International urnal of Progressive Sciences and Technologies (IJPSAT)
ISSN: 2509-0119.

https://ijpsat.org/
Vol. 49 No. 1 February 2025, pp. 452-457

Synthesis Gold Nanoparticles as Advanced Computed Tomography Contrast Agents Using Pulsed Laser Ablation Method

Nadia Maulika Purnama Wafi, Eko Hidayanto, and Ali Khumaeni*

Department of Physics, Faculty of Science and Mathematics, Diponegoro University, Jl. Prof. Soedharto, S.H., Tembalang, Semarang 50275, Indonesia

*Corresponding email: khumaeni@fisika.fsm.undip.ac.id

Abstract– In this study, gold nanoparticles (Au NPs) were successfully synthesized using the pulsed laser ablation technique with an Nd:YAG laser. The successful formation of these nanoparticles was evidenced by the color change of the colloid from translucent to purple. The synthesized Au NPs were then evaluated and compared to iodine-based contrast agents at three different kVp settings: 80 kVp, 100 kVp, and 120 kVp. When applied as CT contrast agents, Au NPs exhibited superior performance, as demonstrated by the maximum CT Number value of 7.43 HU and the maximum Contrast-to-Noise Ratio of 2.85, which significantly surpassed the performance of the widely used iodine-based contrast agent across the tested kVp variations. The results in this experiment hints that Au NPs hold significant potential as effective contrast agents for CT-Scan imaging techniques.

Keywords – Pulsed laser ablation; gold nanoparticles; Computed Tomography; Contrast agent.

I. Introduction

Computed tomography (CT) is a widely used diagnostic modality that is employed in both clinical and preclinical applications. This is due to the fact that CT possesses a high degree of diagnostic efficiency, enabling the provision of detailed anatomical information about tumors, as well as its ease of accessibility [1]. While CT provides detailed anatomical information, it frequently necessitates the utilization of contrast agents to effectively visualize structures with comparable radiographic densities. Molecular contrast agents are commonly administered during CT scans, serving to enhance image clarity and enable the delineation of specific anatomical structures [2,3]. Commercially available iodinated contrast agents are the most frequently utilized contrast agents in routine clinical practice [4]. However, these agents exhibit several limitations, including short blood circulation times attributed to rapid renal clearance, which often constrains their utility for targeted imaging and angiography. Furthermore, high doses of iodinated molecules can induce significant adverse effects in patients [5]. In this case, novel variations of X-ray computed tomography contrast agents are garnering increased research interest.

Metallic nanoparticles with high atomic numbers and excellent X-ray attenuation properties, including gold nanoparticles, are being investigated as potential contrast agent alternatives. Notably, these nanoparticles demonstrate good biodistribution, low toxicity, and favorable pharmacokinetics, as well as resulting in longer circulation times compared to iodine-based contrast agents, and can also be used for a wider range of target tissues [6,7,8]. The synthesis of gold nanoparticles commonly employs

International urnal of Progressive Sciences and Technologies (IJPSAT)
ISSN: 2509-0119.

https://ijpsat.org/
Vol. 49 No. 1 February 2025, pp. 452-457

both chemical and physical methods. Chemical methods such as microemulsion, turkevich method, and others are frequently utilized [9,10]. Additionally, physical methods such as pulsed laser ablation in liquid media offer an alternative synthesis approach. In contrast to chemical synthesis method, the pulsed laser ablation method offers a simpler process, is more environmentally sustainable, and can generate nanoparticles with higher purity levels [11]. Most important factors in evaluating capability of nanoparticles as contrast agents are CT number or Hounsfield Unit (HU) value, and Contrast-to-Noise Ratio (CNR). HU value represents degree of X-ray attenuation, while CNR reflects contrast difference between different tissues [12,13].

In this study, an Nd:YAG pulsed laser will be employed to produce gold nanoparticles (Au NPs) with high purity. The Au NPs will be synthesized in distilled water as the liquid media. Furthermore, the produced nanoparticles will be further investigated for their potential application as a computed tomography contrast agent. The primary objective of this research is to assess and compare the contrast performance of the Au NPs with the widely used iodine-based contrast agents. This evaluation will be conducted by analyzing and comparing the HU values and CNR of the two contrast agent formulations.

II. EXPERIMENTAL PROCEDURE

2.1. Materials

Gold plates with 99.95% purity were used as the bulk material. An Nd-YAG laser with a wavelength of 1064 nm and laser energy of 80 mJ was employed to ablate the gold plates. Beaker glass, vial tube, distilled water, and alcohol were used in the experiment procedure.

2.2. Au Nanoparticles Synthesis

The gold plates, measuring 2 x 2 cm^2, were initially cleaned with distilled water and subsequently washed with 70% alcohol to remove any impurities on the plates. Afterward, the plates were then rinsed again with distilled water to eliminate the residual alcohol. Following the washing process, the cleaned plates were dried and then placed into a beaker containing 10 mL of distilled water. The sample preparation is shown in **Figure 1**.

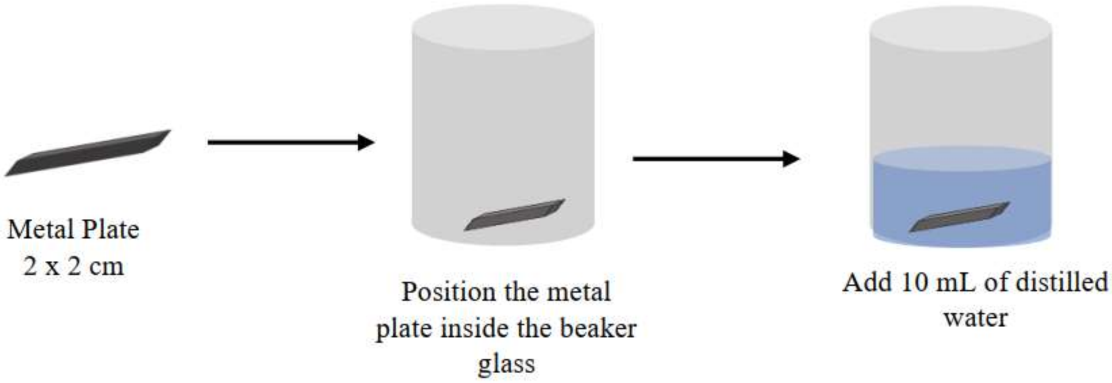

Fig. 1. Preparation for the synthesis of Gold nanoparticles (Au NPs)

Au NPs were synthesized using the pulsed laser ablation technique in distilled water as the liquid medium. An Nd:YAG laser operating at a wavelength of 1064 nm, energy of 80 mJ, focal distance of 10 cm, pulse width of 7 ns, and frequency of 10 Hz was directed onto the gold plates submerged in distilled water for 3 hours, leading to the formation of colloidal nanoparticle. **Figure 2** illustrates the schematic of the synthesis process for Au NPs colloids in distilled water.

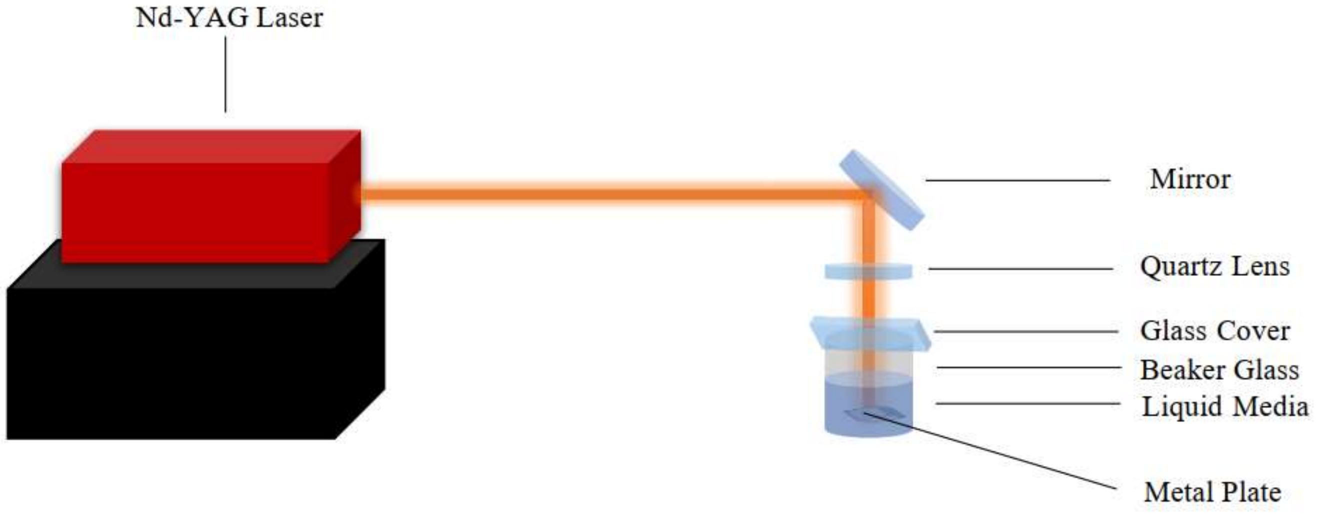

Fig. 2. Setup for the synthesis of Gold Nanoparticles (Au NPs)

2.3. Gold Nanoparticles (Au NPs) Applied as Contrast Agent Computed Tomography

The synthesized Au NPs were loaded into vial tubes for further evaluation. These vial samples were then exposed to X-rays in a computed tomography scanner, enabling the measurement of their HU values and CNR. To perform the HU and CNR analyses, regions of interest were first defined on the indoQCT system. The acquired data was then plotted and compared against the performance of widely utilized iodine-based contrast agents in CT imaging.

III. Result And Discussion

Au NPs were synthesized using the pulsed laser ablation technique with an Nd-YAG laser. The formation of the nanoparticles using the pulsed laser ablation Nd-YAG method is further demonstrated in **Figures 3**. **Figure 3a** shows the liquid medium before laser irradiation. In contrast, **Figure 3b** shows liquid medium after the gold was irradiated with a laser, which resulted in the formation of gold nanoparticles exhibiting a distinctive purple coloration. The successful formation of gold nanoparticles is indicated by the color change from clear to purple [14,15].

International urnal of Progressive Sciences and Technologies (IJPSAT)
ISSN: 2509-0119.

https://ijpsat.org/
Vol. 49 No. 1 February 2025, pp. 452-457

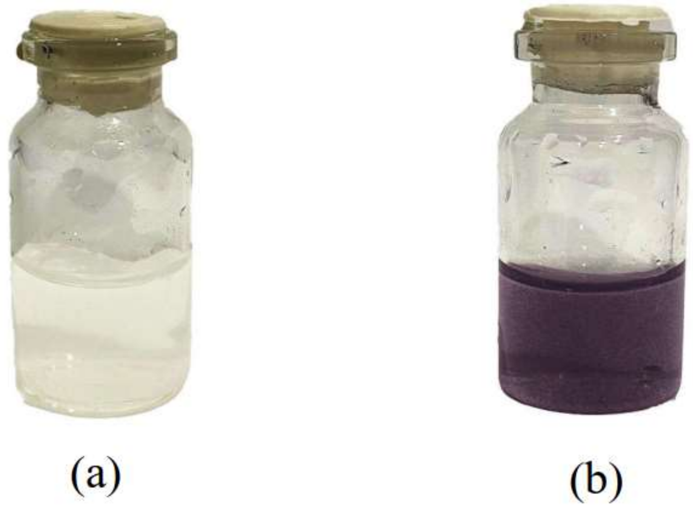

Fig. 3. Gold nanoparticles in distilled water media (a) liquid medium before laser irradiation (b) liquid medium after the formation of gold nanoparticles (Au NPs)

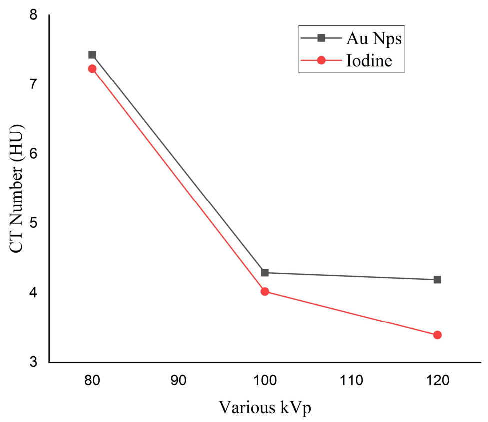

Fig 4. Graphs of CT Number for Au NPs and Iodine with variations of 80 kVp, 100 kVp, and 120 kVp

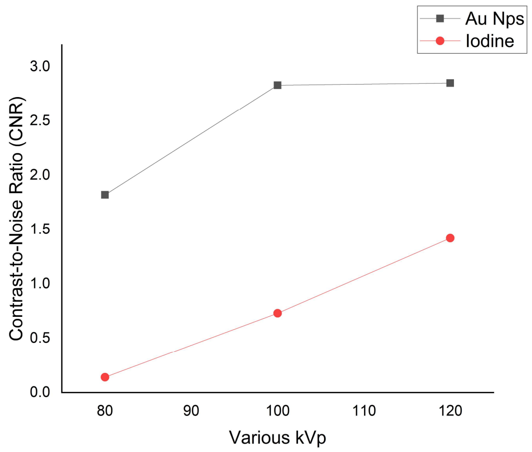

Fig. 5. Graphs of CNR for Au NPs and Iodine with variations of 80 kVp, 100 kVp, and 120 kVp

The efficacy of the synthesized Au NPs as a CT contrast agent was evaluated by comparing their HU values and CNR to the widely employed iodine-based contrast agent. HU and CNR measurements were analyzed using IndoQCT software, with scanning performed at standard tube voltages of 120 kVp, 100 kVp, and 80 kVp, and a background CT number of 0 HU. As shown in **Figure 4**, Au NPs exhibited higher HU values than the iodine-based contrast agent at equivalent concentrations. Specifically, the HU values for Au NPs were 7.43, 4.29, and 4.19, while the iodine-based contrast agent values were 7.23, 4.02, and 3.39. This can be attributed to the higher atomic numbers of gold compared to iodine, leading to enhanced X-ray attenuation and improved contrast in the CT images [15,8]. The study found that HU values decreased with increases in kVp, as the higher energy photons could penetrate the tissue with less attenuation [16].

Furthermore, Au NPs exhibited a higher CNR values compared to the iodine-based contrast agent, as shown in **Figure 5**. The

CNR values for Au NPs were 1.82, 2.83, and 2.85, while the iodine-based contrast agent had CNR values of 1.42, 0.73, and 0.14. Overall, a higher tube voltage (kVp) produced superior CNR values across all the CT scanners. Specifically, there were significant increases in CNR values when the voltage was raised from 80 to 120 kVp. The impact of kVp on image quality, as measured by CNR, was as expected, with elevated kVp increasing photon penetration and the radiation component, even though the radiation component is not directly proportional to kVp. As a result, the noise is reduced, and the CNR is enhanced [17].

IV. CONCLUSIONS

Gold nanoparticles were successfully synthesized using the pulsed laser ablation technique with an Nd:YAG laser, as evidenced by the color change of the colloid from translucent to purple. These nanoparticles demonstrated exceptional performance as a computed tomography contrast agent, achieving a maximum Hounsfield Unit value of 7.43 and a maximum Contrast-to-Noise Ratio of 2.85, surpassing the widely employed iodine-based contrast agent. The enhanced X-ray attenuation and contrast characteristics of gold nanoparticles can be attributed to their higher atomic numbers compared to iodine, leading to greater X-ray absorption and scattering. This improved X-ray interaction resulted in enhanced contrast in the CT images, positioning the tantalum-doped gold nanoparticles as a promising candidate for CT imaging applications.

ACKNOWLEDGMENT

The authors extend their profound appreciation to all members of the Laser and Advanced Nanotechnology (LAN) Group for their exceptional support and collaborative engagement. The invaluable contributions and assistance provided by each group member have been integral to the successful completion of this research endeavor. Furthermore, the authors would like to express their sincere gratitude to Indriati Solo Hospital for their support and facilitation throughout the duration of this research project.

REFERENCES

[1] J. Zukhi, D. Yusob, A. A. Tajuddin, V. Lim, and R. Zainon, “Evaluation of image quality and radiation dose using gold nanoparticles and other clinical contrast agents in dual-energy Computed Tomography (CT): CT abdomen phantom,” May 01, 2017, IOP Publishing. doi: 10.1088/1742-6596/851/1/012008.

[2] T. C. Owens, N. Anton, and M. F. Attia, “CT and X-ray contrast agents: Current clinical challenges and the future of contrast,” Sep. 20, 2023, Elsevier BV. doi: 10.1016/j.actbio.2023.09.027.

[3] A. Mazhit, K. Zhumanova, B. Duisenbayeva, and T. Sh. Atabaev, “Highly efficient CT contrast agent based on barium-doped mesoporous silica nanoparticles (SiO2-Ba NPs),” Sep. 28, 2023, Elsevier BV. doi: 10.1016/j.matlet.2023.135318.

[4] F. Cui et al., “Synthesis of PEGylated BaGdF5 Nanoparticles as Efficient CT/MRI Dual-modal Contrast Agents for Gastrointestinal Tract Imaging,” Aug. 01, 2020, Elsevier BV. doi: 10.1016/s1872-2040(20)60039-1.

[5] Z. Liu et al., “Long-circulating Er3+-doped Yb2O3 up-conversion nanoparticle as an in vivo X-Ray CT imaging contrast agent,” Jul. 06, 2012, Elsevier BV. doi: 10.1016/j.biomaterials.2012.06.033.

[6] A. Khumaeni et al., “Gold and silver nanoparticles as computed tomography (ct) contrast agents produced by a pulsed laser ablation technique: study in-vitro and in-vivo,” jan. 01, 2023. doi: 10.31788/rjc.2023.1618202.

[7] J. Jäntti et al., “Cationic tantalum oxide nanoparticle contrast agent for micro computed tomography reveals articular cartilage proteoglycan distribution and collagen architecture alterations,” Dec. 05, 2023, Elsevier BV. doi: 10.1016/j.joca.2023.11.020.

[8] N. N. T. Sisin, R. A. Rashid, A. Z. Harun, M. Geso, and W. N. Rahman, “Comparative evaluation of gold nanoparticles as contrast agent in multimodality diagnostic imaging,” Aug. 23, 2024, Elsevier BV. doi: 10.1016/j.jrras.2024.101079.

[9] M. Mihaly, M. C. Fleancu, N. L. Olteanu, D. Bojin, A. Meghea, and M. Enăchescu, “Synthesis of gold nanoparticles by microemulsion assisted photoreduction method,” Nov. 01, 2012, Elsevier BV. doi: 10.1016/j.crci.2012.09.013.

[10] A. E. F. Oliveira, A. C. Pereira, M. A. C. de Resende, and L. F. Ferreira, "Gold Nanoparticles: A Didactic Step-by-Step of the Synthesis Using the Turkevich Method, Mechanisms, and Characterizations," Jun. 08, 2023, Multidisciplinary Digital Publishing Institute. doi: 10.3390/analytica4020020.

[11] A. Qona'ah, M. M. Suliyanti, E. Hidayanto, and A. Khumaeni, "Characteristics of copper oxide and tin oxide nanoparticles produced by using pulsed laser ablation method and their application as an antibacterial agent," Jul. 17, 2023, Elsevier BV. doi: 10.1016/j.rechem.2023.101042.

[12] H. Lusic and M. W. Grinstaff, "X-ray-Computed Tomography Contrast Agents," Chemical Reviews, vol. 113, no. 3. American Chemical Society, p. 1641, Dec. 05, 2012. doi: 10.1021/cr200358s.

[13] M. S. Kandanapitiye, M. Gao, J. Molter, C. A. Flask, and S. D. Huang, "Synthesis, Characterization, and X-ray Attenuation Properties of Ultrasmall BiOI Nanoparticles: Toward Renal Clearable Particulate CT Contrast Agents," Sep. 09, 2014, American Chemical Society. doi: 10.1021/ic5011709.

[14] B. S. Lakshmi, M. H. Brindha, N. A. Kumar, and G. Krishnamurthi, "Impact of gold-decorated tantalum oxide (TaOx-Au) nano-probes for low energy cancer diagnostic agent," Nov. 08, 2021, Elsevier BV. doi: 10.1016/j.matlet.2021.131234.

[15] S. Jongjinakool, K. Palasak, N. Bousod, and S. Teepoo, "Gold Nanoparticles-based Colorimetric Sensor for Cysteine Detection," Jan. 01, 2014, Elsevier BV. doi: 10.1016/j.egypro.2014.07.126.

[16] P. F. FitzGerald et al., "CT Image Contrast of High-ZElements: Phantom Imaging Studies and Clinical Implications," Sep. 10, 2015, Radiological Society of North America. doi: 10.1148/radiol.2015150577.

[17] A. M. Jaafar, H. Elsayed, M. M. Khalil, M. N. Yaseen, A. S. Alshewered, and H. Ammar, "The influence of different kVs and phantoms on computed tomography number to relative electron density calibration curve for radiotherapy dose calculation," Nov. 26, 2022, Wiley. doi: 10.1002/pro6.1177.

[18] H. Alsleem and H. Almohiy, "The Feasibility of Contrast-to-Noise Ratio on Measurements to Evaluate CT Image Quality in Terms of Low-Contrast Detailed Detectability," Jul. 06, 2020, Multidisciplinary Digital Publishing Institute. doi: 10.3390/medsci8030026.