Cardio IQ™ Lipoprotein Subfractionation

Fractionation of lipid subclasses has been used to gain additional insight for management of cardiovascular disease (CVD) in at-risk patients for over 15 years.

LDL and HDL subclasses have strong scientific literature support, with a legacy of NIH-funded studies that show lipid subclasses are predictive of short- and long-term CVD risk, atherosclerotic progression, and multiple intervention events.

The insights provided by the lipid subclasses allow for a customized approach to CVD risk management that may ultimately lead to improved patient outcomes.

Since initial analytical ultracentrifugation characterization of lipoprotein subclasses by Dr. John Gofman at University of California, Berkeley, a number of lipid fractionation methods have been developed, including density-gradient ultracentrifugation, particle analysis by spectrum, and gel, gradient gel, and 2-D gel electrophoresis.

While these various technologies each had unique strengths, they all represented some degree of compromise between capturing all lipoprotein types, separating the lipid subclasses with high resolution, and delivering direct quantification of the amount of particles within each lipid subclass.

Evolution of Lipoprotein Subfractionation

Priorities in Interpretation and Management of Key Clinical Indicators

1. What is the total LDL particle number? Does it indicate residual risk?
   - Follow to assess statin efficacy
   - Follow progressive lowering of particle number to monitor progress toward goal
   - Follow size movement toward larger Pattern A peak

2. What is the quantitative amount of Large HDL subclass within respective risk category?
   - Consider LDL-raising strategy
   - Follow progressive increase of particle concentration to: a) Assess patient response to therapy and optimize as needed, and b) Assess patient response toward goal

3. What are the quantitative amounts for Small and Medium LDL subclasses, and where do they fall within respective risk category?
   - Consider degree of risk when formulating aggressiveness of therapy
   - Follow progressive lowering of particle concentration to: a) Gauge patient response to therapy and optimize as needed, and b) Track progress toward goal

References
9. Sonora Quest Laboratories. All rights reserved. 10/2014
Cardio IQ™ Ion Mobility is the latest technology evolution, with a pedigree reaching back to the first lipoprotein characterization work at University of California, Berkeley.

The Latest Technology: Cardio IQ™ Ion Mobility

Cardio IQ Ion Mobility fractionation is the latest technological evolution in advanced lipid subclass measurement. It combines high resolution separation of the full spectrum of lipoprotein particles, along with direct quantification of particles in each lipid subclass fraction.

Cardio IQ Ion Mobility separation allows lipoprotein particles to be characterized without any modification of the particles that could potentially impact their apparent size. Ionized lipoprotein particles are electrophoretically separated in a gas phase, distinguishing lipoprotein particles on the basis of size. Size-selected particles are detected and counted by light scattering.

Cardio IQ™ Ion Mobility Advantages

Cardio IQ Ion Mobility represents the future of advanced lipid analysis in clinical practice. By moving beyond the past compromises of other advanced lipid subclass measurements, this toll provides physicians with increased insights to better manage treatment decisions for their patients.

Cardio IQ Ion Mobility is strongly supported by literature and experts in the field as the leading method for lipoprotein size assessment. It is being proposed as the new standard in the field. Dr. Ron Krauss, developer of segmented gradient gel technology, developed Cardio IQ Ion Mobility as the next generation in lipid subclass separation.

Cardio IQ Ion Mobility provides:

- Direct, accurate, and reproducible measurement of lipoprotein particles
- Insights that allow customization of therapy for potential improvement in patient outcomes

Clinical Utility

The presence of small LDL subclasses has long been associated with increased CVD risk and progression of atherosclerotic disease. Early observations from analytical ultracentrifugation and gradient gel electrophoresis regarding the association of lipoprotein subclasses with risk led to the definition of an “atherogenic lipoprotein phenotype” (ALP). ALP is characterized by a predominance of small LDL particles and associated with elevations of triglycerides and reductions in HDL cholesterol and large HDL particles. Further, the particle diameter of the major LDL peak could be used in the majority of individuals to discriminate carriers of this higher-risk phenotype (referred to as small LDL diameter predominate, or pattern B) from noncarriers (larger LDL diameter, or pattern A).

The Malmö Diet and Cancer Study indicates that Ion Mobility-determined subclasses have been associated with increased CVD risk. An analysis of 4,594 initially healthy men and women (mean follow-up 12.2 years, 377 incident cardiovascular events, with 206 being coronary events) showed an increase in the number of LDL particles, Small and Medium LDL subclasses from Cardio IQ™ Ion Mobility, along with elevated triglycerides, to be positively associated with increased event risk. This same study revealed Large HDL subclass levels to be inversely associated with event risk, thus supporting the cardioprotective aspect of high HDL-C. This finding is consistent with previous literature defining ALP.

Treatment via pharmaceutical options such as statins, niacin, or fibrates, as well as lifestyle changes, has been impactful in correcting ALP, i.e., reducing LDL particle numbers, changing the distribution of LDL particles from atherogenic small LDL to larger LDL particles, and shifting small HDL particles to large HDL particles associated with cardio-protective mechanisms (see Figure 2). The high-resolution subclass separation provided by Cardio IQ Ion Mobility allows healthcare practitioners to follow the change in the lipid profile as the patient responds to therapy. This provides the opportunity to evaluate treatment efficacy and optimize the aggressiveness of therapy in a manner that is personalized to the patient.
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Figure 1. Cardio IQ® Ion Mobility separation of lipoprotein

Ionized lipoproteins migrate across a laminar gas-phase flow based on size and electrical field. Only a single size of lipoprotein will exit the field and be isolated (blue line) at any point during the voltage gradient; larger and smaller lipoproteins (dotted black lines) are not collected. At the voltage ramps across the gradient, all of the lipoproteins are captured.

Figure 2. Key clinical management subclasses and treatment strategy
Cardio IQ™ Ion Mobility: A More Powerful Approach of Lipid Subclass Characterization

By taking into consideration a more powerful risk assessment based on total LDL particles and key lipid subclasses, healthcare practitioners can identify residual risk not revealed by the Lipid Panel or the Lipoprotein Phenotype Pattern B (see Figure 3).

Figure 3. LDL Phenotype versus CVD Risk

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References

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