



Published in final edited form as:

*PET Clin.* 2018 October ; 13(4): 551–565. doi:10.1016/j.cpet.2018.05.008.

## MR Imaging of the Musculoskeletal System Using Ultrahigh Field (7T) MR Imaging

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### Keywords

MR imaging; 7T; Bone; Muscle; Cartilage

### INTRODUCTION

In vivo musculoskeletal MR imaging plays a critical role in the modern medical practice. The excellent soft tissue contrast and multiplanar and multiparametric capabilities of MR imaging contribute to an unparalleled evaluation of all musculoskeletal tissues. Since the advent of diagnostic MR imaging, one of the most significant technological advancements has been the progressive increase in field strength ( $B_0$ ) of the clinical MR imaging systems. MR imaging at higher field strength offers several advantages, including increased signal-to-noise ratio (SNR), higher spatial resolution, improved spectral resolution, improved sensitivity for X-nucleus imaging, and decreased image acquisition times.<sup>1</sup> The physics of imaging at higher field strengths also, however, poses technical challenges, some of which include radiofrequency (RF) coil design, increased chemical shift and susceptibility artifacts, increased RF energy deposition (specific absorption rate [SAR]), and changes in relaxation times compared with the lower field strength scanners.

In October 2017, the US Food and Drug Administration (FDA) approved the first 7T-Magnetom Terra (Siemens, Munich, Germany) MR imaging system for clinical diagnostic imaging of the head and the extremities. In this timely narrative review, we discuss the many potential opportunities as well as the challenges presented by 7T MR imaging systems. We also highlight recent developments in in vivo imaging of musculoskeletal tissues, including anatomic, structural, compositional, and functional imaging of cartilage, bone, and skeletal muscle, using these systems.

### TECHNICAL ADVANTAGES AT HIGHER FIELD STRENGTHS

The SNR is often referred to as the “currency” of MR imaging and is an objective measure of image quality. Increasing SNR has been the primary driving force behind the development

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Conflict of Interest Statement: The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or nonfinancial interest in the subject matter or materials discussed in this article.

of higher field strength MR systems. Increasing field strength results in increased magnetization (also referred to as spin polarization), which provides a higher SNR and improved resolution.<sup>2</sup> Magnetization can be expressed by the following formula:

$$M_0 = B_0 \left( \gamma^2 \hbar^2 / 4kT \right) P_D$$

where  $P_D$  is proton spin density,  $\gamma$  represents the gyromagnetic ratio,  $\hbar$  is Plank constant divided by  $2\pi$ ,  $k$  is the Boltzmann constant,  $T$  is the absolute temperature (Kelvin), and  $B_0$  is the static magnetic field strength. The importance of field strength for magnetization can be easily delineated from the described formula. The calculation of SNR increase with increasing field strengths is, however, quite complicated and a detailed discussion can be found in the chapter by Collins<sup>1</sup> titled “Radio-frequency field calculations for high-field MR imaging.” For those of us who prefer a simple statistic, moving from 3T to 7T results in a gain of SNR by a factor of approximately 2.3.<sup>3</sup> This SNR gain translates to greater spatial resolution as well as reduced scan times, because SNR scales with square root of acquisition time.<sup>3</sup> Additionally, higher field strength allows parallel imaging to be performed with higher speed reduction factors, which can further reduce acquisition time.<sup>4</sup>

The SNR gain at 7T also improves the spectral resolution of (<sup>1</sup>H) magnetic resonance spectroscopy (MRS), allowing identification of biological molecules that would not be possible at lower field strengths.<sup>5</sup> Furthermore, there are many biologically relevant nuclei besides <sup>1</sup>H, such as sodium and phosphorous, which occur in lower concentrations and are therefore difficult to image at conventional clinical field strengths. The utility of 7T in evaluating these nuclei has already been shown. Sodium is closely associated with the glycosaminoglycan, an important component of the cartilage extracellular matrix. Sodium (<sup>23</sup>Na) MR imaging of cartilage at 7T has been used to map the sodium distribution and therefore indirectly detects early cartilage damage.<sup>6</sup> Phosphorous (<sup>31</sup>P) is an important skeletal muscle metabolite and localized dynamic (<sup>31</sup>P) MRS at 7T has been used to study mitochondrial oxidative metabolism in vivo.<sup>7</sup>

## TECHNICAL CHALLENGES AT HIGHER FIELD STRENGTHS

Besides the enormous cost of acquiring and operating a 7T MR imaging system, there are technical challenges that need to be overcome for it to be routinely used in clinical imaging. Five of these are described. First, inhomogeneous tissue excitation is a problem at 7T and RF-related artifacts have been described in multiple in vivo studies.<sup>8</sup> At 7T, RF frequencies are higher, and wavelengths may be shorter than the object of interest, resulting in decreased penetration and inhomogeneous excitation. Artifacts may result with the  $B_1$  magnitude and signal intensity much higher in the center of the field than at the periphery, therefore distorting the image.<sup>8</sup> These effects are more likely to be seen in the head or body than the extremities, which on average have smaller dimensions. RF coils for 7T MR imaging must be designed to control RF field propagation and minimize energy deposition.<sup>9</sup> RF shimming and parallel RF transmission techniques may be used to improve image quality at 7T.<sup>10,11</sup>

Second, increasing field strength leads to changes in relaxation times;  $T_1$  values increase<sup>12</sup> while  $T_2$  values decrease.<sup>13</sup> Pulse sequences, therefore, need to be optimized to produce images with the contrast necessary to answer the diagnostic inquiry. Third, there is an increased sensitivity to susceptibility effects (decreased  $T_2^*$ ) at higher field strengths.<sup>13</sup> Although this may be beneficial for susceptibility-weighted imaging, susceptibility artifact related to orthopedic hardware can hinder interpretation of clinical MR imaging. Both conventional static  $B_0$  and dynamic shimming<sup>14</sup> can be used to reduce susceptibility effects.

Fourth, there is a substantial increase in chemical shift artifact in the frequency-encoded direction at 7T.<sup>15</sup> The chemical shift difference between water and fat resonance is 1040 Hz at 7T compared with 440 Hz at 3T, which at a bandwidth of 130 Hz/pixel amounts to a chemical shift of 8 pixels at 7T versus 3.4 pixels at 3T.<sup>15</sup> The increase in chemical shift improves spectral resolution of MRS; however, chemical shift artifact may hinder interpretation of clinical images. Several techniques, such as using adiabatic refocusing pulses<sup>16</sup> have been used to reduce chemical shift displacement artifacts, but resulting in increases in SAR.

Last, but most importantly, patient safety is paramount. Increased RF at 7T results in higher energy (heat) deposition in tissues. SAR is the measure of RF absorption and scales with essentially the square of the magnetic field. At 7T, SAR needs close monitoring to avoid tissue heating. The FDA has established limits for SAR for both pediatric and adult patients.<sup>17</sup> Although the FDA considers MR imaging under 8T to pose no health risk to adults and children older than 1 month, minor side effects have been reported at high field strengths.<sup>18,19</sup> Table 1 provides a brief summary of some of the advantages and disadvantages of imaging at higher field strengths.

## CARTILAGE

### Cartilage Microarchitecture

Cartilage is composed of 70% to 80% fluid. The remainder is the extracellular matrix (ECM), a network of collagen fibrils and proteoglycan molecules. Proteoglycans consist of negatively charged glycosaminoglycan (GAGs) attached to protein core.<sup>20</sup> Cations such as sodium ( $\text{Na}^+$ ) counter the negative charge of GAGs and maintain neutrality. The flow of water within the ECM provides the known biomechanical properties of cartilage.<sup>21</sup> In osteoarthritis (OA), the initial histologic changes include cartilage breakdown with proteoglycan loss and disorganization and/or loss of the collagen fiber network.<sup>22</sup>

### Morphologic Imaging of Cartilage

Standard protocols for imaging cartilage morphology at 7T are yet to be established; however, will foreseeably follow the techniques used with 3T MR imaging systems. Springer and colleagues<sup>23</sup> recently performed comparable routine knee imaging at 3T and 7T and found diagnostic confidence of radiologists for cartilage defects to be higher with 7T. The turbo spin echo (TSE) pulse sequence used in this study is the workhorse for the clinical musculoskeletal imaging due to its excellent soft tissue contrast and rapid acquisition. Fast Spin Echo and TSE are also part of the International Cartilage Repair Society's cartilage

imaging protocol.<sup>24</sup> Fat saturation is also essential for clinical musculoskeletal imaging and chemical shift selective fat saturation is easier to perform at 7T.

An in-plane resolution of 0.3 mm resolves the earliest fraying of the cartilage surface.<sup>25</sup> Jin and colleagues<sup>26</sup> acquired high-resolution 2-dimensional (2D) and 3D image of the knee and ankle joints at 7T with a 0.3 mm in-plane resolution for TSE and 0.47 mm for isotropic sequences, such as dual echo steady state (3D-DESS). The open architecture 8-channel transmit-receive coil in this study even allowed dynamic imaging during continuous knee and ankle flexion-extension cycles. Regatte and Schweitzer<sup>15</sup> previously described the acquisition of sagittal knee images with a resolution of 0.25 mm using a gradient-based isotropic fast low-angle shot pulse sequence (3D-FLASH) with fat suppression.

Isotropic sequences obviate the need for multiplanar acquisition and reduce acquisition time.

<sup>27</sup> The diagnostic accuracy of isotropic fast spin echo (FSE) for cartilage morphology is similar to 2D FSE at 3T; however, this remains to be studied for images obtained at 7T.<sup>28</sup> Other isotropic sequences, including 3D spoiled gradient recoiled echo (SPGR) and 3D-FLASH produce images with cartilage signal more intense than the surrounding tissues<sup>26</sup> and may be better suited for quantitative analysis of cartilage rather than morphologic assessment (Fig. 1).<sup>29–31</sup>

### Compositional Imaging of Cartilage

By the time morphologic changes in cartilage are evident on clinical MR imaging, cartilage degeneration is in its advanced stages. Compositional imaging techniques have primarily been used in few research centers; however, allow detection of biochemical and microstructural changes in the cartilage ECM. These methods can, therefore, help identify cartilage breakdown at its earliest stages. We briefly describe some of these techniques and related recent developments at 7T.

### T<sub>2</sub> Mapping and T<sub>2</sub>\* Mapping

T<sub>2</sub> mapping has been the most widely studied of all compositional imaging techniques and was an integral part of the knee imaging protocol in the large multicenter osteoarthritis initiative cohort study.<sup>32</sup> After application of an RF pulse, the rate constant of dephasing in the transverse plane equates to T<sub>2</sub> relaxation time. This value measured in milliseconds reflects water content and indirectly the collagen content in the cartilage ECM.<sup>33</sup> There is a laminar variation of T<sub>2</sub> values in cartilage with higher values at the articular surface compared with the bone interface.<sup>34</sup> Higher cartilage T<sub>2</sub> values have been shown to be predictive of the development of morphologic changes of cartilage deterioration.<sup>35</sup>

Welsch and colleagues<sup>36</sup> found less variation in T<sub>2</sub> measurements performed at 7T. This study reported cartilage T<sub>2</sub> values to be intrinsically lower compared with 3T and the laminar variation to be less pronounced. T<sub>2</sub> mapping at 7T has been shown to be able to discriminate between repaired knee cartilage and adjacent healthy cartilage (Fig. 2).<sup>37–39</sup> It has also been shown to detect maturation of reparative tissue after autologous chondrocyte transplantation.<sup>40</sup> Additionally, the increased resolution and decreased partial volume effects at 7T may allow T<sub>2</sub> and T<sub>2</sub>\* mapping of thinner cartilage in the hips and ankles.<sup>41</sup> Juras and colleagues<sup>42</sup> have compared within-subject T<sub>2</sub> values in the knee and ankle cartilage at 7T

and found these to be significantly different owing to their varying biomechanical and biochemical properties.

$T_2^*$  mapping measures transverse-plane dephasing using multi-echo gradient echo techniques, which are faster to acquire than  $T_2$  but are also more vulnerable to local field inhomogeneity.<sup>36,43</sup>  $T_2^*$  values are also lower at 7T than at 3T.<sup>36</sup> Both  $T_2$  and  $T_2^*$  are affected by magic angle effect; that is, the values increase as the angle between collagen fibers and  $B_0$  approaches  $55^\circ$ .

### T1rho Mapping

T1rho evaluates the spin-lattice ( $T_1$ ) relaxation in the rotating frame.<sup>44</sup> It can evaluate the interaction between free (bulk) water and adjacent molecules and is understood to reflect particularly the proteoglycan content of the ECM.<sup>45</sup> T1rho, like  $T_2$ , predicts morphologic deterioration of articular cartilage.<sup>46</sup> T1rho imaging is more challenging to perform due to  $B_0$  and  $B_1$  inhomogeneity, specialized RF pulse sequence requirements, and long acquisition times. The long scan time is particularly a concern at 7T due to increased SAR. A recent study, however, leveraged the SNR advantage of 7T to acquire high-resolution T1rho images ( $0.2 \text{ mm}^2$  in-plane resolution) in reasonable acquisition times (<30 minutes) and within SAR constraints.<sup>47</sup> This study reported T1rho times lower at 7T than at 3T. It also found T1rho values to be higher in the medial femoral condyles of volunteers with meniscal tears compared with those without tears. Wyatt and colleagues<sup>48</sup> found T1rho values to be higher in patients with OA compared with healthy subjects, with the differences being higher and statistically significant in more regions at 7T than at 3T. Kogan and colleagues<sup>49</sup> compared T1-rho at 7T to the gagCEST sequence (described later in this article) and reported good agreement between the 2 techniques. The same investigators have also described combining the 2 methods at 7T to form a CESTrho sequence, which can quantify proton exchange at intermediate exchange rates, without being affected by confounding factors, which can affect proton exchange rates.<sup>50</sup>

### Ultrashort Echo Time and Zero Echo Time Imaging

Musculoskeletal tissues such as cortical bone, tendon, ligaments, and the deep calcified part of cartilage contain a high fraction of components with “ultrashort” transverse relaxation times and therefore produce no signal on standard MR images as their signal decays before it can be acquired.<sup>51</sup> Ultrashort echo time (UTE) and zero echo time use specialized acquisition and reconstruction techniques to capture these ultrashort components before signal decay. The application of these techniques at 7T has primarily focused on tendons and cortical bone. At lower field strengths, UTE has been used to delineate the calcified deepest cartilage layer<sup>52</sup> and has also been used to evaluate the integrity of this layer in osteochondral allografts.<sup>53</sup> UTE also enables  $T_2$  and  $T_2^*$  mapping of tissues with a high fraction of ultrashort components. Chu and colleagues<sup>54</sup> reported UTE  $T_2^*$  to be helpful in evaluating cartilage healing after anterior cruciate ligament reconstruction.

### Delayed Gadolinium-Enhanced MR Imaging of Cartilage

Gadopentetate dimeglumine ( $\text{Gd-DTPA}^{2-}$ ), the commonly used MR imaging contrast, is an anion and therefore repelled by the negatively charged GAGs. dGEMRIC takes advantage of

this to map GAG content within cartilage. An area of damaged cartilage will accumulate Gd-DTPA<sup>2-</sup> and therefore have a shorter T<sub>1</sub> relaxation time. In vivo delayed gadolinium-enhanced MR imaging of cartilage (dGEMRIC) studies at 7T are scarce. A feasibility study by Welsch and colleagues<sup>39</sup> found dGEMRIC to be promising at 7T. In this study of 5 healthy volunteers, T<sub>1</sub> values differed between tibial and femoral cartilage.

At lower field strengths, dGEMRIC has been used for a wide range of musculoskeletal conditions, including cartilage repair,<sup>55,56</sup> tibial osteotomy,<sup>57</sup> inflammatory arthritis,<sup>58</sup> and chronic joint unloading.<sup>59</sup>

The disadvantages of dGEMRIC include the large doses of Gd-DTPA<sup>2-</sup> required. There is also the delay between injection, joint exercise for efficient diffusion into the joint, and long acquisition times.<sup>60</sup> There is, however, a possibility of obtaining an indirect MR arthrogram during this delay, which can aid morphologic evaluation of intra-articular structures, particularly the hip labrum. A recent study by Lazik-Palm and colleagues<sup>61</sup> found that gadolinium administration at 7T did not significantly impact either T<sub>2</sub> or T<sub>2</sub>\* relaxation times and improved morphologic image quality. The investigators suggest morphologic and quantitative analysis including dGEMRIC can, therefore, be combined to perform a comprehensive examination during a single visit.

### Sodium (<sup>23</sup>Na) Imaging

The negatively charged GAGs in cartilage ECM attract positive <sup>23</sup>Na<sup>+</sup> counter-ions, the distribution of which reflect local GAG concentration. Loss of GAG content with cartilage degeneration will result in a lower concentration of <sup>23</sup>Na<sup>+</sup> ions.<sup>62</sup> <sup>23</sup>Na has a spin magnetic moment; however, its concentration is only 0.08% that of <sup>1</sup>H, which makes it difficult to elicit signal, resulting in noisy MR images and long acquisition times. The SNR gain at 7T MR imaging is hence particularly useful for <sup>23</sup>Na imaging, as it increases its sensitivity<sup>63</sup> and improves resolution. <sup>23</sup>Na imaging has been shown to correlate well with dGEMRIC.<sup>64</sup> Unlike dGEMRIC, <sup>23</sup>Na imaging can assess cartilage proteoglycan without intravenous contrast injection. The Larmor frequency of <sup>23</sup>Na<sup>+</sup> is much lower than that of <sup>1</sup>H, so specialized transmit-receive coils are, however, required.<sup>65</sup> SAR is also a concern with sodium imaging at long acquisition times; however, Medelin and colleagues<sup>66</sup> have demonstrated that compressed sensing image reconstruction can reduce scan times to less than 10 minutes without losing sodium quantification accuracy. Additionally, sodium inversion recovery pulse sequences can be designed to mitigate RF absorption while improving quality through suppression of free sodium in the synovial fluid.<sup>67,68</sup> As with T<sub>2</sub> Mapping, sodium imaging has been shown to be able to discriminate between cartilage repair tissue and healthy cartilage (Fig. 3).<sup>68,69</sup> The investigators of this study reported lower sodium signal intensity in repair tissue after microfracture surgery or matrix autologous chondrocyte transplantation (MACT) compared with healthy cartilage, suggesting diminished GAG content. A different study by the same group found repair tissue after MACT to have higher sodium signal intensity than after bone marrow stimulation, leading them to imply that MACT repair is of better quality.<sup>70</sup>



## Diffusion Tensor Imaging

The cartilage collagen network is highly organized resulting in anisotropic water diffusion within the ECM. Diffusion tensor imaging (DTI) can assess both proteoglycan content through mean apparent diffusion coefficient (ADC) and collagen microarchitecture through fractional anisotropy (FA). Raya and colleagues<sup>71</sup> used a line-scan DTI imaging sequence at 7T to compare articular cartilage of healthy subjects with cartilage in subjects with osteoarthritis. They found that both mean ADC and FA values to be good discriminators between the groups, with FA having higher specificity. Ex vivo imaging performed by the same group at 17.6 T found DTI to be excellent for detecting cartilage damage (95% accuracy) and demonstrate good performance for grading cartilage damage (75% accuracy).<sup>72</sup> DTI imaging of cartilage is overall challenging to perform in vivo owing to the short T2 of articular cartilage and the high resolution needed to depict the cartilage anatomy.

## Glycosaminoglycan Chemical Exchange Saturation Transfer Imaging

Water protons bound to macromolecules exchange their magnetization with free water protons within the ECM. Water protons bound to macromolecules have unique RF frequency and can be saturated using off-resonance RF pulses. Subsequently, the magnetization exchange with free water results in a loss of image signal intensity, and this effect can be measured to estimate local macromolecule content. With GAG chemical exchange saturation transfer imaging (gagCEST), GAGs are the macromolecules being evaluated with the off-resonance RF saturation pulses applied to saturate exchangeable protons residing on the hydroxyl groups of cartilage GAGs (Fig. 4).<sup>73</sup> gagCEST has been shown to be sensitive to cartilage proteoglycan content.<sup>73</sup> It also correlates well with <sup>23</sup>Na<sup>+</sup> imaging and feasible at 7T.<sup>74</sup> Singh and colleagues<sup>75</sup> compared CEST in knee cartilage at 3T and 7T and found CEST measurements to be negligible at 3T, whereas the results were more promising at 7T. Kogan and colleagues<sup>49</sup> recently described a volumetric multislice gagCEST technique, which can reduce acquisition time.

## SKELETAL MUSCLE

### Morphologic Images of Skeletal Muscle

Morphologic imaging of skeletal muscle at 7T is similar to imaging at lower field strengths. Routine clinical protocols will need to be optimized to maintain contrast desired by the radiologists to respond to the diagnostic inquiries.

### Chemical-Shift-Encoded Water-Fat Separation MR Imaging

As previously described, chemical shift is increased at 7T resulting in improved spectral resolution. Chemical-shift-encoded water-fat separation (WFI) techniques have been used for intramuscular adipose tissue quantification. WFI captures the phase difference between water and fat protons by acquiring 2 echoes and can provide high-resolution 3D imaging of fat composition.<sup>76</sup> This technique is yet to be applied in vivo in human subjects at 7T. At lower field strengths, fat-fraction (FF) estimated using WFI is reliable in comparison with biopsy<sup>77</sup> and more accurate than visual fat grading.<sup>78</sup> The distribution of MR imaging measured intramuscular fat is different in type 2 diabetes compared with healthy subjects<sup>79</sup>

and intramuscular FF also progressively increases in patients with neuromuscular disorders. Quadriceps muscle FF is associated with osteoarthritis,<sup>80</sup> whereas shoulder rotator cuff muscle FF correlates with the success of repair as well with pain and range of motion.<sup>81</sup>

## MR Spectroscopy

Glycogen, intramyocellular lipid (IMCL), and extramyocellular lipid (EMCL) and phosphocreatine (PCr) are all sources of energy for skeletal muscle, which can be measured in vivo using  $^{13}\text{C}$ ,  $^1\text{H}$ , and  $^{31}\text{P}$  MR spectroscopy (MRS).<sup>82</sup> The frequency difference between IMCL and EMCL is too small to delineate with chemical-shift imaging but can be assessed with  $^1\text{H}$  MRS.<sup>83</sup> At 7T, the increased resolution of lipid spectra allows identification of additional lipid peaks, which are not visible at lower field strengths.<sup>84</sup> Compared with 3T, the  $T_1$  relaxation times of skeletal muscle metabolites are increased at 7T, whereas  $T_2$  relaxation times are decreased.<sup>84</sup> MRS is particularly of interest to endocrinologists, as IMCL levels are elevated in subjects with insulin resistance.<sup>83</sup>

$^{31}\text{P}$  MRS provides information about skeletal muscle bioenergetics. It can detect phosphorylated compounds including phosphocreatine (PCr), inorganic phosphates (Pi), the phosphate groups in ATP, and phosphomonoesters (Fig. 5). The advantages of performing this technique at 7T are clear. Bogner and colleagues<sup>85</sup> found 7T  $^{31}\text{P}$  MRS in the human calf muscle has shorter measurement times with increased SNR and improved temporal resolution in dynamic studies. Parasoglou and colleagues<sup>86</sup> developed a spectrally selective 3D TSE sequence, which can provide simultaneous measurement of PCr resynthesis rates in several muscles of the exercising body part.  $^{31}\text{P}$  MRS has shown that athletes have higher PCr/Pi ratios for a given workload and a faster recovery of PCr.<sup>87</sup> Both of these measurements have been proposed to provide MR-based functional measures of mitochondrial density.<sup>88</sup>  $^{31}\text{P}$  MRS has also been used as a tool to study several diseases, including peripheral arterial disease<sup>89</sup> and type 2 diabetes.<sup>90</sup>

## $T_2$ Mapping

The advantages of skeletal muscle  $T_2$  mapping at 7T remain to be determined. Preliminary work, including optimization of sequence parameters and the determination of how perfusion and oxygenation might affect  $T_2$  mapping at 7T, is ongoing.<sup>91</sup> Theoretically, the higher spatial resolution would allow more accurate and more automated for quantitative analysis. A preliminary study at New York University performed  $T_2$  mapping in a small cohort of volunteers after plantar flexion exercises and found  $T_2$  values to decrease after exercise. The calculated  $T_2$  values for skeletal muscle and the time course of recovery for  $T_2$  values after exercise were similar to those described at lower field strength.<sup>9</sup>

At lower field strengths,  $T_2$  mapping has been shown to correlate with nonquantitative MR scores for fatty infiltration and proposed as a potential imaging biomarker for neuromuscular disorders, such as Duchenne muscular dystrophy<sup>92</sup> and Pompe disease.<sup>93</sup> It also may be valuable for measuring therapeutic effects of corticosteroids on the skeletal muscle in these patients.<sup>94</sup>



## **<sup>23</sup>Na MR Imaging**

Sodium concentration gradients across the cell membrane contribute to the resting membrane potential and help generate action potentials leading to muscle contraction.<sup>9</sup> The general challenges of sodium imaging, as well as advantages of 7T sodium MR imaging, were previously discussed in the cartilage section. The feasibility of <sup>23</sup>Na MR imaging at 7T was demonstrated by Chang and colleagues<sup>95</sup> in a study comparing the effect of exercise on skeletal muscle sodium concentrations in healthy subjects and diabetic individuals. Sodium signal intensity increased within the muscle in both groups after exercise; however, the diabetic individuals demonstrated a delayed return to preexercise sodium signal intensity.

At lower field strengths, <sup>23</sup>Na MR imaging has been used to study skeletal muscle in health volunteers as well as patients with neuromuscular disorders such as Duchenne muscular dystrophy<sup>96</sup> and paramyotonia congenita.<sup>97</sup> Increased sodium signal intensity in the skeletal muscle of patients with the neuromuscular disorder has been proposed as being a contributor to the pathogenesis via intracellular muscle edema.

## **BONE**

Osteoporosis is characterized by a decrease in bone mineral density (BMD) resulting in susceptibility to fragility fractures.<sup>98</sup> Dual-energy x-ray absorptiometry (DXA), the current screening standard for osteoporosis, may artificially underestimate or overestimate fracture risk.<sup>99</sup> A big component of bone imaging research, therefore, focuses on establishing better measures of bone quality and strength and improving prediction of fragility fractures. Normal bone is composed of an outer compact cortical component, internal trabecular component, and bone marrow. The SNR gain and increased resolution of 7T makes it easier to quantify apparent trabecular structural parameters. MR imaging of trabecular bone has been validated via comparisons with micro-computed tomography and histology,<sup>100,101</sup> and these measurements have also been shown to be reproducible.<sup>102</sup> Chang and colleagues<sup>103</sup> demonstrated the feasibility of performing a comprehensive hip MR imaging protocol at 7T that included high-resolution imaging of bone microarchitecture and cartilage, as well as clinical imaging. They also found that same 7T MR imaging of bone microarchitecture can discriminate between women without and with fragility fractures who do not differ by DXA-derived BMD (Fig. 6).<sup>104,105</sup> On the other hand, a study of bone microarchitecture in Olympic fencing athletes found them to have better bone quality than controls.<sup>106</sup> Micro-finite element analysis (FEA), traditionally an engineering tool, has also been performed on 7T high-resolution MR imaging of the distal tibia and proximal femur. MR imaging-based FEA provides bone stiffness measures as a potential imaging marker for bone strength.<sup>107</sup> Professional dancers, for example, were found to have increased bone stiffness in comparison with inactive controls.<sup>108</sup> Feasibility of performing these bone MR imaging techniques at 7T in smaller joints such as the wrist has been demonstrated.<sup>109</sup>

Due to its short T<sub>2</sub> components, cortical bone demonstrates low signal on routine MR imaging. UTE can, however, improve assessment of cortical bone and at lower field strengths has been successfully applied to study cortical water content, which is related to cortical porosity.<sup>110,111</sup> A feasibility study by Krug and colleagues<sup>3</sup> used an isotropic UTE sequence at 7T and 3T. The investigators reported an SNR gain by a factor of 1.7 (from 3T

to 7T) and significantly shorter  $T_2$  values. Further studies are needed to fully explore the potential of UHF MR imaging for imaging cortical bone.

## SUMMARY

The recent approval of 7T MR imaging for clinical use is a major advancement that will drive the development of both clinical and research applications for musculoskeletal imaging. The SNR gain at 7T is an irrefutable advantage. The technical challenges are plentiful but RF inhomogeneity and coil design are the 2 that are underlined. Future musculoskeletal imaging protocols will likely include a combination of clinical morphologic and compositional imaging sequences. Advancement of compositional imaging techniques at 7T will likely be rapid. Further development of CEST techniques will enable high-resolution imaging of organic molecules, such as glucose and proteins, which play critical roles in disease pathogenesis. Higher SNR will permit X-nuclei MRS, including  $^{23}\text{Na}$ ,  $^{39}\text{K}$ ,  $^{31}\text{P}$ ,  $^{13}\text{C}$ ,  $^{17}\text{O}$ , and so on, which will provide vital information regarding cellular processes, metabolic turnovers, energy metabolism, and oxygen consumption rate. MR imaging at 7T is another big step in the continued drive toward precision personalized medicine.

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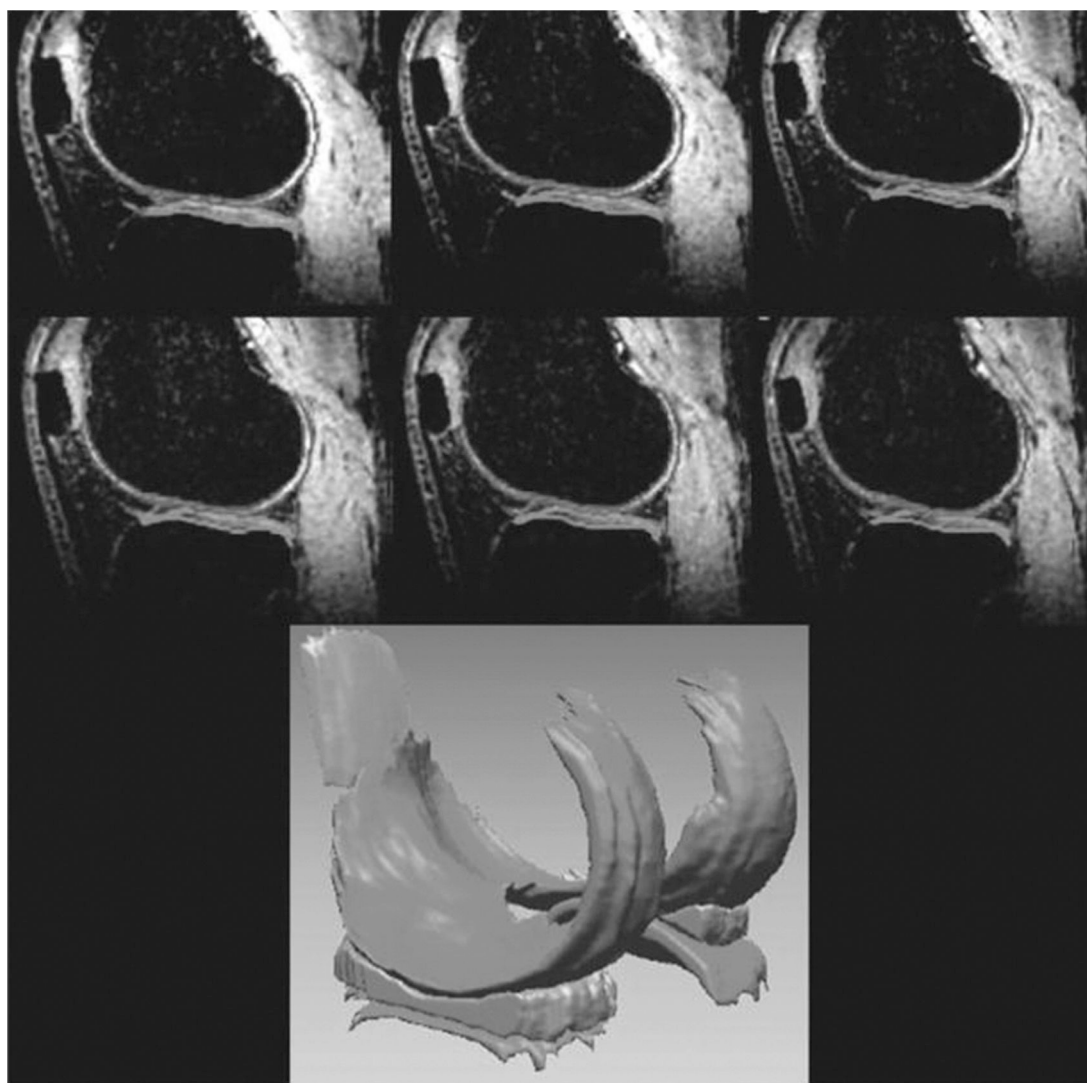
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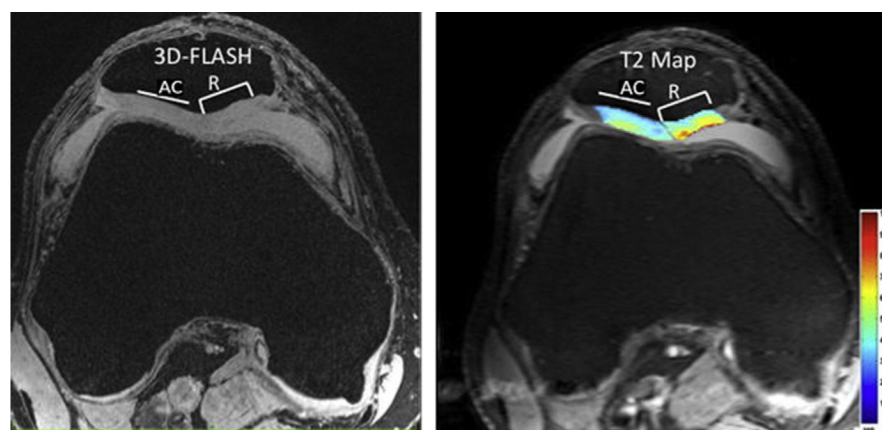
**KEY POINTS**

- The signal-to-noise ratio gain of 7T MR imaging benefits both clinical and research musculoskeletal imaging.
- RF and  $B_0$  inhomogeneity and coil design are the major challenges of MR imaging at 7T.
- Future musculoskeletal imaging protocols will likely be a hybrid of morphologic, compositional, and functional MR imaging sequences.

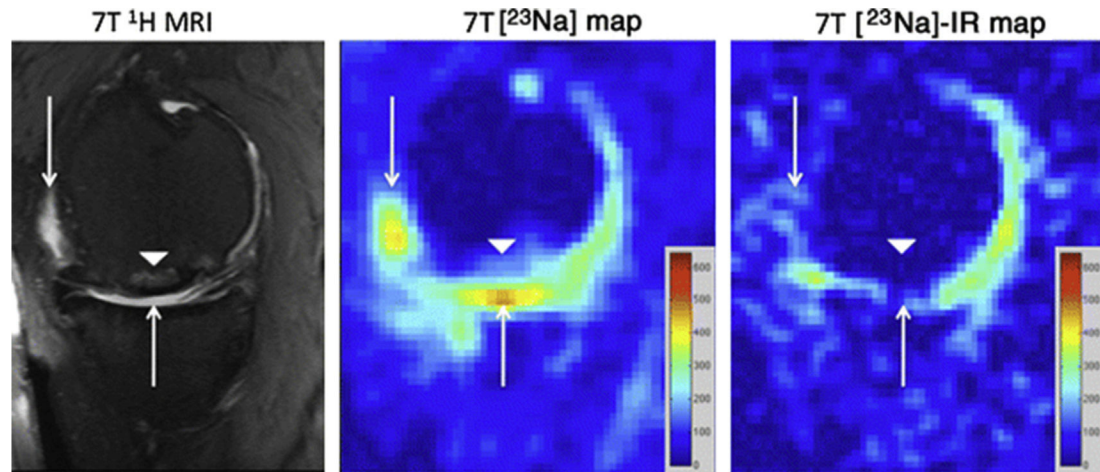


**Fig. 1.**

Representative high-resolution (3D fast low-angle shot) sagittal knee images with fat suppression were acquired on a healthy volunteer at 7T for better visualization of cartilage and surrounding structures. Three-dimensional cartilage and menisci volume were reconstructed from corresponding segmented regions; 160 slices were acquired in approximately 13 minutes with  $500\ \mu\text{m} \times 500\ \mu\text{m} \times 500\ \mu\text{m}$  isotropic resolution. (From Regatte RR, Schweitzer ME. Novel contrast mechanisms at 3 T and 7 T. *Semin Musculoskelet Radiol* 2008;12(3):266–80; with permission.)



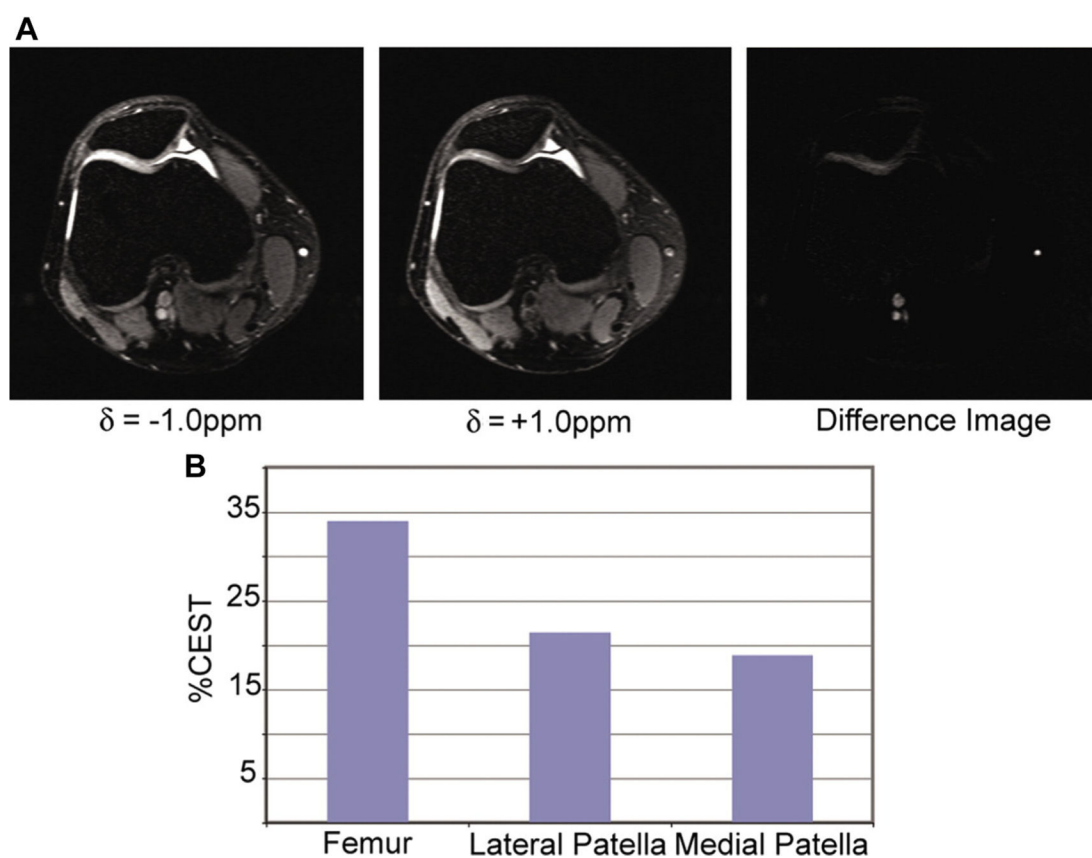
**Fig. 2.** Juvenile cartilage cell implantation. High-resolution 7T 3D-FLASH image (*left panel*, repetition time/echo time [TR/TE] = 20 ms/5.1 ms, 0.234 mm × 0.234 mm × 1 mm) and T2 map (*right panel*, TR/TE = 3000 ms/15, 30, 45, 60, 75, 90 ms, 0.586 mm × 0.586 mm × 2 mm) demonstrate close to normal thickness, but higher T2 values in the repair (R) tissue compared with adjacent cartilage (AC). (*From* Chang G, Xia D, Sherman O, et al. High resolution morphologic imaging and T2 mapping of cartilage at 7 T: comparison of cartilage repair patients and healthy controls. *MAGMA* 2013;26(6):539–48; with permission.)



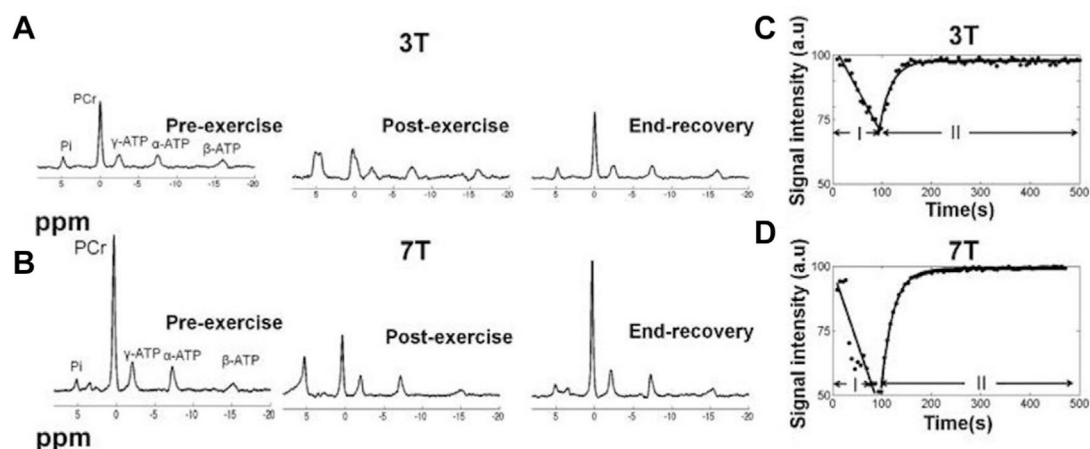
**Fig. 3.**

Sagittal T2-weighted 7T MR image (*left panel*) of the right knee demonstrating an osteochondral allograft (*arrowhead*) at the weight-bearing aspect of the medial femoral condyle. There is synovial fluid at the articular surface (*arrows*). On the conventional  $^{23}\text{Na}$  concentration map (*middle panel*), hyperintense signal is seen from synovial fluid at the articular surface (*arrows*) and to a lesser extent in a subchondral location at the repair site (*arrowhead*). On the sodium concentration map generated from  $^{23}\text{Na}$ -IR MR imaging (*right panel*), there is suppression of signal from free sodium within synovial fluid (*arrows*) and also in the subchondral location (*arrowhead*). The sodium images represent concentration maps, with colored bars indicating range of  $[\text{Na}^+]$  in mM (*red* = 600 mM, *blue* = 0 mM). The larger apparent joint space size on sodium maps compared with proton images is likely due to partial volume averaging from the lower resolution of the sodium maps (2 mm  $\times$  2 mm vs 0.546 mm  $\times$  0.546 mm  $\times$  2 mm). (*Reprinted from* Chang G, Madelin G, Sherman OH, et al. Improved assessment of cartilage repair tissue using fluid-suppressed  $^{23}\text{Na}$  inversion recovery MR imaging at 7 T: preliminary results. *Eur Radiol* 2012;22:1341–9; with permission.)

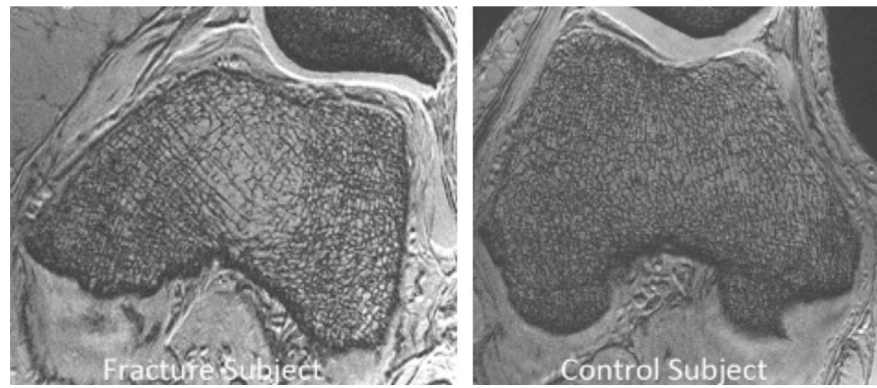


**Fig. 4.**

Images of a human patella in vivo with irradiation at  $\delta = -1.0$  ppm,  $\delta = +1.0$  ppm, and the difference image (*A*) along with the extracted CEST contrast from the femur and the lateral and medial sides of the patella (*B*). The total duration of the presaturation pulse sequence was 320 ms at an average rf power of 42 Hz. (From Ling W, Regatte RR, Navon G, et al. Assessment of glycosaminoglycan concentration in vivo by chemical exchange-dependent saturation transfer (gagCEST). *Proc Natl Acad Sci U S A* 2008;105(7):2266–70; © 2008 National Academy of Sciences, U.S.A. with permission.)

**Fig. 5.**

MR spectra of the same volunteer before and after exercise, and at the end of the recovery period (A) at 3T and (B) at 7T. We have normalized the amplitude of all postexercise spectra to the preexercise ones. We observed an almost threefold increase of SNR at 7T relative to 3T. Evolution of the phosphocreatine (PCr) MRS signal intensity during the execution of the exercise (I) and the recovery period (II) from the same volunteer. PCr depletion rates were estimated by fitting a linear function to phase I, whereas the PCr recovery kinetics were characterized by fitting a mono-exponential growth function to phase II of the exercise. (C) At 3T, the PCr depletion rate is  $0.35 \text{ s}^{-1}$  (estimated from the slope of the fitted line,  $r = 0.997$ ) and the recovery rate constant is  $22.4 \text{ s}$  ( $r = 0.981$ ). (D) At 7T, the PCr depletion rate is  $0.49 \text{ s}^{-1}$  ( $r = 0.945$ ) and the recovery rate constant is  $23.89 \text{ s}$  ( $r = 0.998$ ). (From Parasoglou P, Xia D, Chang G, et al. Dynamic three-dimensional imaging of phosphocreatine recovery kinetics in the human lower leg muscles at 3T and 7T: a preliminary study. *NMR Biomed* 2013;26(3):348–56; with permission.)



**Fig. 6.**

MR imaging at 7T reveals deterioration in distal femur trabecular bone microarchitecture in a fragility fracture subject (*left*) compared with a control subject (*right*). The fracture subject demonstrates fewer trabeculae, which are disconnected, and more widely spaced apart. (From Chang G, Boone S, Martel D, et al. MR imaging assessment of bone structure and microarchitecture. *J Magn Reson Imaging* 2017;46(2):323–37; with permission.)

A summary of potential advantages and disadvantages of high and ultrahigh field systems in musculoskeletal imaging

Table 1

Characteristic	Trend	Positive	Negative
SNR	↑	Higher resolution, shorter scan time, X-nuclei	NA
SAR	↑	NA	Fewer slices, smaller flip angles
Physiologic side effects (7T)	↑	NA	Dizziness, nausea, metallic taste
Relaxation times	$T_1$ ↑ $T_2$ ↓ $T_2^*$ ↓		Scan time increase, DWI/DTI
		Facilitates BOLD, SWI at 7T	
RF homogeneity	↓	Parallel reception, parallel transmission	Poor inversion, poor contrast
Susceptibility effects	↑	$T_2^*$	Geometric distortions Metal artifact
Chemical shift	↑	Fat saturation, spectral resolution	Fat/water Misregistration

Abbreviations: BOLD, Blood Oxygen Level Dependent contrast; DTI, diffusion tensor imaging; DWI, diffusion-weighted imaging; NA, not applicable; SAR, specific absorption rate; SNR, signal-to-noise ratio; SWI, Susceptibility weighted imaging; ↑, Increase; ↓, Decrease.

Adapted from Moser E, Stahlberg F, Ladd ME, et al. 7-T MR—from research to clinical applications? NMR Biomed 2012;25(5):695–716; with permission.