White Paper

An insight in EACVI-ASE-INDUSTRY Initiative to Standardize Deformation Imaging

esaote
Creativity in Healthcare

Background

Deformation imaging, based on Speckle Tracking techniques, is a promising technology for the evaluation and quantification of cardiac mechanics. In particular, during the last decade , a growing body of scientific evidences has shown that this technology, can provide incremental information in many clinical settings[1,2,3]. However, still the main drawback for a fully clinical exploitation of the technique is nowadays represented by the perception that global strain measurements differ between vendors. Reasons for this potential difference could be found in the different tracking algorithms, differences in values definition as well as the underestimation of the impact that some imaging acquisition parameters, such as the images acquisition FR, Telediastolic triggering frame positioning, may have on the final results.

Aim of the initiative

In order to assess the real situation on the ground, the European Association of Cardiovascular Imaging (EACVI), in cooperation with the American Society of Echocardiography (ASE) and Industry Partners, launched an initiative aimed to standardize Deformation Imaging[4,5]. A working group was created to investigate the possible causes of the perceived inter-vendor variability of deformation measurements and trying to reduce them thus making speckle tracking based strain imaging a clinically accepted and useful parameter.

Working Group composition

Esaote, as an established pioneer in 2D Speckle-Tracking Echocardiography (STE) and as first company to introduce this technology (XStrain™) on ultrasound portable devices in 2006, joined and supported the initiative since the very beginning (ASE meeting, Montreal, June 2011). Besides Esaote and the representatives of EACVI and ASE associations other , six ultrasound vendors and two software solutions providers are currently involved in the Working Group[4,5].

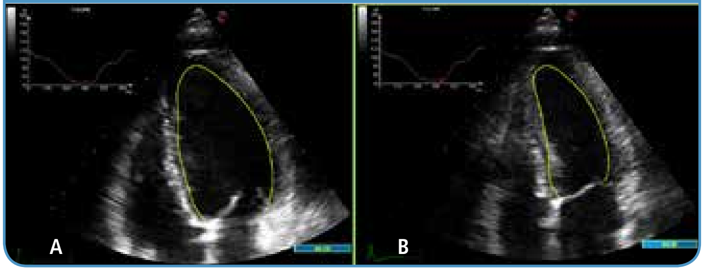
Working Group here-to-date activity and results

The first action taken by the working group was to run a survey among all the different vendors and SW solution providers to verify the mathematical formulas, definitions and conventions used computing the longitudinal strain in order to verify the related degree of agreement. Starting from this initial survey, the working group decided to start a more comprehensive effort whose aim was to deliver a technical document providing a common framework including the definitions, names, abbreviations, formulas and procedures for the computation of the measures derived from speckle tracking echocardiography. This technical document has been published both by the *European Heart Journal Cardiovascular Imaging (Eur Heart J Cardiovasc Imaging)*[6] and by the *Journal of the American Society of Echocardiography(JASE)*[7].

Comparative validation on synthetic data

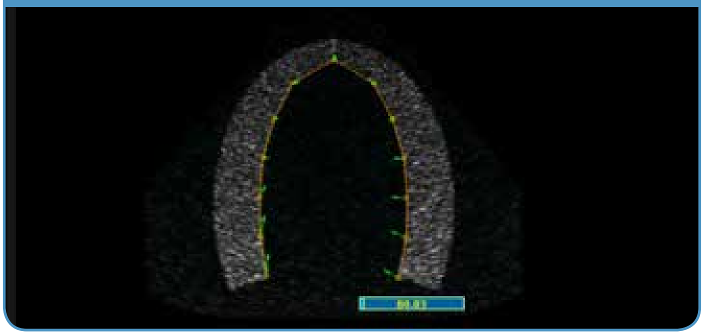
In parallel it was decided to start a technical activity to verify the behavior of the different vendor tracking algorithms on synthetic data (Imaging Phantoms). The validation was based on the Global Longitudinal Strain (*Gls*) parameter that is the deformation calculated over the entire ventricular border length as described in Fig. 1. University of Leuven provided all the vendors an executable program able to generate different datasets to mimic 4 different heart models (Normal, Hypertrophic, Dilated and Exercising Heart) and able to include different level of random noise (20%, 40%, 60%). Each phantom model contained a specific degree of global longitudinal strain, whose value will be referred in this document as "ground truth" value. The ground truth value was not disclosed to the vendors in order to perform a completely "blind test".

Figure 1 Peak Global Longitudinal Strain
(A) $L_0 = L(t_o)$ full diastolic length of the Left Ventricle
(B) $L = L(t)$ full systolic length of the Left Ventricle
$\epsilon(t)\,[\%] = (L(t) - L_0) / L_0 * 100)$



The Study protocol asked each vendor to:
- Create a 36 set of different image data set (4 models x 3 noise levels x 3 runs);
- Analyze the data set obtained three time to account for measurement variability;
- Provide the 108 measurements performed on the dataset (4 models x 3 noise levels x 3 runs x 3 analyses = 108 analyses) on excel files back to Leuven University for data elaboration and comparison (see Fig. 2).

Figure 2 Example of the endocardial tracking on LV Hypertrophic imaging phantom with 20% noise level and HR 70 bpm



The results related to absolute e relative inter-vendor errors reported in this pilot study were recently published on the European *Heart Journal - Cardiovascular Imaging*[8] and can be summarized as follows:
- the relative error for all vendors remained within 10%. This means that the accuracy of commercially available software packages to measure global longitudinal strain is in line with other standard measurements currently used in clinical echocardiography (e.g. left ventricular ejection fraction by 2D echocardiography);
- overall, increasing noise levels results in higher errors (greater deviation from ground truth), the impact of noise on the measurement accuracy of global longitudinal strain varied significantly amongst vendors with some algorithms being more sensitive to noise than others and with some vendors, among which Esaote, showing better accuracy with relative errors below 5% for almost all noise levels and models;
- Consistently amongst all vendors was the fact that high heart rate (i.e. 150 bpm) at a conventional frame rate of 70 Hz resulted in underestimation of the global longitudinal strain. This was another "expected" result as higher heart rate at a fixed frame rate will result in more speckle de-correlation between frames making accurate tracking more challenging
- Overall, intra-vendor reproducibility was fairly good with coefficients of variation below 5% for most vendors.

These tests on synthetic datasets showed promising results. Anyhow, due to the test design that had as pure "technological aim", the question whether these results could be extrapolated to real clinical settings still remained "on the ground". For this reason the EACVI/ASE/Industry Task Force decided to address the topic by designing a specific comparative test to be run on real patients and volunteers.

Comparative scanning on patients and volunteers

This test involved the live scanning of patients with the different vendors ultrasound devices and then the data acquired have been processed using the different SW solutions available on the market. The imaging data acquisition was performed in Leuven (University Hospital Gasthuisberg) from April 22 to April 26, 2013. Seven ultrasound vendors attended the event as shown in the table below Esaote was the only one attending the context with its premium portable ultrasound device MyLabAlpha as show in the following Table 1.

Table 1 Vendors participating in the study with the version of the equipment provided – Ref. "Head-to-Head Comparison of Global Longitudinal Strain Measurements among Nine Different Vendors: The EACVI/ASE Inter-Vendor Comparison Study"[10]

Vendor	Ultrasound Machine	Type
Hitachi-Aloka	Prosound α7 CV v.6.1	high end
Esaote	**MyLabAlpha**	**portable**
GE	Vivid E9 v.112.1.3	high end
Philips	iE 33 Vision 2012	high end
Samsung	EKO7	high end
Siemens	SC2000 v.3.5	high end
Toshiba	Artida V3.0	high end
Epsilon[1]		
TomTec[1]		

1. Software-only vendor

Comparative scanning on patients and volunteers: Imaging Acquisition Protocol

Sixty-three (63) patients and volunteers with normal and abnormal cardiac function were enrolled and scanned during 5 full working days. Each patient/volunteer was assigned to a specific sonographer who had the task to acquire the imaging data on all the different ultrasound platform moving from one device to the other platforms.

In order to allow an analysis of the test-retest-variability, at the end of each scanning section, the three apical views acquisition were acquired by a different sonographer and again by the original sonographer assigned to the patients under analysis repeated the same data acquisition.

University of Leuven elaborated the data set acquired on the 7 vendors devices both using specific vendors software solutions and on two different SW solutions provided by software solution providers. During EUROECHO 2013 Congress the first results of the study were presented by mean of a moderated poster entitled "Variability in global longitudinal strain measurements between different vendors: where do we stand? The EACVI-ASE-Inter-Vendor Comparison Study"[9]. The final results of this study were recently published on the *Journal of the Anerican Society of Echocardiography (J Am Soc Echocardiogr.)*[10]. The study demonstrated that, in a well-controlled setting, close to clinical reality,:

- STE-based GLS measurements are feasible in patients with sufficient image quality.
- **The inter- and intraobserver reproducibility of GLS proved to be comparable with or superior to that of EF and other conventional echocardiographic parameters.**
- A moderate but statistically significant, bias between vendors, was reported. This bias is however, within acceptable limits for most combinations of software packages.

The vendors specific results related to regression line, correlation coefficient and Bland-Altman plot and related limit of agreement are reported in Fig. 2A & 2B of the article "Head-to-Head Comparison of Global Longitudinal Strain Measurements among Nine Different Vendors: The EACVI-ASE Inter-Vendor Comparison Study"[10].

Figure 3 Dr. Farsalinos acquiring patient data on MyLabAlpha CrystaLine in Leuven

Figure 4 XStrain 2D Graph Comparison environment with CRM (Color Rendering M-Mode), Strain and Strain Rate graphs simultaneously displayed on the screen

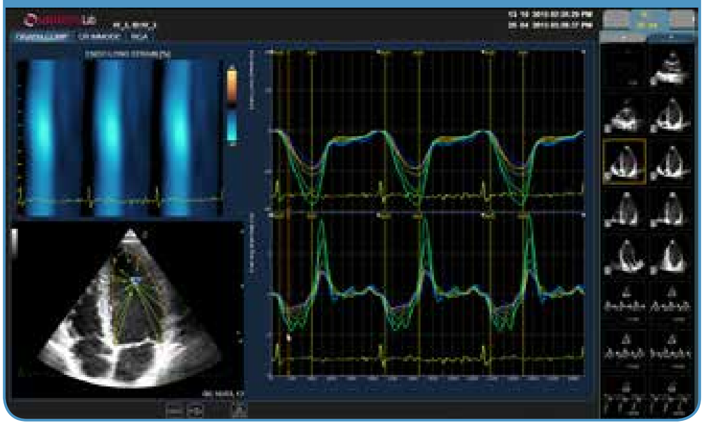


Figure 5 XStrain 2D data elaboration: Regional Curve Analysis (RCA) enviroment with Global Longitudinal Strain (GLS) value

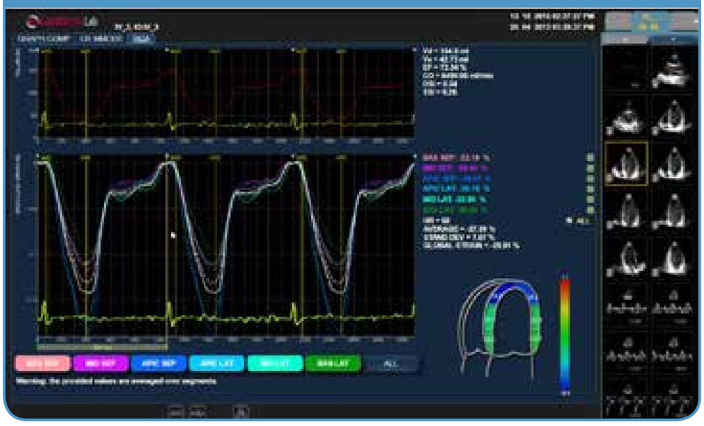
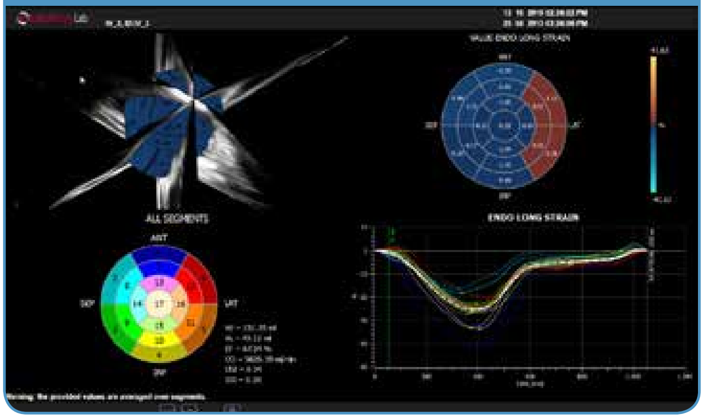


Figure 6 XStrain 4D elaboration and data presentation



Initiative: looking to the future

In 2015, Ase and Eacvi invited the Industries partner to go further in the project to standardize deformation imaging by conducting another comparative scanning of patients with the focus on the sensitivity and reproducibility to detect and quantify regional dysfunction. A formal invitation letter for comparative scanning on patients to the industry partners mid February 2015. All the industries partners attending the 2013 round test on patient accepted the invitation to this second round of test.
The live scanning on the patients took place at the Department of Cardiovascular Diseases, University Hospital Gasthuisberg, Catholic University Leuven, from April 20th until April 24th, 2015.

Interview with Dr. Farsalinos

We're interviewing Dr. Farsalinos, Research coordinator at the Department of Pharmacology at University of Patras and who, in 2013, was serving as Clinical Observer and Researcher at the Department of Cardiovascular Diseases, Medical Imaging Research Center, University Hospital Gathuisberg, Leuven-Belgium thanks to a research grant from the Greek Society of Cardiology to conduct the comparative test on patients.
He is the first author of the publication "Head-to-Head Comparison of Global Longitudinal Strain Measurements among Nine Different Vendors: The Eacvi/Ase Inter-Vendor Comparison Study"[10].

Dear Dr. Farsalinos, what is your opinion about your experience within the Eacvi/AseIndustry Initiative to standardize deformation imaging?

I would say it was a once in a lifetime experience. It was a unique opportunity to work with the research team at the University of Leuven and with all vendors into such an important project for echocardiography. It is a project that will probably redefine the echocardiographic evaluation of left ventricular systolic function by introducing Global Longitudinal Strain into everyday clinical practice. I consider myself lucky for working with all the vendors and getting experience with all the echocardiographic machines and software during this project.

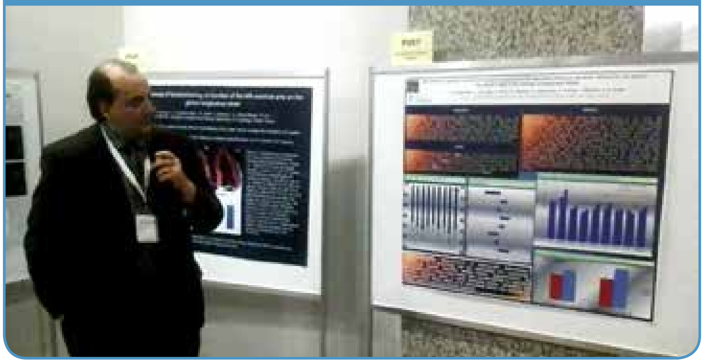
What are the most important and significative clinical results coming out from the Inter-Vendor Comparison study on Global Longitudinal Strain (Gls)?

The most important finding is that the vendors have made some very important steps in this field. We are at a point where reproducibility of Global Longitudinal Strain measurements is very good, comparable or superior to conventional echocardiographic measurements. The variation between vendors was small, and there is room for further improvement. I am confident that we are close to the point where Global Longitudinal Strain will be the method of choice for the evaluation of systolic function for all patients in the daily clinical routine.

The Inter-Vendor Comparison Study gave you a fantastic opportunity to work side-by-side with a wide range of ultrasound devices from different manufacturers. What is your opinion about Esaote MyLabAlpha, the only portable device in the lot, in terms of quality and performance and about our Deformation Imaging tool (XStrain) software?

The Esaote MyLabAlpha is a very practical device because of its small size but large capabilities. The software had a very pleasant user interface, which makes work easier. As in every other case, there is always room for further improvement and I am sure Esaote will strive for perfection.

Figure 7 Euroecho 2013, Dr. Farsalinos presenting the Moderated Poster P957 entitled "Variability in global longitudinal strain measurements between different vendors: where do we stand? The Eacvi-Ase-Inter-Vendor Comparison



Bibliographic References

1. **Assessment of myocardial mechanics using speckle tracking echocardiography: fundamentals and clinical applications**, Geyer et al. (J Am Soc Echocardiogr. 2010;23(4):351-369)
2. **Expert Consensus Statement: Current and Evolving Echocardiographic Techniques for the Quantitative Evaluation of Cardiac Mechanics: ASE/EAE Consensus Statement on Methodology and Indications**, Victor Mor-Avi, et. al. (J Am Soc Echocardiogr 2011;24(3):277-313)
3. **Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging**, Lang et al. (J Am Soc Echocardiogr 2015;28:1-39.)
4. **EACVI-ASE-industry initiative to standardize deformation imaging: a brief update from the co-chairs**, James D. Thomas and Luigi P. Badano (European Heart Journal – Cardiovascular Imaging 2013 14, 1039–1040)
5. **ASE President's Message: A Unique Collaboration to Advance Strain Imaging**, Benjamin F. Byrd III (J Am Soc Echocardiogr 2013,26.(11), A21-A22
6. **Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging**, Voigt et al. Eur Heart J Cardiovasc Imaging. 2015 Jan;16(1):1-11. doi: 10.1093/ehjci/jeu184. Epub 2014 Dec 18
7. **Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging**, Voigt at al. J Am Soc Echocardiogr. 2015 Feb;28(2):183-93. doi: 10.1016/j.echo.2014.11.003
8. **Two-dimensional speckle tracking echocardiography: standardization efforts based on synthetic ultrasound data**, Jan D'hooge et al., Eur Heart J Cardiovasc Imaging. 2015 Aug 18. pii: jev197
9. Moderated Poster presentation EUROECHO 2013 **Variability in global longitudinal strain measurements between different vendors: where do we stand? The EACVI-ASE-Inter-Vendor Comparison Study,** K Farsalinos et-, al.,Eur Heart J Cardiovasc Imaging Abstracts Supplement (2013) 14 (Supplement 2), ii173 Ref: P957
10. **Head-to-Head Comparison of Global Longitudinal Strain Measurements among Nine Different Vendors: The EACVI/ASE Inter-Vendor Comparison Study**, Farsalinos et. al., J Am Soc Echocardiogr. 2015 Oct;28(10):1171-1181.e2. doi: 10.1016/j.echo.2015.06.011. Epub 2015 Jul 23]

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Esaote S.p.A.

International Activities: Via di Caciolle 15 - 50127 Florence, Italy - Tel. +39 055 4229 1 - Fax +39 055 4229 208 - international.sales@esaote.com - www.esaote.com
Domestic Activities: Via A. Siffredi, 58 16153 Genoa, Italy, Tel. +39 010 6547 1, Fax +39 010 6547 275, info@esaote.com