Challenges and Clinical Value of Automated and Patient-Specific Dynamically Timed Contrast-Enhanced Liver MRI Examination

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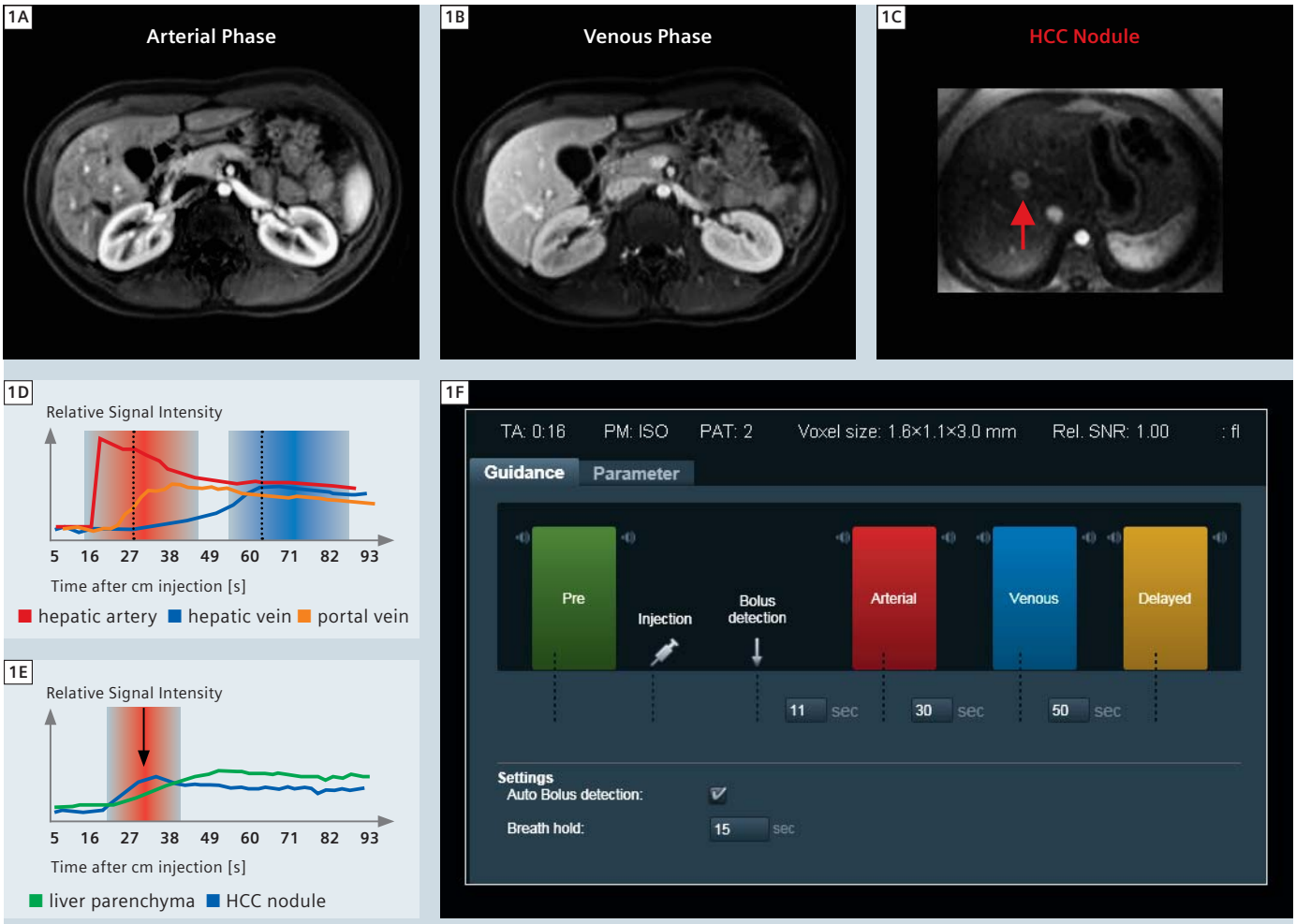
It has been widely accepted that optimal capture of multi-phase (dynamic) contrast media enhanced (DCE) liver images are an important and often critical component to diagnostically optimized MRI examination [1-8]. Especially the arterial-phase images are frequently a unique additional marker for differentiating characteristics of benign, malignant, primary and metastatic liver tumors [3, 4, 8, 9]; also it is known that arterial-phase images do help to analyze active hepatitis in the setting of acute and chronic liver diseases [5, 10]. In this article we describe the technical and clinical requirements for optimized DCE liver imaging and how our developments for patient-adopted scanning help to overcome some of the limitations in clinical routine. And finally, a short outlook on the further implementations of these developments for DCE liver MRI is provided.

The technical requirement for capturing the critical arterial-phase is defined by the dynamic imaging point where there is a maximal image contrast between arterial-enhancing liver lesions and the surrounding liver parenchyma. The commencement and duration of this arterial window however depends greatly on subject-specific vascular transit times. Therefore it is essential to understand the relationship between the contrast enhancement behavior of the liver vessels, parenchyma and liver pathologies and to adopt these requirements to DCE liver MRI. In figure 1A detailed analysis of the signal intensity (SI) time curves, optimal timing of the DCE phases and exemplary SI time curve of an arterialized tumor (HCC nodule) is displayed. Figures 2–4 show the relevance of optimal timing of the DCE liver MR exam in selected cases. In each patient scan presented there is transient important diagnostic information that can only be captured during a narrow time window related to the arterial phase. Based on our observations derived from a large patient cohort, approximately 30% of our patients show a large variation of vascular transit times from the mean population. While imaging the diagnostically important arterial-phase depends upon capture of a transient period that spans approximately 10 seconds in most cases, the time-window for capture of the venous and late phases are relatively broader and therefore less error-prone. Therefore, adoption of a patient specific dynamically timed arterial phase DCE liver MRI technique is essential for reproducible optimal diagnostic images. However, in a clinical setting, DCE liver MRI is very often performed with rigid and therefore sub-optimal timing delays between initiating the contrast infusion and initiating the image acquisitions.

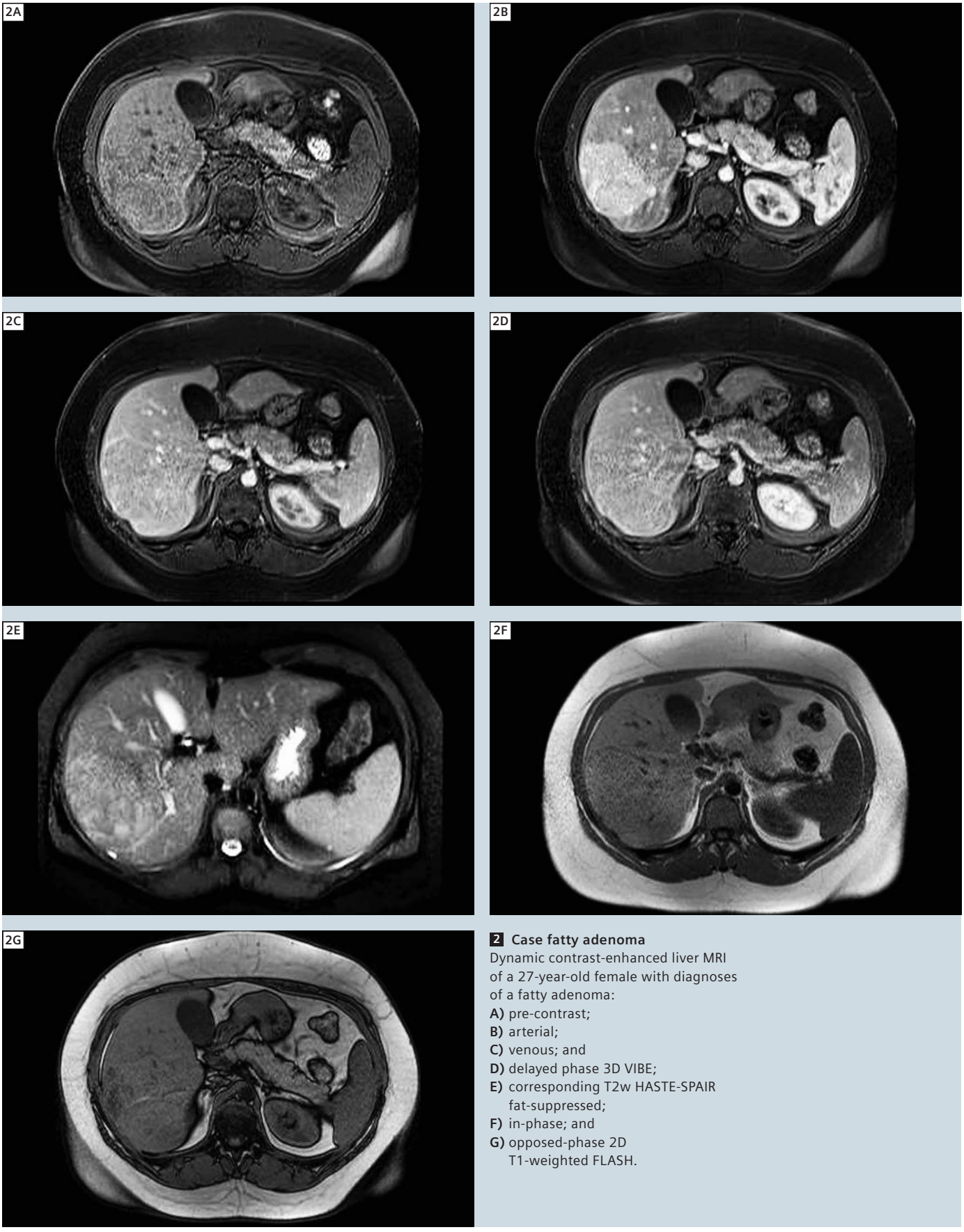
Individually-tailored timing for the phases of DCE liver MRI has been suggested for optimized arterial phase imaging. This can be achieved by applying a test bolus for calculation of circulation time [3], or tracking bolus arrival in the descending aorta using real-time image acquisition [11]. To further simplify the arterial-phase timing calculations, this imaging step can be incorporated into the arterial phase acquisition by applying a real-time bolus tracking methodology similar to the strategy employed for contrast enhanced MR angiography [11–14]. A real-time contrast bolus-triggering methodology for liver offers technical simplification and speed as compared to pre-scan test bolus techniques. In addition to accounting for differences in the vascular transit times between patients, adjustments of the optimal time-point for read-out of the central k-space data must be taken into consideration when using gradient echo technique, such as VIBE. Sequence parameters that affect the peak central k-space acquisition timing include use of centric versus non-centric k-space sampling schemes, but also include field-of-view, resolution, breath-hold duration, and number of slices.

Until now, the usage of bolus-tracking sequences has not been in widespread use for dynamic liver imaging because of the complexity of patient-specific DCE



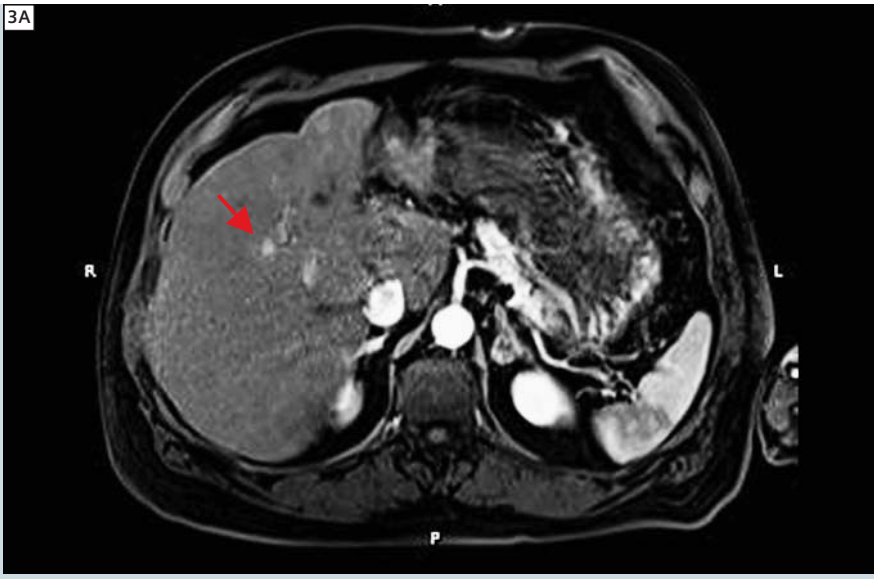
1 Patient-specific DCE liver MRI

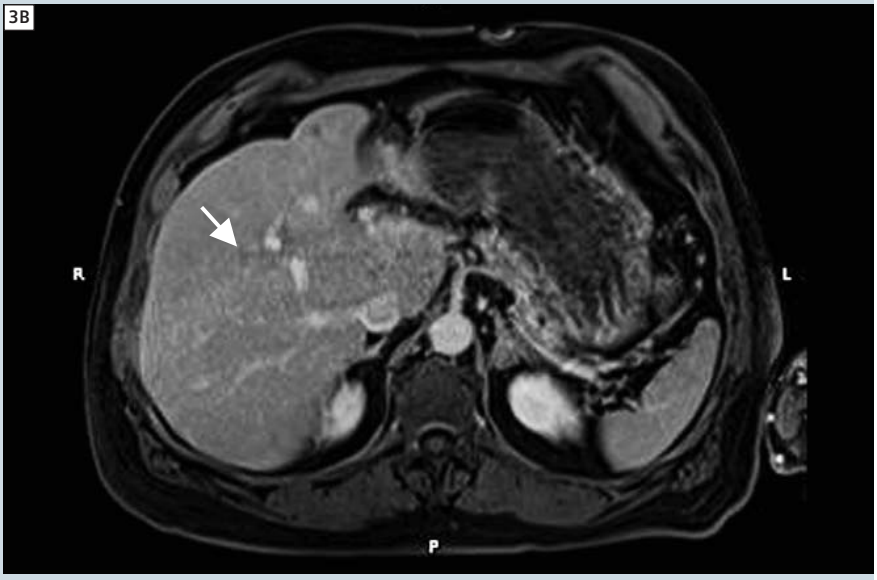
For optimized diagnostic imaging, an individualized patient-specific liver DCE technique is essential for reproducible capture of the arterial phase. An ideal arterial **(A)** and venous phase **(B)** image is shown. To understand the relationship between the different phases and the clinical relevance for optimal timing, especially for the arterial phase images, an example of an arterialized hepatocellular carcinoma (HCC) nodule is provided captured during the arterial phase **(C)**. In this image the enhancing nodule is conspicuous during the transient period when the lesion-to-liver background contrast ratio is elevated. The relative changes in signal-intensities (SI) within the hepatic artery, portal and hepatic veins are provided as a function of time for this patient **(D)**. Additionally the time-windows for capturing an arterial (red zone) and venous (blue zone) image are displayed. The time during which the HCC nodule enhances above the adjacent liver parenchyma is used to define the arterial phase and the basis for this calculation is shown for this patient **(E)**. Note that the time window for capture of the transient arterial tumor enhancement is short (~10 s) and that imaging the arterial enhancement is critical for detection, diagnosis, and for assessing treatment response. A screenshot from the Abdomen Dot Engine is provided **(F)**. This Dot Engine* optimizes timing delay between the arrival of contrast bolus, provides the breath-hold commands, initiates sequence acquisition and also adopts the imaging sequence programming to bolus-timing specifications. Also, the user can adjust the time delays between the detection of the contrast media bolus and the optimal time-point for read-out of the VIBE central k-space acquisition data. All phases of the DCE study may be subsequently acquired without the need of any further manual interactions with the sequence parameters.

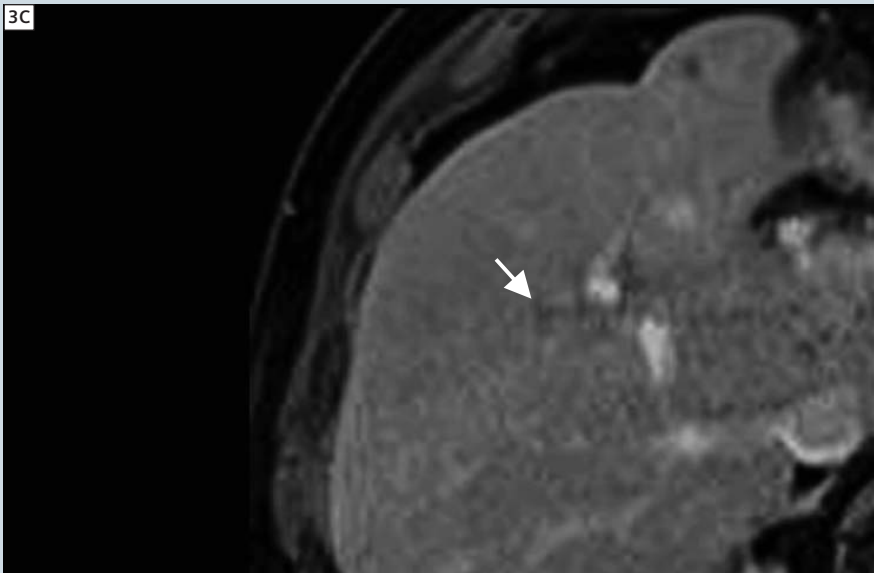


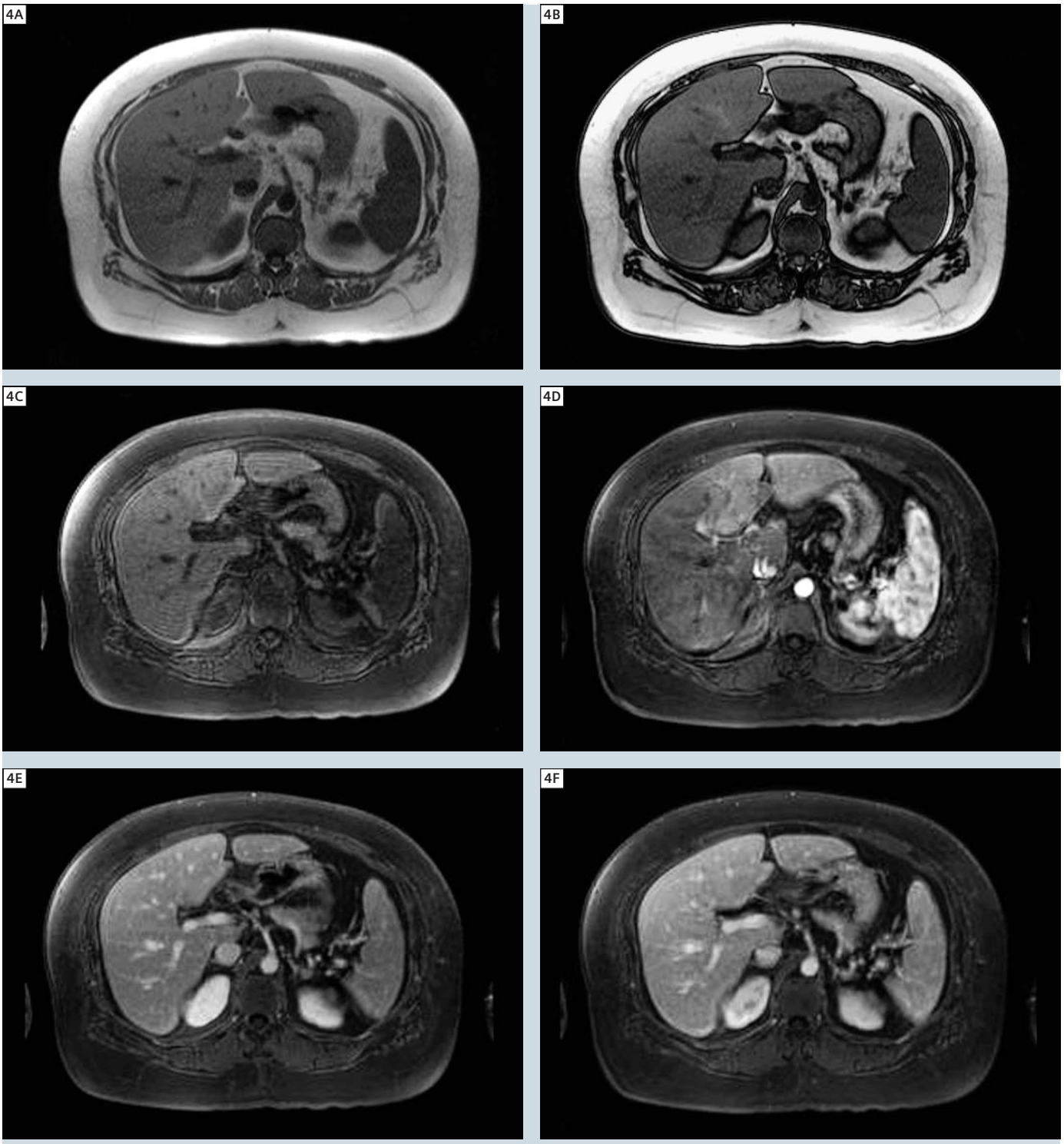
2 Case fatty adenoma
Dynamic contrast-enhanced liver MRI of a 27-year-old female with diagnoses of a fatty adenoma:
A) pre-contrast;
B) arterial;
C) venous; and
D) delayed phase 3D VIBE;
E) corresponding T2w HASTE-SPAIR fat-suppressed;
F) in-phase; and
G) opposed-phase 2D T1-weighted FLASH.

3 Case hepatocellular carcinoma (HCC)
Patient with liver cirrhoses: a small HCC nodule (red arrow) with a maximum diameter of 1 cm can be seen only because of an optimally timed arterial phase liver scan **(3A)**.
On venous (70 s after contrast media injection) and delayed phase (180 seconds delay) a corresponding focal washout lesion with subtle capsule enhancement can be seen progressively on the more delayed image (white arrows).
In addition, the delayed enhanced images show a fine reticular pattern of contrast uptake characteristic of hepatic fibrosis.
The patient had two HCC nodules of similar size, both identified on MRI and confirmed on explanted liver pathology acquired after liver transplantation.
This patient had hepatitis C viral infection, associated with increased risk for HCC at even relatively early stage chronic liver disease, as in this patient.
On a background of chronic liver disease, a transiently arterial enhancing lesion (on arterial phase images) with progressive washout and capsule enhancement (on venous and delayed phase images) represents HCC.
MRI diagnosis is accepted over biopsy for purpose of liver transplant evaluation. While all phases of the DCE MRI are necessary for comprehensive evaluation, sub-optimal arterial phase timing would seriously impair diagnostic sensitivity and specificity of HCC diagnosis.









4 Case non-alcoholic steatohepatitis (NASH)
Patient with biopsy-proven NASH: **(A)** FLASH in-phase; and **(B)** opposed-phase; **(C)** pre-contrast; **(D)** arterial; **(E)** venous; and **(F)** delayed phase DCE 3D VIBE. Images show diffuse steatosis (note liver signal drop on opposed phase images with mild focal sparing in segment 4). While the pre, venous, and delayed phase images show uniform liver signal and enhancement, the arterial phase images show transient marked non-uniform enhancement. This finding has been previously shown to correlate in magnitude to the degree of active hepatitis and requires optimal arterial phase timed image capture for diagnosis. Venous phase images are used to assess portal system and abdominal vasculature and the delayed images may be used to assess chronic changes of hepatitis (for example, **Fig. 3C**). In this case, no evidence of hepatic fibrosis or sequelae of portal hypertension is identified, correlating with only minimal stage bridging fibrosis on the pathology specimen.

liver MRI timing methods. Based on the clinical need to improve DCE liver exams, we developed and implemented a bolus tracking technique which we call Automated Breath-hold Liver Exam (ABLE) for our clinical routine protocols. Through the combination of our observations and techniques, and in close cooperation with Siemens Healthcare, a fully automatic procedure was developed that provides a clear simplification of timing methodology and MR image acquisition for the average user. This new workflow optimizing approach (Abdomen Dot Engine*) offers patient-specific DCE liver MRI for routine clinical application. This software helps to define or even provide full automation of

1) defining vascular reference points;
2) optimizing timing delays between the arrival of contrast bolus, providing the breath hold commands, and initiation of sequence acquisition; and
3) adapting imaging sequence programming to bolus-timing specifications.

The images presented in this article were all generated with the ABLE bolus tracking technology. The real-time bolus track imaging was implemented in this approach using a fast 2D FLASH sequence, with acquisitions every 0.5–1.0 second and on-the-fly image reconstruction (450 mm FOV, 256 matrix, TR/TE = 4.1/1.23 ms, flipangle 10°, 50 mm slice thickness, 100 dynamics, scan time = 100 seconds). The sequence was oriented along the abdominal aorta, and initiated at the same time as contrast administration. The real-time images were then displayed using an Inline viewer on the console and the software triggered the DCE scan upon reaching a certain threshold within a manually placed region of interest (ROI). For the shown DCE liver images in this article, a 3D VIBE imaging sequence with a segmented k-space acquisition was used with the following parameters: 360 mm FOV (75–90% phase FOV), 256 matrix (70% phase resolution), TR/TE = 4.1/1.7 ms, flipangle 10°, 400 Hz/pixel bandwidth, 94 slices, 3 mm slice thickness, acceleration factor = 2 (*syngo* GRAPPA) and SPAIR fat saturation. Following acquisition of the arterial phase image set, venous and delayed interstitial phase image sets were obtained. Based on our clinical experience with the ABLE technique, this approach leads to a clear improvement in reproducible DCE liver scan arterial timing with improved diagnostic yield. This approach provides optimized images for tumor detection and characterization and for therapy monitoring DCE protocols. Uniformity of arterial phase timing between patients with liver tumors, and for an individual patient who is studied by multiple MRI scans over time, is critically improved using the bolus-timing strategy described here.

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*The information about this product is being provided for planning purposes. The product is pending 510(k) review, and is not yet commercially available in the U.S.

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