The Multifunction CardioGram – MCG:

The First Computational Electrophysiological Technology Adopting a Systems Analysis Approach to Non-Invasive Diagnosis of Coronary Ischemia

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Disclosure

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Overview

▶ *The theoretical basis for MCG?*

▶ *How MCG works*

▶ *Comparison to conventional ECG*

▶ *Historical timeline for MCG*

The Systems Analysis Approach

➢ Systems <u>theory</u> focuses on the communication between different parts (e.g., inputs and outputs) of a system.

➢ Systems <u>analysis</u> is the dissection of a system into its component parts in order to study how those parts interact and work.

➢ Systems <u>synthesis</u> is the re-assembly of a system's parts back into a whole system – hopefully with an improved understanding of the system.

➢ In the case of MCG, the "system of interest" is the human heart.

MCG Systems Analysis Approach vs. ECG Approach

▸ The traditional ECG approach examines electrical conduction in the myocardium via six segments of <u>individual</u> cardiac cycles, (P wave, P-Q interval, QRS complex, S-T segment, T weave and Q-T interval) using 12 leads. Analog data from these leads is analyzed separately - by segment – and "integrated" by human experts for interpretation. There is no information about the "relationship" of the electrical data between leads.

▸ The MCG systems analysis approach takes a much different (broader) view of the heart by looking at the interaction (relationship) of the information from two "signal sources," leads V5 and II, on a continuous basis, integrating all the data points obtained over multiple cardiac cycles (82 seconds), thereby providing new, more detailed information about cardiac function.

▸ To do this, MCG digitizes the data, applies six mathematic transformations, which yield 166 indices used for rapid digital-integration/pattern-recognition which reveal heretofore unknown information about the "entire heart" (i.e., "the system of interest") – including the relationship between the myocardium and intracardiac blood flow.

The Mathematics and Physics of MCG

➢ Intracardiac blood flow and myocardial contraction produce ongoing stress and strain which can be normal or abnormal and which varies within and between cycles.

➢ Mathematically, the non-linear visco-elastic property of the myocardium as a whole is depicted by the <u>LaGrange Coordinate.</u>

➢ Mathematically, blood is a non-Newtonian fluid which is depicted by the <u>Euler Coordinate.</u>

➢ The Laplace Transformation is applied to these coordinates resulting in six mathematical transformations and 166 indices that provide different pieces of information about the stress and strain of a patient's myocardium in relationship to intracardiac blood volume alterations.

➢ The integrated patterns of the166 indices from a patient are compared to similar patterns from over 40,000 patients (13,000 without cardiac disease) in a database to determine the "pattern" of the patient's indices.

The Six Mathematical Formulae used in MCG

|	
1) Auto Power Spectrum	$Gxx = Sx(f) \cdot Sx(f)i$
2) Phase Angle Shift	$\theta xy = \tan^{-1} \dfrac{Txy(I)}{Txy(R)}$ $= \tan^{-1} \dfrac{Gxy / Gxx(I)}{Gxy / Gxx(R)}$
3) Impulse Response	$Pih = F^{-1}Txy$
4) Cross Correlation	$Vxy = F^{-1}Gxy$
5) Coherence Function	$\gamma^2 = \dfrac{Gxy^2}{(Gxx)(Gyy)}$
6) Transfer Function	$Txy = \dfrac{Gxy}{Gxx} \qquad Txy = A, \phi$

How MCG is performed

Local Client
- Two Cardiac Electric Signal Sources
- Amplified, digitized, encrypted & transmitted

Local Client
- Automatic diagnostic report (PDF file)
- Final Diagnosis Severity Score

Decryption ➡ FFT

Digital Signal Processing To Increase S/N Ratio

Six mathematical transformations

G_{xx} P_{ih} γ^2 θ_{xy} V_{xy} T_{xy}

Identification of 166 indices

Pattern matching in 40,000 patient database

Premier Heart Network Operation Center (NOC) where the web-based MCG database is housed

The MCG Database (1)

➤ An empirical clinical database of more than 40,000 cases has been accumulated over the last 20 years and is the benchmark reference used for rapid digital pattern recognition.

➤ The database was built using 100,000 individual cases, 1/3 without cardiac disease and 2/3 with known cardiac pathology of various types (i.e., not just ischemia). 60% of the cases were not included in the database because of incomplete or poor quality data.

➤ Clinical data verified by two independent experts, a third to break an impasse.

➤ No bias was introduced by exclusion of these cases due to the requisite age and sex normalization process applied to the data set.

➤ Data from each case includes, sex, age, results from MCG, coronary angiography and other noninvasive testing.

➤ 50% of cases are women; age range is 14-100.

The MCG Database (2)

➢ The database includes patients with a wide variety of cardiac disease.

➢ Database has been internally validated on an going basis and externally validated by the clinical trials you will hear about.

➢ Patients with CAD comprise a significant portion of the database including patients with varying degrees of coronary artery blockage in different epicardial arteries, with or without other coexisting pathologies, e.g. systemic hypertension, diabetes, renal or liver failure, anemia, cancer, etc.

➢ Patients without CAD, as confirmed by angiography, are also included.

➢ All 166 indices have been repeatedly verified and validated both retrospectively and prospectively against the growing empirical clinical database to establish thresholds for reproducibility and reliability as required by FDA cGMP and CE regulatory requirements (ISO 13485).

# *Example: Comparison of ECG data to MCG data*

Lead Vs Resting ECG

Auto Power Spectrum from Lead V5
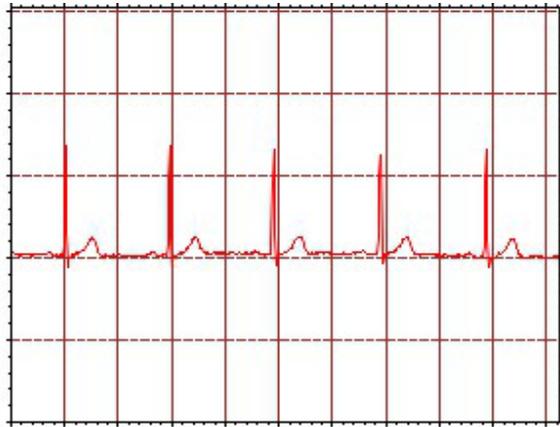
Abnormal Indexes

P	Q	QRS	ST	T
QT	TQT	R-R		
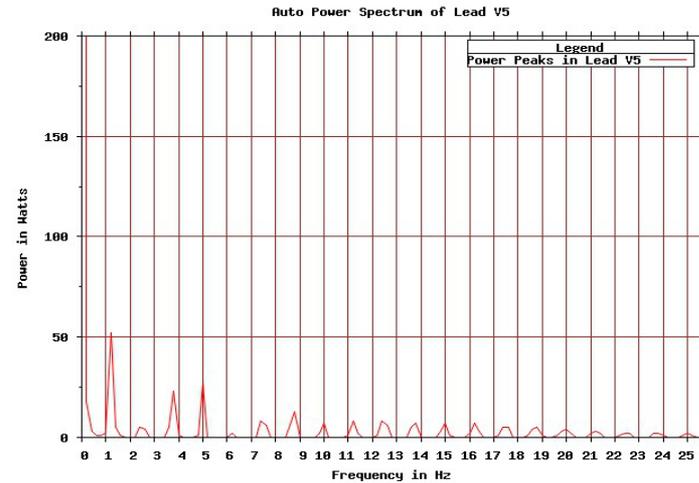
25 Abnormal Index Examples of Pv5

1/2	U_{3xy}	SS	A_3	UNK_1
Ω	U_4	F	A_4	UNK_2
U_1	N_1	FF	A_5	UNK_3
U_2	N_3	A_1	A_{55}	UNK_4
U_3	S	A_2	N_2	UNK_5

Example: Pre and Post Stenting Change in the Auto Power Spectrum Index
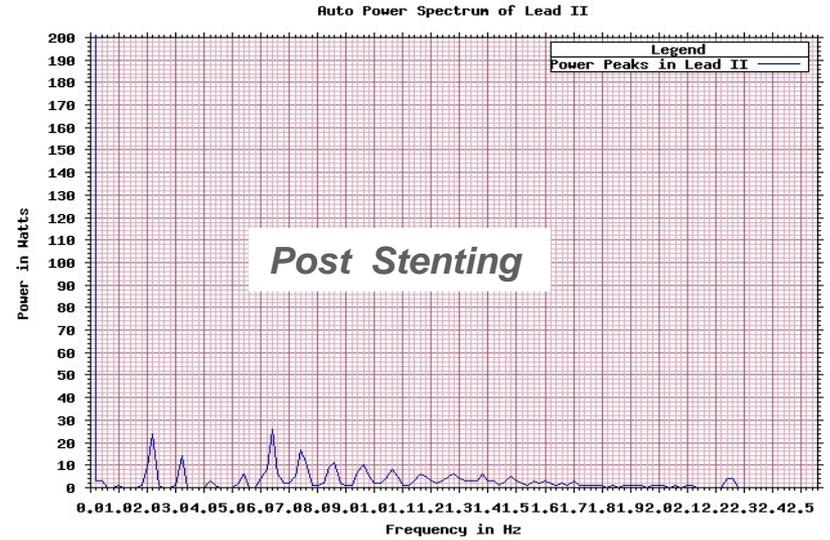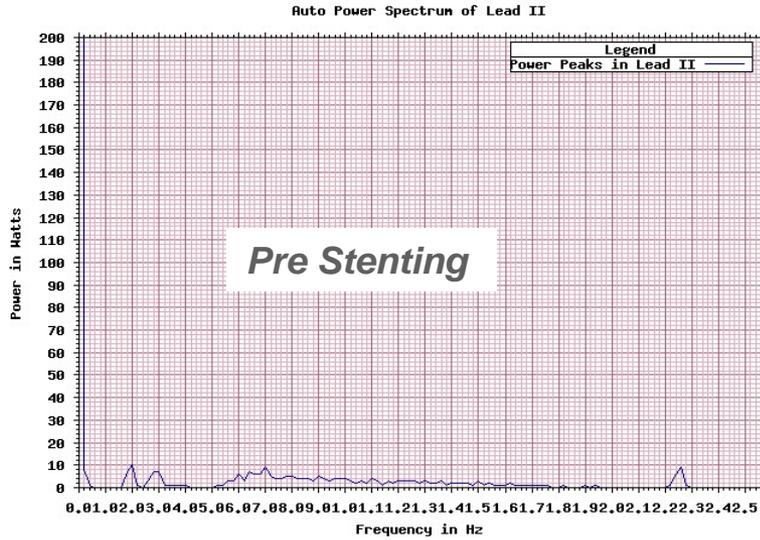
Same Age Male Normal Control
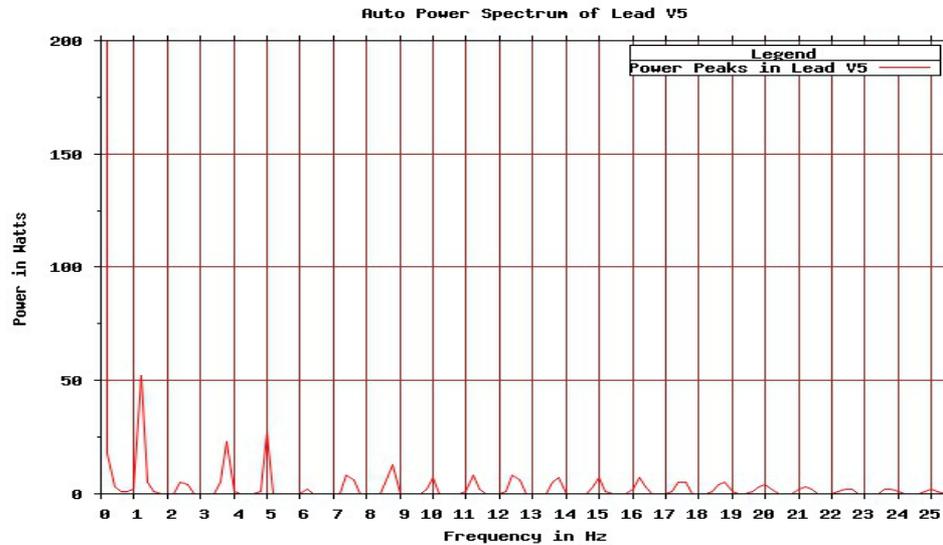
MCG vs. ECG

	ECG, a Reductionist Tool	*MCG, a Systems Analysis Tool*
A	**A theoretical single dipole, plotted on an <u>Einthoven ECG 2-D scale Model</u> (time vs. voltage).**	**Multiple mathematical functions based on the <u>LaGrange-Euler model</u> and Systems Theory**
B	**single-cycle approach, single lead and evaluating segments of the waveform (e.g. ST Segment, T-Wave, QT intervals,...)**	**Leads II & V5 and across multiple cardiac cycles to extract multiple non-linear mathematical relationships.**
C	**Requires an on-site experienced clinician for subjective over-read**	**Automatic computer generated evidence based objective and reliable reporting**
D	**Accuracy <u>impaired</u> by bundle branch blocks, paced rhythms**	**Accuracy <u>unaffected</u> by ECG wave morphology, such as BBB, or Paced rhythms**
E	**No instantly and automatically accessible normalized and validated digital empirical clinical database**	**Dependent to a large normalized, validated and readily accessible digital empirical database for report automation**
F	**dependent on risk factors clinical presentation/History and expert opinions**	**Independent of risk factors, patient history or clinical presentation, or expert opinion**

Practical lessons learned from the experience

➢ There is a fundamental need to include all the information from multiple complete cardiac cycles to understand the dynamic behavior of the heart.

➢ There is disproportionately more information available using interactive data from a pair of signal sources than is available from 12 signal sources examined segmentally and individually.

➢ Computerized mathematical transformation with dissection and resynthesis of the digitized electrical data in order to obtain comprehensive information about cardiac function are essential components of being able to obtain this reproducible and reliable information.

➢ Index integration and pattern recognition using a large validated digital database are essential parts of this approach.

MCG developed own technology through more than 30 years

1976-1979   Theoretical Model Research/Animal Experiments….

1979-1983   Data Collection and Analysis by a TEAC® Tape Recorder to measure the effects of environmental noises on human's transformed ECG and EEG Waveforms on Tsinghua University's 7T08 IBM mainframe computers.

1983-1985   First PC Based (DOS) Analytical Stand-alone System was created for large scale data collection and clinical trials for potential differential diagnosis.

1985-1997   Started limited clinical testing in the USA, data collection continued…

1998   Premier Heart was founded.

1998-2000   Developing new generations of software for a web based system using open source software. Obtain FDA 510K clearance.

2001-2005   First Differential Diagnosis for Local or Global Ischemia and Disease Severity Scores were developed and validated clinically.

2003-2008   First modern web based system communicating with a centralized relational database had been designed and tested in clinical trials in eight countries/three continents on ~1,200 patients.

2008-2011   Additional applications produced and clinical trials performed.

Thank you!

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