# **RESEARCH ARTICLE**



# Prepolarized MRI of hard tissues and solid-state matter

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Prepolarized MRI (PMRI) is a long-established technique conceived to counteract the loss in signal-to-noise ratio (SNR) inherent to low-field MRI systems. When it comes to hard biological tissues and solid-state matter, PMRI is severely restricted by their ultra-short characteristic relaxation times. Here we demonstrate that efficient hardtissue prepolarization is within reach with a special-purpose 0.26 T scanner designed for ex vivo dental MRI and equipped with suitable high-power electronics. We have characterized the performance of a 0.5 T prepolarizer module, which can be switched on and off in 200 µs. To this end, we have used resin, dental and bone samples, all with T<sub>1</sub> times of the order of 20 ms at our field strength. The measured SNR enhancement is in good agreement with a simple theoretical model, and deviations in extreme regimes can be attributed to mechanical vibrations due to the magnetic interaction between the prepolarization and main magnets.

#### KEYWORDS

MRI, low field, prepolarization, hard tissues, solid state

Abbreviations: ART, algebraic reconstruction technique; FID, free induction decay; GPA, gradient power amplifier; LF-MRI, low-field MRI; PETRA, pointwise encoding time-reduction with radial acquisition; PMRI, prepolarized MRI; P-PETRA, prepolarized pointwise encoding time-reduction with radial acquisition; SNR, signal-to-noise ratio; ZTE, zero echo time.

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# 1 | INTRODUCTION

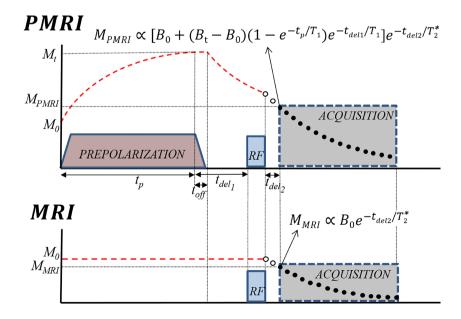
Low-field MRI (LF-MRI) is gaining momentum as an affordable alternative to clinical MRI, the current gold standard in numerous medical imaging applications, but also extremely expensive and often inaccessible. The main cost driver in an MRI scanner is the superconducting magnet required to generate the strong, static magnetic field ( $B_0$ ) that enables the high-quality images typical for clinical MRI. By lowering the field strength, the need for superconducting magnets is removed, resulting in a drastic reduction of the economic and energetic needs. On the other hand, the signal-to-noise ratio (SNR) of the magnetic resonance signals and reconstructed images depends supra-linearly on field strength ( $\propto B_0^{3/2}$ , Reference 2), leading to longer scan times if resolution and SNR are to be maintained.

Prepolarization is a long-established technique designed to partially compensate for the SNR loss in LF-MRI<sup>4-8</sup> and could be of special relevance for hard biological tissues, where hydrogen content is sparse and signals decay very fast. In prepolarized MRI (PMRI), the Boltzmann equilibrium magnetization of the sample is boosted by an intense, not necessarily homogeneous, magnetic pulse of amplitude  $B_p$  before the start of the imaging pulse sequence, which is then executed at a lower but highly homogeneous  $B_0$ . For efficient PMRI, the prepolarization pulse must be turned off in a time  $t_{off}$  much shorter than the sample  $T_1$  relaxation time over which the extra magnetization is lost. This is easily met for liquids and soft biological tissues, where spin-lattice interactions are averaged out by the molecular tumbling of water, leading to relaxation times above  $100 \, \text{ms}.^{11}$  Indeed, PMRI has already demonstrated its potential for ex vivo and in vivo imaging of soft samples at field strengths ranging from hundreds of militesla to hundreds of microtesla. 10.12-16 For solid-state matter or hard biological tissues (e.g., dental tissues), which feature short  $T_1$  times, prepolarization is much more challenging: the suppressed proton mobility prevents the averaging out of dipolar interactions by molecular tumbling of protons in water. This effect is even more pronounced at low field strengths, where the Larmor frequency is closer to proton tumbling frequencies. These challenges have so far precluded PMRI of short- $T_1$  samples, which include tendons and bones, 10.12-10.1

In this paper, we demonstrate prepolarization and imaging of samples with ultra-short  $T_1$ , down to a few tens of milliseconds. After brief introductions to the relevant theoretical framework and experimental equipment in Sections 2 and 3 respectively, we analyze in Section 4 the signal strength boost for an inorganic solid-state sample as a function of pulse sequence parameters. In Section 5, we present the first prepolarized magnetic resonance hard-tissue images (of a cattle bone and a human tooth), which show an SNR increase of a factor of 2 with respect to an equivalent acquisition without prepolarization.

# 2 | THEORY

To quantify the effect of the prepolarization on hard tissues, in the remainder of the paper we compare the signals resulting from magnetic pulse sequences based on those in Figure 1. These sequences are identical except for the fact that the prepolarization pulse has an amplitude  $B_p$  in the



**FIGURE 1** PMRI (top) and MRI (bottom) pulse sequences used in this work, with analytical expressions for the magnetization at the start of FID acquisition. Their ratio  $\alpha$  represents the SNR gain due to prepolarization, as per Equation (2).  $M_t$  and  $M_0$  are the magnetizations in thermal equilibrium with and without prepolarization and are directly proportional to  $B_t$  and  $B_0$  respectively. Red dashed lines represent the longitudinal magnetization. Black points represent k-space data measured during the acquisition, while white points are not measured and lead to a gap in k space



PMRI sequence and zero in the standard MRI sequence. For an homogeneous sample of characteristic relaxation time  $T_1$ , we define the prepolarization gain  $\alpha$  as the ratio between the sample magnetizations during the data acquisitions:

$$\begin{array}{ll} M_{PMRI} \propto & \left(B_0 + (B_t - B_0)\left(1 - e^{-t_p/T_1}\right)e^{-t_{del1}/T_1}\right)e^{-t_{del2}/T_2^*}, \\ M_{MPI} \propto & B_0 e^{-t_{del2}/T_2^*}. \end{array} \tag{1}$$

SO

$$\alpha \equiv \frac{M_{PMRI}}{M_{MRI}} = 1 + \frac{B_t - B_0}{B_0} \left( 1 - e^{-t_p/T_1} \right) e^{-t_{del1}/T_1}, \tag{2}$$

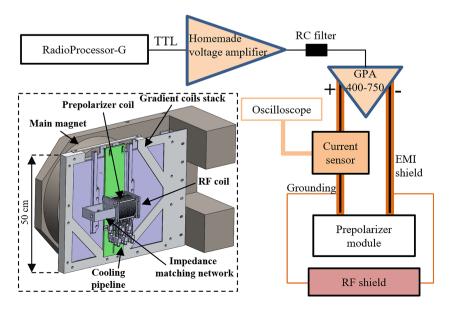
where we neglect the duration of RF pulses. Here  $B_t = |\mathbf{B}_0 + \mathbf{B}_p|$  is the total field strength during the prepolarization pulse, where the main and prepolarization fields need not be parallel;  $t_p$  is the prepolarization pulse length, during which the magnetization asymptotically reaches equilibrium with  $B_t$ ;  $t_{off}$  is the ramp-down time of the prepolarization pulse;  $t_{del1} \ge t_{off}$  is the time from the moment the prepolarization pulse starts to be switched off until the beginning of the RF excitation;  $t_{del2}$  is the time between the RF pulse and the start of the data acquisition and  $T_2^*$  is the sample- and scanner-dependent dephasing characteristic time over which the magnetization decoheres. Admittedly, this definition of SNR enhancement tends to overestimate the benefits of PMRI, since the standard MRI sequence could be shortened and its SNR increased by further averaging in the same overall acquisition time, as discussed in Section 6. Nevertheless, this is the simplest possible comparison and it is often used as a reference (see, e.g., References  $^{12,24}$ ).

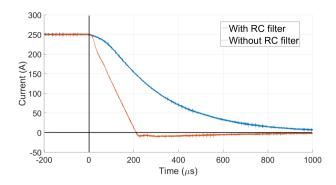
## 3 | APPARATUS

As a result of the short  $T_1$  timescales typical of solids, hard-tissue prepolarization poses a significant engineering challenge to achieve fast enough  $t_{off}$  times. Our solution to this follows.

The "DentMRI—Gen I" 0.26 T scanner, RF transmission and reception (Tx/Rx) coil and prepolarization modules employed for this work (see Figure 2) are described in detail elsewhere. Sessentially, our group has designed, built and characterized a prepolarizer coil with inductance  $L \approx 600 \mu H$ , resistance  $R \approx 75 m\Omega$  and efficiency  $\eta \approx 1.9 mT/A$ . The gap between the planar gradient stacks is  $\approx 210 mm$ , placing a hard boundary on the prepolarizer module size and, consequently, on the maximum achievable coil inductance. Due to geometric limitations, and to ease accessibility, we placed the prepolarizer module so that  $B_p$  is perpendicular to  $B_0$ . This reduces the maximum achievable  $B_t$  from  $|B_0| + |B_p|$  to  $(B_0^2 + B_p^2)^{1/2}$ , but has the advantage that the generated eddy currents and the residual energy in the prepolarization coil barely disturb the longitudinal field  $B_0$  (e.g., when  $B_0$  falls to 1 mT, the total field deviates from the original  $B_0$  by only 2  $\mu$ T).

In order to cope with the short  $T_1$  of hard biological tissues, the high-power electronics setup for the prepolarizer module has been substantially upgraded with respect to the system introduced in Reference  $^{10}$ . In the current apparatus, a digital output from the RadioProcessor-G board





**FIGURE 3** Falling edge of the prepolarization pulse current from 250 A ( $B_p \approx 0.475$  T) with the GPA 400-750, with and without the low-pass RC filter. With the RC filter, the prepolarizer field is 15.6 mT after approximately 1 ms (1 mT at approximately 1.73 ms)

(SpinCore Electronics) is amplified in two stages, first in a home-made variable-gain low-voltage amplifier, and then in a high-power (400 A and 750 V) gradient power amplifier from International Electric Co. (GPA 400-750). The latter can ramp currents from 0 to ±260 A in about 200 μs in our approximately 600 μH load, where we were previously limited to about 35 ms. <sup>10</sup> Figure 3 also shows a smoother transition corresponding to the case where we low-pass filter the digital output with an RC circuit of characteristic time constant approximately 350 μs. We have found this necessary to avoid significant mechanical displacements in the module due to the sudden appearance of strong magnetic interactions between the main magnet and the prepolarizer. This also reduces the generation of eddy currents and, thereby, distortions in the acquired signals and image reconstructions due to uncontrolled magnetic field dynamics. All the measurements below are with the low-pass filter.

# 4 | SNR ENHANCEMENT

For calibration and first tests we employed a sample made of a photopolymer resin,<sup>25</sup> which is highly homogeneous, abundant in hydrogen and features relaxation parameters comparable to the enamel in human teeth. At our  $B_0$ , we have measured  $T_1 \approx 23.1$  ms and  $T_2 \approx 650 \mu s$  with inversion recovery<sup>26</sup> and CPMG<sup>27,28</sup> pulse sequences, respectively.

In a first set of experiments we check whether the SNR is enhanced by prepolarization as predicted by the model in Equation (2). To this end, we set  $t_p=160$  ms ( > 7 $T_1$ ) in the sequence in Figure 6 to prepolarize close to the saturation magnetization. Next, a resonant  $\pi/2$  RF pulse coherently rotates the magnetization to the transverse plane (RF pulse time  $t_{RF}\approx 10\mu s$ , with amplitude  $B_1\approx 590\mu T$ ). The two pulses are separated by a wait time  $t_{del1}=3ms$ , longer than strictly required to switch  $B_p$  off, to avoid Larmor frequency shifts and distortions in the acquired free induction decay (FID) signals due to residual magnetic energy in the setup. The signal readout starts  $t_{del2}=100\mu s$  after the RF pulse to avoid ring-down from the RF coil. The resulting FID is acquired for  $t_{acq}=2$  ms with a readout bandwidth BW = 200 kHz. This protocol is repeated for four different voltage gains of our home-made amplifier, generating  $B_p\approx 0.21$ , 0.29, 0.40 and 0.49 T, which correspond to  $B_t\approx 0.33$ , 0.39, 0.47 and 0.56 T. Figure 4 shows the absolute values of the FIDs for these cases and for the standard MRI sequence ( $B_p=0$  and  $B_t\approx 0.26$  T). For a given value of  $B_p$ , we estimate the prepolarization boost  $\alpha$  as the mean ratio of the PMRI and standard MRI data:

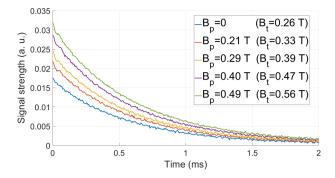
$$\frac{1}{N_{\text{points}}} \sum_{i=1}^{N_{\text{points}}} \frac{s_{B_p}(t_i)}{s_0(t_i)},\tag{3}$$

where  $N_{\text{points}} = t_{\text{acq}} \cdot \text{BW}$ ,  $s_{\text{B}_p}(t_i)$  is the signal amplitude measured for the PMRI with prepolarization strength  $B_p$  for the time bin  $(t_i)$ , and  $s_0(t_i)$  is the amplitude measured for the standard MRI sequence at  $t_i$ . The values of  $\alpha$  estimated by this procedure are  $1.240 \pm 0.005$ ,  $1.430 \pm 0.008$ ,  $1.705 \pm 0.008$  and  $1.964 \pm 0.011$  for the above prepolarization field strengths, where the given uncertainties indicate the standard error of the mean

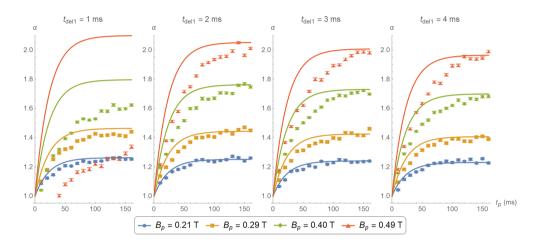
$$\sigma_{\alpha} = \frac{1}{N_{\text{points}}} \sqrt{\sum_{i=1}^{N_{\text{points}}} \left(\frac{s_{\mathsf{B}_{p}}(t_{i})}{s_{\mathsf{0}}(t_{i})} - \alpha\right)^{2}}.$$
 (4)

The corresponding theoretical  $\alpha$  values for  $T_1 \approx 23.1$  ms can be calculated from Equation (2):  $\alpha \approx 1.24, 1.44, 1.72$  and 1.98.

The small experimental deviations from the theoretically calculated values could arise from (i) mechanical vibrations due to magnetic forces, (ii) induced eddy currents, (iii) off-resonant spin evolution due to a time-dependent Larmor frequency or (iv) dependence of  $T_1$  on  $B_t$ . All four are more pronounced for intense  $B_p$  values and short  $t_{del1}$  times. To find a working regime where these effects are suppressed, we have characterized their influence on the SNR gain with the measurements shown in Figure 5.



**FIGURE 4** FIDs after prepolarizing the photopolymer resin sample with pulses of  $t_p = 160$  ms and  $t_{del1} = 3$ ms for different  $B_p$  values



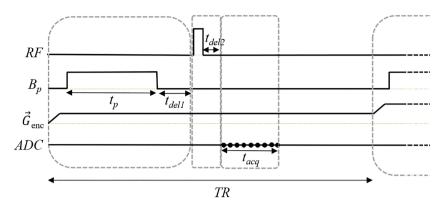
**FIGURE 5** Comparison between theoretical (continuous curves) and experimentally estimated (data points) gain  $\alpha$  for different values of  $t_{\rm p}, B_{\rm p}$  and  $t_{\rm del1}$ , using the photopolymer resin sample. The data for  $B_{\rm p}=0.49$  T and  $t_{\rm del1}=1$  ms are heavily corrupted by the sharp magnetic transitions. The experimental data for the stronger  $B_{\rm p}$  seem to grow more slowly than the corresponding theoretical curves, consistent with longer  $T_{\rm 1}$  at higher field strengths

For the plots in Figure 5 we sweep the prepolarization pulse duration from  $t_p = 10$  to 160 ms and  $t_{del1}$  from 1 to 4 ms, for the same four  $B_p$  values as above. The gain and uncertainty for every data point are estimated according to Equations (3) and (4). The solid lines in the figure correspond to calculations employing the model in Equation (2).

Unsurprisingly, for the weaker prepolarization currents we measure FID curves that follow closely theoretical predictions, even for  $t_{\text{del1}}$  as short as 1 ms. Deviations are stronger for short wait and prepolarization times. In the extreme case of  $B_p \approx 0.49$  T and  $t_{\text{del1}} = 1$  ms, the measured data were heavily corrupted and did not follow the typical exponential behavior (i.e., as in the FIDs in Figure 4). Moreover, the curve for  $B_p \approx 0.4$  T is lower for  $t_{\text{del1}} = 1$  ms than for  $t_{\text{del1}} = 2$  ms. It is unlikely that these issues are due to drifts in the Larmor frequency as the prepolarizer relaxes, since a residual orthogonal field perturbs  $B_0$  very weakly (e.g., for  $B_p \approx 0.49$  T and  $t_{\text{del1}} = 1$  ms, the Larmor frequency shifts by only 250 Hz). On the other hand, eddy currents and especially mechanical vibrations could be behind the aforementioned deviations. In fact, we have observed that these unwanted effects are more prominent if the prepolarizer is not rigidly fixed to the scanner. With the mechanical fixation in place (see Figure 2), the system performs well away from this extreme regime. A further deviation from theory occurs for higher  $B_p$  values, probably because at these  $B_t$  fields  $T_1$  is higher than the one we have measured at  $B_0$ . All in all, the plots in Figure 5 demonstrate that the measured SNR gain is compatible with theoretical predictions for prepolarization pulses longer than 120 ms and  $t_{\text{del1}} \ge 2$  ms.

# 5 | HARD TISSUE PMRI

In this section we demonstrate the system's capability for imaging hard biological tissues with PMRI. To this end, we employ (i) an adult human molar tooth (Figure 7(c)) extracted one year before these experiments and dried so that primarily mineralized matter (dentin and enamel) remains and (ii) a piece of cattle rib (Figure 8(c)) including cortical and spongy bone tissues. We have measured the  $T_1$  times of both samples by inversion recovery at  $B_0$  in our system, and found  $T_1 \approx 20.3$  and 19.3 ms for the tooth and bone, respectively. Using CPMG we have obtained  $T_2 \approx 308 \mu s$  and 200  $\mu s$ . The cattle bone contains both cortical and spongy tissues, so the estimated  $T_1$  is an averaged quantity. The  $T_1$  times of all the



**FIGURE 6** P-PETRA pulse sequence integrating the PMRI sequence in Figure 1 with PETRA. P-PETRA is employed for the prepolarized hard-tissue images in Figs. 7 and 8. Here,  $G_{enc}$  represents the (radial or pointwise) encoding gradient, and the ADC (analog-to-digital converter) acquisition is marked with black points. For pointwise encoding, only the first point in the acquisition is used

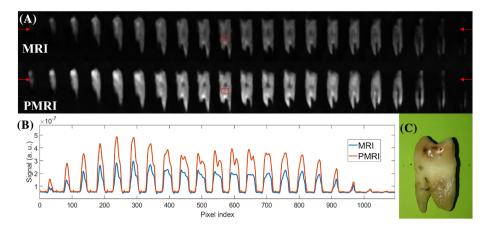
employed samples are very similar, so we can determine suitable parameter regimes from the measurements on the photopolymer resin (Figure 5).

The ultra-short  $T_2$  times typical of hard tissues impose the use of dedicated MRI sequences, such as those in the zero echo time (ZTE) family.<sup>29</sup> These are characterized by radial k-space acquisitions beginning immediately after the RF excitation, to capture as much as possible of the short-lived signal. Ramping the gradient is time consuming, so in ZTE sequences the spatial encoding gradients are switched on before the RF pulse. In this work, we even switch on the frequency encoding gradient before prepolarization<sup>30</sup> to limit mechanical vibrations and the influence of eddy currents during data acquisition. Having the gradient on during resonant excitation imposes the use of hard (short and intense) RF pulses, leading to spurious signals, which could corrupt the data acquisition. To prevent this, we introduce a delay  $t_{\text{del}2}$  before the readout, resulting in a gap without data at the center of k space. This can be filled with additional acquisitions.<sup>31</sup> One possibility is to do so in a pointwise fashion, as in PETRA (pointwise encoding time-reduction with radial acquisition<sup>32</sup>). For the following images we employ a PETRA sequence with a prepolarization stage before the RF excitation (P-PETRA, Figure 6).

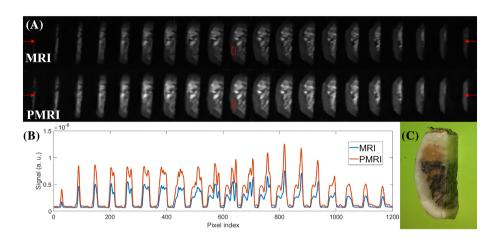
In Figure 7 we show prepolarized images of a human molar tooth obtained following the scheme in Figure 6. The size of the field of view is set to  $21 \times 13 \times 13mm^3$  and the image is reconstructed with algebraic reconstruction techniques (ARTs $^9.33.34$ ) into  $42 \times 26 \times 26$  voxels. The acquisition has a bandwidth BW  $\approx 30$ kHz, it starts  $t_{del2} = 130\mu s$  after the RF pulse ( $t_{RF} \approx 10\mu s$ ) to avoid the effect of ring-down and it lasts  $t_{acq} = 700\mu s$ . The repetition time is set to  $T_R = 250$ ms, limited by the maximum duty cycle of the GPA 400-750 at this current regime. We use 446 radial spokes for each of the 16 vertical planes, corresponding to a total k-space undersampling factor $^{\dagger}$  of  $\approx 8$  with respect to the Nyquist criterion, where ART reconstructions are still robust, with 136 single Cartesian points in the center. Every image contains 12 averages for a total scan time of approximately 29 min. The bottom row of images in Figure 7A corresponds to scans in which a prepolarization pulse is triggered with a current intensity of approximately 260 A ( $B_t \approx 0.56T$ ), which lasts  $t_p = 90$  ms and where  $t_{del1} = 2ms$ . The pulse sequence for the top row of Figure 7A is identical, but the prepolarization pulse is not triggered ( $B_p = 0$ ,  $B_t = 0.26$  T). The brightness scale is common to the two datasets. Both images have been denoised using a block-matching filter.  $^{9.35}$  To quantify the influence of prepolarization, we plot in Figure 7B the same profile along a horizontal line around the upper portion of the images in A, in the region of the tooth crown. We estimate the prepolarization boost  $\alpha$  as the ratio SNR<sub>PMRI</sub>/SNR<sub>MRI</sub>, which we average over a region of interest of constant bright pixels around the dentin before filtering (red boxes in Figure 7A). This yields approximately 1.94, where SNR<sub>PMRI</sub> =  $\bar{s}_{PMRI}/\bar{n}_{PMRI} \approx 22.97$ , and SNR<sub>MRI</sub> (analogously defined) is approximately 11.84. The mean signal and noise values ( $\bar{s}$  and  $\bar{n}$ ) are estimated, respectively, as the mean va

We have applied an analogous protocol to image a piece of a cattle rib bone. The size of the field of view is set to  $36 \times 15 \times 15 \text{mm}^3$  and the image is reconstructed with ART into  $72 \times 30 \times 30$  voxels. The acquisition starts  $t_{\text{del}2} = 125 \,\mu\text{s}$  after the RF pulse and lasts  $t_{\text{acq}} = 800 \,\mu\text{s}$ , with a bandwidth BW  $\approx 45 \,\text{kHz}$ . The repetition time is  $T_R = 280 \,\text{ms}$ . The k-space undersampling factor is again approximately 8 (870 radial spokes, 18 vertical planes, 176 Cartesian central points). Every image contains 11 averages for a total scan time of approximately 53 min. The bottom row of images in Figure 8A corresponds to scans in which a prepolarization pulse is triggered with a current intensity of approximately 260 A ( $B_t \approx 0.56 \,\text{T}$ ), which lasts  $t_p = 90 \,\text{ms}$  and where  $t_{\text{del}1} = 1.5 \,\text{ms}$ . The pulse sequence for the top row of Figure 8A is identical, but the prepolarization pulse is not triggered ( $B_p = 0, B_t = 0.26 \,\text{T}$ ). The ratio SNR<sub>PMRI</sub>/SNR<sub>MRI</sub> yields approximately 1.97, where SNR<sub>PMRI</sub>  $\approx 30.95 \,\text{and}$  SNR<sub>MRI</sub>  $\approx 15.70 \,\text{(defined as in the previous paragraph)}$ . The expected prepolarization gain from Equation (2) is approximately 2.00.

 $<sup>^\</sup>dagger$ The undersampling factor here is defined as the ratio of outermost k-space cell areas in the Nyquist and undersampled cases.



**FIGURE 7** A, PETRA (top) and P-PETRA (bottom) images of an ex vivo adult human molar tooth. B, Signal intensity along the horizontal line defined by the red arrows in A. The experimentally obtained value for the prepolarization gain is  $\alpha \approx 1.94$  (expected value  $\approx 2.02$ ). C, Photograph of the sample



**FIGURE 8** A, PETRA (top) and P-PETRA (bottom) images of an ex vivo piece of cattle rib bone. B, Signal intensity along the horizontal line defined by the red arrows in A. The experimentally obtained value for the prepolarization SNR gain is  $\alpha \approx 1.97$  (expected value  $\approx 2.00$ ). C, Photograph of the sample

# 6 | DISCUSSION

The preliminary results shown in this work have been obtained in a highly constrained setup in terms of prepolarizer alignment, hydraulic capacity and prepolarizer duty cycle. If the prepolarization field had been aligned with the main static field, we could have approached  $B_t = 0.74$  T, leading to an increase in SNR of  $\times 2.85$ . Also, limitations in the cooling system forced us to work under 260 A, although the system could have taken up to 320 A. This corresponds to  $B_t \approx 0.66$  T with the crossed configuration or  $B_t \approx 0.87$  T if  $B_0$  and  $B_p$  are aligned. In this last situation, we could achieve  $\alpha \approx 3.5$  compared to  $\alpha \approx 2$  with the actual setup, resulting in a 2.4-fold time reduction for same SNR. On the other hand, working with a prepolarizer field perpendicular to  $B_0$  can be beneficial for faster switching off of  $B_p$  and to reduce eddy currents, even if the total  $B_t$  is lower. Thus, the benefits of an aligned configuration will largely depend on the ability to reduce eddy currents and to perform a well controlled switch-off of  $B_p$ .

A further limitation of our setup is the maximum duty cycle of the GPA 400-750 module, which enforces repetition times  $T_R \ge 250$ ms. These are significantly longer than strictly required by the  $T_1$  values of the samples. Assuming a hypothetical  $t_p \ge 4T_1$ , enough to thermalize at  $\approx 98\%$  of the longitudinal magnetization, the  $T_R$  could be shortened to around 80 ms for PMRI of teeth (actually, slightly longer due to the increased  $T_1$  time). Increasing the duty cycle can be achieved, for example, by custom fabrication of an efficient cooling system for the high-power gradient amplifier, as compared with the fan-based cooling in our GPA module. This can transfer the total SNR boost into a net gain in SNR per unit time, which is the relevant metric. Taking the example of the human molar tooth and our present setup, a duty cycle defined by  $T_R = 80$  instead of 250 ms would translate to the same SNR gain in only approximately 9 min (three times faster). All in all, the combination of prepolarizing at 320 A,  $\mathbf{B}_0 \parallel \mathbf{B}_p$  and  $T_R = 80$  ms can shorten the acquisition from 29 to less than 4 min for the image in Figure 7.

Finally, in order to provide a fairer comparison, we could have shortened the MRI sequence by  $t_p + t_{off} + t_{del,1}$ . However, if we disregard regimes exploiting steady-state magnetization to shorten the  $T_R$  (which is not possible with PMRI), the standard MRI sequence must include a time for thermalization similar to the prepolarization pulse duration. Hence, the two sequences would be comparably long and a prepolarized setup with an optimal duty cycle could lead to a match between  $M_{PMRI}/M_{MRI}$  and the real SNR boost per unit time.

## 7 | CONCLUSION AND OUTLOOK

We have demonstrated that it is possible to enhance the quality of magnetic resonance images of hard tissues at low field strengths by means of a high-power prepolarizer module, for a total cost of approximately 20 k $\epsilon$ , where the GPA 400-750 module is around 13 k $\epsilon$ . The major challenges we have faced are (i) integrating a high-power drive capable of switching off the prepolarization pulse fast enough and (ii) coping with mechanical vibrations due to the strong magnetic interaction between the main and prepolarization fields. We have shown SNR enhancements for ex vivo imaging of a human molar tooth (29 min) and a cattle rib bone (53 min) by a factor of approximately 2, although a low duty cycle in the high-power gradient amplifier did not allow us to translate this gain into a real boost in SNR per unit time. Nevertheless, a more efficient dissipation of the heat from the power electronics could lead to a significantly higher duty cycle and therefore to PMRI within shorter scan times.

The results in this paper could be of potential application to clinical dental MRI. While X-rays are commonplace in dental clinics, it is known that they can increase the risk of meningioma and other cancers if performed often.<sup>36-38</sup> In fact, in recommending X-rays, dentists follow the ALARA principle (as low as reasonably achievable), in direct conflict with medical practice, which would recommend diagnosis and medium-term monitoring as much as required.<sup>39</sup> There is, hence, a clear motivation for advances in MRI that aim to replace scanners based on ionizing radiation. Standard (high-field) MRI has proven useful for dentistry, but is too costly for massive use,<sup>40</sup> and often impractical due to artifacts induced by the magnetic susceptibility of metallic implants.<sup>41</sup> Both problems can be a priori overcome in low-field systems, but the only experimental evidence so far has required excessively long acquisition times.<sup>9</sup> Hard-tissue PMRI may be a first step towards viable dental MRI. In Section 5 we have demonstrated dental PMRI in 29 min acquisitions. This can be sped up by a factor of 3 or more in our setup with more powerful water cooling for the high-current amplifier (see Section 6), bringing it to scan times under 10 min, albeit in a field of view significantly smaller than a full human jaw. Realistic PMRI in dental practice would seemingly require a combination of techniques, yet to be demonstrated, which could include slice-selective ZTE sequences,<sup>22</sup> hybrid filling of the dead-time gap in ZTE,<sup>42</sup> intra-oral RF detection coils,<sup>43</sup> or acceleration schemes based on *k*-space undersampling,<sup>44</sup> besides exquisite engineering, for scan-time reduction. This constitutes a formidable technical challenge, but holds the promise of safe dental imaging with the added value of soft-tissue visualization.

## **AUTHOR CONTRIBUTIONS**

The high-power electronics for prepolarization were designed and installed by JMG, JB, JPR and JA. The prepolarizer and mechanical holder were designed, assembled and characterized by JPR, JMG, EP and JB, with contributions from DG-R and JA. Experimental data in the "DentMRI—Gen I" scanner were taken by JB and JMG, with help from JMA, FG, RP and JA. Data analysis was performed by JB and JMG, with input from JMA, FG, RP and JA. Animal handling and manipulation of biological tissues were performed by JB. The paper was written by JB, FG and JA, with input from all authors. Experiments were conceived by JMB, JA and AR.

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## ETHICAL APPROVAL

All animal parts were obtained from a local butcher and research was conducted following the 3R principles. Experiments using human teeth were approved by the medical center Clínica Llobell Cortell S.L. Procedures were conducted following the approved protocols, and informed consent was obtained from participants prior to study commencement.

## **CONFLICTS OF INTEREST**

JB, JMA, FG, JMB and JA have patents pending that are licensed to Tesoro Imaging S.L. JMB is a co-founder of Tesoro Imaging S.L. JB, JMG, JPR, RB, DG-R and AR are research scientists and engineers at Tesoro Imaging S.L. All other authors declare no competing interests.

#### **DATA AVAILABILITY STATEMENT**

The data that support the findings of this study are available from the corresponding author upon reasonable request.



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