GRASP: Tackling the Challenges of Abdominopelvic DCE-MRI

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Introduction

Dynamic contrast-enhanced (DCE) T1-weighted acquisition after injection of a gadolinium-based contrast agent is an integral part of most diagnostic abdominopelvic MRI examinations and essential for identifying and properly characterizing lesions and tumors, such as the hepatocellular carcinoma (HCC) or renal cancer [1]. Because tumors show a specific temporal contrast-enhancement pattern, it is necessary to obtain images of the whole region-of-interest at multiple short time points following the injection. While technically infeasible years ago, parallel-imaging acceleration techniques such as GRAPPA [2] have made it possible to achieve the required acquisition speed using standard clinical MRI systems, so that these scans can nowadays be performed at almost all imaging centers.

However, in routine practice abdominopelvic DCE-MRI exams remain challenging and the failure rates are undesirably high.

One main challenge is that the data has to be collected precisely at defined time points relative to the arrival time of the contrast agent in the aorta (see Fig. 1). To this end, usually a small test bolus is injected prior to the actual diagnostic scan and monitored using a bolus-tracking sequence to determine the patient-specific circulation delay [3]. Once estimated, the delay is then incorporated into the timing calculation of the dynamic scans, which are scheduled relative to the injection time of the contrast dose. This procedure is, of course, prone to inaccuracies and mistakes – with the potential risk of missing the important arterial phase (AP) of contrast enhancement. As additional complication, the dynamic acquisitions have to be performed during a strict breath hold of the patient and, thus, need to be properly synchronized with breath-hold commands. While the latter can be automated using computer-controlled voice instructions [3], it cannot be guaranteed that the patient is actually following these breath-hold instructions. Continued respiration occurs due to various reasons, including inability to hold breath for the scan duration (usually ~15 sec per acquisition), hearing or language problems, and uncertainty when exactly to stop breathing after hearing the command. Especially elderly or severely sick patients often struggle to properly suspend respiration, resulting in compromised or even fully non-diagnostic image quality. A particular problem here is that once the injection has been done, the acquisitions cannot be repeated before the contrast agent has been extracted from the body, which takes several hours and requires

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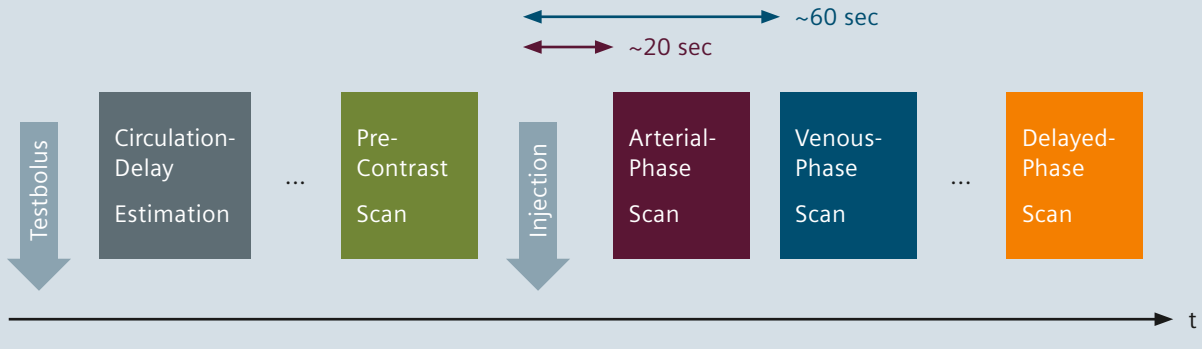

1 Conventional scheme for abdominopelvic DCE-MRI exams, starting with the injection of a test bolus to determine the circulation delay. Afterwards, a pre-contrast image is acquired as well as images in arterial, venous, and delayed phases of contrast enhancement. The acquisitions must be properly timed relative to the injection and accounting for the circulation delay, which makes the procedure prone to timing errors. Furthermore, the scans need to be performed during breath holding.

rescheduling of the examination on a different day. Strongly compromised image quality is also obtained when examining sedated or anesthetized patients, where suspending the respiration is not possible at all.

DCE-MRI with continuous radial acquisition

The requirement to perform abdominal scans during breath-holding results from the high motion sensitivity of conventional MRI techniques, as motion translates into appearance of numerous overlapping object copies known as ghosting artifacts. This problem can be ameliorated by using non-Cartesian acquisition techniques such as radial *k*-space sampling, which inherently prevent the appearance of motion-induced ghosting artifacts. Radial scanning techniques, such as the Radial VIBE or StarVIBE sequence [4], have recently become available for routine imaging, and it has been demonstrated that these sequences can be used to image the abdomen during free-breathing [5]. However, the higher motion robustness of radial *k*-space trajectories comes at the price of lower scan efficiency. With typical scan durations of around 60 sec per image volume, sequences such as Radial VIBE are by itself too slow for dynamic abdominopelvic imaging as it would be impossible to separate the arterial and venous phases of enhancement.

To overcome this problem, our group has recently developed a technique called GRASP[1] that enables using the Radial VIBE sequence for DCE-MRI applications and that resolves many of the aforementioned challenges [6]. The key idea of GRASP is that, instead of performing several individual acquisitions for the required time points, data is acquired continuously throughout the whole exam while the contrast agent is injected (see Fig. 2). Image sets for the needed time points are then calculated from the continuously acquired data using an iterative reconstruction procedure (as described in the next section).

This concept leads to a significant simplification of the overall clinical workflow. Because data is acquired all the time during the examination, it is not necessary anymore to determine the circulation delay using a test bolus. Also, the possibility of missing one of the important enhancement phases as a result of a timing or synchronization error is eliminated. Furthermore, because based on radial *k*-space acquisition, GRASP examinations can be performed during continued breathing [7], which removes the need for breath-hold commands, improves patient comfort, and makes the technique well-suited for patients where holding breath is impossible, such as pediatric[2] patients. Hence, with GRASP, the formerly complex and stressful abdominopelvic DCE-MRI exams now become a simple one-click procedure.

[1] WIP, the product is currently under development and is not for sale in the US and in other countries. Its future availability cannot be ensured.

[2] MR scanning has not been established as safe for imaging fetuses and infants under two years of age. The responsible physician must evaluate the benefit of the MRI examination in comparison to other imaging procedures.

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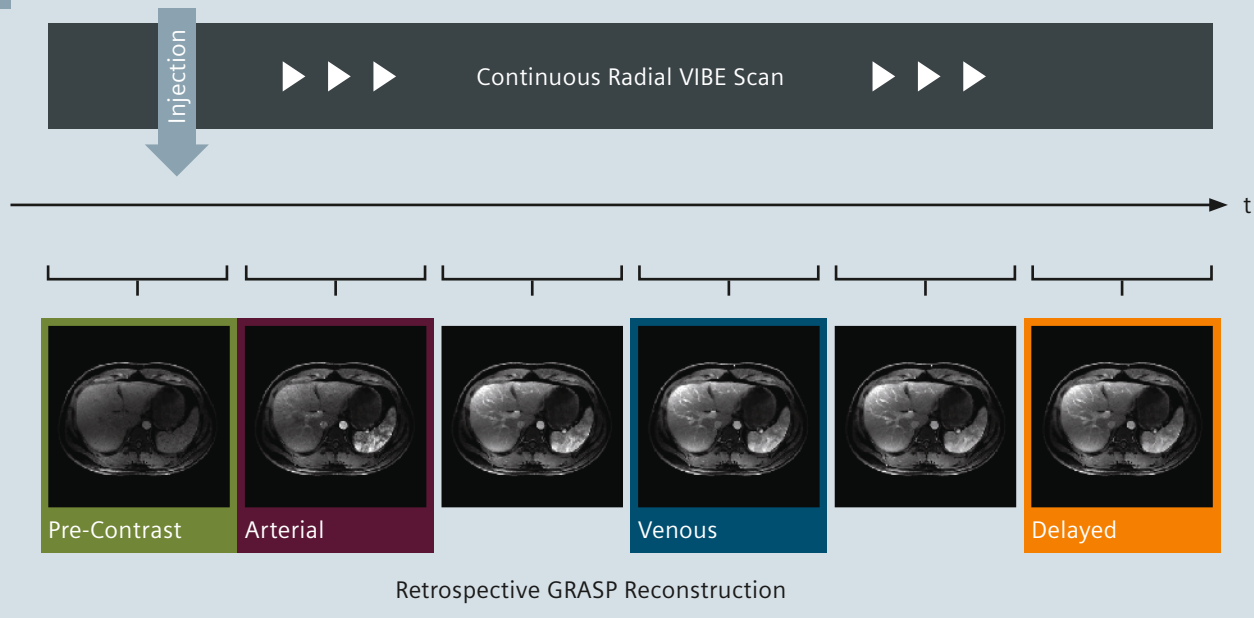


2 GRASP scheme for DCE-MRI, which uses a single continuous acquisition while the contrast agent is injected. Because radial sampling of k-space is used, the data can be acquired during free-breathing. Images are calculated from the continuous data using an iterative reconstruction that allows selecting the desired time points and temporal resolution retrospectively. This eliminates the possibility of timing errors and leads to significant simplification of the workflow.

Technical background

On a technical level, GRASP combines several concepts for MRI scan acceleration that have been described previously as individual techniques. The data acquisition is based on the radial golden-angle ordering scheme, which was originally proposed by Winkelmann et al. [8]. When acquiring radial data with constant angular increment of 111.25 degrees (referred to as 'golden angle' because it corresponds to 180 degrees multiplied by the golden ratio), successively sampled radial spokes always add complementary *k*-space information to the previously acquired data, and any number of grouped spokes cover *k*-space approximately uniformly. This means that if data is acquired continuously over some time, any number of successively acquired spokes can be combined into an individual image (e.g., 144 spokes for low temporal resolution, or 21 spokes for high temporal resolution). Furthermore, the reconstruction window can be placed at any time point of the scan. In other words, it is possible to retrospectively decide which temporal resolution and which time points should be reconstructed.

When grouping only few spokes into each image to achieve high temporal resolution, as needed in DCE-MRI for separating the phases of enhancement, the data available for each time point is highly incomplete or, according to MR terminology, undersampled. For radial sequences, this means that the images are affected by severe 'streak' artifacts, which render the images diagnostically unusable. However, GRASP applies two known tricks to suppress this effect and to recover artifact-free images from the undersampled data: Compressed sensing [9] and parallel imaging [10]. The use of compressed sensing is motivated from the fact that the streak artifacts lead to strongly flickering patterns if viewed along time, whereas the true contrast enhancement occurs in a 'smooth' non-flickering fashion. In other words, flickering pixel intensities can be considered as artificial effects. Therefore, artifact-free images can be obtained by employing an iterative reconstruction procedure that, during each calculation step, matches the solution with the available undersampled data and, in addition, suppresses flickering pixels. Mathematically, this is achieved by calculating the total variation (TV) of each pixel along time and using this value as penalty measure during the iterations (because the true solution should have low total variation). By running the iterative procedure for a certain number of iterations, the streak artifacts disappear and the underlying true solution is recovered – even for severely undersampled data. As second mechanism, parallel imaging is integrated into the iterative scheme by using a CG-SENSE-type formalism [11], which contributes to the suppression of streaking artifacts by exploiting local coil sensitivities. Due to the synergistic combination of these two MR acceleration techniques, GRASP is able to compensate for the lower scan efficiency of radial sampling and achieves even higher temporal resolution than possible with most conventional DCE-MRI techniques. The key advantage, however, consists in the aforementioned workflow simplification.

Clinical integration and evaluation

The downside of using such an iterative reconstruction approach is that the image calculation involves a very computationally demanding numerical process (because the solution has to be mapped between image space and radial *k*-space over and over again). This property is not specific to GRASP and applies to other compressed-sensing techniques likewise. However, a difference is that the amount of data acquired during continuous GRASP acquisitions is enormous (up to 10 GB per scan). Processing such a vast amount of data with the described algorithm is not feasible using the computer components of current clinical MRI scanners, as the MRI systems would be blocked from clinical scanning for an unacceptable long time. Hence, for validating the feasibility of the GRASP technique in actual clinical practice, it was necessary for us to derive a workflow-friendly solution that completely circumvents the normal reconstruction pipeline. Therefore, we developed an offline-processing framework [12] that automatically transfers the acquired GRASP data from our various clinical MRI scanners to a central reconstruction server. Incoming reconstruction tasks are queued according to urgency (clinical vs. research scan) and processed with a parallelized and performance-optimized C++ implementation of the GRASP algorithm. Upon completion, the reconstructed images are sent into the clinical PACS without any user interaction. Our radiologists can then read the GRASP exams side-by-side with other scans that were reconstructed directly on the MRI scanner. Using our current reconstruction server with 64 CPU cores, GRASP images are available in the PACS within 5 to 45 minutes after the exam (depending on the exact scan/reconstruction protocol). With this seamless integration of the GRASP prototype into our routine clinical workflow, a stable solution is now in place to evaluate the technique in a large number of patients and across our different MRI systems. Over the last two years, already several thousand GRASP reconstructions have been performed at our institution, and the setup has recently also been disseminated to multiple collaboration sites for an independent evaluation.

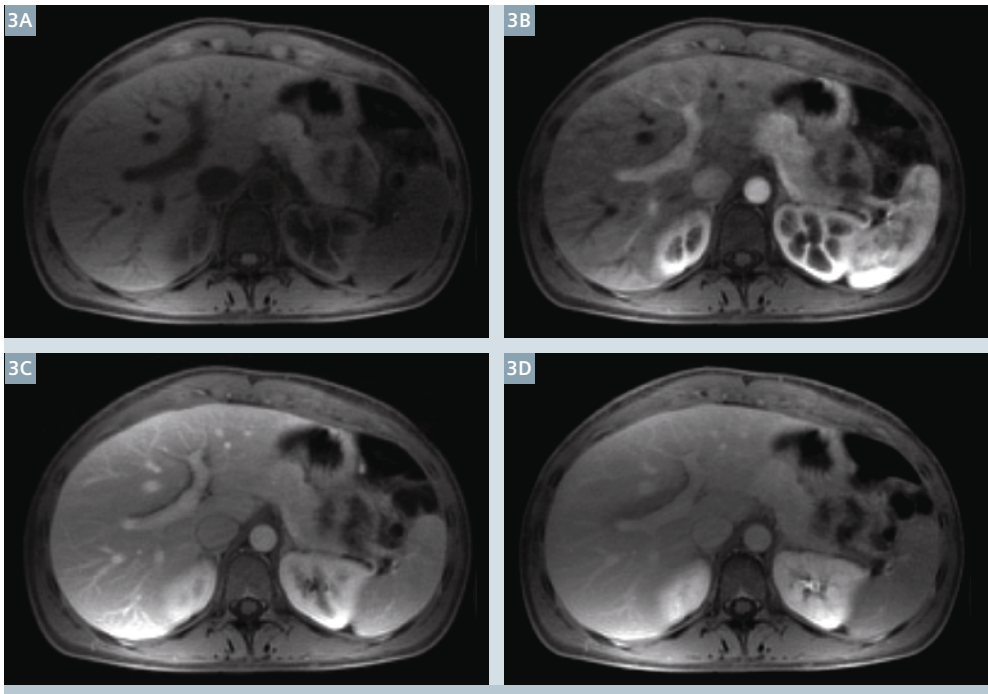
Initial applications

As the development of GRASP was aimed at improving abdominal DCE-MRI, liver and kidney scans are logically among the main applications. Figure 3 shows exemplary images from a free-breathing GRASP liver exam of an adult patient, which are free from the typical MRI ghosting artifacts for continued respiration. In this reconstruction, 55 spokes were combined into each image, which yields a temporal resolution of 8.8 sec per image volume and fulfills the timing requirements for diagnostic abdominal DCE-MRI. However, a very powerful feature of GRASP is that the same dataset can be reconstructed with different temporal resolution as well.

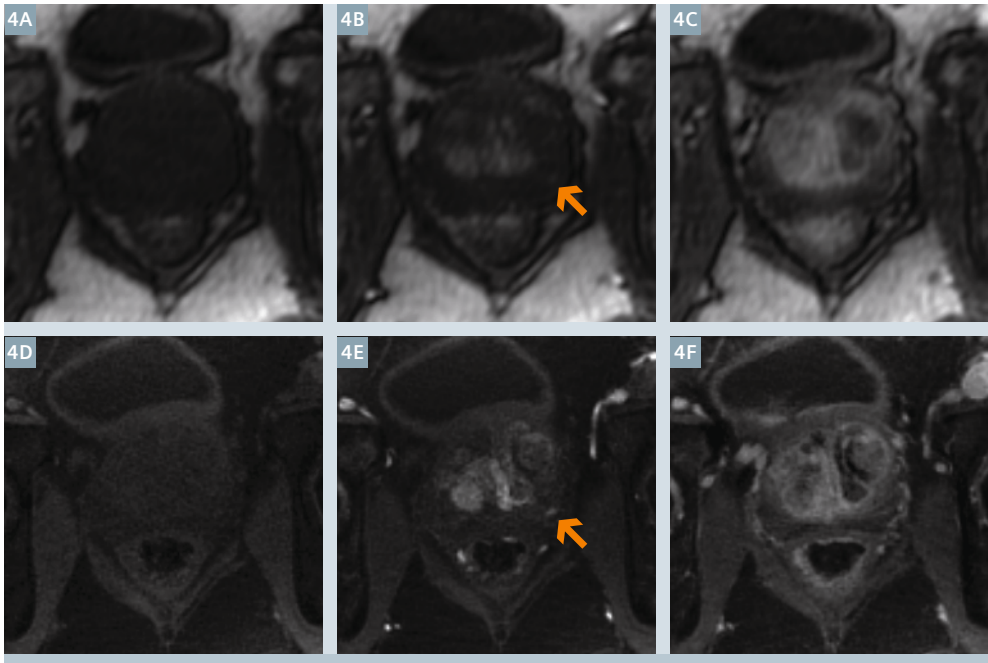
When grouping only 13 spokes into each image, the resulting temporal resolution is 2.1 sec and, thus, fast enough for quantitative tissue-perfusion analysis. Researchers in our group are currently exploring this possibility for assessment of the liver function via dual-input dual-compartment modeling [13] and for assessment of the kidney function via estimation of the glomerular filtration rate (GFR). The key advantage here is that the perfusion information is obtained simultaneously without need for additional contrast injection or scan time. Thus, in the future, the GRASP concept might not only help to make abdominal examinations more robust but also provide new diagnostic measures.

Due to the high scan efficiency and simple workflow, GRASP is also very interesting for dynamic imaging of the prostate [14], which has become the GRASP application with the largest clinical scan volume at our institution. In prostate DCE-MRI, which is also with conventional techniques acquired during free breathing due to the required long readout (to properly capture the contrast washout), the main benefit of using GRASP consists in the higher achievable resolution (both spatially and temporally), which translates into an improved detectability and characterization of small tumors. Figure 4 shows images from our current GRASP protocol with 1.1 x 1.1 x 3.0 mm spatial and 2.2 sec temporal resolution, which represents a significant improvement in comparison to our former protocol and allows more precise assessment of the uptake/washout characteristics of suspicious lesions. In this application, data is acquired over a total duration of 5:38 min while the contrast agent is injected 20 sec after the start of the scan to ensure that sufficient pre-contrast data is available. In addition to the higher resolution, also the motion robustness of GRASP contributes to the achieved improvement in image clarity, as conventional prostate scans are often affected by ghosting artifacts caused by motion of the rectum or adjacent bowel loops.

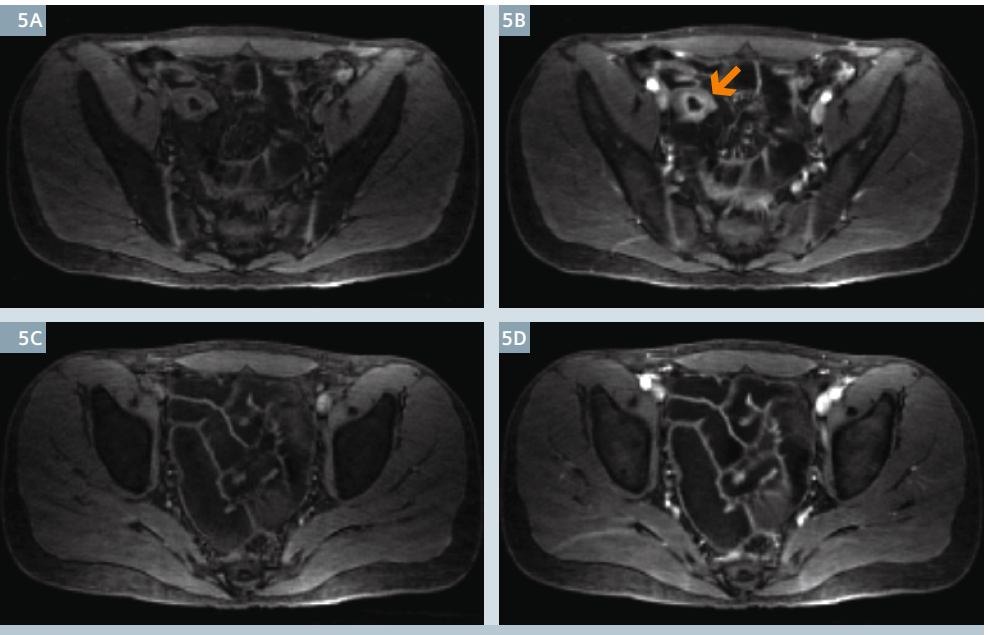
Because GRASP handles such motion effects in a relatively benign manner, our clinical researchers have started



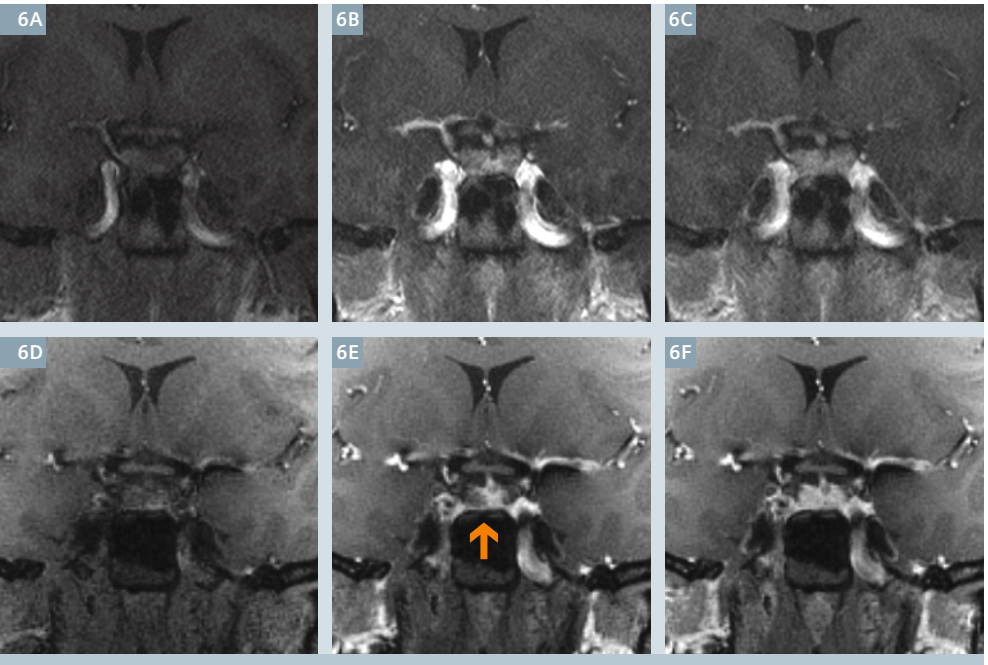
3 Free-breathing dynamic liver GRASP exam in an adult patient. Shown are images of the **(3A)** pre-contrast, **(3B)** arterial, **(3C)** venous, and **(3D)** delayed phase of enhancement. The reconstruction used 55 spokes per frame, corresponding to 8.8 sec per image (spatial resolution 1.5 x 1.5 x 3.0 mm, acquired at 1.5 Tesla).



4 Dynamic prostate exam in a patient on active surveillance using **(4A, B, C)** conventional 3D FLASH with 5.5 sec temporal resolution and **(4D, E, F)** GRASP with 2.2 sec temporal resolution (both acquired at 3 Tesla). Images are shown from **(4A, D)** before the injection, **(4B, E)** the time of contrast arrival, and **(4C, F)** a late phase. Due to the higher spatial resolution (1.1 mm vs. 1.9 mm), a suspicious lesion in the peripheral zone with early enhancement and rapid washout (arrow) is more clearly visible on the GRASP scan. Note that the GRASP acquisition used fat suppression due to the off-resonance behavior of radial k-space sampling [4].



5 Bowel imaging using GRASP in a patient with Crohn's disease (acquired at 1.5 Tesla). Shown are time points **(5A, C)** before and **(5B, D)** shortly after the contrast injection. In the upper images **(5A, B)**, a bowel section with increased wall thickness and mucosal hyperenhancement can be seen (arrow), which indicates active inflammation. For comparison, the lower row **(5C, D)** shows a different slice with normal-appearing bowel sections.



6 Dynamic imaging of the pituitary gland using **(6A, B, C)** a conventional 2D GRE sequence and **(6D, E, F)** GRASP (both acquired at 3 Tesla). Shown are images **(6A, D)** before the injection, **(6B, E)** shortly after contrast arrival, and **(6C, F)** at a later phase. A small area with delayed contrast uptake is visible in the inferior right gland (arrow), which likely reflects a microadenoma. Because of much thinner slices (1 mm vs. 3 mm) and higher overall image quality, such findings are easier to identify with GRASP.

using GRASP also for bowel imaging to investigate inflammatory bowel diseases such as Crohn's disease [15]. Inflamed bowel sections are characterized by increased wall thickness and reduced motility, as well as increased vascularity. Therefore, these bowel sections can be easily identified on GRASP scans, as shown in Figure 5. In addition, signal-enhancement curves can be generated from region-of-interests of the dynamic GRASP images and used to calculate quantitative perfusion measures that have been found to correlate with inflammation [15]. These parameters can potentially be used to non-invasively predict disease progression as well as response to treatments. Again, an advantage is that the perfusion images are obtained together with morphologic information from the same dataset through GRASP reconstruction with variable temporal resolution.

Finally, applications of GRASP are of course not confined to abdominopelvic imaging. GRASP can be used as robust imaging technique for any other dynamic T1-weighted examination as well, and a large portion of our recent GRASP scans are actually done in the head and neck region, including dynamic imaging of the orbits, the neck, and the pituitary gland. In the latter application, it is again the improvement in spatial resolution that makes GRASP attractive. When compared to our previously employed 2D GRE protocol (see Fig. 6), GRASP provides much higher spatial resolution along the slice direction and, thus, makes it easier to accurately localize tiny lesions such as microadenomas or small cysts. The possibility to incorporate also perfusion information into the diagnosis adds to its value [16].

Additional motion compensation

So, is GRASP now the ultimate solution for abdominopelvic DCE-MRI? Unfortunately, not quite yet. Our clinical evaluation showed that free-breathing abdominal GRASP exams work well in many patients with convincing results, but in a certain percentage of patients the image quality is still suboptimal. The problem here is that some patients perform deep respiration in

the moment when the contrast agent is injected, most likely because they are surprised by the sudden onset of the injection and the resulting sensation. Some patients even start to cough, so that the liver and adjacent organs rapidly move up and down by up to 10 cm during the initial circulations of the contrast agent. While GRASP handles moderate motion relatively well, compromised image quality is obtained if the data for each time point is affected by strong inconsistencies due to varying motion states. For example, if during 50% of the spokes the liver was in an end-expiratory position and during the other 50% of the data in an end-inspiratory position, GRASP will not be able to find one reconstruction that is consistent with both of these motion states. As a result, the images show motion blurring and streak artifacts.

However, since GRASP is based on radial sampling, it is possible to apply additional tricks to resolve this situation. Because all of the spokes pass through the center of *k*-space, it is possible to extract a respiration curve from the *k*-space center that indicates how the patient was breathing during the examination [17]. This is possible because the percentage of (dark) lung tissue in the field-of-view changes during respiration, which leads to a modulation of the total signal power. The latter is reflected by the signal intensity at the *k*-space center, which therefore can be used to generate the respiration curve. Once it is known from the curve what the respiratory state for each acquired spoke was, the data can be sorted according to the respiratory state and the GRASP reconstruction can be extended to treat the respiratory state as an extra dimension, which allows freezing the respiration in the reconstructed images [18]. This extended approach, which we call XD-GRASP[1], is still under active development and accompanied by a further increase of the computational complexity. However, as shown in Figure 7, initial results look promising and we are convinced that the motion-compensated XD-GRASP approach is a leap towards the future of abdominopelvic DCE-MRI, soon delivering 100% reliability in every patient and at every imaging center, regardless of the patient's cooperation and regardless of the operator's training level.

Conclusion

GRASP is a new concept to simplify DCE-MRI exams by acquiring all information using a single continuous scan instead of several individual scans, which eliminates the possibility of timing or synchronization mistakes. Because GRASP is based on radial sampling, acquisitions can be performed during free breathing, thus making abdominal DCE-MRI accessible for patients unable hold breath. Sufficiently high acquisition speed is achieved by synergistically combining the compressed-sensing and parallel-imaging principles. Due to use of the golden-angle scheme, the temporal resolution and desired image time points can selected retrospectively, which enables reconstructing both morphologic and perfusion information from the same exam. GRASP has already been tested in thousands of patient exams in our routine practice, making it one of the first compressed-sensing techniques that have been evaluated on a large scale for clinical feasibility. While results are convincing for patients with regular breathing activity, limitations still exist for those patients performing deep respiration/coughing during the injection. This remaining issue is now being addressed by integrating active motion compensation based on the radial self-navigation principle.

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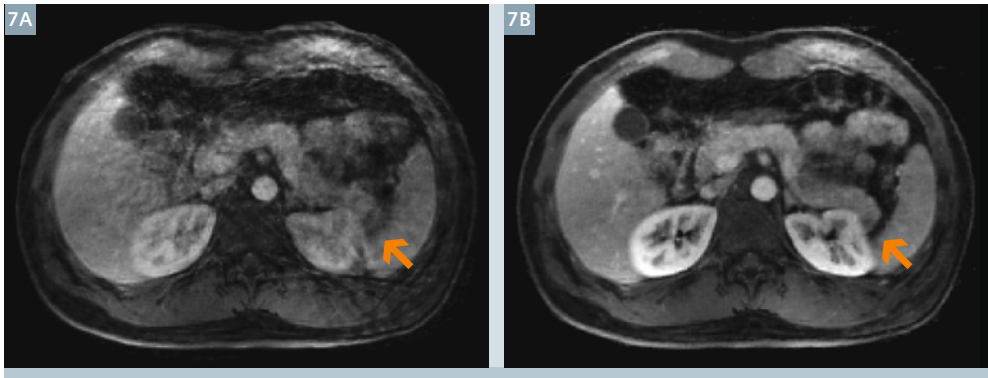

7 GRASP liver exam of a patient breathing deeply after the injection. Due to the inconsistent motion state of the acquired data, the normal GRASP reconstruction **(7A)** is affected by streak artifacts and motion blurring (arrow). These artifacts are clearly reduced when employing XD-GRASP with additional motion compensation **(7B)**.

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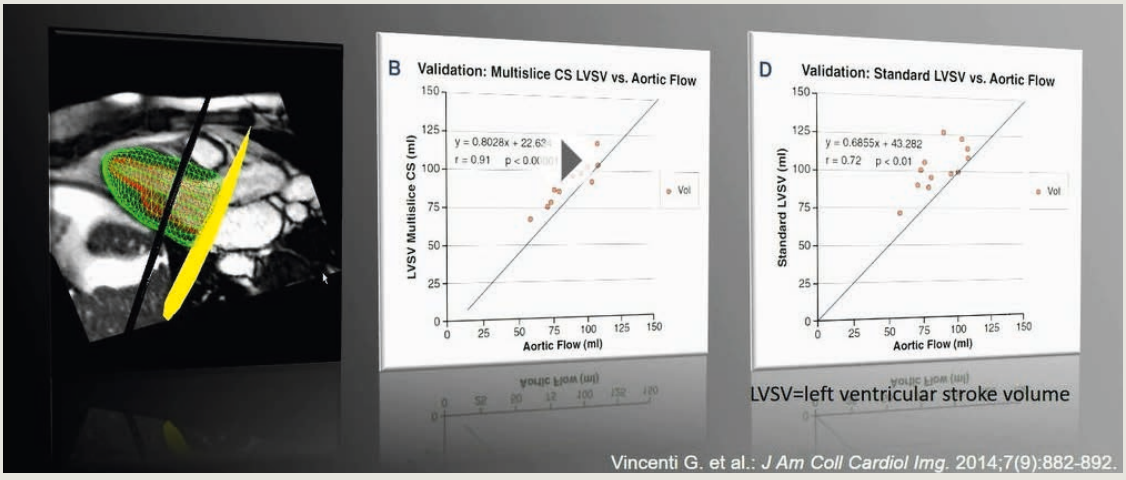

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