASOUND IMAGING**

The following comparison studies reveal that the AngioDefender™ system is statistically equivalent to the gold standard brachial artery ultrasound imaging (BAUI) technique as used to measure %FMD.

1. **Moscow Medical Academy, Moscow, Russia. 2010.**
   Each of twenty-two subjects with a range of CVD risk factors underwent testing with both procedures, separated by a one-hour interval, with each test administered in random order. Figure 2 illustrates a Passing-Bablok regression of the data, showing a close matching of the regression line with the line-of-identity (Pearson correlation coefficient = 0.84, p<0.0001). No significant adverse events were reported.

2. **Medanta Heart Institute, New Delhi, India. 2011.**
   Each of thirty-three subjects underwent FMD testing using BAUI and the AngioDefender™ system, with the two tests being performed on consecutive days for each individual. A Passing-Bablok regression of the data also showed statistical equivalence. No significant adverse events were reported. Graph not shown.
**ENDOTHELIAL DYSFUNCTION PREDICTS EARLY-STAGE CARDIOVASCULAR DISEASE**

“Extensive literature documents that endothelial dysfunction is associated with almost every condition predisposing to atherosclerosis and cardiovascular disease.”

Studies have long demonstrated a correlation between endothelial dysfunction and conditions predisposing to CVD, including: arterial hypertension\(^1\), normotensive subjects with a family history of hypertension\(^2\), smoking\(^3\), dyslipidemia\(^4\), ageing\(^5\), diabetes mellitus\(^6\), and obesity\(^7\). Table 1 highlights some of the most significant studies from the last twenty years.

### Table 1: Significant studies support endothelial dysfunction’s association with the pathogenesis of early atherosclerosis

<table>
<thead>
<tr>
<th>Study</th>
<th>Authors &amp; Publication</th>
<th>Size</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impairment of endothelium-dependent dilation is an early event in children with familial hypercholesterolemia and is related to the lipoprotein (a) level.</td>
<td>Sorensen KE, Celermajer DS, Georgakopoulos D, et al. Journal of Clinical Investigation 1994; 93:50-55.</td>
<td>Children with and without familial hyper-cholesterolemia (n=60)</td>
<td>Impaired endothelium-dependent dilation is present in children with familial hypercholesterolemia as young as 7 yrs. of age and the degree of impairment is related to the lipoprotein (a) level.</td>
</tr>
<tr>
<td>Comparable prognostic value of vasodilator response to acetylcholine in brachial and coronary arteries for predicting long-term cardiovascular events in suspected CAD.</td>
<td>Takase B, Hamabe A, Satomura K, et al. Circulation 2006; 70:49-56</td>
<td>Patient suspected of having coronary artery disease (n=70)</td>
<td>The brachial artery vasodilator response to optimal ACh dosage can be used as a surrogate prognostic predictor for coronary endothelial function tests in patients with suspected CAD.</td>
</tr>
<tr>
<td>Coronary endothelial dysfunction in patient with early coronary artery disease is associated with the increase in intravascular lipid core plaque.</td>
<td>Choi B-J, Prasad A, Gulati R, et al. European Journal of Heart Journal 2013; 34:2047-2054</td>
<td>Patients with chest pain who had diameter stenosis (n=52)</td>
<td>Patients with early coronary artery disease and endothelial dysfunction had a higher lipid content in the vascular wall than patients with normal endothelial function.</td>
</tr>
</tbody>
</table>

Further reading: Comprehensive review papers summarize the substantial research linking endothelial dysfunction with CVD\(^2,3\).

**FLOW-MEDIATED DILATION ACCURATELY MEASURES ENDOTHELIAL DYSFUNCTION**

Table 2 summarizes longitudinal studies using the gold standard — brachial artery ultrasound imaging — to measure %FMD. In these large population studies, the correlation between overall CVD risk and %FMD is apparent.

### Table 2: Large longitudinal studies reveal FMD as a strong predictor of endothelial dysfunction

<table>
<thead>
<tr>
<th>Study</th>
<th>Authors &amp; Publication</th>
<th>Size</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow-mediated dilation and cardiovascular risk prediction: A systematic review with meta-analysis</td>
<td>Ras RT, Streppel MT, Draijer R, Zock PL, et al. Int J Cardiol 2012; 168:344-351</td>
<td>23 studies involving nearly 15,000 subjects</td>
<td>For studies reporting continuous risk estimates, the pooled overall CVD risk was 0.92 (95% CI: 0.88; 0.95) per 1% higher FMD. A higher association was observed in diseased populations.</td>
</tr>
<tr>
<td>Predictive value of brachial flow-mediated dilation for incident cardiovascular events in a population-based study the Multi-Ethnic Study of Atherosclerosis (MESA)</td>
<td>Yeboah J, Folsom AR, Burke GL, et al. Circulation 2009; 120:502-509</td>
<td>6 clinical sites with over 3,000 subjects free of clinical CVD</td>
<td>Brachial FMD is a predictor of incident cardiovascular events in population-based adults and improved the classification of subjects as low, intermediate, and high CVD risk compared with the FRS.</td>
</tr>
</tbody>
</table>


The AngioDefender™ system is not commercially available in the United States.

REF:110004