We want to thank reviewer 2 for his/her helpful comments. Our answers are given below.

General Comments:

This manuscript addresses the characterization of kidney stones (KS) – complex calcium oxalate composites of variable structure and composition – focusing on the molecular composition and structure of primarily the biomineral. The central methodology devised herein is multinuclear ssNMR spectroscopy combined with DFT calculations, as essential ingredients with X-ray diffraction and FTIR.

The authors synthesized the three hydrate standards – mono-, di- and tri-hydrate calcium oxalates (COM, COD, COT) and carried out their NMR characterization as a basis to identify the CO (calcium oxalate) content in the KSs.

Initially the authors screen a variety of possible $^1$H MAS NMR techniques and parameters ($^1$H-$^1$H homonuclear decoupling – DUMBO, fast- to very fast-MAS and field strengths); following, they conclude that the DUMBO sequence is best suited to discriminate (resolve) the CO content and apply that one also the two KS1 and KS2 samples in which they identify COM and COD as the major components. A detailed DFT study of the standards is used to correlate the isotropic $^1$H chemical shifts with the hydrogen bond lengths and assign the water peaks to belong to structural, dynamic or zeolitic type of water content in these materials.

Secondly, natural abundance $^{43}$Ca MAS NMR (at 20 Tesla) was applied to the standards and the KS (1 and 2) samples. While the $^{43}$Ca MAS NMR appeared to discriminate between the standards, it showed in the KS samples primarily COD content (contrary to $^1$H and $^{13}$C data). This issue may have to be further studied in the future as to enhance its analytic capability.

Yes: it will be specified in the final version of the MS.

Thirdly, $^{13}$C CP MAS NMR spectra clearly distinguish the COM and COD standards and identifies their occurrence as mixtures of different proportions in the KS1 and KS2 samples. The proportions seem to the naked eye different than seen in the $^1$H spectra. A
point that may be further discussed in the MS.

*This is a very good comment that will be emphasized in the final version of the manuscript. Indeed, DUMBO experiments are quite sensitive to local dynamics, especially in the intermediate regime. It may involve discrepancies between $^1\text{H}$ and $^{13}\text{C}$ NMR data. We will stress on the capabilities of the various NMR spectroscopies ($^1\text{H}$, $^{13}\text{C}$, $^{31}\text{P}$, $^{43}\text{Ca}$) to achieve qualitative/semi-quantitative/quantitative data.*

Information on the organic content present in a third KS sample (KS3) was obtained by T$_2$($^1\text{H}$) filtering and $^1\text{H}-^1\text{H}$ 2D DQF (all MAS) experiments whose spectra showed a small fraction of (highly mobile) unsaturated fatty acids and bulkier proteinaceous content. This insight was further refined using T$_1r$($^1\text{H}$) filtering ($^{13}\text{C}$ CP MAS) and $^1\text{H}-^{13}\text{C}$ INEPT which allowed to select the highly mobile components. Finally, representative data on P-content was shown for two other KSs (4 and 5) ascribing it primarily to inorganic hydrated orthophosphates.

I find this work broad and of importance to the biomaterials community, highlighting a glossary of ssNMR techniques and demonstrating analytical capabilities (as well as limitations) to analyze the complex and diverse composites of KSs. Certainly, this MS emphasizes the crucial role of ssNMR as a unique molecular-level complement to the more common and far less detailed techniques.

*Thank you.*

I find this MS suitable for publication after a minor revision.

**Specific Comments:**

As quite a large number of KS samples were examined and as not all were subjected to all characterization techniques, I find it instructive to illustrate the variability of organic content and include a Figure (Appendix) which shows all KS’s (for which spectra are available) with full range $^{13}\text{C}$ CP MAS spectra (250 ppm). It appears that the limited range spectra of the KS samples in Fig. 7 are deficient of organic content – were they measured with 9ms contact time? please note that in caption. In such a case also a comparison of the limited range would be desirable to show extent of robustness of identification for the different KSs.

*This is a very interesting suggestion. A new Figure will be added in SI, including the contact time used for each experiment.*

If similar information is available for the P-content throughout the different KSs, it will be as instructive to have it presented as well. From my limited experience with KSs, P-content was not negligible as described herein (line 370) "The acquisition time is ~ 2 to 3 hours demonstrating that the amount of phosphate species is indeed small in all samples".

*We will add a Figure in SI as well. The experimental time will be added in order to get a qualitative idea of the P content for the various KS.*

**Technical Corrections:**

Line 101: Spinning induced temp. increase is referred to in numerous places in the MS (as this may affect the CO); herein I suggest to state how much is moderate? 20C ? 10C ?

*It will be specified for the probes we used. For 2.5 mm probe: < 5 K at 5 kHz, 40 K at 30 kHz. For 7 mm probe: order of magnitude : 5 K at 5 kHz.*
Line 125: Throughout the text referral to e.g. "Table S1"; the supporting materials appear as Table A1.

*It will be corrected according to the Editorial policy.*

Figure 7: There appears to be a mismatch between the $^{13}$C chemical shifts of COM here and those seen in the 2D HETCOR DNP in Fig. A2

*Good observation indeed. The purpose of Figure A2 is initially to demonstrate to the reader that 4 isotropic peaks are indeed observed in the $^1$H dimension (this is an essential point for the 1H discussion). But the temperature used (100 K) has an impact on the $^{13}$C chemical shifts as well. It will be emphasized in the final version.*

Line 323: "~ 0.8% of the whole $^{13}$C isotropic chemical shift range " I am not sure what is meant by this statement.

*I agree that this sentence is confusing and not very informative in itself. It will be suppressed.*

Line 325: " evidenced and could be quantified if necessary (by increasing the signal-to-noise ratio significantly) " The S/N seems adequate for coarse quantification which I suggest to include and briefly discuss.

*You are right. A brief discussion will be added including the new potentialities of denoising (Laurent, Bonhomme, 2019 and 2020).*