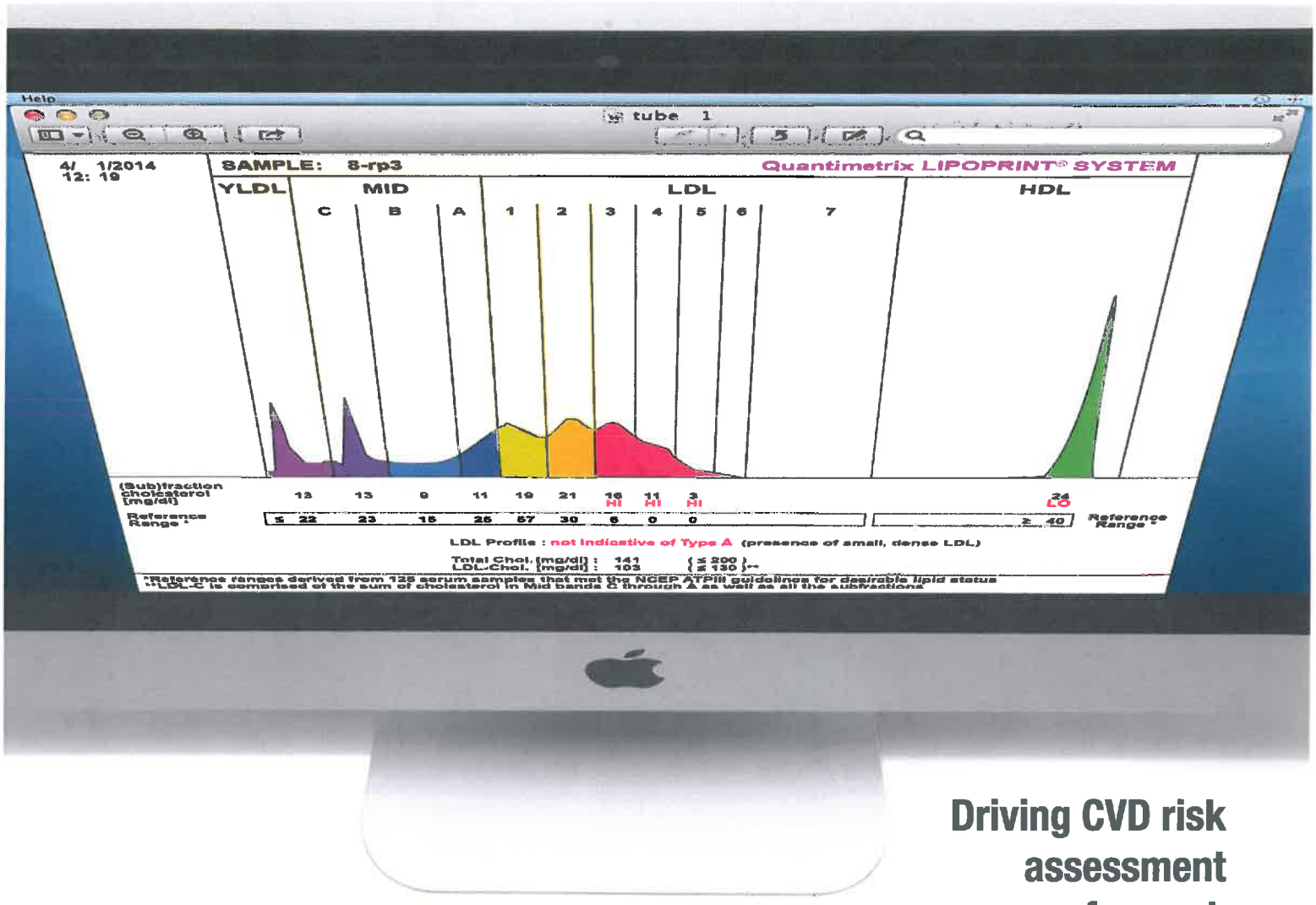
Lipoprint®

Personalized Diagnostics



Driving CVD risk assessment forward.

Quantimetrix®

laboratory solutions made simple®

It was with an unflinching entrepreneurial spirit and a distinguished PhD in biochemistry that, Dr. Robert Ban, my father, founded Quantimetrix. He pioneered a liquid control stabilization technology that simplified laboratory quality control methods and launched an industry that previously offered freeze-dried products.

He believed in the importance of applying the most rigorous standards in research, development and manufacturing, giving his customers confidence that their test results were accurate and clinically sound.

That was more than 40 years ago, and today, Quantimetrix continues to develop next-generation laboratory technologies that will change how clinicians test, laboratories research, and patients interact with their physicians.

Lipoprint® Lipoprotein Subfractions Testing System is our commitment to these core principles. Bringing Lipoprint to the marketplace has been a personal achievement for the Quantimetrix family. Many of us have known people who may have benefitted from more advanced clinical information about their cardiac health. Take a moment to review our Lipoprint brochure and see how our test could benefit you.

Monty Ban
Chairman, President and CEO
Quantimetrix Corporation

Lipoprint®
Lipoprotein Subfractions Testing System

The Lipoprint Lipoprotein Subfractions Testing System analyzes all lipoprotein fractions and subfractions in fasting serum or plasma. It is the only method that identifies and measures cholesterol of all atherogenic and non-atherogenic LDL and HDL subfractions. The Lipoprint Subfractions Test assists clinicians in developing individualized strategies for the management of dyslipidemia in patients at risk for CVD.

PERSONALIZED CVD RISK ASSESSMENT BY LIPOPRINT

There has been much controversy over the current ACC/AHA cholesterol treatment recommendations for primary and secondary ASCVD risk management. Until recently, LDL cholesterol (LDL-C) was accepted as the primary target for Coronary Artery Disease (CAD) treatment. The current cholesterol treatment guidelines uses an ASCVD risk calculator that relies heavily on non-lipid risk indicators while ignoring well-established factors such as LDL-C, Apo-B, and other emerging lipid and lipoprotein risk factors like Non-HDL cholesterol, VLDL remnants, or IDL and highly atherogenic small dense LDL subfractions. These new recommendations may significantly increase the number of individuals qualifying for statin treatment, which could result in overtreatment of individuals at low risk, while raising concerns of possible undertreatment for at risk individuals that would benefit from primary prevention treatment.

Coronary artery disease continues to be the leading cause of death in most developed countries and much of the developing world in spite of growing awareness and increased treatment of individuals at risk. The role of lipids and lipoproteins in atherosclerosis has been documented

by numerous studies, but the methods for assessing CAD risk continue to be the subject of much debate.

A recent study[1] comparing the ACC/AHA ASCVD Risk Calculator against various risk assessment methods demonstrates that the risk calculator may underestimate the risk associated with some dyslipidemias while overestimating risk based on age, gender and other non-modifiable risk factors.

The study subjects were tested for CVD risk using the current ASCVD risk calculator. In addition, the samples were tested by other traditional and non-traditional methods including: LDL-C, NMR LDL-particle number, total cholesterol, triglycerides, non-HDL cholesterol, total cholesterol to HDL-C ratio, and LDL-C to HDL-C ratio. The samples were also analyzed using the Lipoprint Lipoprotein Subfractions Testing System, which discriminates atherogenic from non-atherogenic LDL subfractions.

The results of the study showed significant discordance between the various methods (See Table 1 on the next page). Based on the ASCVD risk calculator, 31.8 % of the total subjects were at high risk of CVD, 71.4 % of those considered at high risk were based on non-lipid risk factors such as hypertension, diabetes and advanced age, while only 28.6 % were classified high risk due to dyslipidemias. The Lipoprint LDL test measures VLDL remnants, IDL and small dense LDL subfractions, in addition to the non-atherogenic large buoyant LDL. Based on the Lipoprint LDL subfractions test, 68.2 % of the individuals were classified intermediate or high risk in contrast to the only 31.8 % identified as high risk by the ASCVD risk calculator. It appears that younger individuals with atherogenic normolipidemia may not be identified by the risk calculator, as well as individuals under 40 years of age who are not covered by the risk calculator.

A more recent study[2] has identified an atherogenic normolipidemia and a non-atherogenic hyperlipidemia using the Lipoprint Lipoprotein Subfractions Testing System. The individuals with atherogenic normolipidemia had increased levels of atherogenic small dense LDL particles while individuals with non-atherogenic hyperlipidemia had predominantly non-atherogenic large buoyant LDL particles. The study reports: "... normolipidemic healthy individuals with an atherogenic lipoprotein profile among clinically healthy volunteers puts in doubt our former belief and generally accepted statement that normolipidemia per se represents an optimal healthy lipid profile."[2]

In summary, these recent studies suggest that the Lipoprint LDL Subfractions test may supplement the present ASCVD risk calculator by identifying and measuring the cholesterol in the individual atherogenic and non-atherogenic particles, providing clinicians a more specific CVD risk assessment approach. Considering the fact that CVD is a life-long progressive disease, early recognition is very important in primary prevention and treatment of individuals at risk.

LIPOPRINT LDL SUBFRACTIONS TESTING

The Lipoprint LDL Subfractions Test from Quantimetrix is intended to measure cholesterol levels in all lipoprotein fractions and LDL subfractions in fasting serum or plasma.The Lipoprint system uses polyacrylamide gel electrophoresis to separate the various lipoprotein subfractions on the basis of size (See Figure 1). The electrophoresed gels are analyzed with Lipoware, a configured software that calculates the levels of cholesterol in each LDL subfraction. A color coded profile is generated for ease of interpretation.

The Lipoprint LDL Subfractions Test reveals emerging heart disease risk factors not indicated by conventional lipoprotein cholesterol measurements. To determine the clinical significance of emerging risk factors, the ATP III requires the following criteria: "Laboratory or clinical measurements must be widely available, well standardized, inexpensive, have accepted population-reference values, and be relatively stable biologically."[3]

The Lipoprint LDL Subfractions Test meets the ATP III criteria with the following features:

- Available for use in any clinical or research laboratory anywhere in the world.
- Correlates to established methods such as direct LDL and HDL cholesterol tests, and to the CDC beta quantification and ultracentrifugation methods.
- Accurate, easy to perform, and relatively inexpensive.
- Test report includes normal reference ranges for all lipoprotein fractions and LDL subfractions (derived from

Table 1: CVD Risk Data

Sample ID	ACC/AHA	Lipoprint						
	10-Year ASCVD Risk	VLDL	IDL-C	IDL-B	IDL-A	LDL-1	LDL-2	LDL-3+
	%	[mg/dL]	[mg/dL]	[mg/dL]	[mg/dL]	[mg/dL]	[mg/dL]	[mg/dL]
002	8.6	49	26	23	14	23	31	20
005	17.7	28	24	20	25	52	40	6
006	4.8	33	19	18	22	37	49	21
008	1.8	43	23	17	12	18	25	12
009	8.6	43	29	20	15	23	26	17
010	3.6	42	22	19	13	20	25	22
011	4.4	22	23	15	18	46	40	7
012	7.1	35	21	23	27	43	32	6
016	1.7	28	20	15	16	45	46	9
017	1.6	31	20	14	20	54	31	2
022	1.7	23	21	16	23	58	43	5
023	5	36	20	12	14	37	18	0
026	11.9	26	17	14	20	41	30	4
028	5.7	43	21	13	9	22	33	14
029	21.8	36	22	16	15	30	32	11
030	0.6	33	21	14	20	55	27	2
031	4.2	17	14	13	28	42	11	0
034	9.7	22	14	13	16	32	26	7
036	0.5	21	13	15	27	51	8	0
037	4.5	44	22	13	11	27	30	7
039	1.9	22	15	16	21	49	45	8
040	18.8	42	22	13	11	30	25	5
	< 7.4 % Desirable	≤ 22	≤ 23	≤ 15	≤ 25	≤ 57	≤ 30	≤ 6
		23-30	24-26	16-18	26-28	58-60	31-33	7-9
	≥ 7.5 % High	> 30	> 26	> 18	> 28	> 60	> 33	> 9

a normal population, as defined by NCEP ATP III guidelines for desirable lipid levels).

› Performed on fasting serum or EDTA plasma. Refrigerated samples are stable for up to 7 days. (For prolonged storage, cryogenic freezing of the samples is recommended.)

The Lipoprint LDL Subfractions Test provides a detailed analysis of the LDL subfractions which aids clinicians in a more specific assessment and management of CVD risk.

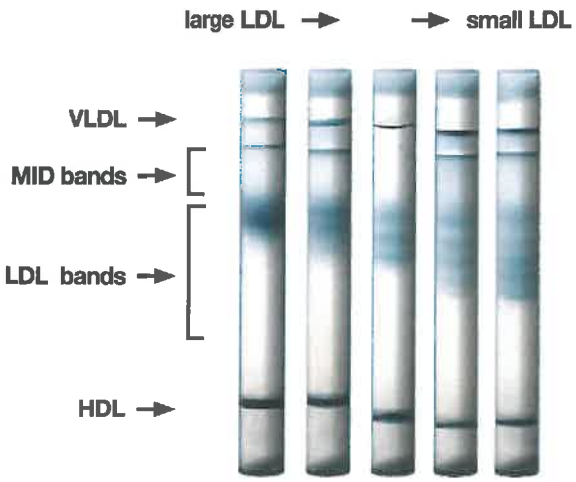


Figure 1: Lipoprint Subfractions

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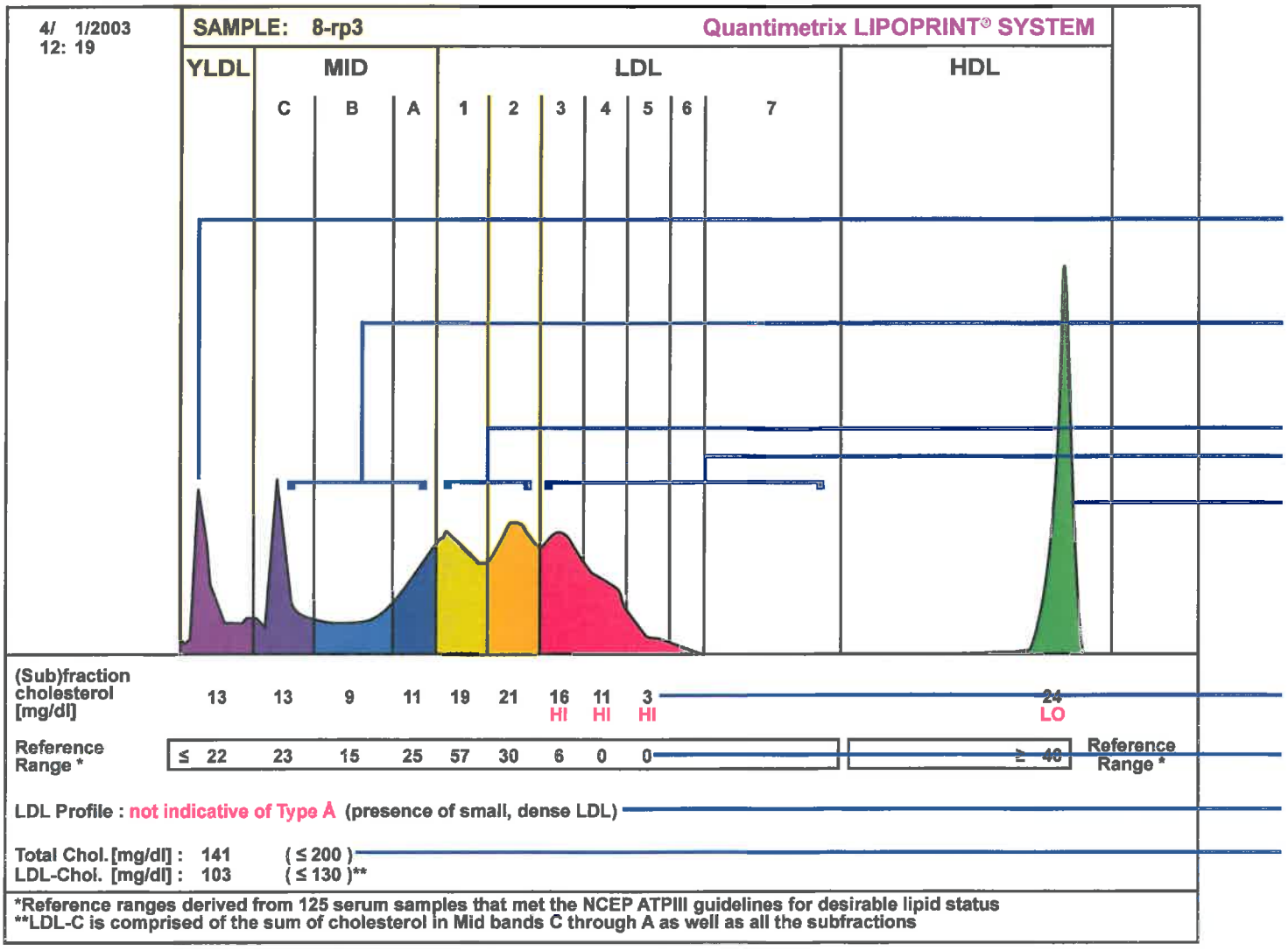
	HDL-C	Mean LDL Particle Size	NMR LDL-P	ATP III TC	ATP III TRIGS	ATP III LDL-C	ATP III Non-HDL	ATP III TC:HDL-C	ATP III LDL-C: HDL-C
	[mg/dL]	Å	(nmol/L)	[mg/dL]	[mg/dL]	[mg/dL]	[mg/dL]	Ratio	Ratio
	38	258	1281	235	471	147	197	6.2	3.9
	43	269	1761	238	103	166	195	5.5	3.9
	26	263	2425	228	186	169	202	8.8	6.5
	33	262	1152	185	321	108	152	5.6	3.3
	35	260	1376	215	245	136	180	6.1	3.9
	27	254	1772	208	284	139	181	7.7	5.1
	50	268	1936	222	115	149	172	4.4	3.0
	37	268	1843	223	139	150	186	6.0	4.1
	37	266	2038	217	153	152	180	5.9	4.1
	48	270	1641	220	116	141	172	4.6	2.9
	48	269	1980	237	101	165	189	4.9	3.4
	31	272	1236	169	173	101	138	5.5	3.3
	45	269	1690	196	105	125	151	4.4	2.8
	30	262	1723	186	219	114	156	6.2	3.8
	33	265	1445	196	196	127	163	5.9	3.8
	54	271	1656	226	169	139	172	4.2	2.6
	54	274	1299	180	55	108	126	3.3	2.0
	51	266	1283	183	109	109	132	3.6	2.1
	60	275	1484	196	71	115	136	3.3	1.9
	32	266	1375	186	233	111	154	5.8	3.5
	40	267	1998	216	83	153	176	5.4	3.8
	51	267	939	199	287	107	148	3.9	2.1
	≥ 50 High	≥ 269 Type A	< 1000 Low	< 200 Desirable	< 150 Desirable	< 100 Desirable	< 130 Desirable	< 4.0 Desirable	< 3.0 Desirable
	40-49					100 - 129 Average	130 - 159 Average	4.0 - 5.0 Average	3.0 - 4.0 Average
		> 265 ≤ 268 Intermediate	1000-1299 Moderate	200 - 239 Borderline high	> 150 ≤ 199 Borderline high	130 - 159 Borderline high	160 - 189 Borderline high	> 5.0 - 6.0 Borderline high	> 4.0 ≤ 6.0 Borderline High
	< 40 Low	≤ 265 Type B	> 1300 High	≥ 240 High	≥ 200 High	≥ 160 High	≥ 190 High	> 6.0 High	> 6.0 High

Understanding the Lipoprint® Profile



Measurement of up to twelve lipoprotein fractions and subfractions. Results for every lipoprotein subfraction reported as mg/dL cholesterol which should be the basis for patient treatment.

VLDL increased levels - associated with hypertriglyceridemia; CVD risk uncertain.

Midbands A, B and C (include VLDL remnants and IDL) - associated with atherogenic Type III dyslipidemia and combined hyperlipoproteinemia.

LDL 1 and 2 (large buoyant LDL) - not associated with CVD risk.

LDL 3 through 7 (small dense LDL) - component of the lipid triad associated with 3 fold increase of CVD, metabolic syndrome and diabetes.

HDL cholesterol (good cholesterol) - Low HDL is a component of the lipid triad associated with increased CHD risk.

Cholesterol values outside the normal reference range are flagged in red for ease of interpretation. Elevated Mid B, Mid C (IDL and VLDL remnants) and small-dense LDL 3 through LDL 7 pose the highest risk for CVD.

Normal Reference Range for each subfraction based on NCEP ATP III guidelines for desirable lipid levels.

Lipoprotein Profile Classification - predominance of large LDL is classified as Type A and predominance of small dense LDL is classified as Not Indicative of Type A.

TRADITIONAL RISK FACTORS

Total cholesterol - CHD risk factor.

COLOR-CODED PROFILE

The Lipoprint Profile is color-coded, making it easy for doctors and patients to understand the results of the test at a glance. Good HDL is shown in green; large low risk LDL 1 and 2 in yellow, for caution; and the atherogenic, small dense LDL 3 through 7 in red, for high risk.

Add Lipoprint® Testing to Your Laboratory

Lipoprint
Lipoprotein Subfractions
Testing System Components

TEST FEATURES

- Easy to interpret color coded profile
- Results available in less than 3 hours
- Fasting serum or EDTA plasma
- LDL subfractions cholesterol derived from total cholesterol assay
- Normal reference ranges derived from NCEP ATPIII guidelines
- Costs are reimbursable (CPT Code: 83701)*

LIPOPRINT CONSUMABLES INFORMATION

LDL Subfractions	48-7002	100 Tests	
HDL Subfractions**	48-9002	100 Tests	
Liposure Serum Lipoprotein Control	48-7060	Level 1	4 x 0.5 mL

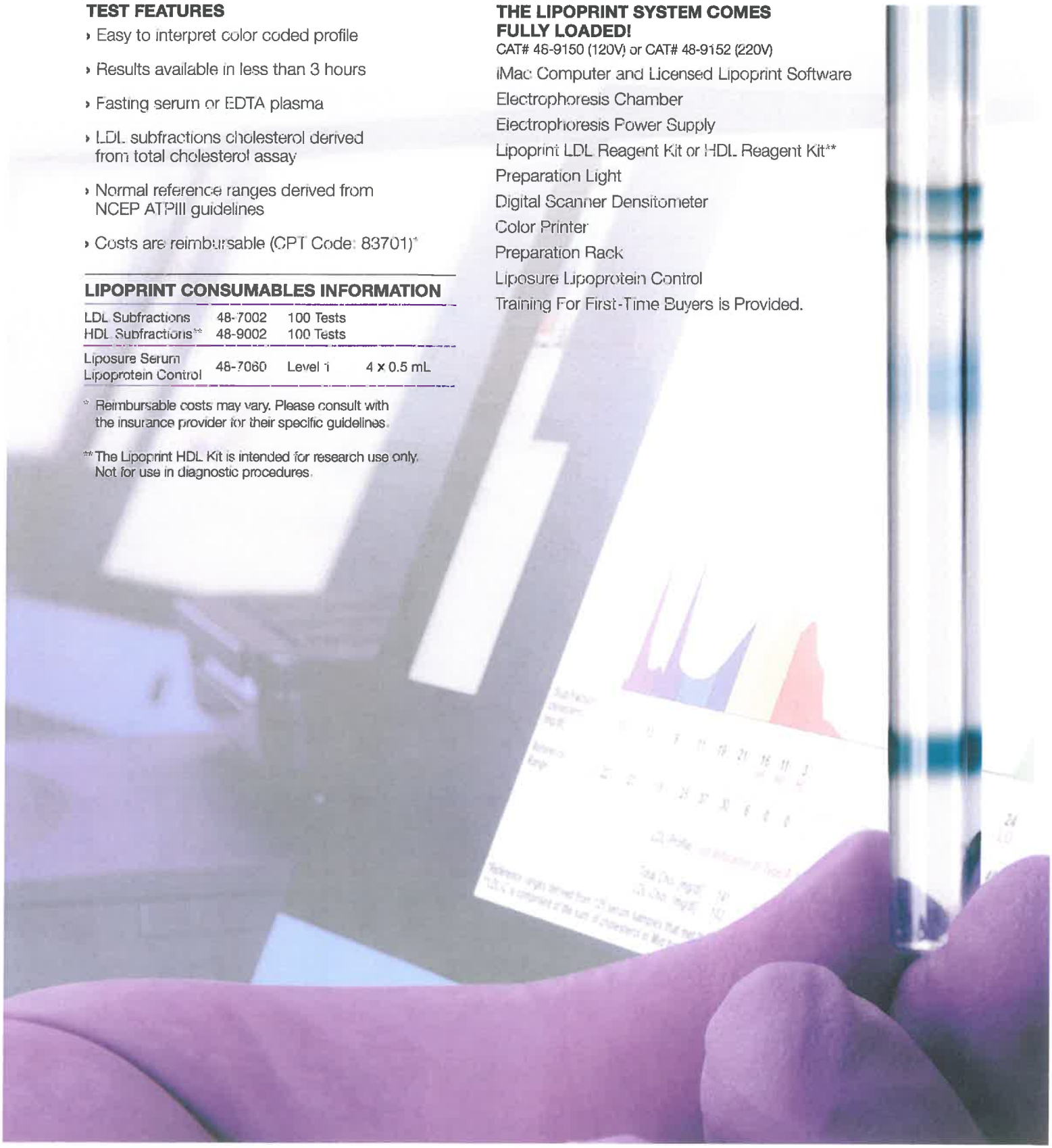
* Reimbursable costs may vary. Please consult with the insurance provider for their specific guidelines.

** The Lipoprint HDL Kit is intended for research use only. Not for use in diagnostic procedures.

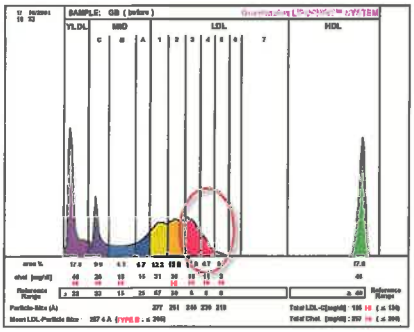
THE LIPOPRINT SYSTEM COMES FULLY LOADED!

CAT# 48-9150 (120V) or CAT# 48-9152 (220V)

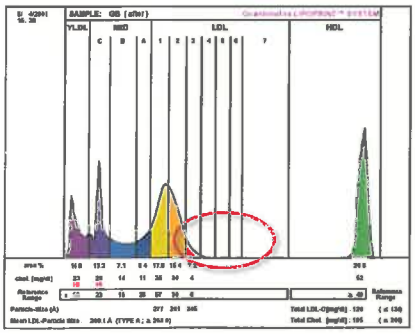
iMac Computer and Licensed Lipoprint Software
Electrophoresis Chamber
Electrophoresis Power Supply
Lipoprint LDL Reagent Kit or HDL Reagent Kit**
Preparation Light
Digital Scanner Densitometer
Color Printer
Preparation Rack
Liposure Lipoprotein Control
Training For First-Time Buyers is Provided.



Case Study 1



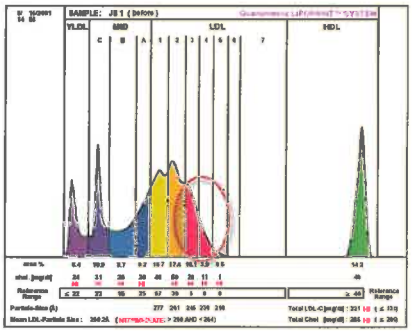
Before Treatment



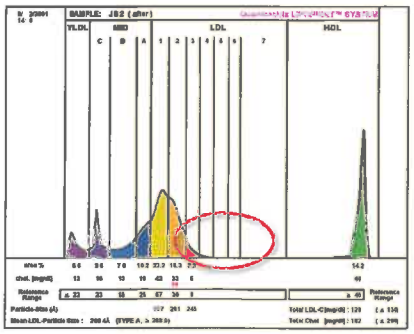
After Treatment

George, a 65 year-old Caucasian male had a Lipoprint LDL Profile showing a predominance of small dense LDL 3, 4 and 5, which has been associated with increased risk of cardiovascular disease (Case Study 1: Before Treatment). After 3 months of niacin and dietary therapy, his profile became normal (Case Study 2: After Treatment).

Case Study 2



Before Treatment



After Treatment

James, a 42 year-old male on a diet rich in carbohydrates and fats had a Lipoprint LDL Profile with high cholesterol levels in most subfractions (Case Study 2: Before Treatment). After 2 months on a vegetarian diet with emphasis on soy protein, low carbohydrates, and exercise, his profile became essentially normal (Case Study 2: After Treatment).

Lipoproteins and Longevity

LIPOPRINT®—IN RESEARCH CLINICAL STUDIES

Recent studies suggest that larger lipoprotein particle sizes of both high-density lipoprotein (HDL) and low-density lipoprotein (LDL) are characteristic of long and healthy lives. A large number of clinical studies have demonstrated that the size of the LDL particles present is a better predictor of cardiovascular and other health risks than the total LDL concentration. It appears that it is not only the amount of cholesterol that is important, but how the cholesterol is distributed among the various LDL and HDL subfractions. Measurements of the cholesterol levels in these lipoprotein subfractions provide a more personalized assessment of the Cardiovascular Disease (CVD) status of the individual than traditional lipid measurements. The Quantimetrix Lipoprint Lipoprotein Subfractions Testing System is now being utilized routinely in the clinical laboratory for assessment of cardiac risk based on the lipoprotein subfractions distribution.

As the world's population grows older, medicine has increasingly turned to questions of longevity and healthy aging. Researchers have reported correlation between a pattern of large lipoprotein particle size and human longevity. They studied a group of Ashkenazi Jews with a mean age of 98.2 years, as well as the children of these long lived individuals.

The researchers found that these individuals and their children had HDL and LDL populations of significantly larger diameter than that of the study control groups. In contrast to the particle size, results were found to be quite similar to the control groups with regard to their concentrations of total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides. Individuals with large buoyant populations of LDL and HDL cholesterol were also found to have a lower prevalence of hypertension, metabolic syndrome, and cardiovascular disease when compared to those of a similar age with small dense particles. A study conducted in the Netherlands reached a similar conclusion with regard to the link between inherited longevity and LDL particle size. This study looked at sibling pairs with an age of 89 or older for men, and 91 or older for women.

The children of these individuals were also studied. Both the long lived siblings and their children were found to have significantly larger LDL populations than the control group. This suggests that inherited longevity may either be due to, or identified by, a pattern of large LDL particles. The significant linkage between LDL particle size and longevity was found to be independent of total cholesterol, HDL cholesterol, and triglycerides.

The study then took the question of LDL particle size and longevity a step further. They wanted to determine whether non-inherited longevity could be predicted by a person's mean LDL diameter. The study attempted to determine the LDL particle size of all the residents of the city of Leiden that had reached an age of 90 or greater, regardless of family history. The elderly population of Leiden was found to have a pattern of large LDL particles similar to the long lived siblings in their study. In this study larger LDL size was again linked to better overall health regardless of family history.

What do the results of these studies mean for people who do not have LDL cholesterol loaded with large particles? Statin drugs commonly taken for lowering cholesterol have been shown to alter the LDL subfraction pattern favorably but the results are inconsistent. Also, Fibrate drugs have consistently improved the LDL subfraction pattern based on a number of studies. In fact, the advice that physicians have been giving their patients for years may be the best approach; maintain a healthy lifestyle, follow a diet rich in fruits and vegetables, and do some moderate aerobic exercise. This not only reduces the total LDL cholesterol, but actually produces a significant increase in the mean size of the LDL particle population, which may be conducive of a longer healthier life.

LIPOPRINT HDL SUBFRACTIONS* TESTING

HDL encompasses a heterogenous class of lipoprotein subclasses that differ in composition and physiological function, and may vary in their anti-atherogenic potential and utility as markers for CVD risk. The Lipoprint HDL test is a convenient, non-denaturing, linear polyacrylamide gel electrophoresis method that separates and quantifies up to 10 HDL subfractions in serum or plasma. The HDL subfractions are classified into three major subclasses: large buoyant HDL lipoproteins (HDL-L), intermediate HDL lipoproteins (HDL-I) and small-dense HDL lipoproteins (HDL-S). The Large HDL subclass (HDL-L) shows an inverse relationship with CVD risk while the Smal HDL subclass (HDL-S) exhibits a direct relationship with CVD risk. The Lipoprint HDL test is used in clinical trials and other research studies involving humans and other species such as mice, guinea pigs, chimpanzees and pigs.

*Lipoprint HDL is for Research use only. Not for diagnostic use.

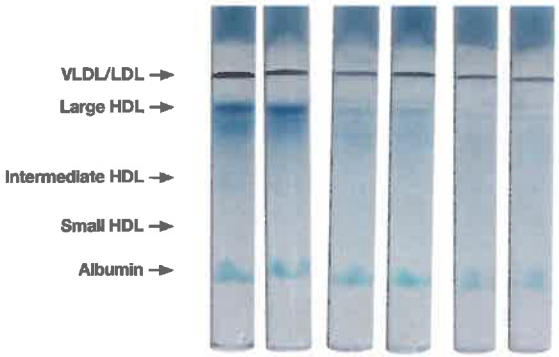


Figure 2: Lipoprint HDL Subfractions

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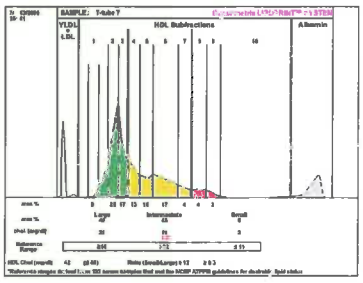


Figure 3. Large HDL
(subfractions 1 to 3)

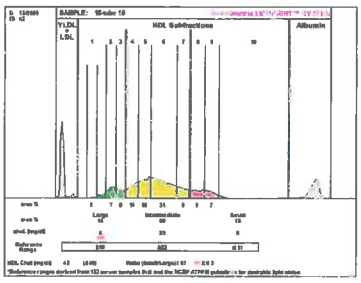


Figure 4. Intermediate HDL
(subfractions 4 to 7)

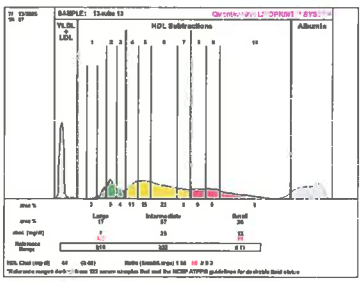
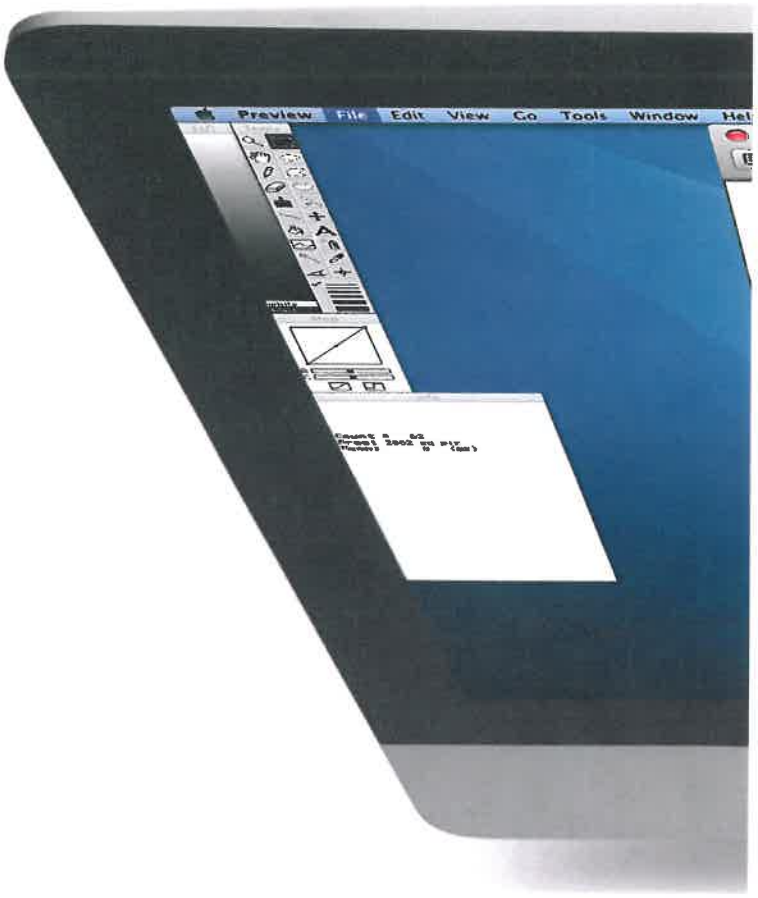


Figure 5. Small HDL
(subfractions 8 to 10)



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