Ambulo™ 2400
Ambulatory Blood Pressure Monitoring Systems
About Tiba Medical

- Private medical device company founded in 2003 and based in Portland, Oregon, USA
- Focused on ambulatory blood pressure monitoring systems
- USA FDA & ISO 13485:2003 / CMDCAS Registered
- Products in the market in US, Canada, EU, Asia, Australia & Latin America
- Technology, price and service leader in supporting
  - Physicians (Cardiology, Nephrology & Primary Care)
  - Clinical Researchers
  - Pharmaceutical Companies, Central Labs & CRO’s
About Blood Pressure

- Blood pressure refers to the force or pressure that is exerted on the body's arteries as blood flows through them. Each time the heart beats or contracts, it produces pressure in the arteries. This blood pressure is what moves blood through the body, supplying oxygen and nutrients to every organ.

- When the heart contracts, it sends blood out into the body. This pressure is referred to as systolic. The pressure that is created as the heart pulls blood back through it is called diastolic. Blood pressure is recorded as systolic over diastolic.
Hypertension

- Left uncontrolled, hypertension places an incredible amount of stress on the heart and arteries, both of which become forced to work harder to keep blood flowing in a healthy manner throughout the body.
- Over time, this stress can result in health problems including enlargement of the heart, loss of elasticity of the arteries, heart disease, stroke and even death.
- Physicians monitor and recommend medications and lifestyle changes to help manage the blood pressure of patients with blood pressure conditions.
- A medical phenomena known as White Coat Hypertension causes many individuals' blood pressure to be higher when taken in a medical office setting. The stress and anxiety of being in the doctor's office may cause blood pressure to raise as much as 20-50 points higher than normal.
BP Guidelines

- Individual levels vary due to a variety of factors, including:
  - temperature (too hot or cold)
  - humidity
  - physical exercise
  - restlessness
  - lack of sleep
  - constipation
  - stress
  - fear
  - hormones
  - anger
  - anxiety
  - food & beverage consumption
  - individual physical conditions

<table>
<thead>
<tr>
<th>Diastolic (mm/Hg)</th>
<th>Normal</th>
<th>Pre-Hypertensive</th>
<th>Borderline</th>
<th>Hypertensive</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>85</td>
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<td>90</td>
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<tr>
<td>95</td>
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</tr>
</tbody>
</table>

Average heartbeats per day: ~100,000
Average heartbeats during office or home BP: ~20
Sampling ratio: 1:5000; 0.02%
## Approaches to Blood Pressure Management

<table>
<thead>
<tr>
<th>Activity/Assessment</th>
<th>Home BP</th>
<th>Office BP</th>
<th>Ambulo 2400 ABPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obtaining a BP measurement</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Assessing White Coat Effect</td>
<td>Limited</td>
<td>Limited</td>
<td>Yes</td>
</tr>
<tr>
<td>Identifying Circadian Pattern</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Identifying diurnal or nocturnal rhythm</td>
<td>Limited</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Identifying true or mean pressure</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Evaluating extent of nocturnal dip and morning surge</td>
<td>Limited</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Determining extent of variability</td>
<td>Limited</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Evaluation of response to treatment</td>
<td>Limited</td>
<td>Limited</td>
<td>Yes</td>
</tr>
<tr>
<td>Determining time dependent effects of treatment – including Phase I cardiac safety trials</td>
<td>Limited</td>
<td>Limited</td>
<td>Yes</td>
</tr>
<tr>
<td>Correlation of activity to BP</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Accuracy of recorded data</td>
<td>Limited</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
What is ABPM?

- A procedure for diagnosis of various hypertension conditions
- A lightweight device that is worn for 24 hours to automatically measure BP and pulse during the day and night
- Used by Primary Care Physicians, Cardiologists & Nephrologists
- Also used extensively by researchers during efficacy or safety clinical trials
- Measurements are uploaded to a computer at the physician’s office and analyzed through software
- Provides reliable information regarding blood pressure, arterial compliance, left ventricular contractility, and dipper/non-dipper classification
- Decreases the need for exhaustive testing and allows quicker, easier diagnosis and treatment program development
Clinical & Research Uses of ABPM

- **White coat hypertension:** The stress and anxiety of being in the doctor's office can cause blood pressure to raise as much as 20-50 points higher than normal. It is estimated that 20% of all people on blood pressure medication don’t have high blood pressure, but rather WCH.

- **Resistant hypertension:** prior to instituting an invasive investigation (e.g. renin vein assays, angiogram for renal artery stenosis) for secondary causes of hypertension for patient's with hypertension that is refractory to medications

- **Evaluation of hypotension:** events that are thought to be related to antihypertensive medications

- **Nocturnal angina:** to investigate BP changes in patients with nocturnal angina

- **Episodic hypertension:** ABPM is covered for patients whose symptomatology (paroxysms of excessive sweating, palpitations, apprehension) suggests episodic hypertension secondary to an adrenal tumor (e.g., pheochromocytoma), and office measurements are repeatedly normal

- **Evaluation of syncope:** ABPM is covered when used in conjunction with a 24-hour holter monitor to determine whether symptoms of syncope or near syncope are the direct result of an arrhythmia

- **Preeclampsia:** to help make the diagnosis of gestational hypertension or preeclampsia, especially in high risk pregnancies

- **Efficacy Trials:** 24-hour control including administration time-dependent effects of poly-therapy

- **Safety Trials:** Cardiac safety including PK/PD studies
### CPT: 93784 - Ambulatory blood pressure monitoring; including recording, scanning analysis, interpretation and report.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>CPT Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>High blood pressure without hypertension (The only ICD-9 code covered by Medicare)</td>
<td>796.2</td>
</tr>
<tr>
<td>Syncope, or near syncope</td>
<td>780.2</td>
</tr>
<tr>
<td>Weakness (generalized)</td>
<td>458.9</td>
</tr>
<tr>
<td>Hypotension, unspecified</td>
<td>785.50</td>
</tr>
<tr>
<td>Cardiovascular collapse</td>
<td>458.0</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>402</td>
</tr>
<tr>
<td>Hypertensive heart disease</td>
<td>429</td>
</tr>
<tr>
<td>Cardiovascular disease due to hypertension</td>
<td>429.2</td>
</tr>
<tr>
<td>Resistant hypertension</td>
<td>997.91</td>
</tr>
<tr>
<td>Hypertensive renal disease</td>
<td>403.1</td>
</tr>
<tr>
<td>Unspecified hypertension complicating pregnancy</td>
<td>642.9</td>
</tr>
<tr>
<td>Transient hypertension of pregnancy</td>
<td>642.3</td>
</tr>
<tr>
<td>Mild preeclampsia</td>
<td>642.4</td>
</tr>
<tr>
<td>Maternal hypotension syndrome</td>
<td>669.2</td>
</tr>
</tbody>
</table>
Considerations for a new ABPM

- Size
- Accuracy
- Durability
- Comfort
- Battery life
- Price
- Synchronization to activity cycles
- Open and extendible software
- Unique needs of the clinical research community
Multi-Disciplinary Design Team

- Development Team Based in the US
  - Industrial designers
  - Mechanical engineers
  - Electronics & firmware engineers
  - Digital signal processing & algorithm experts
  - Software developers
  - Regulatory & quality system experts
  - Soft goods designers

- Complemented with Other Services
  - Testing & validation (EMC, ESD, Safety, Environmental)
  - Clinical partners
  - Contract manufacturing services
Introducing the Ambulo 2400

**Precise:** Highly accurate, and robust oscillometric algorithm based on patented digital signal processing techniques

**Actigraphy:** Automatic categorization of sleep/awake cycles based on patented technology reduces reliance on diaries

**Software:** Sophisticated, intuitive and open software interface for easy programming, data download as well as report generation

**Form Factor:** Beautiful industrial design that is compact, durable and easy to use by patients and clinicians

**Easy to Wear Options:** Integrated on the blood pressure cuff, clipped on the hip or strapped around the shoulder

**Validated:** Validated according to the AAMI SP-10 & British Hypertension Society’s protocols

**Designed & Made in USA**
Specifications

- **Size**
  - 119 mm × 68 mm × 32 mm (4.7”x2.7”x1.2”)

- **Weight**
  - 253 grams (9 oz.)

- **Measurement Ranges**
  - Systolic: 60 to 280 mmHg
  - Diastolic: 30 to 200 mmHg
  - Pulse Rate: 30 to 180 bpm

- **Measurement Accuracy**
  - Blood Pressure: ±5 mmHg mean diff.
  - ±8 mmHg std. dev.
  - Heart Rate: ±3 bpm

- **Measurement Intervals**
  - Four adjustable intervals
  - 0, 5, 10, 20, 30, 45, 60, 90, or 120 min.
  - Optional randomization up to ±75%
  - Optional Sequential Plans for Phase 1 Cardiac Safety Trials

- **PC Interface**
  - USB cable with mini-B connector

- **Cuffs**
  - Standard Adult, Large Adult & Child
  - Optional EasyWear™ Adult

- **Actigraphy**
  - Recording of 3-axis of motion via accelerometer
  - Display & categorization of sleep/awake cycles via application software

- **Memory**
  - Solid-state Flash technology.
  - Sufficient for 3000 blood pressure measurements and 7 days of actigraphy

- **Batteries**
  - 2 x 1.2V AA batteries — NiMH batteries
  - Current: 610mA (max); 1.3 mA (idle)
  - Battery charger NOT included
  - 300 measurements using two 1600mAh NiMH batteries on regular adult cuff
Easy to Wear Options
AAMI SP-10/BHS Validation

- Principle Investigator: Dr. Mateo Aboy
- 85 subjects in Portland, Oregon
- 4 device measurements compared with 4 measurements by two trained observers
- AAMI SP-10: PASS; BHS Grade: A/A
- Report available upon request
- Results to be published in “Blood Pressure Monitoring” journal in the coming months
IEC/ISO 80601-2-30 Validation

- Upcoming global standard for development and validation of all blood pressure devices
- Clinical validation of Ambulo 2400 in 85 adults, adolescents and pediatrics
- Being performed and to be published by Dr. Bruce Alpert of the University of Tennessee in Memphis
Powerful Software

- Intuitive & Feature-Rich Solution
  - For Windows® based platforms (XP, Vista & Windows 7)
  - Allows for configuration of the device including “One Click Configuration”, testing and calibration
  - Measurement download after the procedure
  - Generation of detailed tabular, graphical and statistical data
  - Customized reports in Microsoft® Word, HTML or PDF† formats
  - Comparison reports between measurement sets including automatic sleep/awake pattern synchronization
  - Data import/export in XML or CSV (Excel-compatible)
  - HIPAA compliant
  - Available in English, Spanish & French

† PDF report generation requires 3rd party utility available for free
Unique Features

- **Built-in Actigraphy**
  - Synchronize subject data to awake/asleep patterns unique for each subject & study
  - Incorrect categorization of awake/asleep can skew data due to nighttime dip and morning rise
  - Comparison reports synchronized based on start of awake time
Unique Features

- Flexible and powerful configuration protocol
  - **Period Plans:** 4 periods in a 24-hour timeframe; each with unique attributes such as display, button, buzzer and actigraphy enable/disable features
  - **Sequence Plans:** Up to 80 sets (each set can be multiple equally timed-apart measurements) of sequential measurements based on discrete events. Ideal for PK/PD studies including in Phase I cardiac safety trials. Very granular controls over button, actigraphy, display, buzzer and retry options. Protocol can be saved in XML file and sent to sites for implementation.

- Large, non-volatile data store
  - Storage of up to 3000 measurements and events including up to 7 days of actigraphy in Flash memory
Unique Features

• Robust and Comfortable BP Algorithm
  • Proportional linear deflation; allows us to take measurements in subjects with arrhythmias
  • Significant filtering and signal processing; allows us to do a better job in view of motion and other signal noise
  • Adaptive technology that typically goes 35mmHg above and 20mmHg below last known SYS and DIA respectively; more comfort for the subject

• Flexible data reporting mechanisms
  • Microsoft Word and browser-compatible HTML reports
  • Raw data export to Excel and XML; can be emailed from each site
  • Device serial number and calibration information for each study captured as part of subject data reports
Why the Ambulo 2400?

- State of the art in ABPM technology
- Accurate, robust and easy for clinicians & patients
- Built-in actigraphy
- Powerful and open application software
- Unique features

#1 in technology
#1 in price
#1 in service/support
Why Tiba Medical?

- Dedicated to the success of our partners and customers
- Price & service leader in ABPM technology
- Understand the unique requirements of the clinical & research community
- State of the art research, product development and manufacturing