Study the Effects of Iodine Nanoparticles Contrast Medium to Enhancing the Computed Tomography Imaging

Sarah Majeed Hameed¹, MuhammedMizher Radhi^{1*}, Ahmed A. Mohsin¹

^{1*}Radiological Techniques Department, Health and Medical Technology College-Baghdad, Middle Technical University (MTU), Iraq.

*corresponding author (Prof.Dr. M.M.Radhi) email: mmradhi@yahoo.com

Abstract

The Nano contrast medium of Iodine solution was used in computed tomography scanning (CT-Scan) to test the enhancement of the rabbit heart.

The aim of this research is to see how well Nano iodine solution works as a contrast medium in CT scans.

Iodine nanoparticles were tested on laboratory animals (rabbits) with the heart as the organ of choice to determine the influence of the Nano contrast medium. The heart was chosen to research the Nano iodine contrast media, and the findings were promising in terms of the use of nanoparticles in the field of CT-Scan imaging diagnosis.

It was discovered that injecting the rabbit with iodine nanoparticles improved the rabbit's cardiac imaging by increasing the value of the Hounsfield (HU).

As a result, using iodine nanoparticles solution as a safe contrast medium in a CT-scan with high resolution of the organ's image is recommended.

The anti-oxidative activity of Iodine NPs in blood medium was discovered electrochemically, with only a reduction current peak appearing in the cyclic voltammogram.

Keywords: Iodine contrast, Iodine NPs contrast, CT-Scan, heart's rabbit, cyclic voltammetry

Introduction

X-ray computed tomography (CT) is a form of imaging that is used to visualize and distinguish bones from soft tissue. However, contrast is needed to improve soft tissue visualization using radiopaque formulas [1,2]. This radiopacity is achieved using high atomic number atoms, especially those containing iodine, since it is a good balance between safety, contrasting influence, and cost [3]. Iodine in the blood or a target tissue causes superior radiation scattering and absorption. Despite the fact that current contrast agents have assisted in diagnosis by raising CT attenuation and enhancement, which is directly proportional to the amount of iodine in the environment, they have a number of drawbacks, including a lack of accuracy in tissue comparing and toxicity [4]

Properties such as viscosity, concentration, and osmolality specifically or indirectly describe the tendency of iodinated Contrast to produce adverse effects. The enhancement per volume is better because the concentration is higher. Even, as iodine concentration increases, viscosity rises exponentially, increasing injection pressure and delaying renal Contrast excretion [5].

Researchers are developing novel contrast agents to overcome the challenges of traditional contrast and to increase the accuracy and capability of these techniques [6,4]. Using advances in nanotechnology, researchers are developing novel contrast agents that overcome these

challenges Nanomaterials have a long residence in blood and the capacity to passively aggregate at tumor sites [2], rendering them ideal for use in vascular system imaging and as a blood pool contrast [7], and by confining them to one tissue type, such as a tumor, but not the healthy tissue surrounding it, the diagnostic capabilities of different imaging techniques can be improved [8].

Modifying nanoparticle structures to achieve extended circulation time while ensuring biocompatibility is a major design challenge and the potential to exit the circulatory system and infiltrate other tissues, including tumors [9].

To avoid any long-term toxicity, the nanoparticle must be removed from the body after it has served its function. Nanotechnology allows monitoring the chemical and physical properties of contrast to reduce toxicity, provide useful longer imaging time, tissue specificity, and signal intensity [6].

Iodinated Nano solution is used as an alternative contrast medium for CT scanning of rabbit organs in this research.

Experimental

Materials

GE Healthcare (United States), The comparison media used in CT-scan was the iodinated contrast agent Iohexol (Omnipaque 350 mg I/ml).

Ketamine (10%) from Alfasan Company (Holland) and xylazine (2%) from Alfasan Company (Holland) werethe two anesthesia ingredients used in sedation (Holland).

CT-Scan Apparatus

The Computed Tomography X Ray System used was by United Imaging model uCT520 slices, Shanghai united imaging healthcare.

The rabbit is put on the examination table after being anesthetized and given the prescribed contrast dosage, as seen in Figure 1.



Figure 1: The CT scanner with the rabbit in position.

PreparationofIohexol Nano solution Lyophilization instrument

Lyophilization instrument from LABCONCO Company (USA) was used for the preparation of Iohexol nanoparticles from micro-particles by deep freezing technique as shown in Figure 2.



Figure 2: Lyophilization instrument, LABCONCO Company (USA).

Characterization of Iohexol Nano solution

Atomic Force Microscopy (AFM)

Figures 3 and 4 show the scanning of the prepared Iodine NPs using atomic force microscopy (AFM) and the range of nanoparticle dimensions from 10 to 40 nm, with an average of 25 nm.

The iodine nanoparticles' surface morphology data, which were recognized as findings of the conversion of Iodine to nanoparticles [10].

The park system corporation provided an atomic force microscopy (AFM) instrument (Korea).

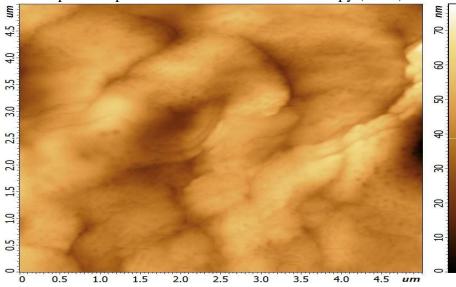


Figure 3: AFM of Iodine NPs

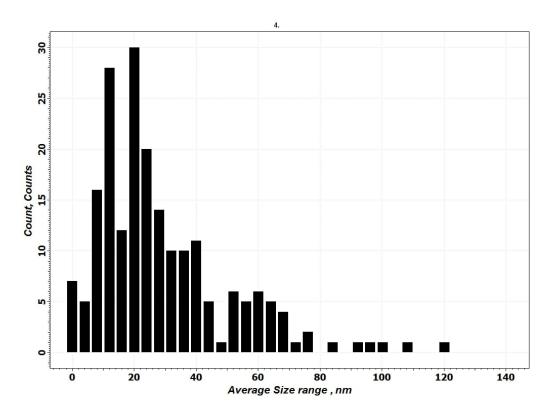


Figure 4: average dimensions of Iodine nanoparticles

Results and Discussion

CT-Scan Exam of Rabbits

Prior to the examination, the rabbits were anesthetized with ketamine and xylocaine, then immobilized on the scanner table. A pre injection scan was taken for each rabbit, followed by post injection of iodinated contrast into the rabbit's heart at doses of 1.4 M of 1, 2, 3, 4, 5ml for the micro iodinated group and doses of 1.4 M of 0.5, 1, 1.5, 2 and 2.5ml for the Nano iodinated contrast the scan was with the following parameters, 1.5mm slice thickness at an increment of 1.5mm using 100kv and 75mAs radiation dose, then Hounsfield numbers measurements were taken of the heart organs.

All statistical analyses were performed with SPSS (version 16.0). The results were expressed as the means and standard deviation for the groups. Data were analyzed by one-way ANOVA and least-significant different tests between groups. All statistics were performed with a 0.05 level of significance.

The following results obtained through CT-scan of the Rabbit's heart in different cases of contrast media used in different doses through which the results can be compared and evaluated.

The results presented in Tables 1 and 2 that there were statistically significant differences between the groups of Iodohexol, the alternative contrast media iohexol Nano solution and the control group when using 1ml of these contrast media (p<0.01). as shown in Figure 5, statistical differences in the expression levels of means were observed betweenIohexol, the alternative contrast media Nano iohexol and the control group (p<0.01). All of these indicators levels with Iohexol and the alternative contrast media iohexol Nanoparticles were higher than those of control group (without contrast media) (p<0.01), Which indicated that the alternative contrast media (Iohexol NPs) can give higher signal intensity like Iohexol as compared to the control group.

Table 1: Distribution of The Means of the Rabbit's heart CT

Dose of contrast			Std.	Std. Error	Range		ANOVA	
media	N	Mean	Deviation		Mini.	Maxi.	test (P-value)	
Control (without contrast media)	10	43.38	2.825	0.999	40	49		
Iohexol (1ml)	10	97.88	8.008	2.831	90	110	P=0.000Highly	
Nano_Iohexol (0.5ml)	10	160.38	46.758	16.531	100	202	sign. (P<0.01)	
Total	30		•	•		•		

Table 2: Multiple Comparisons (fisher test) between (1ml) of Iohexol and (0.5 ml) Nano_iohexol.

Amount	LSD test (P-value)	
Control (without	Nano_iohexol	P=0.000Highly sign. (P<0.01)
contrast media)	Iohexol	P=0.000Highly sign. (P<0.01)
Iohexol(1 ml)	Nano_iohexol	P=0.000Highly sign. (P<0.01)
Nanoiohexol(0.5)	Iohexol	P=0.000Highly sign. (P<0.01)

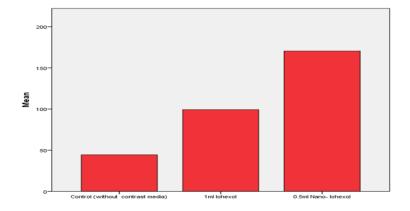


Figure 5: Levels of Mean Values at dose of control, 1ml of Iohexol and 1 ml of Nano iohexol groups

The results presented in Tables 3, and 4 that there were statistically significant differences between the groups of Iohexol, the alternative contrast media Nano iohexol and the control group when using 1ml of these contrast media (p<0.01), Figure 6 shows the statistical differences in the expression levels of means were observed between Iohexol, the alternative contrast media Nano iohexol and the control group (p<0.01). All of these indicators' levels with Iohexol and the alternative contrast media Nano iohexol were higher than those of control group (without contrast media) (p<0.01), Which indicated that the alternative contrast media (Iohexol NPs) can give higher signal intensity like Iohexol as compared to the control group.

Figure 7 illustrated the CT-scan exam of the whole body of the rabbit, and Figures 8, and 9 of the heart's rabbit without contrast, and with different doses of contrast medium such as Iodine

micro solution and Iodine nanoparticles. The imaging of CT-scan has high resolution with Iodine NPS comparison with Iodine micro particles, so we can say the nano contrast medium success more than in micro solution.

Table 3: Multiple Comparisons (fisher test) between (5ml) of Iohexol and (2.5 ml) Nano_iohexol.

Amount of contrast		LSD test (P-value)			
Control (without	Nano_iohexol (4ml)	P=0.00 Highly sign. (P<0.01) P=0.00 Highly sign. (P<0.01)			
contrast media)	Iohexol(2ml)				
Iohexol(5ml)	Nano_iohexol	P=0.000Highly sign. (P<0.01)			
Nano_iohexol(2.5)	Iohexol	P=0.000 Highly sign. (P<0.01)			

Table 4: Distribution of The Means of the Rabbit's kidney CT

Dose of contrast media	N	Mean	Std.	Std. Error	Range		ANOVA		
2 ope of contrast mount			Deviation		Mini.	Maxi.	test (P-value)		
Control (without contrast media)	10	46.60	4.351	1.376	40	53			
Iohexol (5ml)	10	97.70	14.236	4.502	80	130	P=0.000Highly sign. (P<0.01)		
Nano_Iohexol (2.5ml)	10	154.50	21.433	6.778	125	180			
Total	30			I	1	I			

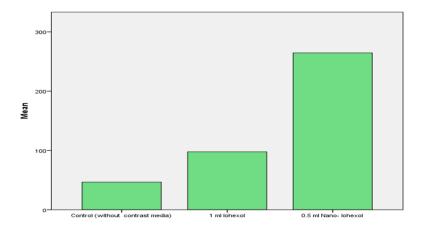


Figure 6: Levels of Mean Values of control, 1ml of Iohexol and 0.5ml iohexol Nanoparticles groups.

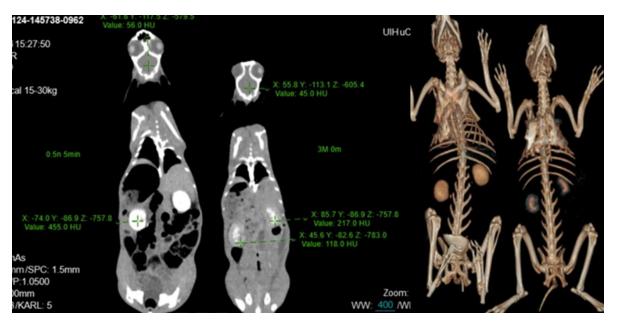


Figure 7: CT-scan of whole body of the rabbit



Figure 8: CT-scan of heart's rabbit injecting 1.5ml of iohexol Nanoparticles

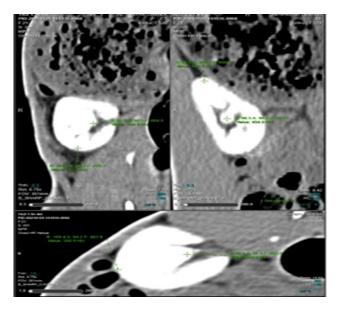


Figure 9: Comparison between the enhancement of 1.5 iohexol nanoparticles and 4ml iohexol of heart's rabbit

Cyclic voltammetric study

Iodine nanoparticles can be used as an alternative contrast medium in CT scans to detect abdominal organs safely and clearly, allowing the doctor to give the picture more brightness and high resolution but still allowing to make the correct diagnostic decision.

Figure 10 indicates an iodine cyclic voltammogram in a stable blood medium, which revealed an oxidation current peak current at a potential of -0.8 V, indicating that iodine serves as an oxidizing reagent [14].

Iodine nanoparticles in blood medium, on the other hand, serve as an anti-oxidative reagent since, as seen in Figure 10, the oxidation current peak of Iodine has vanished

in Iodine NPs.

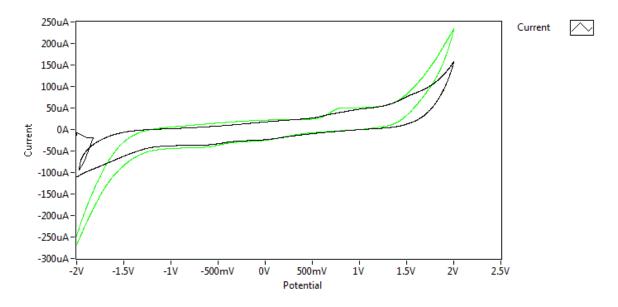


Figure 10: cyclic voltammogram of iodine nanoparticles solution (black line) and iodine solution (green line) in blood medium on glassy carbon electrode as working electrode versus Ag/AgCl as reference electrode at scan rate of 0.1 Vsec-1

Conclusions

Nano iohexol provided high resolution at its most minimum dose, offering maximum contrast and a longer stay overall but most prominently in the heart tissues. Although the Nano iohexol was diluted and less than half the value of iohexol there was a marked distinction between both contrasts in imaging of the heart with the nano contrast achieving the highest enhancement and decreasing slowly. The nanoiohexol contrast shown better contrast stayed longer after administration. Nano iohexol provided high resolution at its most minimum dose, offering maximum contrast and a longer stay overall but most prominently in the heart tissues, which means the nanoiohdexol contrast gets filtered less rapidly than iohexol, that proves its ability to leave the circulation there by its suitable for exams that require a longer time hence a minimum dose which lessons the dose related adverse effects.

References

- Rosen, J. E., Yoffe, S., Meerasa, A., Verma, M., &Gu, F. X. Nanotechnology and diagnostic imaging: new advances in contrast agent technology. J. Nanomed. Nanotechnol, 2(5), 1-12 (2011).
- 2.Liu, Y., Ai, K., & Lu, L. Nanoparticulate X-ray computed tomography contrast agents: from design validation to in vivo applications. Accounts of chemical research, 45(10), 1817-1827 (2012).
- 3. F. Hallouard, N. Anton, P. Choquet, A. Constantinesco and T.Vandamme, Biomaterials, 2010, 31, 6249–6268.
- 4. Bae, K. T. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology, 256(1), 32-61 (2010).
- 5. Yin, Q., Yap, F. Y., Yin, L., Ma, L., Zhou, Q., Dobrucki, L. W., ... & Cheng, J. (2013). Poly (iohexol) nanoparticles as contrast agents for in vivo X-ray computed tomography imaging. Journal of the American Chemical Society, 135(37), 13620-13623.
- 6. Hahn MA, Singh AK, Sharma P, Brown SC, Moudgil BM (2011) Nanoparticles as contrast agents for in-vivo bioimaging: current status and future perspectives. AnalBioanalChem 399: 3-27.
- 7. Hallouard, F., Anton, N., Zuber, G., Choquet, P., Li, X., Arntz, Y., ... &Vandamme, T. F. (2011). Radiopaque iodinated nano-emulsions for preclinical X-ray imaging. RSC advances, 1(5), 792-801.
- 8. Shahid, I., Lancelot, E., &Desché, P. Future of Diagnostic Computed Tomography: An Update on Physicochemical Properties, Safety, and Development of X-ray Contrast Media. Investigative Radiology, 55(9), 598-600 (2020).
- 9. Moghimi SM, Hunter AC, Murray JC (2001) Long-circulating and target-specific nanoparticles: theory to practice. Pharmacol Rev 53: 283-318.
- 10. Lyubchenko, Y. L., Shlyakhtenko, L. S. and Ando, T. 2011. Imaging of nucleic acids with atomic force microscopy. Methods, 54, 274-283.