A review of the contrast mechanisms available with (ultra)low-field MRI

Marta Gironés Sangüesa

Abstract — Since its emergence, magnetic resonance imaging (MRI) has evolved into higher field strengths because of the higher image quality (namely, the signal-to-noise ratio) inherent of high fields. However, in the last years, low- and ultralow-MR field strengths have re-gained interest, opening up a whole world of new applications in this area, thanks to the new advances in hardware and software in MRI. Recent studies have shown that clinical practice might benefit of more affordable, portable machines accessible for developing countries, emergency rooms, intensive care units (ICU), and even surgeries. In this review, the principal applications of low and ultralow-field MRI systems will be provided by focusing on the differences in contrast mechanisms with respect to high-field MRI devices. Understanding and exploiting the characteristics of contrast mechanisms — proton density (PD), longitudinal relaxation time T1, transverse relaxation time T2, diffusion and contrast agents — permits researchers to eradicate some limitations intrinsic of low-fields and achieve the highest image quality possible in low-field MRI.

Index Terms — Low and ultralow-field MRI, signal-to-noise ratio, contrast, T₁ and T₂ relaxation times.

I. INTRODUCTION

The first magnetic resonance (MR) images were acquired in the 1970s at field strengths typically less than 0.3 T [1]. However, because the signal-to-noise ratio (SNR) directly depends on the field strength, continued research of new materials for the construction of magnets drove to higher fields, and eventually, 1.5 and 3 T scanners became the most employed in clinical practice. [1], [2]

In the past decades, current advances in software and hardware in MRI systems have brought attention back to low- and ultralow-field MRI systems. Although these are generally defined as scanners in the range of 0.1 to 0.5 T or below 0.1 T, respectively, a clear definition of what is considered low field strength is not available, as the classification is always relative to the comparison with other field strengths -1.5, 3, 7, 9 and 11 T. The renewed interest in low/field MRI is justified by their multiple advantages: reduced size and weight leading to reduction of costs, lower need for maintenance, decreased susceptibility artifacts and enhanced compatibility with medical devices. Additionally, the limited image quality provided by these magnetic field strengths can be counteracted by signal averaging, high-performance acquisition techniques, high sensitivity detectors, image processing, and modern electronics. These advances permit exploiting the benefits obtained when reducing the field strength without having any significant drawbacks. Its use increases the applications of MRI by providing more affordable, portable machines, accessible for developing countries, emergency

rooms, intensive care units (ICU), and even surgeries. [2], [3]

However, low-field MRI has yet not achieved an optimal performance for clinical practice, as more efforts are needed to improve contrast and image quality before it could be considered for it. One of the most important steps is to understand and exploit how the numerous contrast mechanisms, based on tissue-specific parameters and responsible for generating the images change at low-field MR [4]. Not only is this relevant for varying the image contrast, but also it allows quantitative MR parameters mapping, often specifics for tissues and/or diseases [5].

The primary sources of inherent tissue contrast in MRI are the proton density (PD), the longitudinal relaxation time T_1 , and the transverse relaxation time T_2 . Other parameters that influence the contrast are the relaxation time T_2^* , magnetization transfer, chemical shift, perfusion, diffusion, flow, contrast agents or motion. The different MR sequences exploit these phenomena to obtain the highest image quality possible. [4]

For a better understanding of the following sections, we will provide a definition of the contrast mechanisms that will be discussed. Proton density refers to the macroscopic magnetization dependent on the number of spins involved and the tissue temperature [4]. T_1 relaxation is the process by which the longitudinal magnetization is turned into the transverse plane and realigned again parallel to the magnetic field [4]. T_2 relaxation corresponds to the dephasing of the magnetization in the transverse plane [4]. Diffusion is the random microscopic

Marta Gironés Sangüesa

molecular movement produced by the heat, and is obtained by calculating the apparent diffusion coefficient (ADC) values of the tissue [6]. Contrast agents are introduced in the organism to change the image contrast by decreasing the T_1 and T_2 of water molecules of a specific tissue [7].

In this review, the principal applications of low and ultralow-field MRI systems will be provided by focusing on the differences in contrast mechanisms with respect to high-field MRI devices.

II. DIFFERENCES IN (ULTRA)LOW- AND HIGH-FIELD MRI

As mentioned before, the SNR directly depends on the field strength. Marques et al. [2] acknowledged that, in the range of fields from 0.25 to 1 T, the SNR approximately scales with $B_0^{3/2}$, because there is a relation between the field strength and the MR signal, and between the magnetic field and the noise provided by the coil and the sample. Thus, higher field strengths allow a higher signal-to-noise ratio.

The relaxation times T_1 and T_2 , which influence the resulting image contrast, similarly depend on the magnetic field.

Since the measured longitudinal or T_1 relaxation component rotates with the Larmor frequency, the increase in magnetic field produces a simultaneous decrease in the rotating frequency of the proton and increase of the relaxation time. As a result, shorter T_1 s will be obtained at lower magnetic fields. [8]

Transverse or T_2 relaxation times have a weaker field strength dependency because the function that regulates the rotation frequency of a proton is dominated by a frequency-independent static component. However, stronger magnetic fields can still produce a shortening in the T_2 values. [9]

In the same way, contrast agents alter their effect with a change in the field strength as they modify the T_1 and T_2 relaxation times of the surrounding tissue, but this may result in an increase or decrease of the image contrast depending on the tissue type and contrast agent imaged, so special attention needs to be brought to the investigation of new contrast agents for low-field MRI.

The field strength dependency of the different contrast mechanisms has already been reported in numerous studies since the emergence of MRI. Researchers in [10]–[12] measured the dependence of $1/T_1$ on the magnetic field in different in-vivo and ex-vivo tissue types and calculated a model that fits this variation. Bottomley et al. [13] collected the T_1 and T_2 relaxation times in healthy human and animal tissues in the frequency range of 1 to 100 MHz while changing several parameters like the tissue type, MR frequency and temperature. Oros-Peusquens et al.

[14] studied the field dependence of the T_1 values on whole-brain of healthy volunteers by measuring at 1.5, 3 and 4 T scanners, although they did not provide low-field MR data. In [8], they compared the T_1 relaxation rates in the brain of three healthy individuals while varying the field strengths from 0.2 to 7 T.

Because proton density imaging depends on the macroscopic magnetization of the tissue [4], the signal intensity will increase with the magnetic field.

Unfortunately, the field dependence of diffusion weighted images has not been explored for low-field MRI. Ogura et al. [15] and Donati et al. [16] investigated the field dependence in diffusion weighted images in 1.5 and 3 T MRI scanners. The studies demonstrated that the apparent diffusion coefficient is independent of the field strength and scanner employed when the scanning parameters are unchanged.

To explore how the field dependency influence the different contrast mechanisms and in which way this phenomenon could be exploited, in the present report we will focus on the clinical applications of low- and ultralow-field MRI and its effect on the existent contrast mechanisms.

III. CLINICAL APPLICATIONS IN (ULTRA)LOW-FIELD MRI

The research performed in low- and ultralow-field MRI will be discussed in terms of outcomes, limitations, and future perspectives. The studies will be divided according to the different body parts.

A. Brain

O'Reilly et al. [17] designed a Halbach-based MRI scanner with a magnet of 50 mT. They subjectively tested the scanner by acquiring the T_1 -weighted (T_{1w}) and T_2 -weighted (T_{2w}) scans of the brain of a healthy volunteer.

The same scanner was later employed to obtain the T_1 and T_2 maps of the human brain in healthy volunteers using inversion-recovery and multi-echobased sequences [9].

O'Reilly and Webb reported the T_1 and T_2 values of the gray matter (GM), white matter (WM) and cerebrospinal fluid (CSF). The mean T_1 times across all 3 subjects were 327 ± 10 ms in the GM, 275 ± 5 ms in the WM, and 3695 ± 287 ms in the CSF. The corresponding T_2 values were 102 ± 6 ms, 102 ± 6 ms, and 1584 ± 124 ms. The values were compared with previous studies and in agreement with the theoretic values in low-field. The CSF values, however, were inaccurate due to saturation effects, so an additional scan with a longer repetition time is needed to allow for full longitudinal and transverse relaxation of the CSF.

In this study, the relaxation time maps suffered from partial volume effects, caused by the worse spatial resolution and lower intrinsic SNR that result when working with low field strengths. The authors highlighted the need for specific methods for generating T_1 -weighted images, as the conventional ones, like the inversion-recovery sequence employed in this study, are optimized for the T_1 relaxation times obtained at high-field strengths. These methods may fail when having a small difference in the relaxation times between the different tissues, which is the case when acquiring the images at a low-field strength.

 T_1 and T_2 were also investigated in the brain by Deoni et al. [18]. In this case, they collected wholebrain T_1 and T_2 -weighted MRI data in healthy and typically-developing children, from 6 weeks to 16 years of age, on a commercially available 64mT Hyperfine Swoop imaging system. A 3T scanner was included for comparison.

The results revealed an increase in white and gray matter contrast-to-noise ratio (CNR) with the child's age, similar to previous results seen in 1.5 and 3 T scanners. Additionally, the developmental trajectories reported —the changes in the brain with aging— were in strong agreement with others calculated in previous studies for low- and high-field data. The results demonstrate that this low-field MR scanner can accurately reproduce the brain connections in children.

The limitations mentioned are in line with the previous study, as they emphasized that the sequences and the image reconstructions algorithms employed to acquire and process the data have been designed with the SNR produced by higher-field strengths. Low-field MR scanners suffer from an unavoidable reduction in image SNR which needs to be considered when designing future experiments. Finally, in this study, an additional challenge was to reflect accurate changes in the relaxation properties of the young brains while employing sequences designed for adults.

Campbell-Washburn et al. [19] did not employ an MR system specific for low-field MRI, as in the two previous studies, but modified a commercial 1.5-T MRI system to operate at 0.55 T while maintaining high-performance hardware, shielded gradients, and advanced imaging methods. They performed routine MRI sequences for imaging the brain for both healthy participants and patients with known pathologic abnormalities. They used an inversion recovery sequence for T_1 imaging and a multi-echo sequence for T_2 , by performing spiral acquisitions.

The first results showed a difference in the relaxation parameters with respect to the 1.5 T

images, but part of the signal in the brain could be recovered when using spiral acquisitions, increasing the resulting SNR. For the GM and WM, the mean T_1 of the scanned patients was 327-275, T₂ was 112 and 89 ms, and T_2^* , 86 and 72 ms, respectively. When imaging clinical small-molecular-weight gadolinium-based contrast agents, T_1 and T_2 relaxivity were similar between 0.55 T and 1.5 T. In addition. they demonstrated a decrease in radiofrequency-induced heating and an increase in the safety of metal devices, as well as a higher performance near air-tissue interfaces at low-field MRI.

The study did not obtain a meaningful difference in the relaxation times between their low (0.55 T) and high (1.5 T) field strengths. They measured higher T_1 and T_2 times, and SNR compared to the previous mentioned studies; this is understandable because the field strength in the low-field MRI data was ten times higher —0.55 T VS 0.055 and 0.064 T. However, Campbell-Washburn et al. retuned a 1.5 T scanner, thus the receiver coils were not optimized for low fields which resulted in image shading. Moreover, the MRI scanner was possibly too expensive and not compact enough to be portable, so it may not be beneficial for the intended clinical use of low-field MRI.

To demonstrate the feasibility of imaging diffusion contrast with low-field MRI, diffusion-weighted images (DWIs) of healthy brains were acquired on a 0.35 T MRI in Malawi and compared with images of the same volunteers in a 3 T MR scanner in the US [20].

The SNR decreased for the 0.35 T DWIs compared to the 3 T images, as expected, although it is not easily compared as the images were obtained at different b-values (200 and 900 s/mm² for the 0.35 T images, and 0 and 1000 s/mm² for the 1.5 T images). When visually inspecting the images, contrast and resolution were similar between the scanners, and the ADC contrast was comparable between the scanners for all the subjects. There is, however, a higher contrast between CSF and WM in the 3 T images as the boundaries are better defined.

Because the 0.35 T DWIs have to be acquired by manually changing the diffusion gradients and scanning each imaging plane and b value separately, a higher number of motion artifacts was present compared to the 3 T images; and the slice thickness was larger than for high-field MRIs, having difficulties during co-registration. These conditions are specific to the study and may not be caused by lowering the field strength, but they point out, once again, some limitations intrinsic of low-fields, like the need for specific sequences and protocols for imaging at low and ultralow-field MRI; and the existence of errors due to partial volume effects, especially near the ventricles, which is inevitable in lower fields and mainly induced by inhomogeneous and large voxel sizes.

Several studies were also completed on subjects presenting brain diseases.

Markkola et al. [21] performed, on a 0.1 T clinical MR device, head and neck tumor imaging with multiple-slice spin lock gradient-echo (SL-GRE) sequences, and compared them with spin-echo (SE) T_2 -weighted images.

The mean CNR for tumors did not present any significant difference between the SL images and SE images $(1.1 \pm 0.8 \text{ vs. } 1.0 \pm 0.8)$. The CNR improved in tumors adjacent to the salivary gland tissue when imaging with the SL technique, but this sequence obtained a lower CNR of tumors and the muscle, and no difference between techniques was encountered around fat tissues.

Spin-lock sequences, more often used for specific applications in the musculoskeletal system at highfield [22], at low-field strengths can provide a contrast in tumor imaging similar to spin-echo imaging. This technique has the advantage to reduce motion and susceptibility artifacts.

 T_1 and T_2 -weighted images for patients with hemorrhagic stroke and ischemic stroke were acquired in a 50.9 mT MRI scanner [23].

He et al. showed a higher contrast between cerebrospinal fluid and gray matter or white matter, compared to images acquired with high-field strengths. This is justified by the effect on the T_1 values, as the CSF times barely change with the magnetic field, but the values from the WM and GM are reduced as the magnetic field strength decreases.

In this work, they suggest future improvements like advanced algorithms and hardware to reduce the shielding setup without needing a specific room or even eliminating the Faraday shielding. Other suggestions include the optimization of the algorithms to generate higher contrast in the T_2 -weighted images.

In Liu et al., T_{1w} , T_{2w} , FLAIR and DWI of the brain were acquired in a 0.055 T MRI system to diagnose several major neurological diseases, including brain tumors, ischemic stroke, and intracerebral hemorrhage (ICH) [24]. For comparison, they also scanned the patients using a clinical 3 T MRI scanner.

They identified lower gray matter and white matter contrast compared to the high-field images because the differences in T_1 values between the two tissue types are decreased with the magnetic field,

although the quantitative values were not reported in the paper. Little susceptibility artifacts were observed in the 0.055 T images when imaging metallic clips and cerebrovascular stents.

It is again stated that the lower relative difference in T_1 value between gray matter and white matter, together with the intrinsic low SNR and resolution can limit the achievable contrast and image quality when acquiring ultralow-field T_{1w} images.

B. Upper body

The study performed by Campbell-Washburn [19] also included images of the heart, spine and abdomen for both healthy participants and pathologic diseases in a 0.55 T scanner.

For the myocardium, arterial blood and lungs, the mean T_1 of the scanned patients was 701, 1122 and 971 ms, T₂ was 58, 263 and 61 ms, respectively and T_2^* was 47 ms in the myocardium and 10 ms when imaging the lungs. For the liver, kidney cortex and fat tissue, the mean T_1 of the scanned patients was 339, 651 and 187 ms, T₂ was 66, 101 and 93 ms, respectively, and T_2^* was 43 ms in the liver and 82 ms when imaging the kidney cortex. The advantages of low-field MRI are the same as when imaging the brain, having a higher SNR when using spiral acquisitions and improving the safety with respect to metal implants and the imaging of air-tissue interfaces as compared to the 1.5 T images. The T₁ and T_2 relaxation times of the gadolinium-based contrast agents introduced were similar between 0.55 and 1.5 T.

The limitations mentioned in this study are related to the design of the scanner and were already discussed in the previous section.

A different type of contrast mechanism was investigated by Waddington et al. [25]. They imaged the contrast effect of superparamagnetic iron oxide nanoparticles (SPIONs) in phantoms and rats by acquiring proton density images of the liver and kidneys at a field strength of 6.5 mT.

The measured SNR was 24.4 ± 2.3 and 11.8 ± 1.3 in the adipose and liver tissues, respectively. They observed significant negative contrast in highly perfused organs such as the kidneys and liver due to the presence of SPIONs in images acquired 30 min after injection, but, because positive contrast in MRI scans is often preferred by clinicians, they developed and demonstrated the clinical potential use of a susceptibility-based positive contrast technique for low-field MRI by using SPIONs.

Since the study was developed on phantoms and rats, the decrease in the SNR may not be the same when introducing SPIONs to the human liver and kidneys. Future investigations need to be developed on the effect of this contrast agent on the human body.

C. Extremities and joints

The Halbach-based MRI scan developed by O'Reilly et al. [9], [17] was additionally employed to obtain the T_1 and T_2 maps of the human lower leg in healthy volunteers using inversion-recovery and multi-echo–based sequences.

For muscle and lipid measurements in the lower leg, the mean T_1 across all 3 subjects is 171 ± 11 ms in the muscle and 130 ± 5 ms in the lipid. The mean T_2 across all 3 subjects for muscle is 39 ± 2 ms and 90 ± 13 ms for lipid.

Apart from the challenges mentioned in the brain imaging section, O'Reilly et al. highlighted that lipid suppression at low-field strengths may be limited because of the similar T_1 relaxation times of the muscle and lipid tissues, which results in an undesirable suppression of the muscle signal.

The leg was similarly imaged in [26]. In this study, samples of bovine articular cartilage were imaged in a 0.27 T MRI scan by acquiring T_{1w} and T_{2w} images. The samples were taken from the fresh hip and stifle joints of a femur bone and the T_1 and T_2 relaxation times of these joints were plotted as a function of tissue depth, as they vary depending on the concentration of water in the different parts of the joint.

Rössler et al. demonstrated that T_1 appears to be a superior parameter for characterization across the cartilage tissue and beneath it since the T₁ values show a lower spatial variation across the hip and stifle joint than the T_2 times and the fitting error is significantly lower for the T_1 . While the transverse relaxation times at a field strength of 0.27 T show a similar value as those reported at 7 T, the contrast of the T₁ times is considerably higher at low-field MRI, which suggests an increased image quality and their potential use for systematic investigations of diseased cartilage. When introducing a contrast agent, there was no significant difference in the T_2 relaxation times, but the frequency dependence of the T_1 relaxation times was decreased by the addition of the $(Gd-DTPA)^{2-}$ solution, resulting in shorter T_1 values as the frequency was increased.

The limitations of this study include high acquisition time, the need for a smaller pick-up coil, the possibility to achieve higher sensitivity of the longitudinal relaxation time, the need for an optimum choice of contrast agents —probably the SPIONs investigated by Waddington et al. [25]—, and the option to design different techniques that turn towards order-sensitive multipulse methods and the encoding of diffusion parameters.

D. Dental

Algarín et al. [27] designed a dental MRI scanner that operates at 260 mT. They acquired T_2 images of ex-vivo human teeth, as well as a rabbit head and part of a cow femur with two different and specialized pulse sequences: Pointwise Encoding Time Reduction with Radial Acquisition (PETRA) and Double Radial Non-Stop Spin Echo (DRaNSSE).

Through the dental images, they demonstrated the capability of the scanner to simultaneously image hard and soft biological tissues, but the acquisition times for the human teeth images shown were intolerably long and no quantitative measures were reported for these scans.

Algarín et al. reported high scan times, weight, and size of the scanner. They employed sequences from 15 to 65 minutes that need to be optimized for future investigations, and the scanner was fitted with a permanent magnet of approximately 940 kilograms and 40,000 €. The most urgent change is therefore a switch to an open magnet with the shape of a U, so there is a decrease in the complexity and footprint of the required mechanical structure and additional applications are possible, like head and extremity imaging. These changes will create an optimal dental MRI scanner for use in the clinic.

I. DISCUSSION

Because the majority of the studies did not report the exact numbers in terms of resolution, contrast or relaxivity times, it is impossible to compare the different outcomes. However, to understand the differences between low and ultralow-field scanners, we will be focusing on the results of O'Reilly et al. [9] and Campbell-Washburn et al. [19]

The different field strengths (50 mT vs. 0.55 T) obtained different relaxation times because of the field dependence of these parameters. The obtained mean T_1 values in the gray and white matter had a difference of 52 ms for the ultralow-field MRI, and 224 ms for the low-field MRI. The mean T_2 values did not change in the case of ultralow-field MRI, and the variation was of 23 ms for the low-field MRI. It is worth mentioning that the study from O'Reilly was performed on 3 healthy volunteers, while Campbell-Washburn included 45 women, so the difference in age, sex and number of participants may have influenced the upcoming results. Nevertheless, the decrease in the field strength resulted in lower T_1 and T_2 times, with a greater difference in the first parameter, as occurs when compared to high-field strengths of 1.5 and 3 T. As a result, a higher SNR is present in the images performed with a field strength of 0.55 T as compared to 0.055 T, especially when

employing the spiral acquisition technique. The higher contrast between the brain tissues are obtained as a result of a higher difference in the relaxation times.

In addition, the 0.55 T MRI scanner has been able to achieve a similar reduction in the susceptibility artifacts to the ones observed in lower fields: the image quality near air-tissue interfaces has improved with respect to high-field MRIs, and a reduction of the interferences produced by metal implants opens new possibilities of imaging patients with metal objects and implantable devices inside their body.

Despite the benefits, having a higher field strength increases the size and weight of the scanner, as well as the prize. This may result in a scanner that is not portable or accessible in developing countries, which are two of the most relevant advantages in low-field MRI.

Similarly, many studies did a comparison between low and high fields while focusing on the SNR and image quality. This comparison is not completely fair as we have already demonstrated that lower field strengths will inevitably result in lower SNR, and therefore can derive in a mislead by the reader who would think the method is not clinically valid. Instead, the study should focus on how to exploit the image characteristics to obtain the best contrast possible and should analyze if the different pathologies or anatomy of the body can be correctly identified. It is worth mentioning that low-field MRI does not intend to substitute the high-field but complement it in those applications where the use of more complex, expensive, and bigger scanners is not The different advantages and new feasible. possibilities encountered in the previous papers will be discussed in the following paragraphs.

In the first place, low-field MRIs require a less powerful magnet, which implies lower costs, size, and weight. The shielded gradient configuration is also simpler or even inexistent and does not normally require a big Faraday cage or a special room to avoid any interferences or magnetic distortions. These scanners are then cheaper, more accessible, compact, and often portable. Because of the lower magnetic power, the acoustic noise levels during scanning are also lower, and the scanners are often smaller and open, creating a situation more comfortable for the patients, especially for people with claustrophobia. [24]

Lowering the costs imply more accessibility which not only translates in having scanners in developing countries or in smaller cities where they cannot normally afford this technology, but also Deoni et al. [18] highlights the possibility to perform cheaper and more complete longitudinal studies. The scanners are even portable, allowing to transport them in a truck or to move them around the hospital. Low-field MRI might make the MRI technology more accessible to more patients, especially from places where malnutrition, stress and environmental adversities are common, and an MRI is not always available. In the study of Deoni et al. [18], the development of the brain could be investigated while addressing the differences in sex, gender, place of birth, race, etc.

In the second place, low-field images suffer of fewer susceptibility artifacts as reported in [19], [21], [24]. Susceptibility artifacts are normally produced next to air cavities or metals due to the high difference in the magnetic properties of these particles with respect to the surrounding tissues. The effect is increased with the field strength so, the lowfield studies demonstrated low sensitivity to metallic objects and were able to image implantable devices and accomplish heart catheterization with a guidewire [19], [28]. Air-tissue interfaces could be acquired having less signal loss as compared to higher field strengths.

In the third place, with the new advancements in image acquisition and processing, there is a chance to increase the limited resolution obtained in low-field MRI. Algarín et al. [27] introduced two specialized pulse sequences ---PETRA and DRaNSSE---- to acquire hard and soft tissue images in the same scanning session. These sequences are a variation of the standard zero-echo time pulse sequence [29], and they allowed higher SNR as compared to traditional sequences. The same study revealed a higher performance of an alternative algebraic reconstruction techniques compared to the Fourier transform, as it increases the SNR by obtaining a more homogenous signal and a reduction in the noise levels.

A different way of increasing the SNR and contrast when the parameters are limited by a reduction of the field strength is to employ deep learning and machine learning algorithms for image reconstructions. Several papers have been investigating the possibility to increase the low-field image quality by converting the data into highresolution images. Recent research on this matter has been performed in [30]–[34], with a special interest in ultralow-field MRI.

Finally, a large variety of contrast agents has been employed in MRI to modify the relaxation of the different tissues and increase their intensity in the image. The most widely used contrast agents are those based on gadolinium because it is strongly paramagnetic. However, Rössler et al. [26] reported the choice of these contrast agents may not result optimal as its effects in low-field MRI were minimum or inexistent. In this sense, Waddington et al. [25] introduced the combination of low-field strengths with contrast agents based on superparamagnetic iron oxide nanoparticles, and demonstrated an increase in the SNR and contrast between tissues in the liver and kidney cortex. This suggests that employing the same contrast agents may not be most advantageous for the different field strengths, but it is possible to increase the image contrast if new materials are investigated for lowfield

Despite the benefits examined in comparison with high-field MRI, low-field scanners still need to overcome several disadvantages.

The first and most important is the intrinsic lower signal-to-noise ratio, already explained by a reduction of the field strength. This, however, can be overcome with specific techniques for image acquisition and processing, as mentioned before.

The lower magnetic fields also imply a change in the T1 an T2 relaxation times, which will produce a change in the resulting contrast. This alteration can be both an advantage and disadvantage, depending on the resulting difference. For example, He et al. [23] showed evidence of a higher contrast between CSF and white and gray matter in the T₁-weighted images produced by the decrease in the relaxation times of the last two tissues. However, Liu et al. [24] stated that the contrast between WM and GM is decreased based on the same phenomenon.

Although researchers have already demonstrated that a lower field strength has an influence in the relaxation properties of the tissue and characteristics of the images, the sequences and software employed are those optimized for high-field MRI. There is a need for specialized techniques to acquire and process MR images in low and ultralow-field MRI.

In line with the above, some studies have been carried out by retuning a 3T scanner and converting it to low-field, without perfectionating the hardware components and investigating which configuration will obtain the best image possible at a lower magnetic field.

Apart from the disadvantages in image quality, there is also a limitation in the parts of the body were low-field MRI can be acquired. The main applications reported involved brain or joints which is probably explained by the fact that often MR bores of low-field MRI are small. The difficulty to create a homogenous B_0 field is higher when the bore is larger or when using an open magnet. Thus, a scanner with a limited bore makes it impossible to fit larger parts of the body with the existent hardware.

Lastly, temperature changes have a higher effect

on low-field MR scanners. Vesanen et al. [35] demonstrated that the temperature dependence of an agarose gel increased when lowering the field strength. The increment in the temperature produced an increment in the relaxation rates of the agarose gel, which opens new possibilities of temperature mapping in low and ultralow-field MRI. However, it is also a disadvantage as a change in the room or body temperature may produce a distortion in the intensities and contrast of the MR image.

The effect was measured in several compositions of agarose gel that mimic the T_2 of living tissues. Nevertheless, future experiments investigating the temperature dependence on a human body are necessary, as this change cannot be expected to be the same for the phantoms and the in-vivo human tissue.

In conclusion, low and ultralow-field MRI systems present a variety of advantages that extend the possibilities of MRI into new fields. The difference in contrast and SNR induced by lowering the field strength can be exploited to turn into an advantage or compensate it by processing the images when it becomes a limitation.

In this review we have explored the different contrast mechanisms currently used with low and ultralow-MRI, and the possibilities that this may bring into the clinic.

II. REFERENCES

- R. R. Edelman, "The History of MR Imaging as Seen through the Pages of Radiology," *Radiology*, vol. 273, no. 2, pp. S181–S200, Oct. 2014, doi: 10.1148/RADIOL.14140706.
- [2] J. P. Marques, F. F. J. Simonis, and A. G. Webb, "Low-field MRI: An MR physics perspective," *J. Magn. Reson. Imaging*, vol. 49, no. 6, pp. 1528–1542, Jun. 2019, doi: 10.1002/JMRI.26637.
- M. Sarracanie and N. Salameh, "Low-Field MRI: How Low Can We Go? A Fresh View on an Old Debate," *Front. Phys.*, vol. 8, p. 172, Jun. 2020, doi: 10.3389/FPHY.2020.00172/BIBTEX.
- [4] W. R. Nitz and P. Reimer, "Contrast mechanisms in MR imaging," *Eur. Radiol.*, vol. 9, no. 6, pp. 1032–1046, 1999, doi: 10.1007/S003300050789.
- [5] G. J. Lima da Cruz, C. Velasco, B. Lavin, O. Jaubert, R. M. Botnar, and C. Prieto, "Myocardial T1, T2, T2*, and fat fraction quantification via low-rank motion-corrected cardiac MR fingerprinting," *Magn. Reson. Med.*, vol. 87, no. 6, pp. 2757–2774, Jun. 2022, doi: 10.1002/MRM.29171.
- [6] P. Mukherjee, J. I. Berman, S. W. Chung, C. P. Hess, and R. G. Henry, "Diffusion tensor

MR imaging and fiber tractography: theoretic underpinnings," *AJNR. Am. J. Neuroradiol.*, vol. 29, no. 4, pp. 632–641, Apr. 2008, doi: 10.3174/AJNR.A1051.

- [7] L. M. De León-Rodríguez, A. F. Martins, M. C. Pinho, N. M. Rofsky, and A. D. Sherry, "Basic MR relaxation mechanisms and contrast agent design," *J. Magn. Reson. Imaging*, vol. 42, no. 3, pp. 545–565, Sep. 2015, doi: 10.1002/JMRI.24787.
- [8] W. D. Rooney *et al.*, "Magnetic field and tissue dependencies of human brain longitudinal 1H2O relaxation in vivo," *Magn. Reson. Med.*, vol. 57, no. 2, pp. 308–318, 2007, doi: 10.1002/MRM.21122.
- [9] T. O'Reilly and A. G. Webb, "In vivo T1 and T2 relaxation time maps of brain tissue, skeletal muscle, and lipid measured in healthy volunteers at 50 mT," *Magn. Reson. Med.*, vol. 87, no. 2, pp. 884–895, Feb. 2022, doi: 10.1002/MRM.29009.
- [10] S. H. Koenig and R. D. Brown, "Determinants of proton relaxation rates in tissue," *Magn. Reson. Med.*, vol. 1, no. 4, pp. 437–449, 1984, doi: 10.1002/MRM.1910010404.
- [11] H. W. Fischer, P. A. Rinck, Y. van Haverbeke, and R. N. Muller, "Nuclear relaxation of human brain gray and white matter: analysis of field dependence and implications for MRI," *Magn. Reson. Med.*, vol. 16, no. 2, pp. 317–334, 1990, doi: 10.1002/MRM.1910160212.
- [12] J. P. Korb and R. G. Bryant, "Magnetic field dependence of proton spin-lattice relaxation times," *Magn. Reson. Med.*, vol. 48, no. 1, pp. 21–26, 2002, doi: 10.1002/MRM.10185.
- [13] P. A. Bottomley, T. H. Foster, R. E. Argersinger, and L. M. Pfeifer, "A review of normal tissue hydrogen NMR relaxation times and relaxation mechanisms from 1-100 MHz: dependence on tissue type, NMR frequency, temperature, species, excision, and age," *Med. Phys.*, vol. 11, no. 4, pp. 425–448, 1984, doi: 10.1118/1.595535.
- [14] A. M. Oros-Peusquens, M. Laurila, and N. J. Shah, "Magnetic field dependence of the distribution of NMR relaxation times in the living human brain," *MAGMA*, vol. 21, no. 1–2, pp. 131–147, 2008, doi: 10.1007/S10334-008-0107-5.
- [15] A. Ogura *et al.*, "Apparent Diffusion Coefficient Value Is Not Dependent on Magnetic Resonance Systems and Field Strength Under Fixed Imaging Parameters in Brain," *J. Comput. Assist. Tomogr.*, vol. 39, no. 5, pp. 760–765, Sep. 2015, doi: 10.1097/RCT.0000000000266.

- [16] O. F. Donati *et al.*, "Diffusion-weighted MR imaging of upper abdominal organs: Field strength and intervendor variability of apparent diffusion coefficients," *Radiology*, vol. 270, no. 2, pp. 454–463, Feb. 2014, doi: 10.1148/RADIOL.13130819/SUPPL_FILE/ RADIOL.13130819.SUPPL.
- T. O'Reilly, W. M. Teeuwisse, D. de Gans, K. Koolstra, and A. G. Webb, "In vivo 3D brain and extremity MRI at 50 mT using a permanent magnet Halbach array," *Magn. Reson. Med.*, vol. 85, no. 1, pp. 495–505, Jan. 2021, doi: 10.1002/MRM.28396.
- S. C. L. Deoni *et al.*, "Accessible pediatric neuroimaging using a low field strength MRI scanner," *Neuroimage*, vol. 238, p. 118273, Sep. 2021, doi: 10.1016/J.NEUROIMAGE.2021.118273.
- [19] E. Campbell-Washburn A. et al., "Opportunities in Interventional and Diagnostic Imaging by Using High-Performance Low-Field-Strength MRI," Radiology, vol. 293, no. 2, pp. 384-393, 2019, doi: 10.1148/RADIOL.2019190452.
- [20] Y. Zhuang, M. J. Potchen, S. D. Kampondeni, M. Tivarus, G. L. Birbeck, and J. Zhong, "Validation of diffusion measurements obtained on a 0.35T MR in Malawi: Important insights for radiologists in low income settings with low field MRI," *Magn. Reson. Imaging*, vol. 45, pp. 120–128, Jan. 2018, doi: 10.1016/J.MRI.2017.10.001.
- [21] A. T. Markkola, H. J. Aronen, S. Lukkarinen, U. A. Ramadan, J. I. Tanttu, and R. E. Sepponen, "Multiple-slice spin lock imaging of head and neck tumors at 0.1 Tesla: exploring appropriate imaging parameters with reference to T2-weighted spin-echo technique," *Invest. Radiol.*, vol. 36, no. 9, pp. 531–538, 2001, doi: 10.1097/00004424-200109000-00005.
- [22] L. Wang and R. R. Regatte, "T₁ρ MRI of human musculoskeletal system," J. Magn. Reson. Imaging, vol. 41, no. 3, pp. 586–600, Mar. 2015, doi: 10.1002/JMRI.24677.
- [23] Y. He *et al.*, "Use of 2.1 MHz MRI scanner for brain imaging and its preliminary results in stroke," *J. Magn. Reson.*, vol. 319, Oct. 2020, doi: 10.1016/J.JMR.2020.106829.
- [24] Y. Liu *et al.*, "A low-cost and shielding-free ultra-low-field brain MRI scanner," *Nat. Commun. 2021 121*, vol. 12, no. 1, pp. 1–14, Dec. 2021, doi: 10.1038/s41467-021-27317-1.
- [25] D. E. J. Waddington, T. Boele, R. Maschmeyer, Z. Kuncic, and M. S. Rosen, "High-sensitivity in vivo contrast for ultra-

low field magnetic resonance imaging using superparamagnetic iron oxide nanoparticles," *Sci. Adv.*, vol. 6, no. 29, Jul. 2020, doi: 10.1126/SCIADV.ABB0998.

- [26] E. Rössler, C. Mattea, A. Mollova, and S. Stapf, "Low-field one-dimensional and direction-dependent relaxation imaging of bovine articular cartilage," *J. Magn. Reson.*, vol. 213, no. 1, pp. 112–118, Dec. 2011, doi: 10.1016/J.JMR.2011.09.014.
- [27] J. M. Algarín *et al.*, "Simultaneous imaging of hard and soft biological tissues in a low-field dental MRI scanner," *Sci. Reports 2020 101*, vol. 10, no. 1, pp. 1–14, Dec. 2020, doi: 10.1038/s41598-020-78456-2.
- [28] C. D. E. Van Speybroeck, T. O'Reilly, W. Teeuwisse, P. M. Arnold, and A. G. Webb, "Characterization of displacement forces and image artifacts in the presence of passive medical implants in low-field (," *Phys. Med.*, vol. 84, pp. 116–124, Apr. 2021, doi: 10.1016/J.EJMP.2021.04.003.
- [29] M. Weiger and K. P. Pruessmann, "MRI with Zero Echo Time," *Encycl. Magn. Reson.*, vol. 1, pp. 311–322, Jun. 2012, doi: 10.1002/9780470034590.EMRSTM1292.
- [30] S. C. L. Deoni, J. O'Muircheartaigh, E. Ljungberg, M. Huentelman, and S. C. R. Williams, "Simultaneous high-resolution T2-weighted imaging and quantitative T2 mapping at low magnetic field strengths using a multiple TE and multi-orientation acquisition approach," *Magn. Reson. Med.*, vol. 88, no. 3, pp. 1273–1281, Sep. 2022, doi:

10.1002/MRM.29273.

- [31] N. Koonjoo, B. Zhu, G. C. Bagnall, D. Bhutto, and M. S. Rosen, "Boosting the signal-to-noise of low-field MRI with deep learning image reconstruction," *Sci. Rep.*, vol. 11, no. 1, Dec. 2021, doi: 10.1038/S41598-021-87482-7.
- [32] M. L. de Leeuw den Bouter, G. Ippolito, T. P. A. O'Reilly, R. F. Remis, M. B. van Gijzen, and A. G. Webb, "Deep learning-based single image super-resolution for low-field MR brain images," *Sci. Rep.*, vol. 12, no. 1, Dec. 2022, doi: 10.1038/S41598-022-10298-6.
- [33] M. Manso Jimeno, K. S. Ravi, Z. Jin, D. Oyekunle, G. Ogbole, and S. Geethanath, "ArtifactID: Identifying artifacts in low-field MRI of the brain using deep learning Magnetic Resonance Imaging," *Magn. Reson. Imaging*, vol. 89, pp. 42–48, Apr. 2022, doi: 10.1016/j.mri.2022.03.006.
- [34] D. Yoo *et al.*, "Signal Enhancement of Low Magnetic Field Magnetic Resonance Image Using a Conventional- and Cyclic-Generative Adversarial Network Models With Unpaired Image Sets," *Front. Oncol.*, vol. 11, May 2021, doi: 10.3389/FONC.2021.660284.
- [35] P. T. Vesanen, K. C. J. Zevenhoven, J. O. Nieminen, J. Dabek, L. T. Parkkonen, and R. J. Ilmoniemi, "Temperature dependence of relaxation times and temperature mapping in ultra-low-field MRI," *J. Magn. Reson.*, vol. 235, pp. 50–57, 2013, doi: 10.1016/J.JMR.2013.07.009.