Preliminary Experiences with Compressed Sensing Multi-Slice Cine Acquisitions for the Assessment of Left Ventricular Function: CV_sparse WIP

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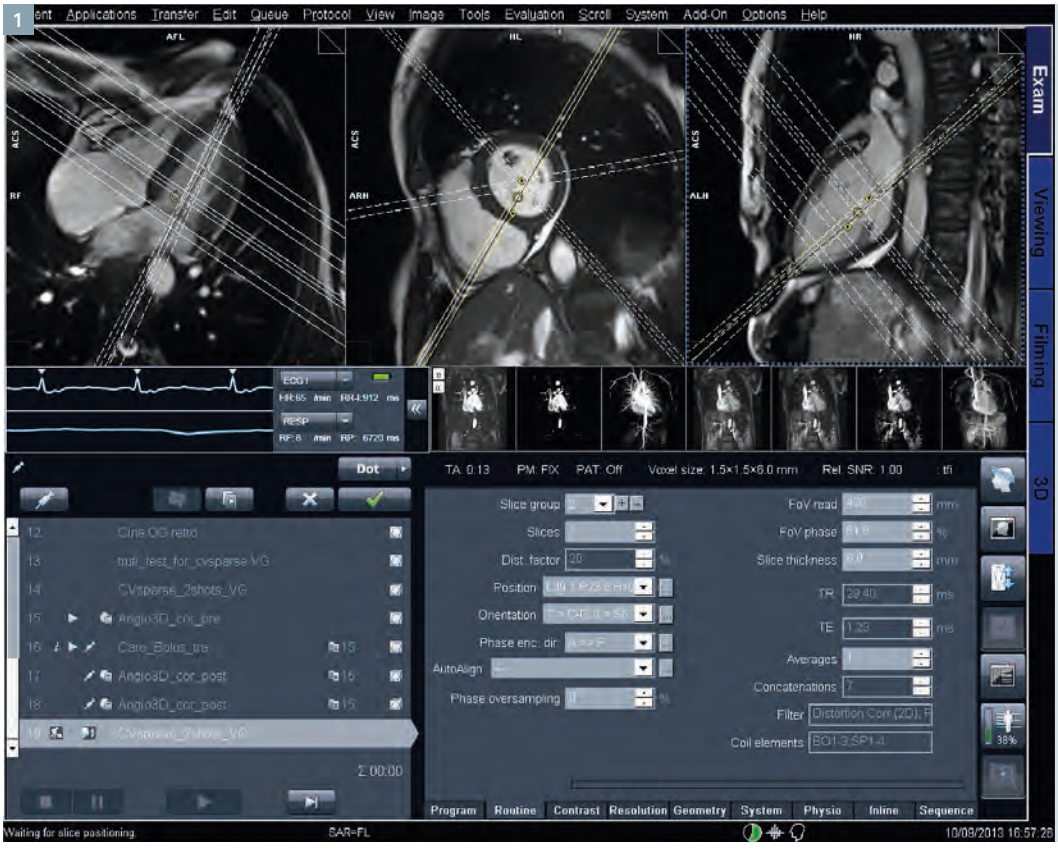
Introduction

Left ventricular (LV) ejection fraction is one of the most important measures in cardiology and part of every cardiac imaging evaluation as it is recognized as one of the strongest predictors of outcome [1]. It allows to assess the effect of established or novel treatments [2], and it is crucial for decision making [3] e.g. to start [4] or stop [5] specific drug treatments or to implant devices [6]. CMR is generally accepted as the gold standard method to yield most accurate measures of LV ejection fraction and LV volumes. This capability and the additional value of CMR to characterize pathological myocardial tissue was the basis to assign a class 1 indication for patients with known or suspected heart failure to undergo CMR in the new Heart Failure Guidelines of the European Society of Cardiology [3].



1 Display of the planning of the 7 slices (4 short axis and 3 long axis slices) acquired within a single breath-hold with the three localizers.

The evaluation of LV volumes and LV ejection fraction are based on well-defined protocols [7] and it involves the acquisition of a stack of LV short axis cine images from which volumes are calculated by applying Simpson's rule. These stacks are typically acquired in multiple breath-holds. Quality criteria [8] for these functional images are available and are implemented e.g. for the quality assessment within the European CMR registry which currently holds approximately 33,000 patients and connects 59 centers [9].

Recently, compressed sensing (CS) techniques emerged as a means to considerably accelerate data acquisition without compromising significantly image quality. CS has three requirements:

1) transform sparsity,
2) incoherence of undersampling artifacts, and
3) nonlinear reconstruction (for details, see below).

Based on these prerequisites, a CS approach for the acquisition of cardiac cine images was developed and tested*. In particular, the potential to acquire several slices covering the heart in different orientations within a single breath-hold would allow to apply model-based analysis tools which theoretically could improve the motion assessment at the base of the heart, where considerable through-plane motion on short-axis slices can introduce substantial errors in LV volume and LV ejection fraction calculations. Conversely, with a multi-breath-hold approach, there are typically small differences in breath-hold positions which can introduce errors in volume and function calculations. The pulse sequence tested here allows for the acquisition of 7 cine slices within 14 heartbeats with an excellent temporal and spatial resolution.

Such a pulse sequence would also offer the advantage to obtain functional information in at least a single plane in patients unable to hold their breath for several heartbeats or in patients with frequent extrasystoles or atrial fibrillation. However, it should be mentioned that accurate quantitative measures of LV volumes and function cannot be obtained in highly arrhythmic hearts or in atrial fibrillation, as under such conditions volumes and ejection fraction change from beat to beat due to variable filling conditions. Nevertheless, rough estimates of LV volumes and function would still be desirable in arrhythmic patients.

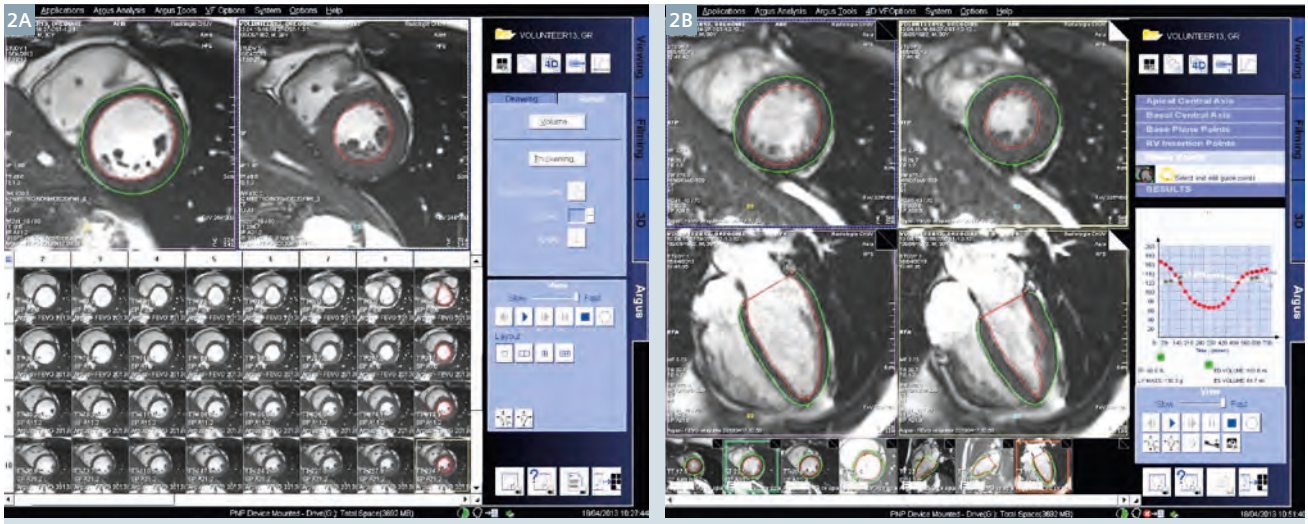
*Work in progress: The product is still under development and not commercially available yet. Its future availability cannot be ensured.

In a group of healthy volunteers and patients with different LV pathologies, the novel single-breath-hold CS cine approach was compared with the standard multi-breath-hold cine technique with respect to measure LV volumes and LV ejection fraction.

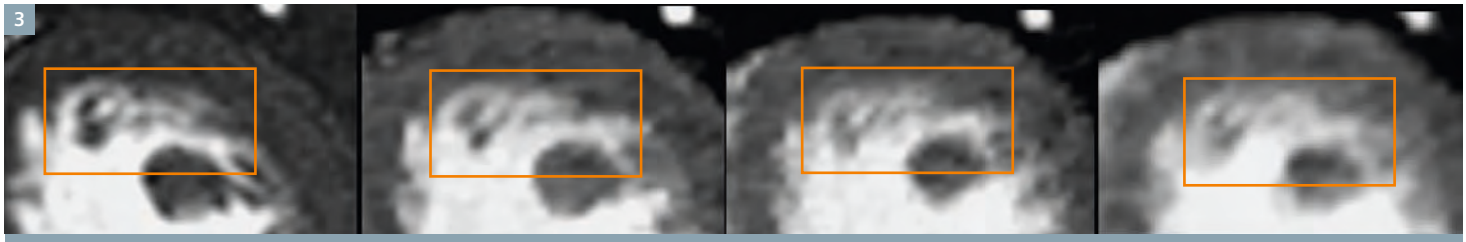
The CV_sparse work-in-progress (WIP)

The CV_sparse WIP package implements sparse, incoherent sampling and iterative reconstruction for cardiac applications. This method in principle allows for high acceleration factors which enable triggered 2D real-time cine CMR while preserving high spatial and/or temporal resolution of conventional cine acquisitions. Compressed sensing methods exploit the potential of image compression during the acquisition of raw input data. Three components [10] are crucial for the concept of compressed sensing to work

I. Sparsity: In order to guarantee compressibility of the input data, sparsity must be present in a specific transform domain. Sparsity can be computed e.g. by calculating differences between neighboring pixels or by calculating finite differences in angiograms which then detect primarily vessel contours which typically represent a few percent of the



2 Displays of the data analysis tools for the conventional short axis stack of cine images covering the entire LV **(2A)** and the 4D analysis tool **(2B)**, which is model-based and takes long axis shortening of the LV, i.e. mitral annulus motion into account. Note that with both analysis tools, LV trabeculations are included into the LV volume, particularly in the end-diastolic images (corresponding images on the left of top row in 2A and 2B).



3 Examples of visualization of small trabecular structures in the LV (in the rectangle) with the standard cine SSFP sequence (image on the left) and the accelerated compressed sensing sequences (images on the right). Despite increasing acceleration most information on small intraluminal structures remains visible.

entire image data only. Furthermore, sparsity is not limited to the spatial domain: the acquisition of cine images of the heart can be highly sparsified in the temporal dimension.

II. Incoherent sampling: The aliasing artifacts due to *k*-space undersampling must be incoherent, i.e. noise-like, in that transform domain. Here, it is to mention that fully random *k*-space sampling is suboptimal as *k*-space trajectories should be smooth for hardware and physiological considerations. Therefore, incoherent sampling schemes must be designed to avoid these concerns while fulfilling the condition of random, i.e. incoherent sampling.

III. Reconstruction: A non-linear iterative optimization corrects for subsampling artifacts during the process of image reconstruction yielding to a best solution with a sparse representation in a specific transform domain and which is consistent with the input data. Such compressed sensing techniques can also be combined with parallel imaging techniques [11].

WIP CV_sparse Sequence

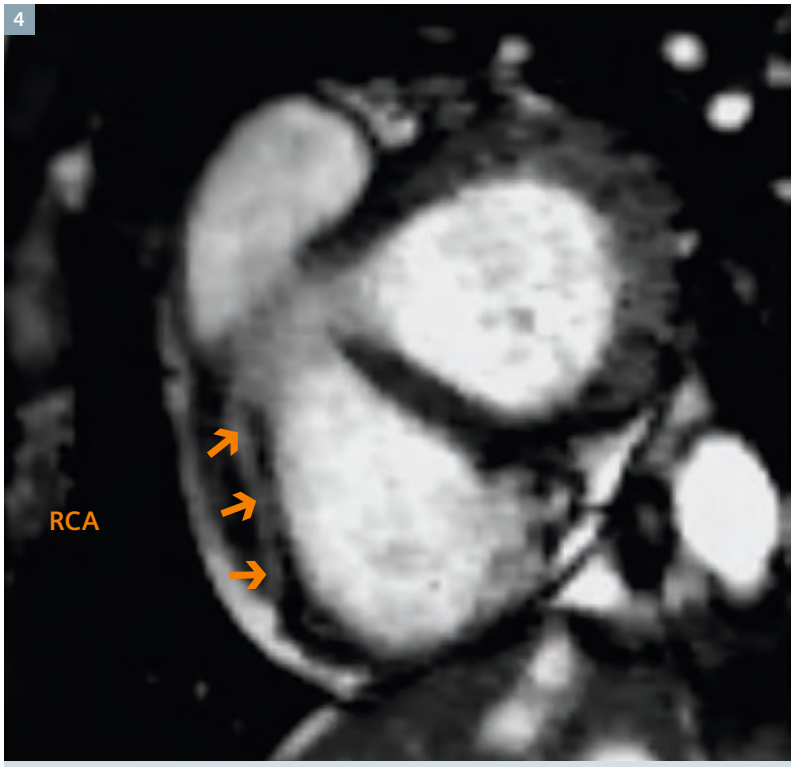
The current CV_sparse sequence [12] realizes incoherent sampling by initially distributing the readouts pseudo-randomly on the Cartesian grid in *k*-space. In addition, for cine-CMR imaging, a pseudo-random offset is applied from frame-to-frame which results in an incoherent temporal jitter. Finally, a variable sampling density in *k*-space stabilizes the iterative reconstruction. To avoid eddy current effects for balanced steady-state free precession (bSSFP) acquisitions, pairing [13] can also be applied. Thus, the tested CV_sparse sequence is characterized by sparse, incoherent sampling in space and time, non-linear iterative reconstruction integrating SENSE, and L1 wavelet regularization in the phase encoding direction and/or the temporal dimension. With regard to reconstruction, the ICE program runs a non-linear iterative reconstruction with *k-t* regularization in space and time specifically modified for compressed sensing. The algorithm derives from a parallel imaging type reconstruction which takes coil sensitivity maps into account, thus supporting predominantly high acceleration factors. For cine CMR, no additional reference scans are needed because – similar to TPAT – the coil sensitivity maps are calculated from the temporal average of the input data in a central region of *k*-space consisting of not more than 48 reference lines. The extensive calculations for image reconstruction typically running 80 iterations are performed online on all CPUs on the MARS computer in parallel, in order to reduce reconstruction times.

Volunteer and Patient studies

In order to obtain insight into the image quality of single-breath-hold multi-slice cine CMR images acquired with the compressed sensing (CS) approach, we studied a group of healthy volunteers and a patient group with different pathologies of the left ventricle. In addition to the evaluation of image quality, the robustness and the precision of the CS approach for LV volumes and LV ejection fraction was also assessed in comparison with a standard high-resolution cine CMR approach. All CMR examinations were performed on a 1.5T MAGNETOM Aera (Siemens Healthcare, Erlangen, Germany). The imaging protocol consisted of a set of cardiac localizers followed by the acquisition of a stack of conventional short-axis SSFP cine images covering the entire LV with a spatial and tem-

poral resolution of 1.2 x 1.6 mm², and approximately 40 ms, respectively (slice thickness: 8 mm; gap between slices: 2 mm). LV 2-chamber, 3-chamber, and 4-chamber long-axis acquisitions were obtained for image quality assessment but were not used for LV volume quantifications. As a next step, to test the new CS-based technique, slice orientations were planned to cover the LV with 4 short-axis slices distributed evenly over the LV long axis complemented by 3 long-axis slices (i.e. a 2-chamber, 3-chamber, and 4-chamber slice) (Fig. 1). These 7 slices were then acquired in a single breath-hold maneuver lasting 14 heart beats (i.e. 2 heart beats per slice) resulting in an acceleration factor of 11.0 with a temporal and spatial resolution of 30 ms and 1.5 x 1.5 mm², respectively (slice thickness: 6 mm). As the reconstruction algorithm is susceptible to aliasing in the phase-encoding direction, the 7 slices were first acquired with a non-cine acquisition to check for correct phase-encoding directions and, if needed, to adjust the field-of-view to avoid fold-over artifacts. After confirmation of correct imaging parameters, the 7-slice single-breath-hold cine CS-acquisition was performed. In order to obtain a reference for the LV volume measurement, a phase-contrast flow measurement in the ascending aorta was performed to be compared with the LV stroke volumes calculated from the standard and CS cine data.

The conventional stack of cine SSFP images was analyzed by the Argus software (Siemens Argus 4D Ventricular Function, Fig. 2A). The CS cine data were analyzed by the 4D-Argus software (Siemens Argus, Fig. 2B). Such software is based on an LV model and, with relatively few operator interactions, the contours for the LV endocardium and epicardium are generated by the analysis tool. Of note, this 4D analysis tool automatically tracks the 3-dimensional motion of the mitral annulus throughout the cardiac cycle which allows for an accurate volume calculation particularly at the base of the heart.



4 Example demonstrating the performance of the compressed sensing technique visualizing small structures such as the right coronary artery (RCA) with high temporal and spatial resolution acquired within 2 heartbeats. Short-axis view of the base of the heart (1 out of 17 frames).

Results and discussion

Image quality – robustness of the technique

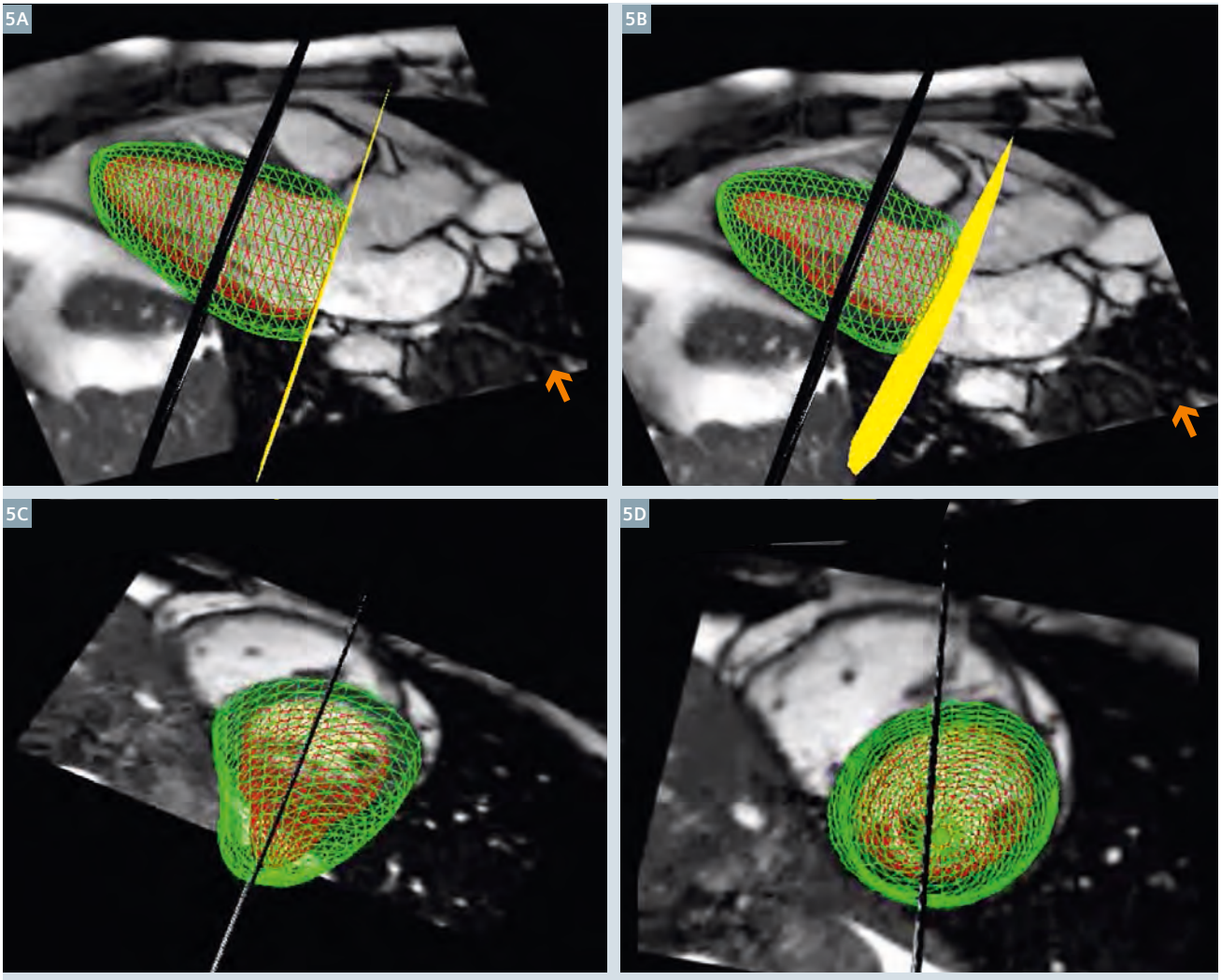
Overall, a very good image quality of the single-breath-hold multi-slice CS acquisitions was obtained in the 12 volunteers and 14 patient studies. All CS data sets were of adequate quality to undergo 4D analysis. Small structures such as trabeculations were visualized in the CS data sets as shown in Figures 3 and 4. However, very small structures, detectable by the conventional cine acquisitions, were less well discernible by the CS images. Therefore, it should be mentioned here, that this accelerated single-breath-hold CS approach would be adequate for functional measurements, i.e. LV ejection fraction assessment (see also results below), whereas assessment of small structures as present in many cardiomyopathies is more reliable when performed on conventional cine images. Temporal resolution of the new technique appears adequate to even detect visually the dyssynchroneous contraction pattern in left bundle branch block. Also, the image contrast between the LV myocardium and the blood pool was high on the CS images allowing for an easy assessment of the LV motion pattern. As a result, the single-breath-hold cine approach permits to reconstruct the LV in 3D space with high temporal resolution as illustrated in Figure 5. Since these data allow to correctly include the 3D motion of the base of the heart during the cardiac cycle, the LV stroke volume appears to be measurable by the CS approach with higher accuracy than with the conventional multi-breath-hold approach (see results below). With an accurate measurement of the LV stroke volume, the quantification of a mitral insufficiency should theoretically benefit (when calculating mitral regurgitant volume as 'LV stroke volume minus aortic forward-flow volume').

As a current limitation of the CS approach, its susceptibility for fold-over artifacts should be mentioned (Figs. 6A). Therefore, the field-of-view must cover the entire anatomy and thus, some penalty in spatial res-

olution may occur in relation to the patient's anatomy. In addition, the sparsity in the temporal domain may be limited in anatomical regions of very high flow, and therefore, in some acquisitions, flow-related artifacts occurred in the phase-encoding direction during systole (Figs. 6B, C). Also, in its current version, the sequence is prospective, thus it does not cover the very last phases of the cardiac cycle and the reconstruction times for the CS images lasted several minutes precluding an immediate assessment of the image data quality or using this image information to plan next steps of a CMR examination.

Performance of the single-breath-hold CS approach in comparison with the standard multi-breath-hold cine approach

From a quantitative point-of-view, the accurate and reliable measurement of LV volumes and function is crucial as many therapeutic decisions directly depend on these measures [3–6]. In this current relatively small study group, LV end-diastolic and end-systolic volumes measured by the single-breath-hold CS approach were comparable with those calculated from the standard multi-breath-hold cine SSFP approach. LVEDV and LVESV differed by 10 ml ± 17 ml and 2 ml ± 12 ml, respectively. Most importantly, LV ejection fraction differed by only 1.3 ± 4.7% (50.6% vs 49.3% for multi-breath-hold and single-breath-hold, respectively, $p = 0.17$; regression: $r = 0.96$, $p < 0.0001$; $y = 0.96x + 0.8$ ml). Thus, it can be concluded that the single-breath-hold CS approach could potentially replace the multi-breath-hold standard technique for the assessment of LV volumes and systolic function.



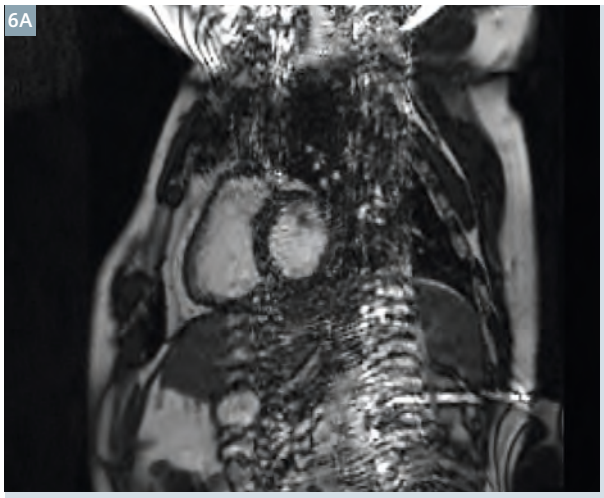
5 Display of the 3D reconstruction derived from the 7 slices acquired within a single breath-hold. Note the long-axis shortening of the LV during systole allowing for accurate LV volume measurements (**5A, 5B**, yellow plane). Any orientation of the 3D is available for inspection of function **(5A–D)**.

What about the accuracy of the novel single-breath-hold CS technique?

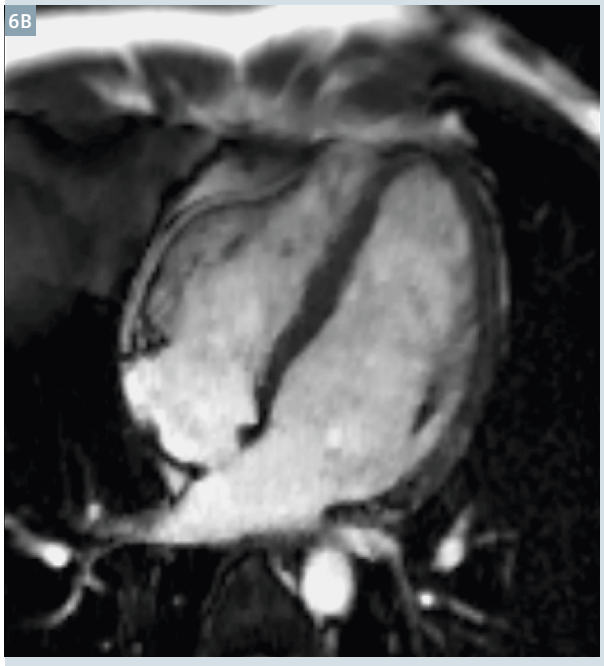
To assess the accuracy of the LV volume measurements, LV stroke volume was compared with the LV output measured in the ascending aorta with phase-contrast MR. As the flow measurements were performed distally to the coronary arteries, flow in the coronaries was estimated as the LV mass multiplied by 0.8 ml/min/g. An excellent agreement was found with a mean of 86.8 ml/beat for the aortic flow measurement and 91.9 ml/beat for the LV measurements derived from the single-breath-hold CS data ($r = 0.93$, $p < 0.0001$). By Bland-Altman analysis, the stroke volume approach overestimated by 5.2 ml/beat versus the reference flow measurement. For the conventional stroke volume measurements, this difference was 15.6 ml/beat (linear regression analysis vs aortic flow: $r = 0.69$, $p < 0.01$). More importantly, the CS LV stroke data were not only more precise with a smaller mean difference, the variability of the CS data vs the reference flow data was less with a standard deviation as low as 6.8 ml/beat vs 12.9 ml/beat for the standard multi-breath-hold approach (Fig. 7). Several explanations may apply for the higher accuracy of the single-breath-hold multi-slice CS approach in comparison to the conventional multi-breath-hold approach:

1) With the single-breath-hold approach, all acquired slices are correctly co-registered, i.e. they are correctly aligned in space, a prerequisite for the 4D-analysis tool to work properly.

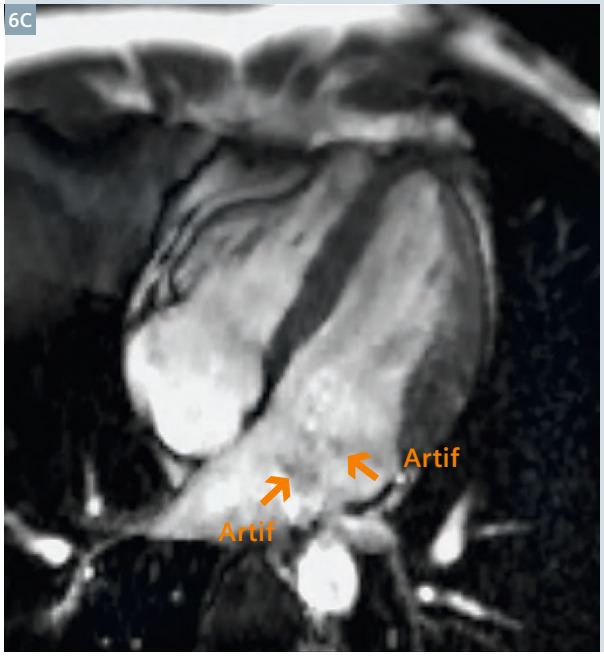
2) This 4D-analysis tool allows for an accurate tracking of the mitral valve plane motion during the cardiac cycle as shown in Figure 5, which is important as the cross-sectional area of the heart at its base is large and thus, inaccurate slice positioning at the base of



6A
A typical fold-over artifact along the phase-encoding direction in a short axis slice, oriented superior-inferior for demonstrative purpose.



6B
No flow-related artifacts are visible on the end-diastolic phases, while small artifacts in phase-encoding direction (Artif, arrows) occur in mid-systole projecting over the mitral valve **(6C).**



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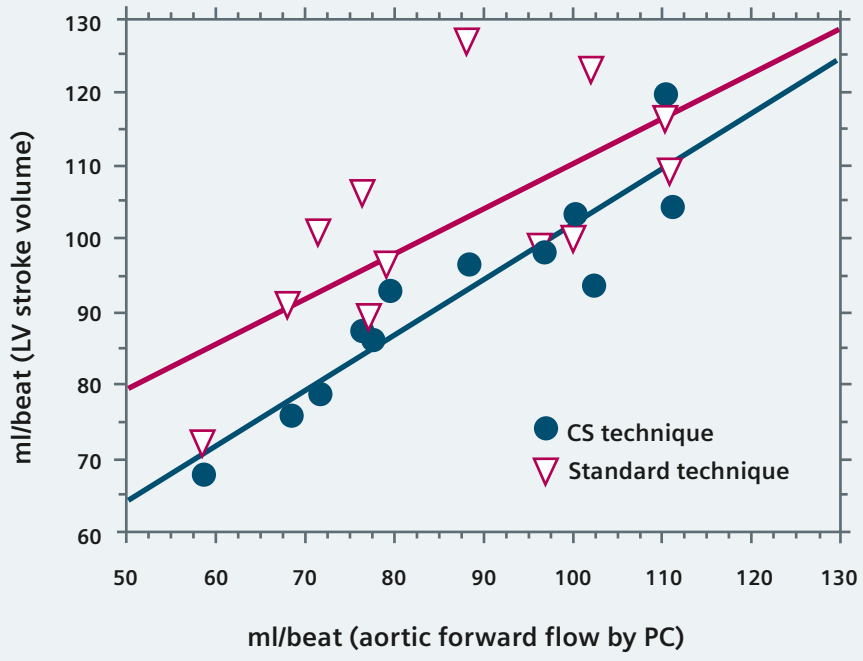


7
An excellent correlation is obtained for the LV stroke volume calculated from the compressed sensing data with the flow volume in the aorta measured by phase-contast technique. Variability of the conventional LV stroke volume data appears higher than for the compressed sensing data.

the heart with conventional short-axis slices typically translate in relatively large errors. Nevertheless, we observed a systematic overestimation of the stroke volume by the CS approach of 5.2 ml/beat in comparison to the flow measurements. In normal hearts with tricuspid aortic valves, an underestimation of aortic flow by the phase-contrast technique is very unlikely [14]. Thus, overestimation of stroke volume by the volume approach is to consider. In the volume contours, the papillary muscles are excluded as illustrated in Figure 8. As these papillary muscles are excluded in both the diastolic and systolic contours, this aspect should not affect net LV stroke volume. However, as shown in Figure 8, smaller trabeculations of the LV wall are included into the LV blood pool contour in the diastolic phase, while these trabeculations, when compacted in the end-systolic phase, are excluded from the blood pool resulting in a small overestimation of the end-diastolic volume, and thus, LV stroke volume. This explanation is likely as Van Rossum et al. demonstrated a slight underestimation of the LV mass when calculated on end-diastolic phases versus end-systolic phases, as trabeculations in end-diastole are typically excluded from the LV walls [15].

In summary, this novel very fast acquisition strategy based on a CS technique allows to cover the entire LV with high temporal and spatial resolution within a single breath-hold. The image quality based on these preliminary results appears adequate to yield highly accurate measures of LV volumes, LV stroke volume, LV mass, and LV ejection fraction.

Testing of this very fast multi-slice cine approach for the atria and the right ventricle is currently ongoing. Finally, these preliminary data show that compressed sensing MR acquisitions in the heart are feasible in humans and compressed sensing might be implemented for other important cardiac sequences such as fibrosis/viability imaging, i.e. late gadolinium enhancement, coronary MR angiography, or MR first-pass perfusion.

The Cardiac MR Center of the University Hospital Lausanne

The Cardiac Magnetic Resonance Center (CRMC) of the University Hospital of Lausanne (Centre Hospitalier Universitaire Vaudois; CHUV) was established in 2009. The CMR center is dedicated to high-quality clinical work-up of cardiac patients, to deliver state-of-the-art

training in CMR to cardiologists and radiologists, and to pursue research. In the CMR center education is provided for two specialties while focusing on one organ system. Traditionally, radiologists have focussed on using one technique for different organs, while cardiologists have concentrated on one organ and perhaps one technique. Now in the CMR center the focus is put on a combination of specialists with different background on one organ. Research at the CMR center is devoted to four major areas: the study of

1.) cardiac function and tissue characterization, specifically to better understand diastolic dysfunction,
2.) the development of MR-compatible cardiac devices such as pacemakers and ICDs;
3.) the utilization of hyperpolarized ^{13}C-carbon contrast media to investigate metabolism in the heart, and

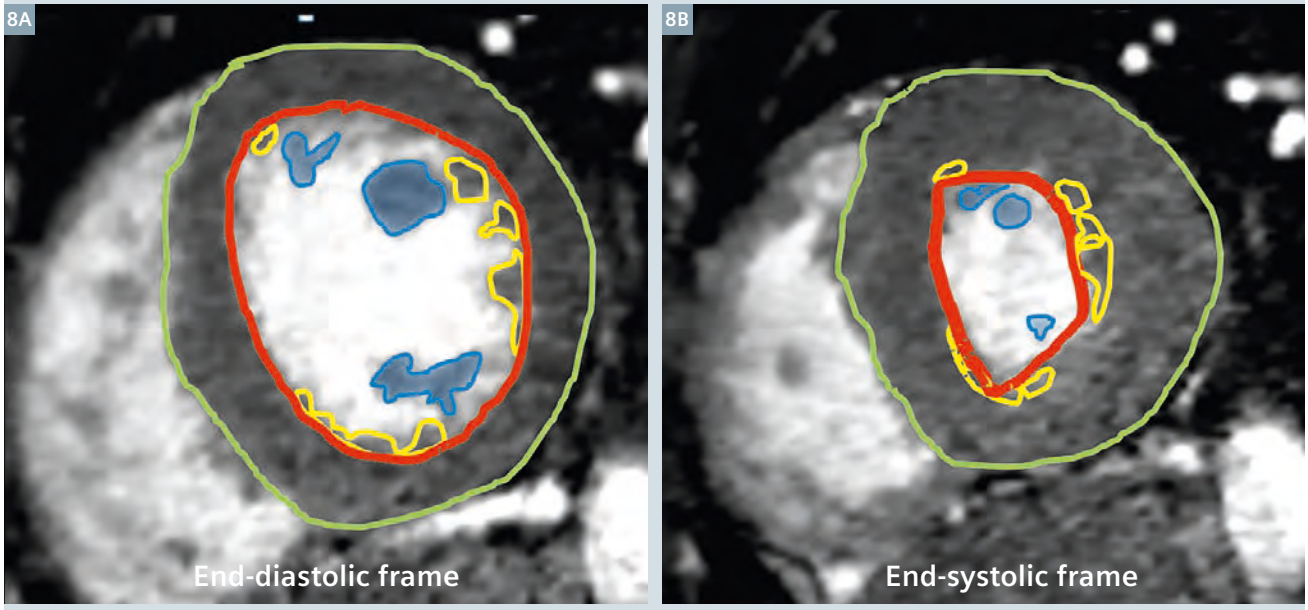
4.) the development of ^{19}F-fluorine-based CMR techniques to detect inflammation and to label and track cells non-invasively.

For the latter two topics, the CMR center established tight collaborations with the Center for Biomedical Imaging (CIBM), a network around Lake Geneva that includes the Ecole Polytechnique Fédérale de Lausanne (EPFL), and the universities and university hospitals of Lausanne and Geneva. In particular, strong collaborative links are in place with the CVMR team of Prof. Matthias Stuber, a part of the CIBM and located at the University Hospital Lausanne and with Prof. A. Comment, with whom we perform the studies on real-time metabolism based on the ^{13}C-carbon hyperpolarization (DNP) technique. In addition, collaborative studies are ongoing with the Heart Failure and Cardiac Transplantation Unit led by Prof. R. Hullin (detection of graft rejection by tissue characterization) and the Oncology Department led by Prof. Coukos (T cell tracking by ^{19}F-MRI in collaboration with Prof. Stuber, R. van Heeswijk, CIBM, and Prof. O. Michielin, Oncology). This structure allows for a direct interdisciplinary interaction between physicians, engineers, and basic scientists on a daily basis with the aim to enable innovative research and fast translation of these techniques from bench to bedside.

The CMRC is also the center of competence for the quality assessment of the European CMR registry which holds currently approximately 33,000 patient studies acquired in 59 centers across Europe.

The members of the CRMC team are: Prof. J. Schwitter (director of the center), PD Dr. X. Jeanrenaud, Dr. D. Locca, MER, Dr. P. Monney, Dr. T. Rutz, Dr. C. Sierro, and Dr. S. Koestner (cardiologists, staff members),

LV short-axis slice: CV_SPARSE



8 Overestimation of end-diastolic LV volumes by volumetric measurements. In comparison to ejected blood from the LV as measured with phase-contrast techniques, the volumetric measurements of LV stroke volume overestimated by approximately 5 ml, most likely by overestimation of LV end-diastolic volume. Small trabculations (yellow contours in 8A) are included into the LV blood volume (red contour in 8A) in diastole, while these trabeculations (yellow contours in 8B) are typically included in the end-systolic phase (red contours in 8B). For the same reasons, LV mass (= green contour minus red contour) is often slightly underestimated in diastole vs systole.

Dr. G. Vincenti (cardiologist) and Dr. N. Barras (cardiologist in training, rotation), PD. Dr. S. Muzzarellli (affiliated cardiologist), Prof. C. Beigelman and Dr. X. Boulanger (radiologists, staff members), Dr. G.L. Fetz (radiologist in training, rotation), C. Gonzales, PhD (^{19}F-fluorine project leader), H. Yoshihara, PhD (^{13}C-carbon project leader), V. Klinke (medical student, doctoral thesis), C. Bongard (medical student, master thesis), P. Chevre (chief CMR technician), and F. Recordon and N. Lauriers (research nurses).

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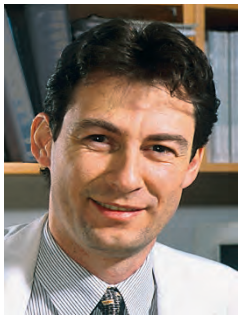

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