

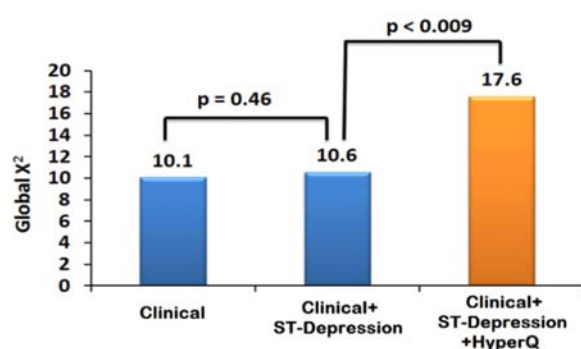
BSP: HyperQ™ Newsletter

Spring 2017

HyperQ in the Clinic: expanding clinical use, gaining wider recognition

HyperQ: a powerful tool for the detection of Myocardial Ischemia, as demonstrated in a multi-center prospective study

A first multi-center blinded prospective study, performed by Balfour et al., compared HyperQ analysis to standard ST-segment analysis for the identification of left ventricular ischemia during exercise test. A cohort of 389 patients from the Cleveland clinic, Minneapolis heart institute and the Univ. of Virginia heart center were analyzed using HyperQ and standard ST analysis, while nuclear imaging was used as the gold standard. The results demonstrated considerable increase in diagnostic accuracy between ST and HyperQ analysis (40% vs 66.7% sensitivity, with no significant change in specificity). Moreover, combining HyperQ analysis with clinical factors and ST results produced an impressive overall



incremental diagnostic utility, in contrast to the poor, if any, incremental value of ST results over clinical factors.

The researchers concluded that HyperQ substantially improves the detection of ischemia over ST-segment analysis in patients undergoing

an exercise stress test. They added that the HyperQ test is a novel non-invasive method that may improve risk stratification in low-intermediate risk patients while reducing radiation exposure compared to an imaging strategy.

[Ref: JACC, 69(11), Supp., 21 March 2017]



HyperQ modality proves easy integration with standard stress ECG devices

HyperQ usually requires ECG recordings at a high sampling rate of 1000Hz. Researchers from Tampere University Hospital in Finland examined the performance of HyperQ in lower-frequency recordings of 500Hz, common in standard ECG devices. They compared the diagnostic performance of HyperQ to a computerized ST analysis in a group of 98 patients who underwent a bicycle stress ECG test; the group was extracted from the Finnish Cardiovascular Study (FINCAVAS) database which was recorded using a commercially available exercise ECG system by GE Healthcare.

Results demonstrated that HyperQ was significantly more sensitive (84% VS 37%) than computerized ST analysis, with no significant change in specificity (67% VS 75%, $p=0.54$).

This is the first study to demonstrate that much of the information required for effective HyperQ analysis exists in the frequency band available from standard ECG devices. HyperQ may therefore be applied to existing devices and significantly improve the diagnosis of ischemia.

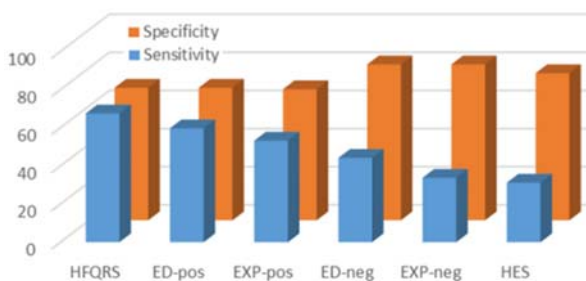
[Accepted for presentation at the EMBEC 2017]

A new paradigm for diagnosing Acute Coronary Syndrome (ACS)

A pioneering study, by Galante et al., tested the use of HyperQ Rest in diagnosing ACS (often referred to as “heart attack”), in the emergency department (ED).

The study included 324 patients, presenting with chest pain and suspected ACS to the ED. ECG and HyperQ were recorded at rest shortly after the patients presented to the ED. HyperQ results were compared to three independent interpretations of conventional ECG diagnosis: by the treating physician, by an expert cardiologist and by an automated computer program. All patients were classified according to their discharge diagnosis and follow up evaluation.

HyperQ analysis demonstrated increased sensitivity of 68% in diagnosing non-ST elevation ACS, compared to sensitivity of 44%, 34% and



31% in the 3 ECG-based interpretation schemes. In the subgroup of patients with non-ischemic chest pain and pathological or inconclusive ECG, HyperQ analysis identified 75% correctly as non-ischemic. Out of the non-ST elevation ACS with normal or inconclusive ECG, HyperQ analysis identified 72% correctly as having acute ischemia.

The researchers concluded that resting HyperQ offers an inexpensive, simple modality with no adverse effects for diagnosing ACS.

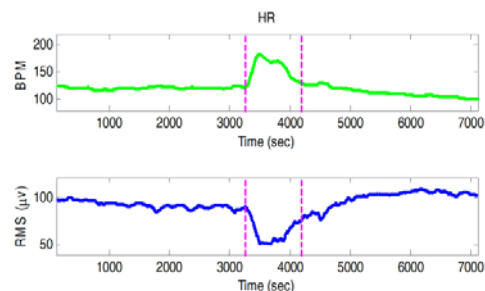
[Ref: JECG, 2017; doi:10.1016/j.jelectrocard.2017.02.009]

Implantable HyperQ: impressive pre-clinical results, vast implementation

First pre-clinical trials demonstrate HyperQ's striking intra-cardiac potential

First animal studies, performed by researchers from the Tel Aviv University, Lahav CRO and BSP, examined HyperQ as an *intracardiac* sensitive marker for the early detection of ischemia.

A chronic scenario study examined continuous high-resolution (1KHz sampling rate) electrogram, recorded 24h a day, for a period of several weeks, in an active, conscious animal. Intracardiac pacemaker leads were placed in standard locations. Gradual occlusion in the LAD was induced by a copper plated stent in the artery, and stenosis progression was evaluated by angiographic procedures throughout the study. Daily troponin levels were also acquired. Continuous HyperQ analysis was performed, particularly at times of increased heart rate, where demand ischemia may be triggered by the partial occlusion of the artery.



The remarkable results of the study demonstrated consistent and significant change (amplitude reduction) in the continuous HyperQ signal, when increased HR was registered. The extent of HyperQ's ischemia indications was correlated with the extent of occlusion, and intensified significantly as the occlusion progressed. HyperQ's response to demand ischemia was considerably more sensitive, more specific and more stable than ST response.

BSP selected to present at the Eureka InnoVest Venture Forum

BSP has been selected to participate in the 2017 InnoVest Venture Forum. The InnoVest Forum is the leading investment event of the European Eureka program, an EU organization for R&D funding and coordination.

BSP has presented in the forum, that took place in Barcelona on May 2017, its new CV-Guard wearable fitness solution, and made initial contacts with potential collaborators towards commercialization of the product. CV-Guard is a wearable device designed for exercise and training. Utilizing HyperQ's unique real-time monitoring capabilities, CV-Guard will provide a highly effective tool for evaluating cardiovascular wellbeing, aiming at the population of physically active adults and mature adults.

HyperQ diagnosis and monitoring: Accurate, Non-invasive, Cost-effective

Recently confirmed by BSP's analysis of over 3000 patients from various clinical studies, HyperQ has all the benefits of ST-segment based exercise ECG (ExECG) but with a considerably improved accuracy – sensitivity improved by 30% without degrading specificity.

	ExECG	HyperQ	ExEcho	SPECT	CTA
<i>Cost</i>	\$	\$	\$\$\$	\$\$\$	\$\$\$
<i>Safety</i>	+	+	+	-	-
<i>Availability</i>	+	+	-	-	-
<i>Accuracy</i>	-	+	+	+	+

Eurostars approves a collaboration project with Roche, Schiller, Basel Univ. Hospital and the University of Luzern

Eurostars, a joint program between Eureka and the European Commission, will participate in financing a collaborative R&D program of BSP,

Roche Diagnostics AG, Schiller AG, Basel University Hospital and the University of Luzern.

This \$1M project aims to develop a diagnostic and a prognostic risk score for patients suffering from suspected or known coronary artery disease (CAD). The scores will combine generally established methods with HyperQ-based novel diagnostic and prognostic methods, quantifying functional myocardial ischemia.

Increasing presence in literature for advanced stress ECG technologies

New technologies for better utilization of exercise ECG testing and innovative paradigms based on this modality gain growing support by researchers, clinicians and opinion leaders worldwide. An invited editorial in the European Journal of Preventive Cardiology, published by Prof. Christiaan Vrints, the editor in chief of the European Heart Journal: Acute Cardiovascular Care, presents the diagnostic advantages of advanced technologies in stress-ECG analysis, as reflected by the latest European Society of Cardiology guideline on the management of stable CAD (Vrints C JM, Refined interpretation of exercise ECG testing: Opportunities for a comeback in the era of expanding advanced cardiac imaging technologies?; Eur J PrevCardiol. 2016 Oct;23(15)).

High frequency QRS analysis (HF-QRS) is specifically noted in a JACC CV imag. paper, published by Prof. Jamieson Bourque and Prof. George Beller of the Univ. of Virginia. HF-QRS is acknowledged by the authors as a viable method to expand the clinical capacity of exercise ECG modality (Bourque et al., Value of exercise stress electrocardiography for risk stratification in patients with suspected or known coronary artery disease in the era of advanced imaging technologies, JACC Cardiovasc Imaging. 2015 November ; 8(11)).