Study of Electron–Nuclear Interactions in Doped Calcium Phosphates by Various Pulsed EPR Spectroscopy Techniques

Fadis Murzakhanov,* Georgy Vladimirovich Mamin, Sergei Orlinskii, Margarita Goldberg, Nataliya V. Petukhova, Alexander Y. Fedotov, Peter Grishin, Marat R. Gafurov, and Vladimir S. Komlev

ABSTRACT: Substituted calcium phosphates (CaPs) are vital materials for the treatment of bone diseases and repairing and replacement of defects in human hard tissues. In this paper, we present some applications of the rarely used pulsed electron paramagnetic resonance (EPR) and hyperfine interaction spectroscopy approaches [namely, electron spin-echo envelope modulation (ESEEM) and electron–electron double-resonance detected nuclear magnetic resonance (EDNMR)] to investigate synthetic CaPs (hydroxyapatite, tricalcium, and octacalcium phosphate) doped with various cations (Li+, Na+, Mn2+, Cu2+, Fe3+, and Ba2+). These resonance techniques provide reliable tools to obtain unique information about the presence and localization of impurity centers and values of hyperfine and quadrupole tensors.

We show that revealed in CaPs by EPR techniques, radiation-induced stable nitrogen-containing species and carbonate radicals can serve as sensitive paramagnetic probes to follow CaPs’ structural changes caused by cation doping. The most pulsed EPR, ESEEM, and EDNMR spectra can be detected at room temperature, reducing the costs of the measurements and facilitating the usage of pulsed EPR techniques for CaP characterization.

1. INTRODUCTION

Numerous studies are devoted to the investigation of bone tissue properties, implants, and biomineralization processes.1–5 One of the key reasons for this research direction is worldwide aging population processes, serious fractures with related consequences, and increasing bone and joint infections. In the surgical treatment method, it is important to choose a suitable material that will serve as an alternative for the defective area of bone tissues.6 Currently, it is known that several inorganic phases are involved in bone biomineralization generally presented as nonstoichiometric carbonate [Ca_{10-x}(PO_4)_{6-x}(CO_3)x(OH)_{2-x}(CO_3)x] or nitrogen-substituted [Ca_{10-x}(PO_4)_{6-x}(NO_3)x(OH)_{2-x}(NO_3)x] calcium phosphates (CaPs), among which hydroxyapatite [HA, chemical formula Ca_{10}(PO_4)_6(OH)_2], tricalcium phosphate (TCP, chemical formula Ca_3PO_4), and octacalcium phosphate [OCP, Ca_9H_2(PO_4)_6·5H_2O] are of the main importance (Table 1). The structures of mentioned CaP materials are similar to that of the mineral phase of the bone. Thanks to their chemical and biological properties, the CaP materials have gained vast interest in recent decades for orthopedic and dental applications,7 as well as items for the bone tissue engineering.8

To tune (improve) chemical, bioactive, and antimicrobial properties of synthesized CaPs, doping and co-doping with various metal impurities such as Zn2+, Mg2+, Na+, Li+, Cu2+, Fe2+/3+, Al3+, Mn2+, and so forth19–27 are widely in use. Thus, the structural, biological, and physicochemical characteristics of CaPs have to be extensively investigated. However, despite the large amount of data obtained, diverse property changes of the initial materials (implants), especially for nanosized CaP or thin CaP coatings and for surrounding tissues depending on the conditions of synthesis and (co)doping, have not been sufficiently studied. Standard analytical tools and histological and biochemical analyses were mainly used to explore these materials. A further advance in this area requires the involvement of other physical and chemical approaches for material characterization.

One of the analytical nondestructive methods for studying CaPs of biogenic and synthetic origins is electron paramagnetic...
Table 1. List of CaP Materials That Are Widely Found in Biological Systems and as Components of Bone Implants

| Ca/P ratio | material                     | chemical formula        |
|------------|------------------------------|-------------------------|
| 1.0        | dicalcium phosphate dihydrate (DCPD, brushite) | CaHPO<sub>4</sub>-2H<sub>2</sub>O |
| 1.0        | dicalcium phosphate anhydrate (DCPA, monetite) | CaHPO<sub>4</sub>         |
| 1.33       | octacalcium phosphate (OCP)  | Ca<sub>6</sub>H<sub>2</sub>(PO<sub>4</sub>)<sub>5</sub>·5H<sub>2</sub>O |
| 1.5        | α-tricalcium phosphate (α-TCP) | α-Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub>                  |
| 1.5        | β-tricalcium phosphate (β-TCP) | β-Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub>                  |
| 1.5        | amorphous calcium phosphate (ACP) | Ca<sub>4</sub>(PO<sub>4</sub>)·nH<sub>2</sub>O |
| 1.67       | hydroxyapatite (HA)          | Ca<sub>10</sub>(PO<sub>4</sub>)<sub>6</sub>(OH)·2H<sub>2</sub>O |
|            | carbonated HA<sup>420</sup> | Ca<sub>10</sub>(PO<sub>4</sub>)<sub>6</sub>(CO<sub>3</sub>)·(OH)<sub>2</sub>·nH<sub>2</sub>O |
|            | nitrato HA<sup>450</sup>     | Ca<sub>10</sub>(PO<sub>4</sub>)<sub>6</sub>(NO<sub>3</sub>)·(OH)<sub>2</sub>·nH<sub>2</sub>O |
| 2.0        | tetracalcium phosphate (TTCP) | Ca<sub>10</sub>(PO<sub>4</sub>)<sub>6</sub>(OH)<sub>2</sub> |

“Including anions substituted via air carbonate and reactant-concomitant nitrate modifications.

A standard way of studying EPR-silent CaPs is the creation of radiation-induced defects and investigations of their spectroscopic properties. Several radiation-induced paramagnetic species (anion radicals) located at hydroxyl or phosphate sites have been identified in CaPs. Among them, oxygen radicals O<sup>-</sup>, trapped atomic hydrogen centers, holes trapped on OH<sup>-</sup> or PO<sub>4</sub><sup>3-</sup>, carbonate radicals CO<sub>3</sub><sup>2-</sup>, CO<sub>2</sub><sup>-</sup>, CO<sub>3</sub><sup>-</sup>, and color centers have been observed. In burnt bones, coal-type C-radicals have been detected.<sup>50</sup> In our previous publications (see ref 31 for review on this topic), we have demonstrated the suitability of the radiation-induced nitrate radical NO<sub>3</sub><sup>-</sup> to serve as an effective spin probe for studying the structure and chemical composition of CaP powders with various anions and cations (e.g., Cu<sup>2+</sup>, Fe<sup>3+</sup>, Al<sup>3+</sup>, Mn<sup>2+</sup>, Ni<sup>2+</sup>, Pb<sup>2+</sup>, etc.) by EPR.

As was shown by a series of publications, introducing impurities in concentrations of less than <0.5 mol % can also significantly affect the CaP properties. For example, the introduction of 0.3–0.5 mol % Ag<sup>+</sup> as well as 0.4 mol % Cu<sup>2+</sup> and Zn<sup>2+</sup> resulted in antibacterial properties of ceramic materials, while the doping by 0.5 mol % Au<sup>3+</sup> led to enhancement of the thermal stability of HA.<sup>39</sup> Conversion of HA → β-TCP occurred at lower temperatures due to incorporation of 0.25 mol % Mg<sup>2+</sup>.<sup>40</sup> Recently nitrato doping of CaP nanoparticles was proposed for potential use as (P, N)-nanofertilizers for agricultural applications,<sup>41</sup> and EPR was recognized as one of the fast methods to evaluate the presence and amount of nitrates. HA is also applied as an adsorbent for water purification.<sup>42,43</sup>

Most of the EPR measurements are limited to CaP study by conventional continuous wave (CW) methods at X- (9.5 GHz) and (sometimes) Q-band (36 GHz) microwave (mw) frequency ranges. A large number of EPR data are gathered mainly in the conventional mode.<sup>44,45</sup> It is known that interpretation of EPR spectra in disordered materials (powders, ceramics) of CaPs in the X-band is a difficult task, especially with the impurity paramagnetic centers in high-spin electron states (S > 1 for Mn<sup>2+</sup>, Fe<sup>3+</sup>) and/or having high nuclear spins (I ≥ 1: 14N, 23Na, 55Mn, 27Al, 63Cu, 65Cu, etc.).<sup>53</sup>

The main spectroscopic parameters [g-factors, zero-field splitting (ZFS) (D and E), and hyperfine interactions (A)] are orientation-dependent. In powder materials, all orientations of (nano)particles are equally probable. Therefore, the EPR spectrum of the sample contains signals from all orientations. Eventually, the resulting EPR spectra are detected as broad structureless lines with unresolved components of fine or hyperfine interactions. Such inhomogeneous broadening leads to the loss of the extremely important data about the values of electron–electron and electron–nuclear interactions and the influence of impurity paramagnetic centers on the crystal lattice.<sup>54,55</sup>

CaP materials consist of the structural elements having nonzero nuclear magnetic moments (I = 1/2 for 31P and 35P). Also, as was already mentioned above, some impurity centers in CaPs have their own nuclear magnetic moments. In such spin systems, details of the electron–nuclear interactions could provide unique information about the localization of impurity ions and lattice distortions. Unfortunately, the hyperfine splittings in CaP powders are usually masked by broad EPR lines. To solve the problems with low spectral resolution and the impossibility of studying the nuclear environment by conventional EPR, it is necessary to apply all available analytical tools that are aimed at studying weak electron–nuclear and quadrupole interactions. Various pulse EPR techniques allow obtaining a complete set of spectroscopic parameters with dynamic features for the distinct impurity center in CaP materials. The explicit identification of a certain paramagnetic center is important for biphase materials (HA + β-TCP), which are now gaining great interest and are still poorly studied.<sup>56</sup> Equally interesting are materials with copoling, that is, with several distinct impurity centers.<sup>57</sup>

Accordingly, for the successful study of mentioned compounds, it is important to have a complete picture of electron–nuclear and quadrupole interactions in single-phase materials with one type of the impurity center.

In the present paper, we aimed to show that X-band pulse EPR techniques including electron spin-echo envelope modulation (ESEEM) and electron–electron double-resonance (ELDOR) detected nuclear magnetic resonance (EDNMR) can significantly complement and deepen the existing EPR approaches for the investigation of hyperfine interactions in CaP materials on examples of HA, TCP, and OCP powders. The experimentally obtained spectroscopic data (anisotropic g-factors and hyperfine A and quadrupole P interaction values) for different impurity centers will become a reference point for further theoretical calculations based on quantum chemistry (e.g., density functional theory—DFT approach), which will allow obtaining structural information about the features of the doped crystal lattice.

### 2. MATERIALS AND METHODS

Powders of "pure" and cation-substituted CaPs (HA, TCP) were synthesized by the wet (precipitation) technique from solutions of nitrates and ammonium hydrogen phosphate. For example, reaction 1 shows the route of synthesis of Li<sup>+</sup>-doped HA with x = 0–2 taking into account the valence states of ions for the charge balance.
(10 − x)Ca(NO₃)₂ + 6(NH₄)₂HPO₄ + 2xLi(NO₃)₃ + 8
NH₄OHCa₁₀−xLi₂x(PO₄)₆(OH)₂ + 20NH₄NO₃ + 6
H₂O

Calcium and lithium-containing salts were dissolved in 250 mL of deionized water to obtain the solutions with selected ratios (x = 0−2). The solution of diammonium hydrogen phosphate was prepared with 150 mL of deionized water. The diammonium hydrogen phosphate solution was added by dropping to the cation nitrate solution during the stirring at room temperature. The pH value of the reaction mixture was maintained at a value of 9.0−9.5 by adding aqueous ammonia. The precipitate was ripened in the mother solution for 21 days at a temperature of 25 °C for its full crystallization. The obtained powders were filtered, washed in deionized water, and dried at 60 °C for 24 h. The powders were heat-treated at 300 °C for 3 h in air to remove ammonium nitrate, an impurity phase.

The powder of OCP was made by hydrolysis of the initial DCPD powder in the buffer solution. 10 g of DCPD powder was immersed in 1000 mL of 1.5 M sodium acetate aqueous solution with a pH value of 8.8 ± 0.2. The powder was kept in 24 h with a constant stirring rate at 35 °C; then, it was thoroughly washed in distilled water and dried overnight at 37 °C.

Samples were characterized by X-ray diffraction to study structural phase composition (D2 Phaser, Bruker, Germany), elemental analysis by atomic emission spectrometry with inductively coupled plasma (HORIBA Jobin Yvon, ULTIMA 2, USA), scanning electron microscopy (SEM) to assess the structural phase composition (D2 Phaser, Bruker, Germany), and Fourier transform infrared spectroscopy (FTIR) in the frequency range (Tescan Vega II SBU microscope, Czech Republic), and transmission electron microscopy (Nicolet Avatar 330 FTIR spectrometer, USA) to follow the presence of various functional groups. EPR spectra interpretation.59

Figure 1. (a) ESEEM pulse sequence scheme; (b) energy levels for the electron–nuclear spin system S = 1/2, I = 1/2 with the corresponding quantum numbers and transitions.

EDNMR was done by using a pulse ELDOR module E580-400U and a dielectric ring resonator ER 4118X-MDS to perform double electron–electron manipulations in the range of 9.3−9.8 GHz (Figure 2). The length of the selective pulse was chosen to be 6 μs, which corresponds to the excitation band in the EPR spectrum with ΔB = 0.072 G (0.0072 mT). The duration of the detection pulse was equal to 300 ns, and the delay time between two pulses was td = 500 ns.

The pulse at the fixed observation frequency (νmew or νchir) serves to create a free induction decay (FID) signal at the value of the magnetic field which corresponds to one of the EPR transitions. Another pulse at the pump frequency (νmew or νpump) with a variable (sweep) value is in need to excite forbidden transitions (Figure 2b). The secondary (additional) frequency that is varied within 9.3−9.8 GHz induces the corresponding forbidden transitions between hyperfine interaction levels of ground and excited states (in our case, mI = −1/2, mI = 1/2, mI = 1/2, mI = 1/2, respectively).

Subsequently, due to the redistribution of the spin population between the hyperfine splitting levels, the FID amplitude at the
Figure 2. (a) Pulse sequence diagram for EDNMR excitation at one mw frequency (mw2—green) in the sweep range of 9.3–9.8 GHz and detection at another one (mw1—red) at a fixed value of the main EPR spectrometer frequency with \( \nu_{\text{mw1}} = 9.59 \) GHz; (b) energy levels for the electron–nuclear spin system with \( S = 1/2, I = 1/2 \), where \( m_S \) and \( m_I \) are the level states. The arrows indicate EDNMR resonance transition (blue) initiated by mw (red and green arrows, correspondingly).

3. RESULTS AND DISCUSSION

3.1. EPR of Intrinsic Paramagnetic Impurities.

Registration of EPR spectra and unraveling the nature of the observed paramagnetic centers are the main steps before conducting experiments by using hyperfine EPR spectroscopy. Nominally "pure" CaP materials according to their chemical formulas are EPR-silent. In some specimens, impurity ions like iron (Fe\(^{3+}\)) or manganese (Mn\(^{2+}\)) as contaminants can be detected. Figure 3 shows an example of the room-temperature spectrum for the nominally "pure" TCP that reveals the presence of a small quantity of Mn\(^{2+}\). The spectrum is mainly due to the hyperfine interaction between the manganese electron spin (\( S = 5/2 \)) and \(^{55}\)Mn nuclei (\( I = 5/2 \)) with \( A = 9–10 \) mT (see refs 14 and 16 for details). The valence of manganese was determined by the following reasons: in TCP, manganese substitutes the calcium ion isovalently, in accordance with the charge balance rule in a crystal lattice and also confirmed by DFT calculations as the most energy preferable.\(^{16,51}\) The value of hyperfine structure \( A \) is found to be of 9.0 mT, which also attributes to the Mn\(^{2+}\) ions.\(^{53}\) From the comparison of the presented EPR spectrum and its integral intensity with the concentration series for the manganese-doped TCP,\(^{16}\) the amount of Mn\(^{2+}\) in the Ca\(_3\)-Mn\((\text{PO}_4\)_3\) sample can be estimated as \( x < 0.001 \) or \(< 0.02 \) wt %.

Figure 4a shows spectra of Cu\(^{2+}\) in the copper-doped HA. A complex EPR signal in the region of the spectroscopic \( g \)-factor \( g \approx 2.02–2.40 \) is due to (1) the rhombic-distorted symmetry of the paramagnetic center in HA nanocrystals, defining the \( g \)-factor anisotropy; (2) the presence of anisotropic hyperfine interactions of the electron magnetic moment \( S \) with the nuclear magnetic moment of copper (\(^{63}\)Cu and \(^{65}\)Cu, both with \( I = 3/2 \)); and (3) averaging over different orientations of nanocrystals in the powder structure.\(^{51}\) Spectra can be registered at room temperature. To identify Cu\(^{2+}\) and extract the EPR parameters, the spectrum presented in Figure 4a was detected at \( T = 15 \) K. By introducing the values of \( g_{zz} = A_{xx}, A_{yy}, A_{zz} \) (for orientation parallel to the external magnetic field \( B \)); \( g_{xx}, A_{xx} \) and \( g_{yy}, A_{yy} \) in the plane \( (x, y) \) for orientation perpendicular to \( B \) (Figure 4a) we can attribute the anisotropic components of the resonance signal to the certain canonical orientation of the Cu-HA nanocrystals relative to the external magnetic field \( B_0 \). Spectra simulation by using EasySpin abilities\(^{64}\) gives the following values: \( g_{zz} = 2.49, A_{xx} = 238 \text{ MHz}, g_{xx} = 2.12, g_{yy} = 2.07 \), and \( A_{xx} \approx A_{yy} \approx 120 \text{ MHz} \). The extracted axially anisotropic parameters with rhombic distortion indicate that Cu\(^{2+}\) is included in the HA crystal structure.\(^{53}\) Figure 4b shows the concentration dependence of the Cu-OCP sample EPR spectra. In this case, due to the room-temperature conditions and the more complex crystal structure, the lines are inhomogeneously broadened, hindering the accurate determination of EPR parameters.

An example of detection of Fe\(^{3+}\) impurity by ESE EPR as a signal in the “half-magnetic-field” \( g = 4.27 \) in the copper-doped sample of TCP is shown in Figure 5. The asymmetric EPR absorption in the low-field regions corresponding to the above-mentioned effective \( g \)-factor is a clear feature of the trivalent iron introduced into the lattice structure of the materials under study. Previously, for HA doped with Fe\(^{3+}\), these signals served as a reliable source of local structural changes depending on the concentration of impurity centers.\(^{56,66}\) More details about the nature of the signal in the “half-magnetic field” are given in our papers.\(^{6,51}\) Examples with the detection of paramagnetic centers (Mn or Fe) in nominally pure samples indicate the possibility of using EPR spectroscopy to control the presence of undesirable/unwanted centers with spin numbers no less than 10\(^2\) per one Gauss of resonance line width.

3.2. EPR of Radiation-Induced Paramagnetic Impurities.

As was already mentioned in the Introduction, ionizing radiation allows detecting various anions and cations (like Pb\(^{2+}\)) with EPR. Powder EPR spectra of the radiation-induced paramagnetic centers in CaPs very often can be described by a spin-Hamiltonian of axial symmetry

\[
H = g_B S_B \cdot B_0 + g_A (B_x S_x + B_y S_y) + A_S S_z + A_I I_z
\]

(2)

where \( g_B \) and \( g_A \) are the main components of the g-tensor; \( A_S \) and \( A_I \) are the main components of the hyperfine tensor; \( B_x, B_y \) and \( I_z \) are the projections of the external magnetic field strength.
and electronic \( S \) and nuclear \( I \) spins, respectively, onto the 
\( i = \{x, y, z\} \) coordinate axis; and \( \beta \) is the Bohr magneton.

The most common and studied radiation-induced signals 
belong to carbonate radicals.\textsuperscript{25,45,48,53} The type of carbonate 
radical as a point defect has an electron spin \( S = 1/2 \) and an 
anisotropic shape of the resonance line with a \( g \)-factor around 
of 1.99–2.01 (namely, \( g_\parallel > g_\perp \)). In studied materials, the 
carbonate anions serve as spin traps and can capture electrons 
under the X-ray or gamma radiation exposure by which 
impurities obtain paramagnetic properties. Figure 6 shows the 
typical EPR spectrum due to the axial CO\(_2^\cdot\) paramagnetic 
center in the jawbone of a Vietnamese mini pig (the mineral 
phase of which consists mainly from HA) in CW and pulsed 
EPR modes.

The HA and TCP EPR spectra of the synthesized 
compounds from the nitrogen-containing reagent samples 
(see eq 1) can be described with \( A_\parallel = 6.65(40) \) mT and \( A_\perp = 3.37(5) \) mT, while the components of \( g \)-factors are \( g_\parallel = 2.002, \) 
\( g_\perp = 2.006 \) (Figure 7). It was concluded that in the irradiated 
HA samples, EPR is mainly due to the stable NO\(_3^\cdot\) ions \( (I = 1 \) 
for \(^{14}\)N nuclei) preferably substituting the PO\(_4^\cdot\) position in 
the HA structure (substitution of the B-type).\textsuperscript{30} In our paper,\textsuperscript{34} 
we have found that for NO\(_3^\cdot\) in TCP, the distribution of \( A_\perp \) 
is larger than that for HA. We have suggested that it could be due 
to three different positions for PO\(_4^\cdot\) group substitution in the 
TCP structure as well as due to the various schemes for charge 
compensation.

Radiation-induced signals in OCP (Figure 8) are the most 
complicated among the considered CaPs\textsuperscript{67} and can be ascribed 
to the presence of three paramagnetic centers—two 
nitrogen-containing and one carbonate-based radiation-in-
duced paramagnetic centers. Their parameters are listed in 
Table 2. The structure of OCP can be imagined as consisting of 
apatite and hydrated layers.\textsuperscript{68} The difference in the obtained 
OCP values of EPR parameters compared to HA most 
probably points out that the radical(s) are not located in the 
bulk of apatite crystallites (A- or B-type substitution) but in the 
hydrated layers.

3.3. Influence of Metal Co-doping on EPR Parameters 
of the Radiation-Induced Paramagnetic Impurities.

As concerning conventional EPR, three EPR parameters (intensity, 
line width, and the position of the lines, i.e., values of \( g \)- 
and \( A \)-tensors) of the radiation-induced centers can be affected 
by metal co-doping. Indeed, as was already mentioned above, 
we found, for example, that Al\textsuperscript{3+} doping reduces the intensity 
of carbonate-related signals (the amount of carbonates).\textsuperscript{15}
the presence of magnetic nuclei in CaP often leads to the appearance of modulations on the decay curves of transverse magnetization caused by the interaction with the neighboring nuclei. ESEEM spectra of NO$_3^-$ in the Li-doped HA with Li$^+$ concentrations are shown in Figure 11a. It demonstrates that the number and shape of the ESEEM lines significantly change with concentration. For the lowest concentration, only the signal for $^{31}$P (natural abundance 100%, $I = 1/2$, gyromagnetic ratio $\gamma = 17,240 \text{ kHz}/T$) that is centered on the Larmor (Zeeman) frequency $f_{\text{Zeeman}} \approx 5.87 \text{ MHz}$ for $B_0 = 340 \text{ mT}$ is observed. This information already indicates that the nitrate radical is located in the HA structure and can be used as an intrinsic spin probe. The frequency band at 6 MHz contains two signals from phosphorus and lithium nuclei. Because of the close values of the Larmor frequencies for $^{31}$P and $^7$Li (natural abundance of 92.41%, $I = 3/2$, gyromagnetic ratio $\gamma = 16,550 \text{ kHz}/T$, $f_{\text{Zeeman}} \approx 5.63 \text{ MHz}$ for $B_0 = 340 \text{ mT}$) and relatively low spectral resolution, their contributions can be separated only for the second ESEEM harmonic at higher Li$^+$ concentrations (Figure 11a). The inhomogeneous broadening of the lines that limits the analysis of the first resonance frequency harmonics is caused by the short $T_M$ time.

ESEEM proves a direct involvement of Li nuclei in the formation of a regular structure around the nitrate radical and, therefore, indicates that lithium ions are included in the crystal structure of the material during the synthesis. The absence of additional splitting (due to hyperfine or quadrupole interactions) is possibly related to the restriction of the spectral resolution of the method at room temperature. However, it is worth noting that in this case, the observation of the lithium signal can already be considered a success since due to the high nuclear spin, some broadening mechanisms appear due to the hyperfine and quadrupole interactions. As can be seen, two low-frequency signals indicated by asterisks in Figure 11a can also be detected by ESEEM in the lithium-doped HA. Obviously, low-frequency lines refer to lithium ions, but due to the presence of two nuclear isotopes ($^7$Li, $I = 1$, 5.626% and $^7$Li, $I = 3/2$, 92.41%) with nonzero quadrupole moments ($Q > 0$) and the combination of the difference frequencies, the interpretation of these signals is extremely difficult. The nature of these broadened lines is still presently unclear and requires additional experiments and efforts. The $^1$H frequency is apparently not observed since the hydrogen nuclear interacted with Li$^+$ ions isotopically (the so-called Fermi contact interaction), which does not lead to the appearance of ESEEM modulations.

Figure 11b shows that ESEEM spectra in the Cu-HA system depend on the value of the magnetic field ($B_1 = 330 \text{ mT}$ or $B_2 = 293 \text{ mT}$). This means that the EPR spectrum is due to the presence of at least two types of paramagnetic centers. In the first case ($B_1$), we observe only the phosphorus nucleus in the near local environment of Cu ions (for $^{31}$P $f_{\text{Zeeman}} = 5.69 \text{ MHz}$ at $B_1$). Changing the value of the magnetic field on $B_2$ has led to the conclusion that one detects the impurity centers of copper in another position in the crystal structure also having

![Figure 8. Field-swept ESE spectra of the barium-doped OCP (10 wt % Ba) sample after X-ray irradiation with the corresponding fitting as a sum of signals from three stable radicals R$_1$–R$_3$ with the parameters listed in Table 2.](https://doi.org/10.1021/acs.omega.1c03238)
hydrogen nuclei $^1$H (natural abundance 99.985%, $f_{\text{Zeeman}} \approx 14.05$ MHz for $B_0$, $I = 1/2$, gyromagnetic ratio $\gamma = 42,570$ kHz/T) around. Thus, one reveals the presence of two structurally nonequivalent positions of copper in the crystal lattice of HA at extremely low impurity concentrations. According to the HA structural information, even at a concentration of 0.23%, Cu$^{2+}$ ions substitute both calcium positions (Ca1 and Ca2) in the HA structure. Such a primary ESEEM analysis allows simplifying the process of simulating and separating overlapping components of the complex EPR spectrum. The first harmonic of $^{31}$P does not change with the magnetic field value $B_0$, unlike the second one that coincides with $\nu_{\text{Larmor}} = \gamma \times B$. The mathematical processing of modulations in a time-limited mode will lead to some error in the quantitative determination of Larmor frequencies (first harmonic) with a small change in the magnetic field. The absence of modulation from copper nuclei can be ascribed to the low concentration of impurity ions, short relaxation times, and line broadening due to the quadrupole interaction.

The ESEEM spectrum registered at $T = 25$ K from Fe$^{3+}$ in HA (signal at $g = 4.27$, see Figure 5) is shown in Figure 12. ESEEM from the surrounding phosphorus nuclei $^{31}$P ($f_{\text{Zeeman}} \approx 2.79$ MHz at $B_0 = 161.7$ mT) definitely indicates that Fe$^{3+}$ ions are embedded into the HA structure of the sample. Therefore, we can conclude that the synthesis of this sample assumes the introduction of undesirable (uncontrolled) impurities.

Radiation-induced radicals in OCP (Figure 8) can also serve to probe the presence of uncontrolled impurities. Figure 13 shows alterations of CW EPR spectra of the radiation-induced radicals in OCP with copper content (left panel) and changes of integral intensity of the radiation-induced defects as a function of the amount of copper (logarithmic scale, right panel).
shows that additional (besides $^1$H and $^{31}$P) signals obtained in the ESEEM spectrum can be ascribed to electron−nuclear interactions with $^{23}$Na nuclei ($f_{Zeeman} \approx 3.57$ MHz at $B_0 = 317$ mT, $I = 3/2$ and, therefore, quadrupolar). The presence of a signal from $^{23}$Na nuclei (Figure 13) is probably due to the incorporation of sodium into the OCP lattice during the synthesis stage (see the section Materials and Methods) and is also obtained in some papers devoted to the apatite investigations (see ref 48 for example) by ENDOR techniques.

3.5. EDNMR for the Nitrate Radical in HA at Room Temperature. Significant anisotropy of $g$- and $A$-tensors and a relatively long transverse relaxation time of NO$_3^-$ radicals on CaPs allow to carry out angular-selected EDNMR measurements at room temperature (Figure 14). Usually, low temperatures (to lengthen relaxation times) and high frequencies (for better spectral resolution) for EDNMR are in need.$^{62}$

Signals corresponding to the Larmor frequencies of $^{31}$P ($\pm 6$ MHz) and $^1$H ($\pm 14.8$ MHz) are shown on the overview spectra at $B_0 \approx 0.34$ T (Figure 14). These signals are expected to be detected because hydrogen and phosphorus ions are structural elements of HA and indicate that the studied nitrogen probes are located in the HA crystal lattice. The lack of additional structures (or splittings) for these nuclei is a sign of insufficient spectral resolution of the EDNMR method at least at room temperature for the X-band. The most interesting signals are those observed at $\nu = \pm 47.5$ and $\pm 95.0$ MHz. Given the theoretical calculations$^{62,69}$ for various electron−electron transitions as well as the known values of $A$ from EPR measurements, it follows that these transitions are caused by the anisotropic hyperfine interaction with $^{14}$N nuclei. Since the value of $A$ is bigger than the Larmor frequency of $^{14}$N nuclei ($\nu_{Larmor} = 1.04$ MHz for $B_0 \approx 340$ mT), this leads to localization of the EDNMR signal in the range at the half value (for single-quantum transitions with $\Delta M_I = \pm 1$) and at the whole value of $A$ (for the double-quantum transitions with $\Delta M_I = \pm 2$).

A more detailed analysis of the spectrum for $\Delta \nu > 0$ ($M_I = -1$) shows the additional splitting for the single-quantum transition exactly localized at the value of $A_{23}I_2/2$ (Figure 15). Using the expression for single-quantum transitions,$^{69}$

$$\Delta = 2\nu_{\perp} \pm 3P$$  

(3)
where $\Delta$ indicates splitting the value of single-quantum transitions and a choice of sign $\pm$ depends on a quantum number of $M_i$ ("+" for $M_i = -1$ and "-" for $M_i = +1$), and we can conclude that the observed splitting is due to the presence of a quadrupole interaction ($P$) of the $^{14}$N nuclei with a gradient of the crystal field. In the assumption that the $A$- and $P$-tensors are collinear, the value (and sign) of the quadrupole splitting is calculated quite easily. Thus, we have established that the value of quadrupole splitting is $P = 1.2$ MHz. Because the value of $P$ is comparable to the Larmor frequency for $^{14}$N, the splitting at the same orientation with $M_i = +1$ is not observed.

The anisotropic EPR spectrum (Figure 7) and a quite narrow excitation band make it possible to conduct angular measurements (Figure 16). The significant shift of the EDNMR resonance lines is caused by the presence of the strong anisotropic hyperfine interaction. The magnetic dipole–dipole interaction with the corresponding angular dependence and the strong coupling case ($A > 2 \times \nu_{\text{Larmor}}$) lead to the considerable change of the frequency values (located just at $A_i/2$) depending on $B_0$. Indeed, in our experiments, we clearly observe that the value of splitting depends on $B_0$ confirming the mentioned assumption. However, it should be noted that $A$- and $P$-tensors are not collinear, which are based on the simple calculation and mutual angular analysis of $A$ and $P$ values. Therefore, in a dipole–dipole approximation, it can be assumed that the quadrupole interaction tensor is rotated relative to the z-axis of the hyperfine interaction tensor.

The spectroscopic parameters of the spin Hamiltonian (anisotropic g-factors, hyperfine $A$ and quadrupole $P$ interaction values) reflect the local symmetry of the impurity center position. The extent of anisotropy and the corresponding amplitudes of $g$- and $P$-tensors depends on the electron density distribution of ions and the gradients of electric fields. Quantum-chemical methods are able to calculate the listed energy characteristics, which are determined by the structural features and localization of impurity ions. Thus, a comparative analysis of experimental data from pulsed EPR spectroscopy with further theoretical calculations will lead to a more complete understanding of the structural features of the crystal lattice of the doped CaP materials.

4. CONCLUSIONS

In this article, we have demonstrated the possibility of using pulsed X-band EPR, ESEEM, and EDNMR techniques to study nominally "pure" CaPs and synthetic CaP (HA, TCP, and OCP) powders doped with various ions ($\text{Li}^+$, $\text{Na}^+$, $\text{Mn}^{2+}$, $\text{Cu}^{2+}$, $\text{Fe}^{3+}$, and $\text{Ba}^{2+}$). The main parameters of the spin Hamiltonian were determined by EPR spectroscopy to describe and identify the nature of paramagnetic centers. The ESEEM method allows to quickly determine the type of nuclear isotopes (also for $I > 1/2$) for the different local environments of various paramagnetic centers or their structurally nonequivalent positions.

It is shown that spectroscopic (including hyperfine) and relaxation characteristics of the radiation-induced stable nitrogen-containing species and carbonate radicals are sensitive to the presence and concentration of the cation impurities. By EDNMR, the values of quadrupole interaction for $^{14}$N (1.2 MHz) for the radiation-induced nitrate radicals with a high degree of anisotropy were determined. The value of quadrupole interaction is shown to be sensitive to the changes of the local environment (to the symmetry of the electric/crystal field). Remarkably, a large portion of the pulsed measurements can be carried out even at room temperatures. It simplifies the experiments and reduces their costs.

The results show the feasibility of using pulsed and hyperfine EPR spectroscopy as an informative complementary tool for studying CaP-based materials.

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

■ AUTHOR INFORMATION

Corresponding Author
Fadis Murzakhanov – Kazan Federal University, Kazan 420008, Russian Federation; orcid.org/0000-0001-7601-6314; Email: murzakhanov.fadis@gmail.com

Authors
Georgy Vladimirovich Mamin – Kazan Federal University, Kazan 420008, Russian Federation
Sergei Orlinskii – Kazan Federal University, Kazan 420008, Russian Federation
Margarita Goldberg – A.A. Baikov Institute of Metallurgy and Materials Science, Russian Academy of Sciences, Moscow 119334, Russian Federation
Nataliya V. Petrakova – A.A. Baikov Institute of Metallurgy and Materials Science, Russian Academy of Sciences, Moscow 119334, Russian Federation; orcid.org/0000-0003-0457-3845
Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.1c03238

Author Contributions
The research work was done through the contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes
The authors declare no competing financial interest.

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ABBREVIATIONS
EPR, electron paramagnetic resonance; NMR, nuclei magnetic resonance; EDNMR, EDLOR (electron nuclei double-resonance) detected NMR; CaP, calcium phosphate; HA, hydroxyapatite; TCP, tricalcium phosphate; OCP, octacalcium phosphate; DCDP, dicalcium phosphate dihydrate; FFT, fast Fourier transformation; ESE, electron spin echo; FID, free induction decay; CW, continuous wave; ZFS, zero-field splitting

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