

# Nanoluminofors based on silicates and germanates of rare earth elements for visualization of biotissues

Mikhail G. Zuev <sup>a\*</sup>, Vladislav G. Il'ves <sup>b</sup>, Sergey Yu. Sokovnin <sup>bc</sup> 

a: Institute of Solid State Chemistry, Ural Branch of the Russian Academy of Sciences, Ekaterinburg 620990, Russia

b: Institute of Electrophysics, Ural Branch of the Russian Academy of Sciences, Ekaterinburg 620016, Russia

c: Institute of Physics and Technology, Ural Federal University, Ekaterinburg 620002, Russia

\* Corresponding author: [zuev@ihim.uran.ru](mailto:zuev@ihim.uran.ru)

This paper belongs to the MOSM2021 Special Issue.

© 2022, the Authors. This article is published in open access under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).



## Abstract

Nanoparticles of silicates and germanates with a general formula  $Sr_2R_{8-x-y}Er_xYb_yM_6O_{26}$  ( $R = Y, La$ ;  $M = Si, Ge$ ) were produced in vacuum by the method of pulse electron beam evaporation. An upconversion photoluminescence of the nanoparticles was detected during the excitation by a laser with a wavelength of 980 nm with a predominance of lines in the red and near infrared regions of the spectrum. Due to their optical properties, the nanoparticles can be excited directly through the biotissues to visualize various pathologies. The obtained nanosamples have K-jumps of X-ray radiation absorption in the 10–100 keV energy region. This opens up prospects for the use of the nanoparticles as X-ray contrast agents. Thus, the nanoparticles have both optical and X-ray contrast characteristics, and therefore have the potential necessary for imaging and diagnosing pathologies in biological tissues.

## Keywords

Er<sup>3+</sup>  
Yb<sup>3+</sup>  
upconversion  
nanoluminofor  
biotissues  
bimodal substances

Received: 19.01.22

Revised: 14.07.22

Accepted: 14.07.22

Available online: 19.07.22

## Key findings

- Silicates and germanates of rare earth elements are promising for visualization of biological tissues.
- Upconversion silicate and germanate nanoluminophores containing Er and Yb ions can be used for optical and X-ray bioimaging.

## 1. Introduction

Single-mode nanoparticles (NP) with optical or magnetic characteristics are widely used in biosensing and biovisualization [1]. However, they do not provide all the necessary information about biological objects. The requirements of modern biomedical technology suggest the development of new, multimodal bioprobes. Multimodal bioprobes combining two or more functions are emerging advances in biology and medicine. A number of nanomaterials with such interesting properties have found various biomedical applications, including imaging, separation, and drug delivery [2]. Inorganic nanoparticles doped with Ln<sup>3+</sup> ions are considered good candidates for multimodal bioapplications, since they have unusual optical and magnetic properties [3]. Narrow width of f-f emission lines, long lifetime of photoluminescence (PL), IR excitation in the field of transparency of biological tissues (700–

1000 nm), large antistox shifts for separation of upconversion photoluminescence (UCPL) from excitation, weak background of intrinsic luminescence of biotissues, low cytotoxicity, high chemical resistance and resistance to photobleaching make them extremely suitable for use in various bio-applications [4–7]. The increased intensity of red radiation could be useful for various UCPL applications, especially for deep tissue imaging [4]. Currently, magnetic resonance imaging (MRI), computed tomography (CT) positron emission tomography (PET), optical imaging, and other methods provide vivid tissue imaging; however, they cannot provide comprehensive information in clinical practice. Therefore, various multimodal imaging technologies have attracted considerable attention [8–11].

In this work, UCPL was studied and the dependencies of mass coefficients of weakening of X-ray radiation on the radiation energy for the nanopowders (NPs) produced by

electronic evaporation of solid solutions with a general formula  $\text{Sr}_2\text{R}_{8-x-y}\text{Er}_x\text{Yb}_y\text{M}_6\text{O}_{26}$  ( $\text{R} = \text{Y, La; M} = \text{Si, Ge}$ ) were considered. NPs can be promising as bioprobes for various biomedical applications, including photoluminescent and X-ray contrast images of body tissues [12]. Currently, iodinated X-ray contrast agents are widely used to contrast organs and systems of the body. However, these means have a number of drawbacks. They have toxic effects on the blood system, liver, kidneys, pancreas, central nervous and endocrine systems. They also have a local irritating effect on the mucous membranes, including the epithelium of the hepatic and pancreatic ducts, the endothelium of the arterial, venous, lymphatic vessels and the heart, and the cerebral membranes. They cause various types of allergic reactions. Therefore, there is a search for new effective X-ray contrast agents that do not have the noted drawbacks. The compounds discussed here can be characterized as two-modal substances promising for simultaneous use in optical and X-ray biovisualization.

## 2. Experimental

Samples of the above compositions were selected to produce NPs. The choice of the compositions is due to two factors. Firstly, they should have a UCPL and, secondly, they should have a sufficiently high X-ray attenuation covering the entire range of X-ray energies (10-100 keV) used in medical X-ray diagnostics. The samples were synthesized by conventional ceramic technology. The high-purity reactants  $\text{SrCO}_3$ ,  $\text{Y}_2\text{O}_3$ ,  $\text{La}_2\text{O}_3$ ,  $\text{Er}_2\text{O}_3$ ,  $\text{Yb}_2\text{O}_3$ ,  $\text{SiO}_2$ ,  $\text{GeO}_2$  were used (the content of the main substance not less than 99.99%). The initial components taken in stoichiometric ratio were thoroughly ground. The obtained mixes were pressed in tablets and burned in air at a temperature of 1350–1400 °C for ~50 h. The X-ray diffraction analysis was carried out by means of the Shimadzu XRD-7000 diffractometer (Cu  $\text{K}\alpha$ -radiation, counter monochromator CM-3121, detector – Scintillation Counter) with use of an ICDD card file. The diffractograms of the samples were processed using the Ritveld full-profile analysis method with the use of an ICDD card-file. The NPs were produced by evaporating the tablets in vacuum by a pulsed electron beam (PEBE) in the NANOBIM-2 unit [13]. The electron energy was 40 keV, electron beam pulse energy 1.8 J, pulse duration 100  $\mu\text{s}$ , repetition rate 100–200 pps. The time of evaporation of the targets was 40–60 minutes. The speed of rotation of the targets was ~8.3 revolutions/min. The specific surface area of the powders was determined by the known BET method in Micromeritics TriStar 3000. The microscopic analysis of the HP was performed on a JEOL JEM 2100 transmission electron microscope. The microscopic analysis of the NP was performed on a JEOL JEM 2100 transmission electron microscope. The PL spectra were recorded on a MDR-204 spectrometer (laser KLM-Hg80-200-5,  $\lambda = 980$  nm, rated power 221 mW; photoelectron multiplier R928 from Hamamatsu).

## 3. Results and Discussion

Figure 1 shows the results of NPs microscopy based on solid solutions of  $\text{Sr}_2\text{La}_{7.85}\text{Er}_{0.075}\text{Yb}_{0.075}\text{Ge}_6\text{O}_{26}$  (I) and  $\text{Sr}_2\text{Y}_{6.8}\text{YbEr}_{0.2}\text{Si}_6\text{O}_{26}$  (II). According to TEM HR microscopy and electronography, it can be seen that the nanoparticles are prone to agglomeration, have irregular shapes and amorphous character (insert) (Figures 1, 2).

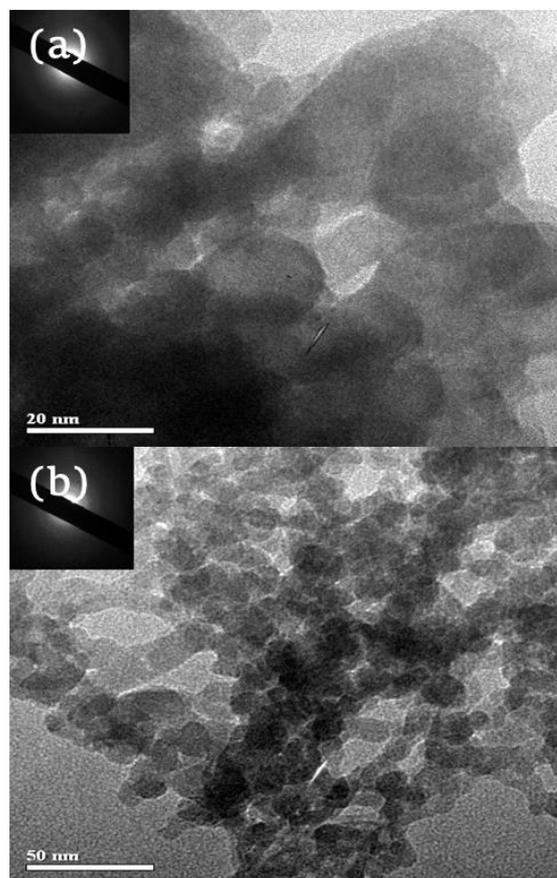
According to BET, the nanoparticles sized ~23 nm (sample based on I) and ~4 nm (based on II) were found.

It is known that nanopowders together with an organic additive obtained by evaporation of solid solutions of the composition  $\text{Sr}_2\text{Y}_{8-x-y}\text{Er}_x\text{Yb}_y\text{Si}_6\text{O}_{26}$  were proposed for diagnostics of pathologies in biological tissues [14].

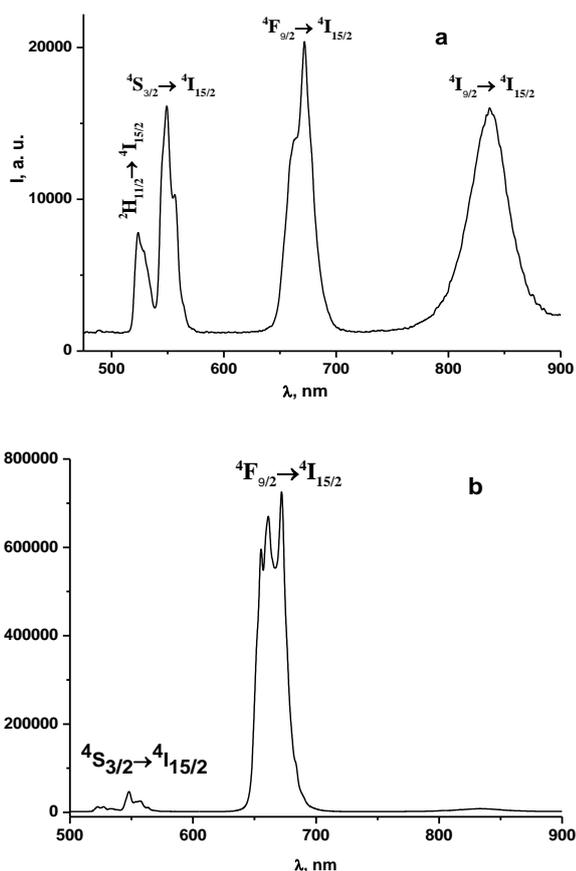
### 3.1. Upconversion photoluminescence

Figure 2 shows the spectra of UCPL nanopowders produced based on  $\text{Sr}_2\text{La}_{8-x-y}\text{Er}_x\text{Yb}_y\text{Ge}_6\text{O}_{26}$  ( $x = y = 0.075$ ) and  $\text{Sr}_2\text{Y}_{8-x-y}\text{Er}_x\text{Yb}_y\text{Si}_6\text{O}_{26}$  ( $x = 0.2, y = 1$ ).

The excitement of UCPL of  $\text{Er}^{3+}$  ions occurs in the presence of  $\text{Yb}^{3+}$  because of the absorption of the 980 nanometer laser radiation upon  ${}^2\text{F}_{7/2} \rightarrow {}^2\text{F}_{5/2}$  transition of  $\text{Yb}^{3+}$  ions with the subsequent transmission of energy in  $\text{Er}^{3+}$  in a state  ${}^4\text{I}_{11/2}$ . In addition, there is a  ${}^4\text{I}_{11/2} \rightarrow {}^4\text{F}_{7/2}$  transition at the excitement by the second photon from a state  ${}^2\text{F}_{5/2}$  of  $\text{Yb}^{3+}$  ion. Besides, the excitation of the state of the  ${}^4\text{F}_{9/2}$  ion  $\text{Er}^{3+}$  occurs directly by two laser photons with the participation of the photons of the matrix.



**Figure 1** TEMHR snapshots and electronograms (inserts) NP based on  $\text{Sr}_2\text{Y}_{6.8}\text{YbEr}_{0.2}\text{Si}_6\text{O}_{26}$  (a) and  $\text{Sr}_2\text{La}_{7.85}\text{Er}_{0.075}\text{Yb}_{0.075}\text{Ge}_6\text{O}_{26}$  (b).



**Figure 2** PL spectra of NP based on samples I (a) and II (b).

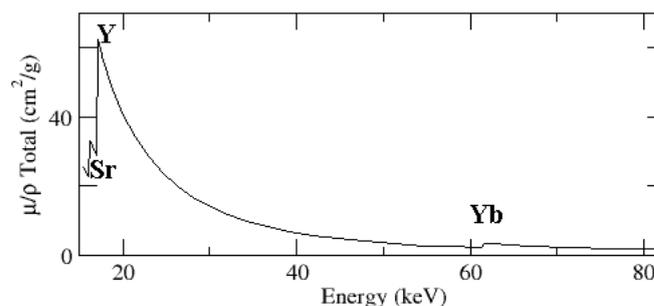
As is known, the primary importance of UCPL in the NIR-to-Red or NIR-to-NIR [15, 16] radiation transformations regions of the spectrum are at the excitation radiation with a wavelength of typically about 980 nm. This is particularly important for biomedical purposes. Excitation in the NIR region of the spectrum in combination with UCNP in the NIR or RED is possible due to the high transparency of biological fluids and low tissue damage.

Two intense peaks in NIR at 836 and RED at 670 nm (Figure 2a), and a very intense RED peak at ~665 nm (Figure 2b) were detected.

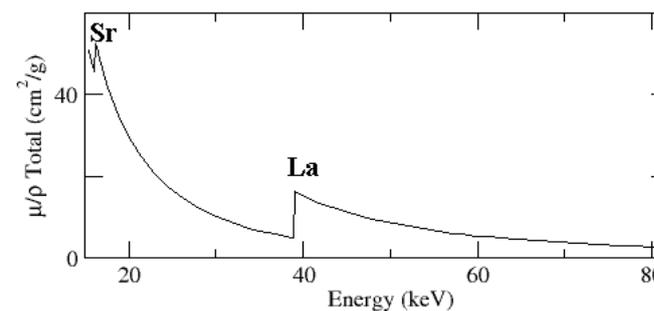
This luminescence can be used in photodynamic therapy (PDT) to excite a photosensitizer (PS) localized in the diseased region. Photodynamic therapy (PDT) uses special drugs called photosensitizing agents that respond to a certain wavelength of light to kill cancer cells [17]. Currently, a new generation of photosensitizers is actively developing, which have a stronger absorption in the near infrared region of the spectrum (NIR), corresponding to the optimal "transparency region" of the biotissue (700–1000 nm) [18]. High red line intensities at  $\lambda_{\alpha_{max}} = 670$  nm and near IR line at  $\lambda_{\alpha_{max}} = 836$  nm (Figure 2a) as well as  $\lambda_{\alpha_{max}} = 664$  nm (Figure 2b) indicate the nanoparticles' promise for deep tissue imaging [19].

### 3.2. X-ray attenuation mass coefficients

Let us consider the dependencies of mass attenuation coefficients ( $\mu$ ) on X-ray energy for the samples  $\text{Sr}_2\text{Y}_{6.8}\text{YbEr}_{0.2}\text{Si}_6\text{O}_{26}$  and  $\text{Sr}_2\text{La}_{7.75}\text{Er}_{0.075}\text{Yb}_{0.075}\text{Ge}_6\text{O}_{26}$  (Figures 3, 4).



**Figure 3** Dependence of mass coefficient of  $\text{Sr}_2\text{Y}_{6.8}\text{YbEr}_{0.2}\text{Si}_6\text{O}_{26}$  attenuation on X-ray energy.



**Figure 4** Dependence of mass coefficient of  $\text{Sr}_2\text{La}_{7.75}\text{Er}_{0.075}\text{Yb}_{0.075}\text{Ge}_6\text{O}_{26}$  attenuation on X-ray energy.

The schedules are constructed according to the previous work [20] ( $\rho$  – X-ray density). K absorption jumps of the elements Sr, Y, Yb, La are indicated. The absorption of radiation by the nanoparticles in almost the entire range of quantum energies used in X-ray diagnostics is ensured by the fact that the NP includes Sr, Y, Yb and La elements, the K absorption jumps of which lie in different parts of this range. Strontium has a K-jump at 16.10 keV, Yttrium – at 17.038 keV, Ytterbium – at 61.30 keV and Lanthanum at 39 keV. It should be noted that due to the low content of Er and Yb in the solid solutions, the K-jumps of these atoms practically do not affect the mass attenuation coefficients of the samples.

## 4. Conclusions

Bimodal nanoparticles were produced by PEBC in vacuum. UCPL of NPs was detected during excitation by a laser with a wavelength of 980 nm with a predominance of RED and NIR lines. Due to their optical properties, nanoparticles can be excited directly through the biotissue to visualize various pathologies. In addition, K-jumps of X-ray absorption in the energy region of 10–90 eV make it promising to use NPs as X-ray contrast agents.

## Supplementary materials

No supplementary materials are available.

## Funding

This work was carried out in accordance with the state assignment of the Institute of Solid State Chemistry, Ural Branch of the Russian Academy of Sciences.

## Acknowledgments

None.

## Author contributions

Conceptualization: M.G.Z.

Data curation: S.Y.S.

Investigation: M.G.Z., V.G.I.

## Conflict of interest

The authors declare no conflict of interest.

## Additional information

Author IDs:

Mikhail G. Zuev, Scopus ID [7003705663](https://orcid.org/0000-0002-7003-7056);

Vladislav G. Il'ves, Scopus ID [57219269059](https://orcid.org/0000-0002-5721-9269);

Sergey Yu. Sokovnin, Scopus ID [6601905930](https://orcid.org/0000-0002-6601-9059).

Websites:

Institute of Solid State Chemistry,  
<https://www.ihim.uran.ru>;

Institute of Electrophysics, <http://iep.uran.ru>;

Ural Federal University, <https://urfu.ru/ru>.

## References

- Erathodiyil N, Ying JY. Functionalization of inorganic nanoparticles for bioimaging applications. *Acc Chem Res*. 2011;44:925–935. doi:[10.1021/ar2000327](https://doi.org/10.1021/ar2000327)
- Kim J, Piao Y, Hyeon T. Multifunctional nanostructured materials for multimodal imaging, and simultaneous imaging and therapy. *Chem Soc Rev*. 2009;38:372–390. doi:[10.1039/b709883a](https://doi.org/10.1039/b709883a)
- Wang G, Peng Q, Li Y. Lanthanide-doped nanocrystals: synthesis, optical-magnetic properties, and applications. *Acc Chem Res*. 2011;44:322–332. doi:[10.1021/ar100129p](https://doi.org/10.1021/ar100129p)
- Zeng S, Yi Z, Lu W, Qian C, Wang H, Rao L, Zeng T, Liu H, Liu H, Fei B, Hao J. Simultaneous realization of phase/size manipulation, up conversion luminescence enhancement, and blood vessel imaging in multifunctional nanoprobes through transition metal Mn<sup>2+</sup> doping. *Adv Funct Mater*. 2014;24:4051–4059. doi:[10.1002/adfm.201304270](https://doi.org/10.1002/adfm.201304270)
- Liu Y, Meng X, Bu W. Up conversion-based photodynamic cancer therapy. *Coord Chem Rev*. 2019;379:82–98. doi:[10.1016/j.ccr.2017.09.006](https://doi.org/10.1016/j.ccr.2017.09.006)
- Wang J, Wang F, Wang C, Liu Z, Liu X. Single-band up conversion emission in lanthanide-doped KMnF<sub>3</sub> nanocrystals. *Angew Chem Int Ed Engl*. 2011;50(44):10369–10372. doi:[10.1002/anie.201104192](https://doi.org/10.1002/anie.201104192)
- Woźny P, Runowski M, Lis S. Emission color tuning and phase transition determination based on high pressure up-conversion luminescence in YVO<sub>4</sub>: Yb<sup>3+</sup>, Er<sup>3+</sup> nanoparticles. *J Lumin*. 2019;209:321–327. doi:[10.1016/j.jlumin.2019.02.008](https://doi.org/10.1016/j.jlumin.2019.02.008)
- Sun Y, Zhu X, Peng J, Li F. Core-shell lanthanide up conversion nanophosphors as four-modal probes for tumor angiogenesis imaging. *ACS Nano*. 2013;7:11290–11300. doi:[10.1021/nn405082y](https://doi.org/10.1021/nn405082y)
- Zhou J, Zhu XJ, Chen M, Sun Y, Li FY. Water-stable NaLuF<sub>4</sub>-based up conversion nanophosphors with long-term validity for multimodal lymphatic imaging. *Biomater*. 2012;33:6201–6210. doi:[10.1016/j.biomaterials.2012.05.036](https://doi.org/10.1016/j.biomaterials.2012.05.036)
- Liu Q, Sun Y, Li C, Zhou J, Li C, Yang T, Zhang X, Yi T, Wu D, Li F. 18F-Labeled magnetic-up conversion nanophosphors via rare-Earth cation-assisted ligand assembly. *ACS Nano*. 2011;5:3146–3157. doi:[10.1021/nn200298](https://doi.org/10.1021/nn200298)
- Li Z, Zhang Y, Huang L, Yang Y, Zhao Y, El-Banna G, Han G. Nanoscale “fluorescent stone”: luminescent calcium fluoride nanoparticles as theranostic platforms. *Theranostics*. 2016;6(13): 2380–2393. doi:[10.7150/thno.15914](https://doi.org/10.7150/thno.15914)
- Zuev MG, Larionov LP, Strekalov IM. New radiopaque contrast agents based on re tantalates and their solid solutions. *SOP Trans Phys Chem*. 2014;1(2):53–64. doi:[10.15764/pche.2014.02005](https://doi.org/10.15764/pche.2014.02005)
- Sokovnin SYU, Il'ves VG, Zuev MG. Production of complex metal oxide nanopouders using pulsed electron beam in low-pressure gas for biomaterials application, «Engineering of Nanobiomaterials Applications of Nanobiomaterials» Elsevier. 2016;2 (Chapter 2). Edited by Alexandru Grumezescu. P. 29–76. doi:[10.1016/B978-0-323-41532-3.00002-6](https://doi.org/10.1016/B978-0-323-41532-3.00002-6)
- Zuev MG, Larionov LP. biomedical material for diagnosing pathologies in biological tissues. Patent RU 2734957.
- Wang C, Tao H, Cheng L, Liu Z. Near-infrared light induced *in vivo* photodynamic therapy of cancer based on up conversion nanoparticles. *Biomater*. 2011;32:6145–6154. doi:[10.1002/adfm.20130427](https://doi.org/10.1002/adfm.20130427)
- Lv Y, Jin Y, Sun T, Su J, Wang C, Ju G, Chen Li, Hu Y. Visible to NIR down-shifting and NIR to visible upconversion luminescence in Ca<sub>14</sub>Zn<sub>6</sub>Ga<sub>10</sub>O<sub>35</sub>:Mn<sup>4+</sup>, Ln<sup>3+</sup> (Ln=Nd, Yb, Er). *Dyes Pigments*. 2019;161:137–146. doi:[10.1016/j.dyepig.2018.09.052](https://doi.org/10.1016/j.dyepig.2018.09.052)
- Huang Z, Xu H, Meyers AD, Iusani A, Wang L, Tagg R, Barqawi AB, Chen YK. Photodynamic therapy for treatment of solid tumors-potential and technical challenges. *Technol Cancer Res Treat*. 2008;7(4):309–320. doi:[10.1177/153303460800700405](https://doi.org/10.1177/153303460800700405)
- Liqiang L, Lanlan D, Weijia Z, Jiawei S, Xiaoqiang Y, Wei L. A phthalocyanine based near-infrared photosensitizer: Synthesis and *in vitro* photodynamic activities. *Bioorg Med Chem Lett*. 2013;23:3775–3779. doi:[10.1016/j.bmcl.2013.04.093](https://doi.org/10.1016/j.bmcl.2013.04.093)
- Zhou J, Sun Y, Du X, Xiong L, Hua H, Li F. Dual-modality *in vivo* imaging using rare-earth nanocrystals with near-infrared to near-infrared (NIR-to-NIR) upconversion luminescence and magnetic resonance properties. *Biomater*. 2010;31:3287–3295. doi:[10.1016/j.biomaterials.2010.01.040](https://doi.org/10.1016/j.biomaterials.2010.01.040)
- Chantler CT. X-Ray form factor, attenuation and scattering tables. *J Phys Chem Ref Data*. 2000;29:597–1048. doi:[10.18434/T4HS32](https://doi.org/10.18434/T4HS32)