Synthesis and structural characterization of Al$_2$O$_3$ nanoparticles: Towards 3D optically stimulated luminescence dosimetry

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Advanced radiotherapy techniques, which plan and deliver a treatment in complicated 3D geometries with steep dose gradients, push 3D dosimetry with correspondingly high spatial resolution to the top of scientific and clinical agendas. This paper presents the first steps taken towards an inexpensive and reusable material for 3D dosimetry based on optically stimulated luminescence (OSL). Carbon-doped alumina (Al$_2$O$_3$:C) nanoparticles were synthesized using supercritical flow synthesis, in which product properties can be finely controlled. The particles were characterized using electron microscopy and powder x-ray diffraction. C-doping did not alter the crystallographic structure appreciably, and a high elemental signal from C could be measured. Nanoparticles of amorphous $\gamma$-Al$_2$O$_3$:C were achieved, however calcining these to produce the OSL-relevant $\alpha$-phase yielded microparticles. Future work will aim at producing phase-pure $\alpha$-Al$_2$O$_3$:C nanoparticles with a narrow size distribution below 10 nm, and controllable C-concentration and O-deficiency.

1. Motivation & Introduction

To spare healthy tissue near a cancer tumor, modern radiotherapy techniques, such as intensity modulated-, proton-, and heavy-ion radiotherapy, plan and deliver a treatment in a complicated 3D geometry with steep dose gradients. In order to assure the quality of the treatment, patient-specific or at least treatment-plan-specific dosimetry also in 3D with high spatial resolution should be performed. Historically, gel- and polymer matrices (e.g. radiochromic [1, 2] or polymerizing) have been used, however problems with their reusability and reproducibility have spurred renewed interest in dosimeters based on optically stimulated luminescence (OSL) that rely on physical properties rather than chemical reactions. This paper presents progress and considerations regarding an inexpensive and flexible dosimetry system based on OSL nanoparticles embedded in a transparent elastomer matrix, which has previously been suggested by our group [3, 4]. Such a system is reusable as it can be reset by emptying the populated trap states responsible for information storage (so-called bleaching) with either light or heat. Readout of this dosimeter can be performed by a movable laser sheet, which illuminates and
stimulates a thin slice of the dosimeter at a time. By imaging this 2D slice onto a suitable sensor such as a CCD camera and then moving the laser sheet down through the dosimeter, the entire 3D shape can be read out (see [5] for a sketch of the readout setup).

Carbon-doped alumina in the crystallographic $\alpha$-phase ($\alpha$-$\text{Al}_2\text{O}_3$:C) is well-known for exhibiting highly sensitive OSL signals in a wide dose range [6]. To achieve high spatial resolution and transparency of a 3D OSL dosimeter, nanoparticles rather than bulk are preferable, in particular for high-refractive index materials like $\text{Al}_2\text{O}_3$ [7]. This article presents synthesis and characterization of $\text{Al}_2\text{O}_3$ nanoparticles in various phases with and without C-doping. To allow fine control of many properties, industry-inspired supercritical flow synthesis was used. Particles are investigated with elemental analysis, electron microscopy, and x-ray diffraction.

Batch-based techniques for synthesis of nanoparticles such as sol-gel or traditional hydrothermal synthesis are limited by relatively long reaction times, where both nucleation and growth occur at the same time. This results in wide size distributions or large particles (via the LaMer model [8]). To accurately control the size of small nanoparticles, a different approach is necessary. In this work, supercritical flow synthesis was used to produce nanoparticles of aluminum oxide. The supercritical state of matter can be achieved by heating while at the same time applying pressure to a liquid. The result is a fluid with properties (solubility, diffusivity, density) between those of a liquid and gas. In supercritical flow synthesis, the decreased solubility of precursor molecules in supercritical solvent compared to the liquid state leads to flash nucleation of nanoparticles [9]. A sketch of the flow reactor can be seen Figure 1. The primary reward of such a setup is full control of both the precursor concentration, flow rates of both precursor solution and solvent as well as the pressure and temperature at the T-mixing section and in the maturing reactor. In this way, the size distribution, shape and phase of the nanoparticles can be largely controlled [9].

![Figure 1. Sketch of the supercritical flow synthesis setup used in this work. The setup consists of pressurized tube lines for the precursor and solvent on each side, as well as a central section, where they are mixed and the reaction takes place. In the lower right corner is a close-up of the T-mixing section, where nucleation takes place. The just-seeded nanoparticles are swept into a maturing reactor, where growth can be precisely controlled by adjusting temperature and flow rates. The particles are cooled before being collected. A barometer or thermocouple is indicated by a P and T, respectively. Adapted from [9].](image-url)
2. Experimental Details

Synthesis of both pure and C-doped Al₂O₃ nanoparticles was performed using the setup seen in 1 with a precursor solution of Al(NO₃)₃. Samples from pure precursor and with an added C-source, corresponding to an expected doping of 4 atomic-%, were prepared for direct comparison between undoped and C-doped particles. At the synthesis temperatures relevant for this work, two competing reactions exist, namely the synthesis of boehmite, γ-AlO(OH), or alumina, γ-Al₂O₃. Both these phases can be calcined (heated) at temperatures above 1000 °C to produce corundum, α-Al₂O₃. To visualize the samples, scanning transmission electron microscopy (STEM) was performed (FEI Talos F200X), along with nanoscale elemental analysis by energy dispersive x-ray spectroscopy (EDS) measuring the characteristic x-rays produced by the electron beam. Structural characterization using powder x-ray diffraction (PXRD) was done on a Rigaku SmartLab II (Cu Kα₁-radiation, λ = 1.54056 Å).

![Figure 2. HAADF STEM (a) of C-doped Al₂O₃ particles. A size distribution (b) of particles measured visible in the HAADF-image and the EDS spectrum (c) is plotted. The large Si peak is from the TEM-grid. The color maps (d-f) show elemental EDS-intensities of Al, O, and C, respectively.](image)

3. Results & Discussion

Results from the STEM-analysis of the C-doped particles can be seen in 2. An image taken in high-angle-annular-dark-field (HAADF) mode (2a) and EDS-maps (2d-f) for Al, O, and C are shown. The particles visible in 2a are clearly outlined in the EDS maps. Although the main feature is larger than the target of sub–10 nm, it seems to consist of a substructure of agglomerated nanoparticles, and around these are smaller particles, closer to the expected size as seen in the histogram of 35 particles visible in the HAADF-image (2b). The C-signal may not look high in the EDS-map or -spectrum (2c) due to a lower interaction cross section for light elements, but the concentration is in fact much higher than expected. Atomic composition of the particle is 20.03 ± 1.11% Al (36.00%), 57.99 ± 1.79% O (60.00%), and 21.97 ± 0.76% C (4.00%) (expected in parentheses, at-%). There is no detectable trace of N in the doped sample, but a small signal is seen in the undoped sample (7.52 ± 1.93 at-%), probably in the form of nitrates, suggesting that doping may facilitate full reaction of Al(NO₃)₃. The high C-concentration is likely due to organic residues from the solvent on the surface, in spite of extensive washing. To avoid this contaminant, supercritical water could be used in future synthesis. The high background O-signal is likely oxidation of the Si surface of the TEM grid.
PXRD reveals the structure of as-synthesized nanoparticles to be primarily amorphous both for the undoped and C-doped samples. This can be seen in 3a. The few discernible peaks are very broad, indicating nanosized crystallites in agreement with the STEM images. For reference, theoretical Bragg peaks of $\gamma$-$\text{Al}_2\text{O}_3$ and $\gamma$-$\text{AlO(OH)}$ are plotted as tick marks, but poor data quality has made an actual refinement impossible. Although hard to say for certain, the particles seem to be a mixture of the two phases in both cases. This can explain the large particle seen in the STEM image (2a), because $\gamma$-$\text{AlO(OH)}$ often acts as a binder between crystallites [10]. Most importantly, the diffractograms show that a C-doping of 4% does little to change the structure. The combined analysis of PXRD and STEM indicates small crystallites of $\gamma$-$\text{Al}_2\text{O}_3$ and $\gamma$-$\text{AlO(OH)}$ merged together into large particles by amorphous $\gamma$-$\text{AlO(OH)}$.

![Figure 3. PXRD diffractograms of C-doped and undoped Al$_2$O$_3$ particles as-synthesized (a) and after heating to 1000 °C (b). C-doped is plotted in red and undoped in blue in both cases. Also plotted for reference are tick marks for theoretical Bragg peaks of $\gamma$-$\text{Al}_2\text{O}_3$ [11] and $\gamma$-$\text{AlO(OH)}$ [12] (top) as well as $\alpha$-$\text{Al}_2\text{O}_3$ [13] and $\theta$-$\text{Al}_2\text{O}_3$ [11](bottom).](image)

After heating to 1000 °C, the particles become highly crystalline (3b). Reference Bragg positions plotted at the bottom (in this case $\alpha$-$\text{Al}_2\text{O}_3$ and $\theta$-$\text{Al}_2\text{O}_3$), reveals that the undoped sample is pure $\alpha$-$\text{Al}_2\text{O}_3$, while the C-doped sample has a small contamination probably of $\theta$-$\text{Al}_2\text{O}_3$. The width of the peaks has contracted dramatically from the broad features in the as-synthesized diffractograms. This signifies microparticles rather than nanoparticles. Together with evidence from the STEM analysis, it could be suggested that a microparticle, consisting before heat treatment of smaller crystallites merged together by amorphous material, grows into a single microcrystallite of primarily $\alpha$-$\text{Al}_2\text{O}_3$ upon calcination. Further refinement and complementary STEM analyses of the calcined samples are necessary before a definite conclusion can be made.

Once developed, the composite 3D dosimeter consisting of these OSL active nanoparticles embedded in a suitable matrix material should in every voxel be comparable to a measurement done by a point dosimeter (such as an ion chamber). This entails a precision of $\sim 2\%$ even at doses as low as 0.1 Gy measured in small voxels of the order of mm$^3$s [14]. Thus even sharp dose gradients in spatially complicated treatment plans will be within the detection limit. Furthermore, due to the nature of the energy storage mechanism involved, the dosimeter will be reusable and relatively insensitive to ambient conditions; as long as it is stored at room temperature in the dark, fading of the signal should be as low as 3 % per year [15]. Further work is warranted to study the effect of long-wavelength ambient work light, which would allow for convenient handling in a clinical environment. Similarly, various methods for bleaching and thereby resetting the dosimeter - such as thermal, UV, or a combination - should be studied.
As mentioned previously, the necessity of very small nanoparticles stems from the desire to minimize scattering of light through the dosimeter. Even though the refractive index of Al$_2$O$_3$:C is relatively high (\(~1.8\)) compared to that of most elastomers (e.g., silicone with 1.4), Mie scattering can be neglected if the particle size is less than 10% of the wavelength of light. Remaining is Rayleigh scattering, which scales as \cite{16}:

$$T = \exp \left( -\frac{32\pi^4 V_p r^3 n_m^4}{\lambda^4} \frac{(n_p/n_m)^2 - 1}{(n_p/n_m)^2 + 2} \right)^2,$$

where $T$ is the transmission at wavelength $\lambda$ through a sample of length $\ell$ with a volume percentage $V_p$ of nanoparticles with radius $r$. $n_p$ is the refractive index of the nanoparticles, whereas $n_m$ is that of the matrix material. Evidently the two most important factors in increasing the transmission is lowering the particle size, matching the refractive indexes and/or lowering the volume percentage. Naturally, there is a lower boundary for the volume percentage so that the signal level is still sufficient and the spatial resolution is not limited by the separation between particles.

4. Conclusion

In conclusion, ideal synthesis parameters to optimize the nanoparticle size distribution and avoid agglomeration have yet to be found. Also, washing procedures must be improved to avoid organic contamination of the surface, which can lead to uncontrollable C-doping during calcination. Furthermore, a different calcination procedure must be used, where crystal growth into microparticles can be avoided. The studies do reveal the possibility of synthesizing nanoparticles down to below 10 nm, especially evident in the C-doped sample, and calcination yielding phase-pure $\alpha$-Al$_2$O$_3$. Apart from the C-concentration, the OSL response of $\alpha$-Al$_2$O$_3$:C also depends on O-deficiency of the lattice resulting in F and $F^-$-centers, which are believed to be responsible for radiative recombination \cite{17}. These have a high energy of formation \cite{18}, which is why conventional samples are produced at very high temperatures ($> 2000 \degree$C). However, as seen very clearly from calcinating the nanoparticles synthesized in the present work, such temperatures are - with current procedures - incompatible with very small particles. The challenge still remains to produce nanosized Al$_2$O$_3$:C with the correct level of O-deficiencies to achieve the desired OSL properties. It is unknown whether the $\alpha$-phase of Al$_2$O$_3$:C is crucial for OSL to be present, or indeed if the directly synthesized $\gamma$-phase can also be utilized as long as the correct level of O-vacancies is present.

In summary, a number of challenges and investigations are still ahead before such a 3D OSL dosimeter is ready for clinical use - from the synthesis of ideal nanophosphors to the embedding of these at volume percentages suitable for both response level and transparency. However, the quest is strongly motivated by the potential for high-accuracy, reusable, and affordable 3D quality assurance of state-of-the-art treatment plans.

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6. References

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