Fast Abdominal Magnetic Resonance Imaging

Schnelle Abdomenbildgebung in der Magnetresonanztomografie

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Abstract

Abdominal imaging is the driving force that necessitates the development of numerous techniques for accelerated image acquisition in magnetic resonance imaging (MRI). Today, numerous techniques are available that enable rapid, high spatial resolution acquisition for both T1 and T2 weighted images. These techniques open new opportunities in the detection and classification of numerous pathologies in the abdomen. However, there is still ongoing progress in the development of fast and ultrafast sequences and promising techniques are currently close to clinical application. With these 4D-technologies, MRI is becoming the central imaging modality for dynamic, motion-compensated imaging of the parenchymal abdominal organs such as liver, pancreas and kidney.

Key points:
- Fast imaging techniques are especially valuable in the upper abdomen, as this region is particularly affected by respiratory motion.
- Parallel imaging and k-space-based acceleration techniques are the basic components of fast 3 D sequences.
- By further accelerating 3 D imaging with high spatial resolution, 4 D techniques become available.

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Zusammenfassung

Die abdominelle Bildgebung ist die treibende Kraft für zahlreiche Techniken und Entwicklungen, die über unterschiedliche Ansätze eine Beschleunigung der Bildakquisition in der Magnetresonanztomografie (MRT) bewirken. Heute stehen für T1- und T2-Kontrast zahlreiche Techniken für die schnelle, räumlich hochaufgelöste Bildaufnahme zur Verfügung. Durch sie eröffnen sich für die MRT neue Möglichkeiten in der Detektion und Klassifikation verschiedenster Pathologien. Gleichzeitig ist die Entwicklung dieser Techniken nicht abgeschlossen und vielversprechende Techniken stehen auch aktuell wieder kurz vor der breiten klinischen Anwendung. Durch diese 4D-Technologien positioniert sich die MRT als das zentrale Verfahren für die dynamische, bewegungskompensierte Bildgebung parenchymatöser Organe wie Leber, Pankreas und Niere.

Introduction

In the last three decades, magnetic resonance imaging (MRI) has become one of the primary clinical imaging methods. Its unmatched soft tissue contrast makes it the diagnostic method of choice in a variety of issues, thus fundamentally revolutionizing diagnostic procedure with respect to numerous diseases. Unlike X-ray-based imaging technologies, MRI is considered uncritical with respect to patient load in cases of repeated examination. Since the widespread introduction of MRI in clinical practice, consequential or late complications have not been observed and are considered to be unlikely on the whole. As with every imaging method, MRI is subject to the conflict between acquired information and the time required to acquire such information; a longer acquisition time can provide more information. Whereas during examination of non-moved body regions, the examination time is of secondary consideration in certain contexts, the time component during examination of organs displaced

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by respiration or other movable organs is a primary variable which supersedes other parameters such as spatial resolution, etc. Although acquisition times of a few minutes during head or joint examinations are less problematic on the whole, signal acquisition during examinations of the upper abdominal organs must normally be obtained in a few seconds. The position of upper abdominal organs, particularly the liver, varies by several centimeters during the course of one respiratory cycle. During typical sequencing, the time available for signal acquisition corresponds to the period during which patients can hold their breath. Rapid image acquisition is also required for patients, who for specific reasons can lie still only briefly, e. g. due to pain, gerontopsychiatric reasons, or in the case of pediatric patients [1]. In addition to movements due to respiration and patient activity, the motion of the organs themselves require rapid image acquisition – cardiac imaging is the best example of this. Likewise, effects in the abdominal area such as intestinal motility can make rapid imaging necessary [2]. Acquisition during a single holding of the breath is a basic prerequisite for an abdominal MRI with respect to imaging speed. For many clinical issues, an even more rapid image capture is desirable, for example when recording the dynamics of contrast agent distribution in tissue [3] or using imaging to assess the effect of antiangiogenic tumor therapies [4]. This article provides an overview of the various techniques, strategies and developments that support rapid image acquisition during abdominal MRI.

Clinical High-field MRI and basic Sequencing Technology

In MRI the signal-noise ratio (SNR) represents a parameter for image acquisition quality. The SNR defines the extent to which actual information and background noise can be differentiated based on the measured and processed signal. As with every measuring method, valid interpretation in MRI is possible only after achieving a defined signal-noise ratio as a function of the examination requirements (e. g. spatial resolution). With respect to most measuring procedures, prolongation of the measurement time with averaging of the recorded values also increases the SNR in MRI. As already mentioned, the recording time in abdominal MRI cannot be extended as desired. Thus, increasing the signal or SNR has to be achieved by optimizing additional factors influencing the signal-noise ratio. One possibility for MRI is increasing the static magnetic field (B_O). Whereas in MRI the measured signal increases proportionally to the square of the strength of B_O, image noise increases only in linear proportion to the strength of B_O. With the introduction of clinical 3-T systems at the start of this century, twice the signal-noise ratio was (theoretically) available compared to 1.5-T systems, although numerous technical difficulties had to be overcome in order to realize the benefit of the theoretical SNR advantage in routine clinical practice [5]. Increasing B_O strength is a foundation for other advancements which, either directly or indirectly, can be employed to speed up image acquisition.

A number of techniques have been developed to achieve optimum SNR yield based on an ideal combination of pulse sequence, k-space filling and image reconstruction. The two most widely-used rapid sequencing technologies employed in routine clinical practice for image acquisition with T1 and T2 contrast are presented here as examples.

T1-weighted Sequences

T1-weighted sequences of the abdomen represent a cornerstone in the assessment of abdominal pathologies [6]. Typically, T1-weighted sequences are acquired dynamically with fat signal suppression at different time points after administration of an intravenous contrast medium. The sequences used for this are based on gradient recalled echo (GRE). Compared to spin echo sequences, no additional radio frequency pulses are used, instead only phasing and dephasing gradients are applied to generate the signal [7]. Omitting the time-intensive 180° refocusing pulse translates into shorter repetition times resulting in more rapid acquisition while emphasizing the (desirable) T1 contrast. However, short repetition times make spoiling techniques necessary in order to cancel remaining transverse magnetization at the start of a new sequence cycle. RF spoiling, i. e. cancelation of transversal magnetization by selectively changing the RF pulse has largely been accepted as a technique [8]. Gradient recalled echo can be employed for both 2 D and 3 D sequences. The advantages of 3 D sequences with respect to abdominal imaging lie in the possibility of quickly acquiring high-resolution isotropic data sets with a high SNR. The result is that RF-spoiled GRE-3 D sequences can be found in the sequence portfolio of all equipment manufacturers (**Table 1**).

In order to speed up the already comparatively rapid GRE technique, these sequences are combined with time-efficient utilization of the k-space. Measured MR signals are collected in the k-space arranged in a matrix [9]. The data matrix of the k-space is used to reconstruct the actual image based on the mathematical Fourier transform method [10]. Typically, filling the data rows in the k-space requires repetitions of the pulse sequence with varying phase encoding. Correspondingly, it stands to reason that techniques providing efficient filling of data points in the k-space have been developed. One of these measures which further accelerates the entire image acquisition is not to examine all k-space data points, but rather to leave specific "gaps" in the k-space matrix (undersampling).

After "translation" by the Fourier transform, the boundary areas of the k-space matrix corresponding to local frequencies result in the detail information of the reconstructed image. Completely filling these regions requires time-consuming phase encoding; at the same time the signal in the boundary areas of the k -spaces is typically very low. Likewise, specifically omitting these boundary regions appears to be useful. Since simply leaving data points empty in the

Table 1 Vendor-specific sequence acronyms.

	GRE	Ultrafast SE	View-Sharing	SENSE
GE	LAVA	SS-FSE	TRICKS	ASSET
Hitachi	TIGRE	SS-FSE	–	RAPID
Philips	THRIVE	SS-TSE	4D-TRAK	SENSE
Siemens	VIBE	HASTE	TWIST	mSENSE
Toshiba	QUICK 3 D	FASE	–	SPEEDER

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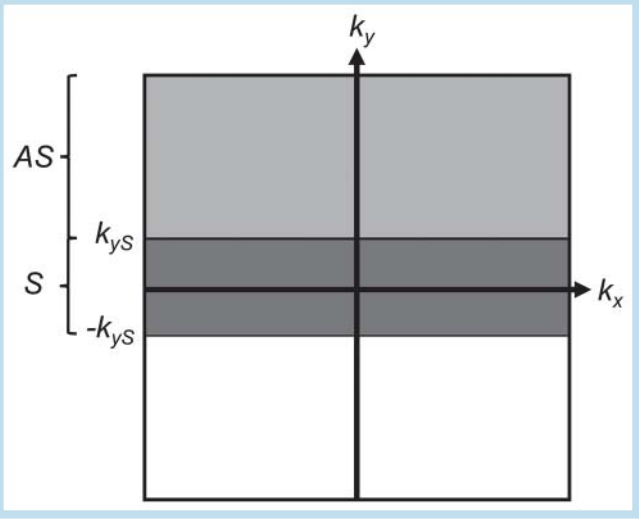

Fig. 1 Schematic diagram of a partial Fourier technique. Only central k-space is acquired symmetrically (S, from kYS to -kYS, dark grey), whereas the other parts of k-space are sampled asymmetrically (AS, grey area) and reconstructed based on prior knowledge on k-space symmetry.

boundary area of the Fourier transform results in artifacts, in standard GRE sequences with incomplete k-space filling, the "omitted" data points are filled with zeroes [11]. A further characteristic of the k-space is its symmetrical structure, since its center functions as a notional "mirror point" (so-called Hermitian symmetry). Theoretically, at least, inclusion of half of the k-space suffices to calculate the data points of the other half of the k-space. In practical application, phase errors during acquisition lead to imperfect symmetry. Reasons for this include minor movements during acquisition, B_O inhomogeneity, physical differences in coil sensitivity or susceptibility effects. In order to offset this, somewhat more than half of the k-space (typically around 60 %) is acquired in clinical 3 D GRE sequences. The additional acquired data points are used to correct phase errors in order to increase the validity of the calculation of the remaining data points based on k-space (**Fig. 1**).

3 D GRE sequences with incomplete asymmetrical k-space filling are currently the clinical standard in abdominal imaging. In the upper abdomen in particular, they allow generation of spatial high-resolution data sets during a breath-hold period, typically prior to administration of contrast agent and multiply in a brief time sequence afterward. The information thus obtained regarding morphology and vascularization contributes significantly to the detection and classification of abdominal pathologies [6, 12].

T2-weighted Sequences

T2-weighted sequences are essential for the differential diagnosis of numerous pathologies in abdominal imaging. Standard spin echo sequences generate a signal via the sequence of excitation pulse, relaxation pulse and signal selection. The k-space is filled line-by-line via a change in phase encoding between each repetition; a repetition of this sequence is required for each line. Additional long repetition times (time between excitation pulses) are required for T2-weighting. To counteract this, after the initial excitation pulse, rapid spin echo sequences use a series of 180° relaxation pulses each with a different upstream phase encoding gradient in order to fill more lines of the k-space within a repetition period. Compared to conventional spin echo sequences, the repetition times are somewhat longer, which on the whole has a beneficial effect on T2 contrast. The sequence of spin echoes generated by the relaxation pulses is called echo train. Ultrafast spin echo sequences expand this concept further, so that after a single excitation pulse, a sufficient number of relaxation pulses are produced to completely fill the k-space (single-shot technique). Since the excitation pulse is not repeated in this case, the repetition time is "interminably" long.

In fat tissue, adjacent protons exhibit interaction, called J-J effect or J-coupling. In conventional spin echo sequences, J-coupling, which particularly occurs in typical T2 echo times of 60 – 80 ms, results in local signal reduction, corresponding to a reduced fat signal. During fast and ultrafast spin echo sequences the 180°pulses transmitted in rapid succession largely eliminate J-coupling, and fat tissue appears correspondingly more hyperintense compared to conventional spin echo sequences.

Use of energy-rich 180° pulses leads to significant tissue warming. Correspondingly, the prescribed limits for the specific absorption rate (SAR) during ultrafast turbine spin echo sequences are quickly reached – particularly for 3 T. Reduction of the flip angle of the RF pulse to below 180° would lead to a reduction of the SAR; the result, however would be the occurrence of a pseudo-ready state with a correspondingly significant reduction of the SNR. To counter this problem, various SAR reduction techniques were developed which have limited effects on SNR. One approach is the use of variable flip angles selected in the course of the echo train to achieve the best-possible compromise between SAR reduction and SNR. A further technique is to use an asymmetrical pulse series at a 180° angle which results in a hyperecho, i. e. a strong echo signal in the echo train of an ultrafast turbine spin echo sequence [13]. In general, these techniques are susceptible to B_1 inhomogeneity and strongly benefit from methods supporting B_1 homogenization such as parallel transmit procedures.

As already described in the section on gradient echo sequences and T1 contrast, these ultrafast spin echo sequences can likewise be combined with time-efficient k-space techniques. In one widely-used technique, the echo train is changed such that only a little more than half the k-space is filled. Prior knowledge of the symmetry of the k-space (which in the case of spin echo sequences is almost perfect, thus requiring no phase correction) is then used to reconstruct the absent data points using the acquired data [14]. Combining ultrafast spin echo sequences with this partial Fourier technique thus allows rapid acquisition of heavily T2-weighted images. Corresponding sequences have been implemented by all equipment manufacturers (**Table 1**). In principle, ultrafast turbine spin echo sequences can be combined with breath triggering techniques. During acquisition and breath holding times in the 10 s range, breath triggering appears to be of reduced significance in this context.

Although these techniques have been available for decades, they continuously benefit from innovations and improvements in scanner hardware. The latest generation of devices offer technologies which produce diagnostically high-quality T2-weighted images with the shortest acquisition time [1].

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Keyhole and View-sharing Techniques

Keyhole and view-sharing techniques are methods originally developed for rapid acquisition of dynamic MR angiographic images, requiring a temporal resolution of 1 – 2 acquisitions per second. The following will briefly describe the basic principles of view-sharing technique, their application in MR angiography, as well as illuminate details of technical aspects. Reference is made to the extensive work of Hadizadeh et al. [15].

Keyhole and view-sharing techniques utilize the structure of k-space to use recorded data points repeatedly for image reconstruction. Typically k-space is virtually divided into two regions, a central and peripheral region. As described above, after the Fourier transform, the central components of the k-space translate into image contrast information, whereas the peripheral components provide detail information. For various clinical issues, the change of image contrast after administration of contrast agent provides the essential information which changes rapidly in the course of time and which must be correspondingly quickly reproduced. In comparison, image detail information typically remains largely constant during the image acquisition time. In the standard keyhole technique, the entire k-space is initially recorded and an image is reconstructed in a known manner. In order to record the changes in image contrast in rapid succession, only the data points of the central k-space are repeatedly acquired. These are then combined with the previously acquired peripheral region data, and the k-space recorded in these two separate steps is used for image reconstruction (**Fig. 2**) [16]. The limited k-space section can be recorded in less time, thus increasing the temporal resolution compared to repeated recording of the entire k-space. This underlying technique forms the basis for various further developments with this common feature: different parts of the k-space are acquired at varying temporal frequencies and are combined to reconstruct high-resolution images. Commercially-available view-sharing sequences based on 3 D technology divide k-space into an oval/ovoid central region with data points that are more frequently completely acquired, as well as a peripheral region. The peripheral region is either recorded anew after multiple complete acquisitions of the central region (e. g. TRAK, Phillips) and then further subdivided into sub-regions which then are filled alternately with the central region (e. g. TRICKS, GE), or recorded alternately with the central region only with reduced density (e. g. TWIST, Siemens, for an overview see **Table 1**, **Fig. 2**).

Parallel Imaging

Parallel imaging (PI) has been one of the most significant developments in MR imaging in the past decade. It relies on simultaneous recording of the magnetic resonance signal using several receiver coils generally placed on the body arrayed in a row. Thus it is possible to perform spatial encoding in the MRI in part using the different sensitivity profiles of the coils. Reduction of phase encoding steps is a fundamental principle of acquisition acceleration in parallel imaging. In doing so, the extent of sampling in the k-space remains unchanged while the sampling density is reduced line-by-line. The spatial information lost by undersampling is then reconstructed using the spatial information contained by the different reception sensitivities of the receiver coils. In parallel imaging, signal reception consists of a combination of gradient and sensitivity encoding, i. e. only a portion of spatial encoding is realized using reception an-

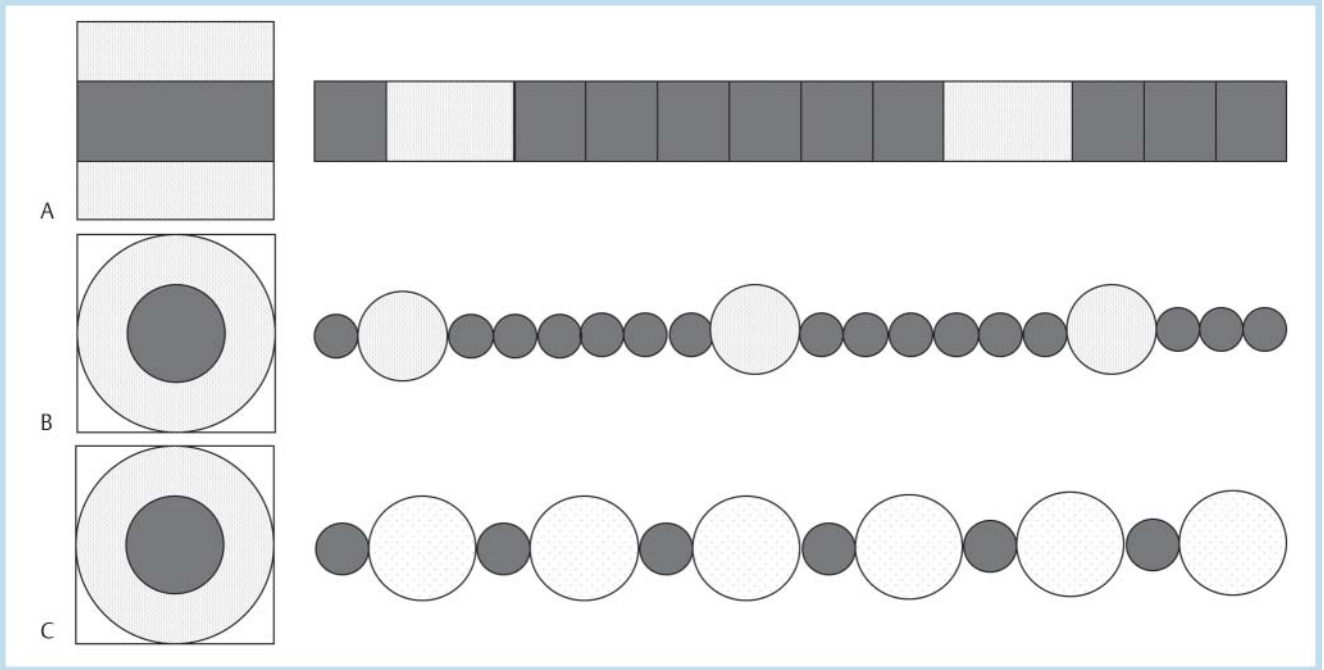

Fig. 2 Diagram of different view-sharing techniques. **A** Keyhole with frequent acquisition of central k-space region, the peripheral space is refreshed only after 6 updates of the central part. **B** 3D-implemenation with ovoid acquisition. **C** Alternating acquisition of undersampled peripheral and fully-sampled central k-space.

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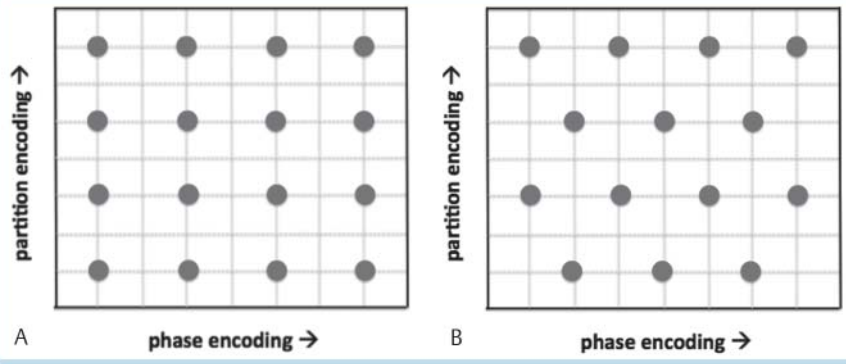

Fig. 3 Two-dimensional undersampling. Undersampling without (as in conventional parallel imaging, left) and with (as in CAIPIRINHA, right) offset, grid-like arrangement of phase-encoding steps.

tennas operated in parallel, while the rest uses conventional gradient encoding. Because of this, parallel imaging is sometimes called partial parallel acquisition (PPA). During PPA a distinction is made between k-space-based and image space-based parallel imaging techniques. In image space-based techniques, such as SENSE, data recorded using a certain degree of undersampling of the individual array elements are first Fourier transformed, then reconstructed [17]. The underlying principle of all k-space PI techniques is compensation for the effect of undersampling through the use of sensitivity data remaining in the k-space and reconstructing a complete k-space which can then be Fourier transformed in the usual way. One of the best-known and widespread representatives of k-space-based technique is GRAPPA (Generalized Autocalibrating Partially Parallel Acquisitions) introduced by Griswold et al. [18]. Actually, SMASH is the underlying technique of k-space-based PI; however it extremely sensitive to changes in the coil position. With GRAPPA, the coil sensitivity profile is recorded during the scan using a few additional fully-recorded central k-space lines which makes the technique more robust with respect to movement artifacts. In the case of time-resolved applications, this results in a noticeable loss of time, unless it is acquired once at the beginning (external reference scan). SENSE offers the disadvantage of a needing a separately acquired coil sensitivity scan that is also sensitive to repositioning (which is why TSENSE is better used for cardiac MRI, for example).

GRAPPA and SENSE typically speed up acquisition through one-dimensional undersampling (in the phase encoding direction). However, it is possible to perform two-dimensional acceleration. This means that undersampling is present in both the phase encoding and slice encoding direction. However, conventional techniques in the abdomen are limited to the extent that the sensitivity profiles of the individual receiver coils differ too little in the slice encoding direction, thus leading to imperfect reconstruction with remaining aliasing artifacts.

An advanced two-dimensional procedure, CAIPIRINHA (Controlled Aliasing In Parallel Imaging Results In Higher Acceleration Factor), has been recently discussed [19]. Similar to other procedures such as 2 D SENSE [20], CAIPIRINHA employs two-dimensional undersampling in the phase encoding and slice encoding direction. However, by using modified radiofrequency pulses similar to Hadamard pulses, displacement of every other phase encoding step is induced in one direction (**Fig. 3**). In this way, aliasing artifacts can be specifically generated during data acquisition. These artifacts can be manipulated to obtain improved spatial mapping, thus enabling improved multi-slice and 3 D volume acquisition [19, 21]. A few recently published studies demonstrated that using CAIPIRINHA when acquiring 3 D GRE sequences in the abdomen resulted in significantly reduced acquisition time, and thus an improvement of image quality through reduction of breath artifacts [22 – 25].

Dynamic 4 D Imaging with Cartesian Selection Technique

Recently the trend in abdominal imaging is to use high-quality 3 D sequences with high temporal resolution (4th dimension). These 4 D techniques typically combine various existing methods for static and dynamic acceleration.

Potential advantages of 4 D techniques include:

- Assurance of acquisition of a perfect arterial, late arterial and portal venous phase.
- Analysis of dynamic contrast agent behavior of lesions
- Perfusion quantification, e. g. for assessing arterial and portal venous perfusion before and after TIPSS
- Time-resolved movement analysis of highly motile structures such as the stomach wall or duodenal colon to better determine space consumption.

The following section discusses the CAIPIRINHA-Dixon-TWIST (CDT) volume-interpolated breath-hold examination (VIBE) sequence, an example of a high-end sequence used for rapid abdominal imaging that combines previously-known techniques [26]. The basis for this sequence is an RF-spoiled 3 D GRE sequence with incomplete interpolated k-space filling, combined with a parallel imaging technique with a fourfold acceleration factor. View-sharing is additionally used in the sequence as well as the Dixon fat suppression technique. Using this method, during an acquisition time of e. g. 29 seconds, 14 high-resolution data sets can be acquired with a slice resolution of $1.2 \times 1.2\,mm^2$ and a thickness of 3 mm. For example, the entire time frame of contrast agent influx in the liver parenchyma can be imaged, from the start of the injection, through the arterial phase and finally to the portal venous or venous phase (**Fig. 4**). Thus, even without patient-specific circulation time measurement, it can be ascertained that at least one data set is available with ideal arterial opacification [27]. This is particularly advantageous in the detection of hyper-

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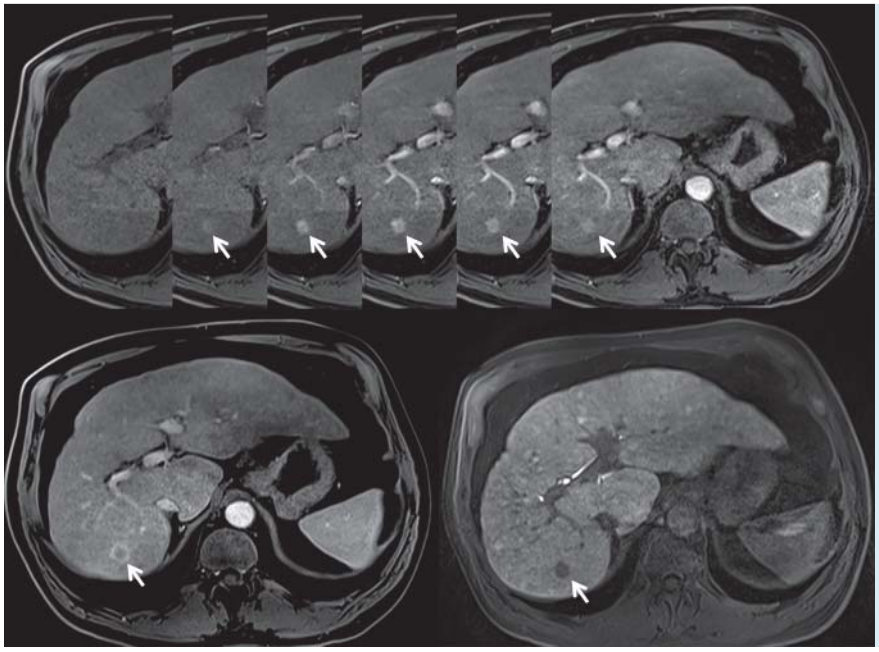

Fig. 4 Example of a CDT-VIBE-sequence acquired during contrast media injection with a temporal resolution of 2.8 s per dataset (top row). Contrast inflow as well as a hypervascularized liver lesion in a patient with chronic hepatitis C are clearly shown. During portal-venous (bottom left) and hepatobiliary phase (bottom right), a sequence with CAIPIRINHA acceleration and Dixon fat saturation is used (acquisition time 10 s). The lesion shows early washout in portal-venous and hypoattenuation in hepatobiliary phase. Histology revealed a hepatocellular carcinoma.

vascularized lesions, which stand out from the rest of the liver parenchyma only during a short time window [28].

Radial Selection Method and Compressed Sensing

Despite the introduction of new parallel imaging procedures and resulting increased speed of sequences, breath artifacts still pose an obstacle during the dynamic examination of the abdomen. Studies by Lee et al. and Krinsky et al. have demonstrated that 7 % of patients registered for an MRI examination of the liver could not hold their breath for 15 seconds [29, 30]. In particular, children, older patients or those with comorbidities such as ascites, pneumonia or cardiac insufficiency may sometimes fail to adequately follow the breath commands.

The Cartesian k-space selection method, usually used for dynamic 3 D GRE sequences, is relatively sensitive to breath movement. In this case, data sampling is performed in the k-space along parallel lines that typically exhibit a fixed phase difference. If the object being examined moves during the examination, phase offsets are generated which negatively influence the phase encoding process. Graphically, movement of the body produces fluttering of the parallel k-space lines resulting in gaps in the k-space coverage, thus leading to the familiar misregistration artifacts after image reconstruction.

Non-Cartesian imaging techniques offer advantages when acquiring images of moving objects. During the radial k-space selection method, data sampling runs along rotating spokes that cross one another in the center of the k-space (**Fig. 5**) [31, 32]. This cross-over in the k-space avoids gaps in k-space coverage, and therefore avoids misregistration artifacts, even if the examined object moves. Instead, streak artifacts result from this technique. On the whole, they are considered minor compared to the influence of artifacts on the image quality resulting from Cartesian methods. The radial selection method is thus unaffected by breath movements, thereby allowing robust and high-quality imaging even during free breathing. However, this method requires significantly longer measuring times than the Cartesian technique. Without additional acceleration methods (see below) it achieves measuring times of about 60 seconds for a volume data set, thereby making dynamic abdominal imaging impossible.

Compressed sensing (CS) is a further strategy to accelerate data acquisition during dynamic 4 D MRI, and is based on utilizing redundancies in the MRI images [33 – 35]. Three conditions must be met for this:

1. The data has to be “sparse”, i. e. can be represented using few coefficients.
2. The data must be recorded uncorrelated, e. g. not every second line in the k space needs to be picked up, as is the case with parallel imaging.
3. At the end, the data is iteratively reconstructed, without using conventional Fourier transformation.

Since the data must be recorded without correlation, radial measurements are more suitable than Cartesian data, since radial selection results in noisy artifacts (incoherent aliasing), which are highly suitable for CS. The combination of radial selection technique and CS enables acquisition of data sets during free breathing with such high temporal resolution that dynamic imaging is possible. The underlying principle of this technique is continuous data acquisition during the entire wash-in and wash-out of the contrast medium, rather than performing individual scans for the different contrast phases (**Fig. 6**). The images are then reconstructed retrospectively from this data set. This occurs with a freely-selectable temporal resolution while a different number of acquired k-space spokes within one time frame are summarized [36, 37]. This concept could lead to a significant simplification of the clinical workflow. Since data are acquired during the entire examination, determining circulation time is no longer necessary. Furthermore, through the free selection of time periods during the retrospective reconstruction, it is possible to generate any desired con-

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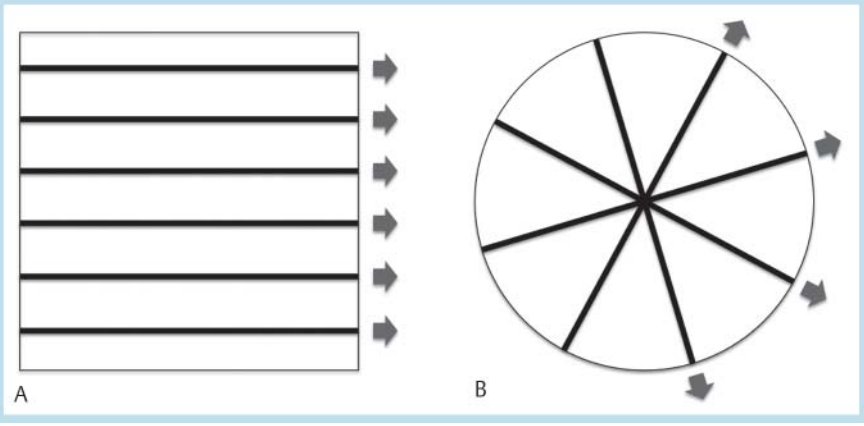

Fig. 5 **A** Cartesian acquisition **B**: radial acquisition with rotating spoke-like sampling, spokes crossing in center of the k-space.

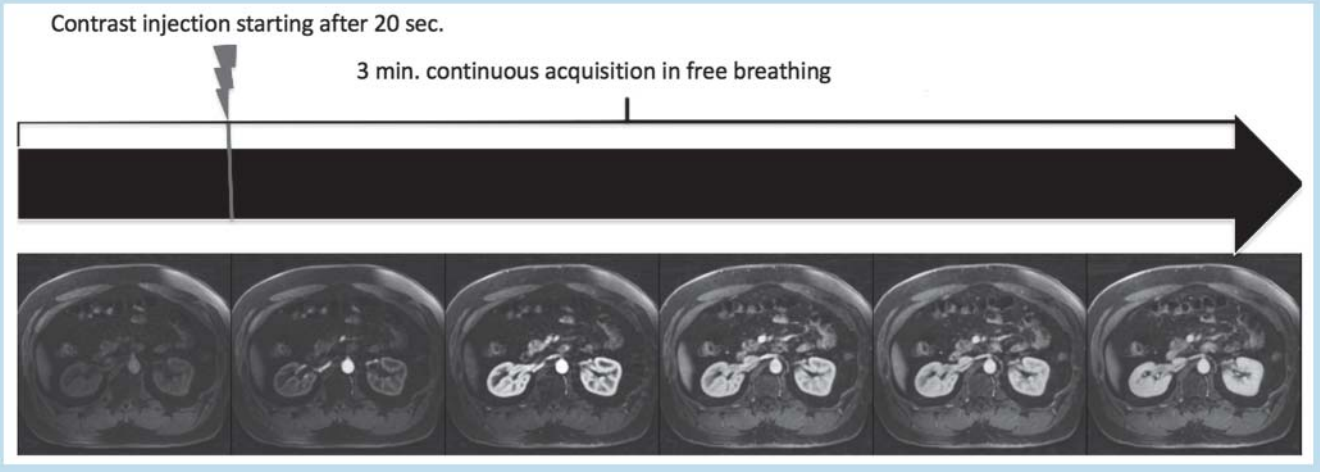

Fig. 6 Example of a radial acquisition scheme combined with compressed sensing techniques. Data acquisition is performed continuously under free breathing. Image reconstruction is performed afterwards with customizable temporal resolution.

trast agent phase as an individual data set. This avoids missing the contrast agent bolus. Since the data are acquired during free breathing, breath commands are no longer necessary, thus improving patient comfort.

Conclusions

Today there are numerous techniques for acquiring rapid, spatially high-resolution images. Various procedures and methods are related to different steps of the acquisition process and can thus be combined to further accelerate image acquisition. These rapid acquisition techniques present new possibilities for MRI to detect and classify various pathologies. Likewise, development of these techniques is not finished, and promising new procedures are currently on the verge of widespread clinical application. In particular, patients who, for various reasons, can hold their breath for only short periods, such as very ill or pediatric patients, can benefit from these techniques. In addition, rapid acquisition enables the recording of dynamic contrast changes in the parenchyma of the upper abdominal organs, which has much to offer, particularly with respect to contrast-enhanced examinations. These 4 D technologies position MRI as the primary procedure for dynamic, movement-compensated imaging of parenchymatous organs such as the liver, pancreas and kidneys.

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