



# Correlation between fat signal ratio on T1-weighted MRI in the lower vertebral bodies and age, comparing 1.5-T and 3-T scanners

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Dominik Sieron<sup>1</sup>, Dionysios Drakopoulos<sup>1</sup>, Laura I Loebelenz<sup>2</sup>,  
Christophe Schroeder<sup>2</sup>, Lukas Ebner<sup>2</sup>, Verena C Obmann<sup>2</sup> ,  
Adrian T Huber<sup>2</sup> and Andreas Christe<sup>1,2</sup> 

## Abstract

**Background:** The hypothesis was that the fat-dependent T1 signal intensity in vertebral bodies increases with age due to red-yellow marrow conversion.

**Purpose:** To analyze the increasing fatty conversion of red bone marrow with age.

**Material and Methods:** A continuous sample of 524 patients (age range 2–96 years) with normal lumbar spine MRIs (T11–L5) was retrospectively selected in order to get a representative sample from our 1.5-T and 3-T MRI units (Siemens, Erlangen, Germany). Four radiologists read the images independently. Absolute T1 signal intensities were measured in the lower vertebral bodies and standardized by dividing their value by the signal of the subcutaneous fat on lumbar and sacral level.

**Results:** The standardized T1 signal correlated significantly with patients' age at the 1.5-T unit, with the best correlation demonstrated by thoracic vertebra T11, followed by lumbar vertebra L1, with correlation coefficients (R) of 0.64 (95% CI 0.53–0.72,  $P < 0.0001$ ) and 0.49 (95% CI 0.38–0.59,  $P < 0.0001$ ), respectively. For women and men, the R values were similar in thoracic vertebra T11 at 0.62 (95% CI 0.49–0.72) and 0.64 (95% CI 0.44–0.77), respectively. The vertebral signal correlated significantly better with age in the 1.5-T compared to the 3-T unit on all vertebral levels: the best R value of the 3-T unit was only 0.20 (95% CI 0.09–0.30,  $P < 0.0001$ ). Our study showed an average increase of the relative T1 signal in T11 of 10% per decade.

**Conclusion:** T1 fat signal ratio increases with age in the vertebral bodies, which could help estimating the age of a person. Best age correlation was found when measuring T1 signal in T11, standardized by the sacral subcutaneous fat signal and using a 1.5-T MRI.

## Keywords

T1 signal of spine, red bone marrow conversion, age, fat signal ratio, vertebral bone marrow

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## Introduction

Bone marrow consists of both hematopoietic (red) and fatty (yellow) components, the proportions of which are thought to be related to the remodeling capacity of bone. There is a well-established, age-related conversion of red to yellow bone marrow (1), and Neumann was the first who reported that active hematopoietic (red) bone marrow declined with age and converted to fatty (yellow) marrow, starting from the periphery and extending towards the axial skeleton (2). From this point forward, this phenomenon was referred to as

<sup>1</sup>Department of Radiology, Division City and County Hospitals, INSELGROUP, Bern University Hospital, University of Bern, Bern, Switzerland

<sup>2</sup>Department of Radiology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

### Corresponding author:

Andreas Christe, Department of Diagnostic, Interventional and Pediatric Radiology, Inselspital, Bern University Hospital, University of Bern, 3010 Bern, Switzerland.

Email: andreas.christe@insel.ch



Neumann's law (3). Both the causes and consequences of this change are uncertain, as is the role of fat in the regulation of the bone marrow (4).

Recently, magnetic resonance imaging (MRI) has become the non-invasive imaging modality of choice in diagnosing bone marrow pathology (5). Red and yellow marrow is easily distinguishable, and marrow composition may be qualitatively assessed from signal intensity variations on an MRI. Previous articles have demonstrated the age-related conversion of bone marrow in cranial bones (6), femoral bones (7), bone epiphyses (8), and pelvic bones (9). In particular, Ricci et al. (10) described three distinct signal intensity age-related patterns in the lumbar spine. In comparison, relatively few MRI studies have tried to present quantitative measurements of bone marrow by inferring red and yellow composition from their water and fat signal contributions. Those studies have tended to focus on a single vertebral body in the lumbar spine, usually L2 or L3 (11).

On the other hand, the reconciliation between skeletal and chronological age is of big importance in the context of criminal proceedings involving living individuals, who frequently lack any associated identification documentation and are referred to the criminal justice system. Many times, a forensic practitioner is requested to perform an assessment of age in a dead or a living individual in order to provide information that carries significant evidentiary value in legal decisions.

Therefore, the purpose for this study was to use the advent of clinical scanners to examine the correlation between age and fat content in the lower vertebral bodies (signal ratio on T1-weighted [T1W] MRI). Furthermore, the influence of field inhomogeneities, sequence parameters, and signal ratios of a 1.5-T and 3-T scanner on this correlation was examined.

## Material and Methods

The institutional review board (IRB) proposal was waived due to the retrospective nature of the study and the anonymity of the patients' exams. A continuous sample of patients with lumbar spine MRI was retrospectively selected in order to get a representative sample from our 1.5-T and 3-T MRI unit (Magnetom Avanto® and Magnetom Skyra®, Siemens Healthineers, Erlangen, Germany).

### Patients

Inclusion criterion was as follows: a lumbar spine MRI with a T1W image of diagnostic quality. Exclusion criteria were as follows: postoperative status, any pathology in the spine interfering with the proper measurement or MRI exam with severe motion or metal artifacts.

During a time period of two years (May 2015 to May 2017), a total of 205 patients were included in the 1.5-T unit (80 men, 125 women; median age = 57 years; age range = 17–96 years) and a total of 319 patients were included in the 3-T unit (151 boys/men, 168 girls/women; median age = 53 years; age range = 2–94 years). Age distribution is provided in Fig. 1.

### MRI exam

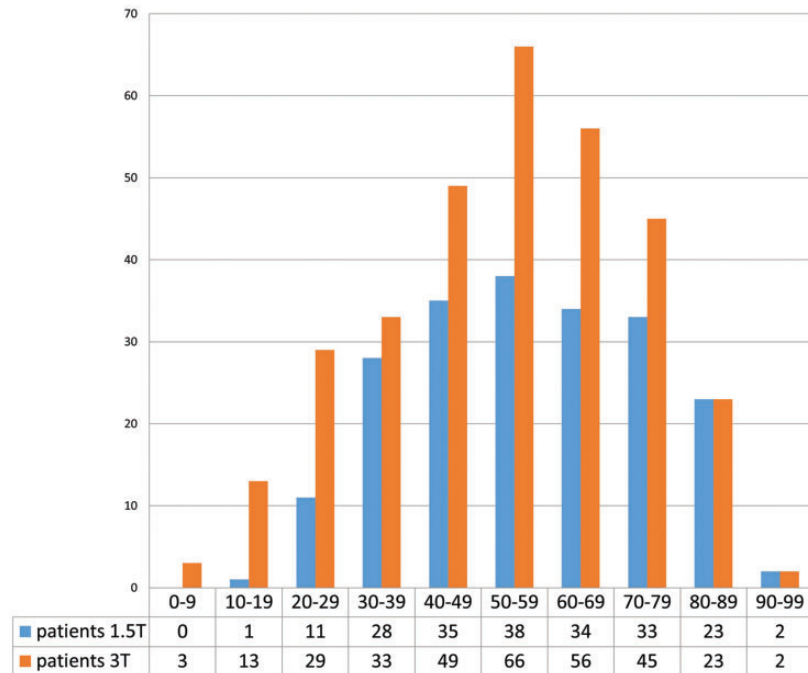
In our routine protocol the entire lumbar spine was scanned, along with most of the adjacent sacral bone and the adjacent lower thoracic vertebral bodies. The standard sagittal T1W parameters of the 1.5-T and 3-T unit are given in Table 1.

### Image analysis

Two radiologists, with 15 and 5 years of experience in musculoskeletal imaging, respectively, read the MRIs of the patients of the 1.5-T unit (Readers 1 and 2) and two radiology fellows of musculoskeletal imaging read the images of the 3-T unit separately (Readers 3 and 4). The readers analyzed the images independently and were blinded to the ages of the patients. The images were read in a random order. Two picture archiving and communication system (PACS, Sectra, Linköping, Sweden and General Electric, Milwaukee, WI, USA) were used. Both groups were instructed to note the T1 signal intensity within the center of all captured vertebra (avoiding variants and pathologies). The region of interest (ROI) should be as large as possible on the sagittal T1W image, without including the cortical plate of the vertebra. Furthermore, the readers measured the T1 signal of the subcutaneous tissue on the level of the lumbar vertebra L1 and the sacral vertebra S1 (Fig. 2). The ROI should be as large as possible, without including the cutis or the muscles. After four weeks, all radiologists were asked to reread half of the patients in another random order.

### Analysis of real fat fraction in the spine (ex-vivo experiment)

From the standardized T1 signal, the relative vertebral fat signal and, consequently, the vertebral age, could be approximated. With a second experiment, we aimed to determine the actual fat content in the vertebral bodies with the following ex-vivo experiment: 20-mL syringes filled with different fat–water mixtures, with administered solvent (having the same signal as water). Sunflower oil (Florin AG, Muttentz, Switzerland) was mixed with tap water and solvent (Splendid, Salzburg, Austria) accordingly to reach a fat fraction of 0, 20%, 40%, 60%, 80%, and 100%. These six syringes were scanned with the 1.5-T and 3-T lumbar spine standard



**Fig. 1.** Age distribution (per decade) of the 205 and 319 patients examined on the 1.5-T and 3-T units.

**Table 1.** Routine sagittal T1 turbo spin-echo protocol for the 1.5-T unit (Magnetom Avanto<sup>®</sup>) and the 3-T unit (Magnetom Skyra<sup>®</sup>).

	TR (ms)	TE (ms)	FOV (mm)	Base resolution	Phase oversampling (%)	Stack	Slice thickness (mm)	Voxel (mm)
1.5 T	604	9.6	360	384	50	19	3	0.9 × 0.9
3 T	506	9.8	300	448	100	17	3	0.7 × 0.7

FOV, field of view; TE, echo time; TR, repetition time.

protocol to determine the T1 signal intensities and calculate the relative signal by dividing the signal in a specific syringe by the signal of the syringe filled with 100% oil. A fitting curve of the graph fat fraction signal/actual fat fraction would allow for absolute fat fraction determination in the vertebral bodies.

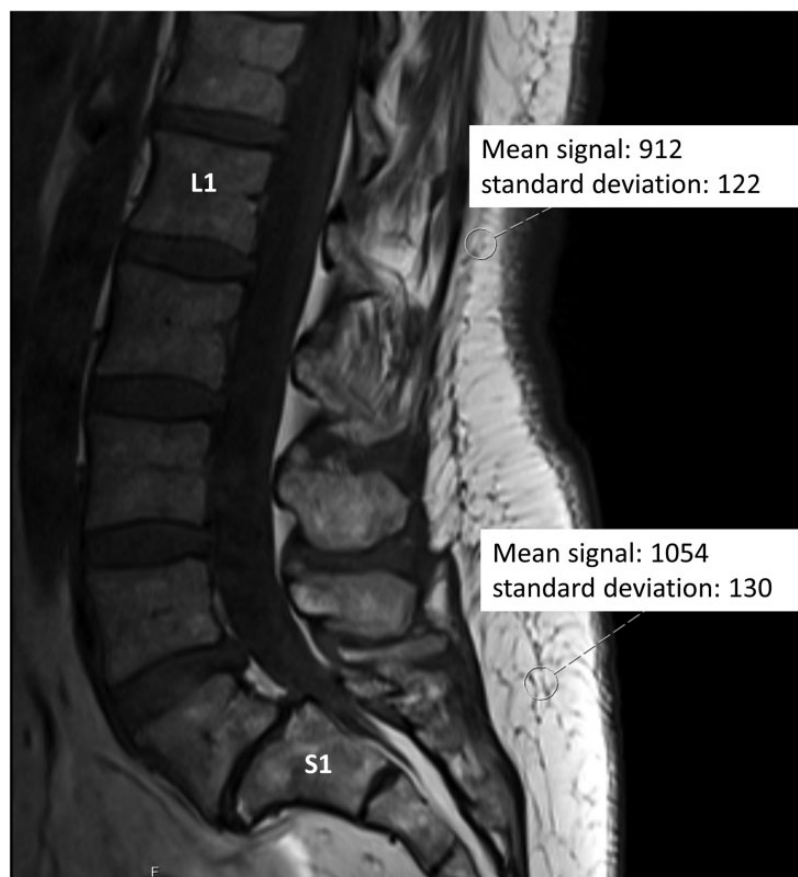
### Statistical analysis

The absolute mean T1 signal intensity measurements were standardized by dividing their signal value by the signal of the subcutaneous tissue (vertebra-to-fat ratio). For each vertebral body, bone-to-fat ratios (for both lumbar and sacral subcutaneous fat) were calculated. After four weeks, all radiologists were asked to reread half of the MRIs of the patients for an intra-reader concordance, in addition to the inter-reader concordance. Both were calculated as Pearson correlation coefficient R values with 95% confidence interval (CI). The age-signal correlation coefficients

(R) were calculated from each spine level and compared to each other for women and men, both separately and together. Furthermore, a comparison of R values of 1.5-T versus 3-T images was performed for each spine level. MedCalc<sup>®</sup> version 15.0 (MedCalc Software, Ostend, Belgium) and a significance level of  $P < 0.05$  were utilized. An age-signal fitting curve was selected for best correlation. The SD of this fitting curve was calculated using the differences of the calculated age and real age, to provide a hands-on tool for physicians.

### Results

The standardized sagittal T1 signal intensity in the spine correlated significantly with the age of the patients. The strongest correlation was demonstrated for the 1.5-T unit in the thoracic vertebra T11, followed by lumbar vertebra L1, showing correlation coefficients (R) of 0.64 (95% CI = 0.53–0.72,  $P < 0.0001$ ) and 0.49



**Fig. 2.** Measurement of the T1 fat signal in the subcutaneous tissue for standardization (L1 and S1).

**Table 2.** R values for best age-signal correlation in the 1.5-T group.

Gender	Fat signal measurement level (standardization)	Age signal correlation coefficient (1.5-T unit)						
		T11	T12	L1	L2	L3	L4	L5
All	SI	0.64	0.44	0.49	0.46	0.39	0.34	0.43
Male	SI	0.64	0.50	0.57	0.50	0.43	0.42	0.52
Female	SI	0.62	0.42	0.44	0.43	0.37	0.30	0.39
All	LI	0.35	0.25	0.29	0.25	0.21	0.17	0.24
		Confidence intervals of T11 and L1						
All	SI	0.53–0.72		0.38–0.59				
Male	SI	0.44–0.77		0.41–0.70				
Female	SI	0.49–0.72		0.28–0.57				
		All with $P < 0.0001$						

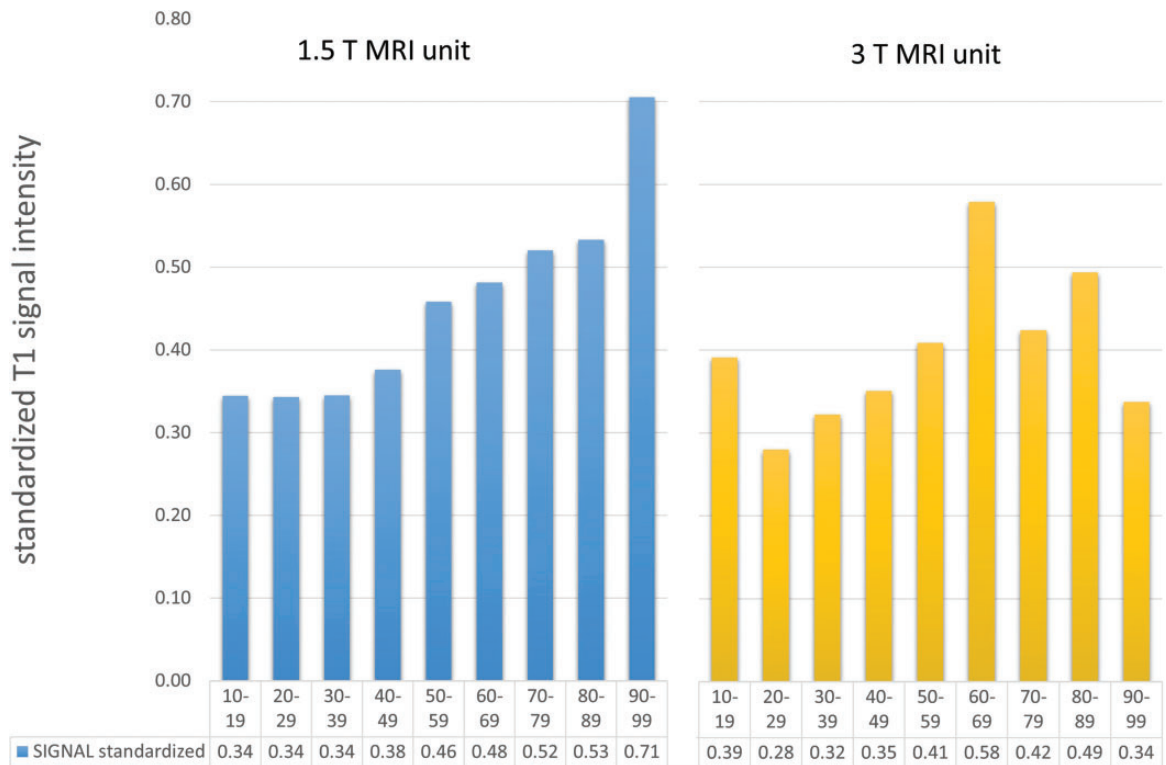
(95% CI = 0.38–0.59,  $P < 0.0001$ ), respectively. For the 125 women and 80 men at the 1.5-T unit, the R values were similar in T11, with 0.62 (95% CI = 0.49–0.72) and 0.64 (95% CI = 0.44–0.77), respectively. The other R values are listed in Table 2.

The R value was significantly higher when the signal in the subcutaneous fat on the sacral level instead of the lumbar level was used for standardization ( $P < 0.02$ ).

The vertebral signal correlated significantly better with age in the 1.5-T unit compared to the 3-T unit on all vertebral levels: comparing the best R values, the 3-T unit demonstrated an R of 0.20 (95% CI = 0.09–0.30,  $P < 0.0001$ ) compared to the 1.5-T unit. On the 3-T images, better R values were obtained by using the lumbar level for standardizing the fat signal, except for the level of thoracic vertebra T11 (Table 3).

**Table 3.** Age-signal correlation in the 3-T group.

Fat signal measurement level (standardization)	Age signal correlation coefficient R (3-T unit)													
	T11		T12		L1		L2		L3		L4		L5	
	R	P value	R	P value	R	P value	R	P value	R	P value	R	P value	R	P value
L1	0.19	0.17	0.18	0.00	0.20	0.00	0.18	0.00	0.15	0.01	0.16	0.00	0.19	0.00
S1	0.20	0.13	0.10	0.08	0.11	0.04	0.11	0.05	0.10	0.07	0.10	0.06	0.10	0.07

**Fig. 3.** Average standardized T1 signal intensity in thoracic vertebra T11 per decade, examined on a 1.5T and 3T MRI unit.

The average standardized T1 signal per decade is shown in Fig. 3 and the age-signal curve is demonstrated in Fig. 4 (for both the 1.5-T and 3-T units), with obvious superiority of the 1.5-T unit. The fitting curve demonstrated the best R value for linear fitting ( $R^2=0.403$ ). Therefore, the formula for age estimation was  $y = 101.68x + 11.813$ , with y representing age and x representing the T1 signal ratio of vertebra-to-fat (subcutaneous fat on level S1). The SD for the age was  $\pm 14.06$  years. This meant that there was an average increase of the relative T1 signal in thoracic vertebra T11 of 0.098 per decade, equaling a 10% increase in absolute T1 signal intensity per decade (Fig. 5). The inferior average relative age-signal curve for thoracic vertebra T11 on the 3-T MRI unit is shown in Fig. 4.

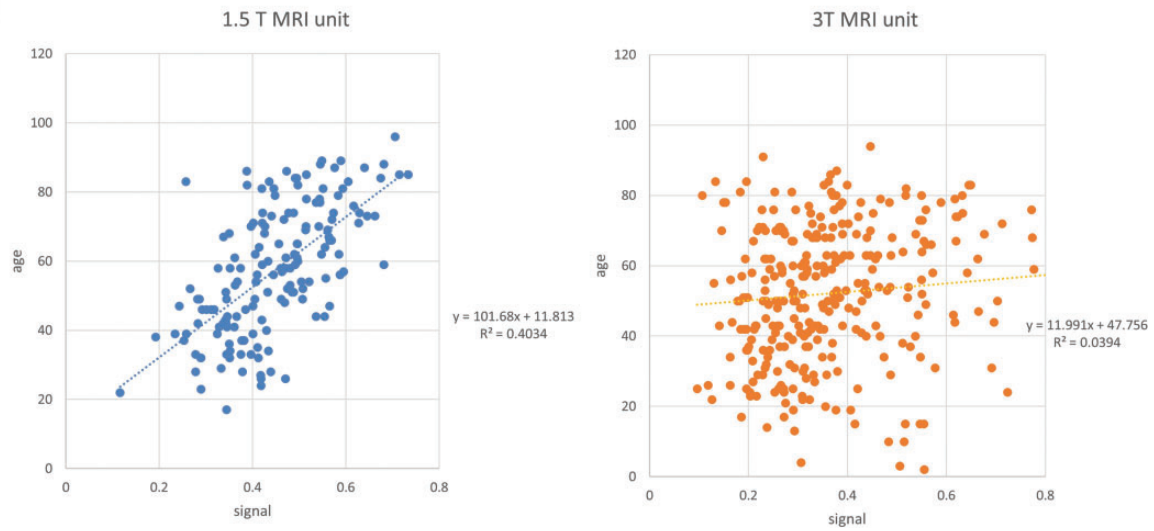
#### Inter- and intra-reader concordance

Inter- and intra-reader correlations were significant for all readers, with an  $R > 0.82$  and  $> 0.88$ , respectively (both with  $P < 0.0001$ ). Intra-reader correlations of Reader 1, 2, 3, and 4 were 0.998 (95% CI = 0.998–0.999,  $P < 0.0001$ ), 0.883 (95% CI = 0.84–0.92,  $P < 0.0001$ ), 0.961 (95% CI = 0.95–0.97,  $P < 0.0001$ ), and 0.930 (95% CI = 0.91–0.95,  $P < 0.0001$ ). Inter-reader correlation between Reader 1/2 and Reader 3/4 was 0.827 (95% CI = 0.74–0.89,  $P < 0.0001$ ) and 0.883 (95% CI = 0.83–0.92,  $P < 0.0001$ ).

#### Calculated absolute vertebral fat fraction

There was a linear relationship between T1 signal intensity and fat content in the syringes in the ex-vivo





**Fig. 4.** Age to T1 signal correlation in thoracic vertebra T11 examined on a 1.5-T and 3-T MRI unit. The formula of the linear fit curve, as well as the  $R^2$  value, are indicated.



**Fig. 5.** Vertebral T1 fat signal ratios (TIFSR). TIFSR of thoracic vertebra T11 and subcutaneous tissue on a 1.5-T scanner (top row) and TIFSR of lumbar vertebra L1 and subcutaneous tissue on a 3-T scanner (bottom row). TIFSR increased with age: (a/f, b/g, c/h, d/i, e/j) T1W images represent examples for the 2nd, 4th, 6th, 8th, and 10th decade, respectively, with increasing vertebral T1 hyperintensity.

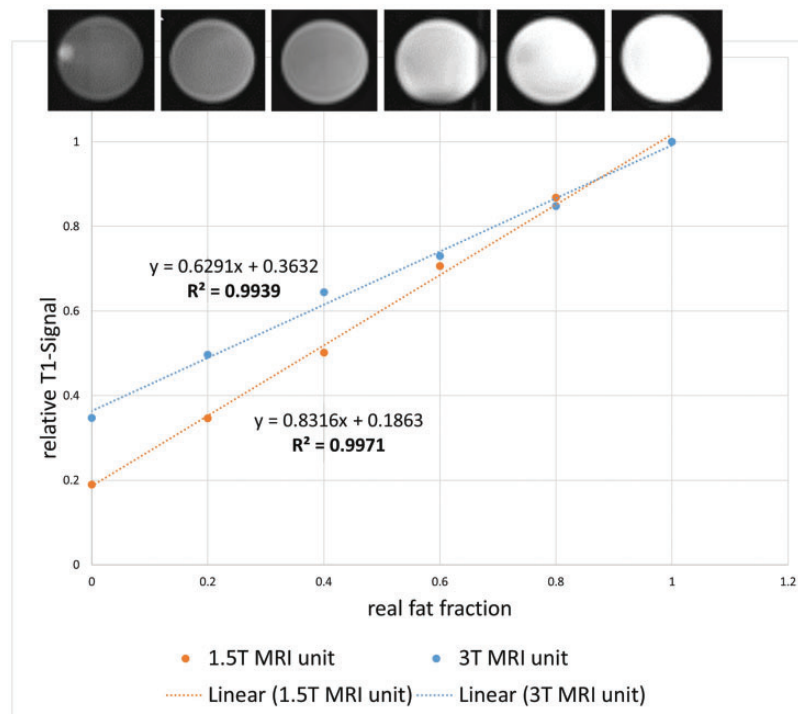
experiment (Fig. 6). The relative T1 signal ratio demonstrated a linear increase parallel to the ex-vivo fat ratio; therefore, the absolute vertebral fat content could be determined. The fitting curve and correlation coefficient are indicated on Fig. 6.

## Discussion

An inverse relationship between increasing marrow fat and trabecular bone loss in osteoporosis has been evident for the past several years (12). It was only recently, through the use of MR-based techniques, that marrow fat content could be quantified on a large scale (13) and at different anatomical parts (14). Several studies examining the physiological changes in marrow fat content have proven that the percentage of marrow fat content gradually increases with advancing years (11,15–17). An easily remembered approximation is that vertebral body marrow fat content increases from 25% at 25 years of age to 65% at 65 years of age (15). Moreover, along with the increase in marrow fat content with age, MR-based studies have shown that a distinct sex difference in marrow fat content exists (11,15). Other studies have suggested that glucose metabolism and weight loss may influence marrow fat behavior, and marrow fat may be a

determinant of bone metabolism (18), with other studies presenting the evidence that specific volumes and types of exercise may influence the age-determined adipose marrow conversion (19). To overcome this sex-, metabolic-, or habit-related predilection, in our study, we investigated different age groups consisting of randomized numbers of male and female patients with different medical status, body mass index, smoking habits, and levels of physical activity. In this way, we intended to investigate the direct connection between the age and the fat content of the lumbar vertebrae. There is a linear correlation between the age and the relative T1 signal of the spine and the real fat fraction in the spine. The syringe with 0% fat/100% water did not produce zero signal because of the remaining signal from the pure water in Fig. 6.

Several previous studies have tried to evaluate the efficacy of MR spectroscopy (MRS) on high field imaging systems (3.0 T) for the assessment of normal bone marrow composition (20); other studies have tried to quantitatively evaluate vertebral bone marrow fat content with chemical-shift MRI (21). Those studies demonstrated an age-related increase in the fat content of the spine, with values greater in men compared to women. There was also a trend in vertebral bodies within the same individuals, with fat content increasing



**Fig. 6.** Ex-vivo experiment with syringes filled with water and oil: 6 syringes with 0%, 20%, 40%, 60%, 80%, and 100% oil (mL), in a 1.5-T and 3-T MRI unit (top line demonstrates cross-section through the syringes 1.5-T). An almost perfect linear correlation was observed between fat content ratio and T1 signal ratio ( $R^2 > 0.99$ ). For example, a patient with a standardized T1 signal ratio of 0.5 on a 1.5-T MRI would have a real fat content of 0.4 in the vertebral body.

from the L1 vertebra to the L5 vertebra (20). In our study, the most reliable vertebra, according to the age-related fat content, was shown to be thoracic vertebra T11. If the thoracic spine is not included in the imaging field, the second-best age assessment could be made in the lumbar vertebra L1. The pathophysiological relevance of this is unknown but may be because of the “peripheral to axial” conversion from red to yellow marrow with increasing age (2). Due to this conversion, the inferior lumbar vertebrae may be prone to show more fatty infiltration with lower age. This may be in opposition with the fact that the lower spine is more sensitive to early degenerative changes, which could be one reason that our results found that vertebrae T11 and L1 were best for age matching. In these previous studies, the results demonstrated an advantage of higher magnetic field (3.0 T) because of the increase in both signal-to-noise ratio and chemical shift dispersion, thus leading to improved spatial resolution, which is crucial in the examination of small vertebral bodies and those vertebral bodies that are anatomically more difficult to identify as L5 (20). Additionally, an improvement in spectral quality at 3.0 T was demonstrated compared to 1.5 T in one individual (20). On the other hand, it was demonstrated that the vertebral bone marrow fat content, when calculated with chemical-shift MRI, is not a reliable parameter for predicting bone mineral density in female patients aged 50–65 years (21). However, chemical-shift-based water–fat separation enables the quantitation of vertebral marrow adiposity with excellent reproducibility, which appears to be a useful method in providing complementary information to osteoporosis-related research fields (22). In our study, we discovered that, because of the higher magnetic field of a 3.0-T imaging system, the results had a lower statistical significance compared to a 1.5-T system due to the regional field inhomogeneity. We avoided the use of chemical shift sequences or spectroscopy in our investigation because we wanted to examine the direct age changes in the fat content of the bone marrow by utilizing a daily used, non-extravagant sagittal T1W imaging system. This type of imaging system is used by almost every radiology department in the imaging of the spine and is accessible by almost every forensic department.

This study had some limitations. First, we had no histological reference standard. To overcome this limitation, we retrospectively examined an efficient number of individuals of different ages and we used a consistent measuring field size. Second, we had to deal with several artifacts, such as the susceptibility, truncation, chemical-shift, third arm, and, particularly, pulsation artifacts, along with choice of slice orientation, for which all options are equally advantageous in all regions of the lower spine and reduce the image quality.

Spine studies in clinical routine are performed with a posterior coil and the subcutaneous adipose tissue on the back side may be artificially too T1-hyperintense which may lead to a biased fat fraction. This problem could be solved with a Dixon sequence because of the inherent B1 correction. In addition, MRS (single voxel) of the vertebral bone marrow could overcome this problem. Furthermore, the retrospective nature of the study is not as powerful as prospectively acquired data: a longitudinal assessment of an individual’s fat signal over time will demonstrate the real correlation.

The T1 signal intensity in spine MRI is not only dependent from fat, several factors influence the signal intensity. First, the localization of the coil and the distance from the spine to the coil influences the signal. Second, the saturation pulse used for suppression of breathing artifacts influences the signal depending on the location of the saturation band. Third, postprocessing image homogenization due to b1 inhomogeneity is a vendor specific T1 variable. We tried to overcome these limitations by including many patients and using relative T1 signal for neutralizing these variables to come forward with a fast and simple age estimation method that can be used in daily clinical or forensic routine. Many of these limitations can be eliminated by measuring the absolute T1 time (T1 mapping) and we are currently recruiting patients for a prospective T1 mapping of the spine for age estimation. In addition, we used sunflower oil in the ex-vivo experiment, without knowing if it is a good “mimic” of the vertebral bone marrow and whether the T1W sequence used really captured the potential differences in fat spectrum (R2\* effects). Until further confirmation of the results with biopsy or spectroscopy, others would have to apply the exact same T1W imaging parameters to utilize the described ex-vivo approach.

In conclusion, these results demonstrate a vertebral fat signal ratio relationship to age. The fatty conversion of the bone marrow during life presented a linear increase of 10% T1 signal ratio per decade with the 1.5-T scanner.

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### Declaration of conflicting interests

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**ORCID iDs**Verena C Obmann  <https://orcid.org/0000-0001-6572-9968>Andreas Christe  <https://orcid.org/0000-0002-2355-2591>**References**

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