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RESEARCH PAPER

Comparison Study between the Contrast Media of Iodine and Iodine Nanoparticles in Physicochemical Properties in CT-scan Imaging

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ABSTRACT

In a new study in a comparison between the contrast medium of Iodine solution which used in the computed tomography scanning (CT-Scan) and the same contrast medium after converting it to nanoparticles by Lyophilization method. The aim of this study is to reduce the different side effects which caused the micro iodine for the patients, but the iodine nanoparticles solution have good physical and chemical properties in blood medium as antioxidant reagent compared with micro-iodine, as well as the new characteristics of nano iodine solution. The micro iodine and nanoparticles were studied on laboratory animals, so the rabbits were chosen in the study to identify the time of remaining the contrast media in the different organs, so that the diagnosis was good, as in the catheter and some organs that need the contrast media to remain for a longer period. The brain, heart, liver, kidney and bladder were selected to study the contrast media at micro and nano iodine, and the results were encouraging in the use of nano iodine in the field of diagnosis by the CT-Scan imaging. It is noticed that after injected the rabbit with the iodine nanoparticles, the value of Hounsfield unit (HU) values was monitored which have the same values after one hour. Whereas, the survival of the micro contrast medium were observed with a shorter period time of survival in the studied the organs compared with the micro contrast medium. Therefore, it is recommended to using iodine nanoparticles solution to monitor the functioning of the organs.

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INTRODUCTION

Research that talks about the use of iodine as a contrast media in computed tomography imaging is the only contrast medium currently used, as of the iodine nanoparticles solution [1-5]. Computed tomography (CT) is a full-body imaging technique based on x-rays and widely used in medicine. Contrast agents clinically approved for CT imaging are small iodized particles or barium suspensions. Nanoparticles have several advantages over small-molecule CT contrast agents, such as long blood pool dwell times, cell traceability and targeted imaging applications. The required large doses of contrast agent require careful toxicology studies prior to clinical translation [6]. Suspensions of nanoparticles from the iodinated polymer are evaluated as a contrast agent for computed tomography (CT). Intravenous injection of iodized

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polymer nanoparticles provides mice with a clear visualization of the cardiovascular system over a period of several hours followed by a gradual accumulation in the liver and spleen. This substance is a "pooling" contrast agent with a very long stay in the bloodstream [3].

X-ray iodine attenuation is not effective in clinical computed tomography that uses high-energy X-rays. Due to these limitations, nanoscale iodized contrast agents have been developed that can increase circulation time and reduce adverse effects. In addition to iodine, nanoparticles based on heavy atoms such as gold, lanthanides and tantalum are used as more efficient CT contrast agents [7]. Nanoparticles (NPs) are being used as novel contrast agents that represent a promising strategy for non-invasive diagnostics. Advances in nanotechnology will provide improved sensitivity and specificity for tumor imaging, enabling early detection of metastases. Nanoparticles are consistent with the development of targeted contrast agents, which are used as contrast agents and the benefits / concerns associated with their use in clinical procedures [8].

Medical imaging techniques allow for the rapid diagnosis and evaluation of a wide range of diseases. In order to increase its sensitivity and utility, many imaging techniques such as computed tomography and magnetic resonance imaging rely on contrast agents administered intravenously. While the current generation of contrast agents has enabled rapid diagnosis, they still have many unwanted defects including a lack of tissue specificity and systemic toxicity problems. Through advances in nanotechnology and materials science, researchers are now creating a new generation of contrast agents that overcome many of these challenges and are able to provide more sensitive and specific information [9,10].

In this study iodine nanoparticle was used as alternative contrast medium of micro iodine solution in different organs of rabbit to monitoring the time remaining in the organ for good diagnosis in CT-scan.

MATERIALS AND METHODS

GE Healthcare USA Iodine contrast Iohexol (Omnipaque 350 mg I/ml) was the contrast media utilized in CT-scan. Anesthesia materials used in sedation include ketamine 10% from Alfasan Company (Holland), xylazine 2% from Alfasan (Holland). Blood samples of rabbits and other chemicals and solvents were of annular grade and were used as received by the manufacturers.

Fig. 1. Lyophilization instrument, LABCONCO Company (USA). ábra Liofilizáló készülék LABCONCO Company (USA)

Deionized water was used to prepare aqueous solutions.

Preparation of nanoparticles of Iohexol contrast medium

Lyophilization instrument

Lyophilization instrument from LABCONCO Company (USA) was used for the preparation of Iopromide nanoparticles from micro-particles by deep freezing technique as shown in Fig. 1.

CT-Scan apparatuses

The CT-Scan screw type United Imaging Computed Tomography X ray System UCT520, Shanghai United Imaging Healthcare, China.

After preparing the rabbit for examination and in the case of anesthesia with the specified dose of the contrast, the rabbit was lying on the examination table to perform the spiral CT-Scan as shown in Fig. 2.

Preparation of rabbit groups for the CT scan

Three groups of rabbits weighing between 1.5 to 2 kg were all before the acquisition, rabbits were anesthetized with ketamine and xylocaine prior to the examination, then, placed on the scanner table and immobilized. The iodinated Nano-solution was injected directly into the heart muscle, Scans were performed before administration for the 1st control group.

The 2nd group had their hearts injected with micro iodinated contrast at doses of (1,2,3,4,5ml) respectively, The 3rd group had their hearts injected with Nano iodinated contrast at doses of (0.5, 1, 1.5, 2 and 2.5ml) exams were taken for each group at different time intervals of (0min, 5min, 10min, 20min, 30min and 1hour) respectively ,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 brain, heart and the abdominal organs.

The Hounsfield unit (HU): radiolucency Absorption coefficient unit of a substance; HU is normalized to water, where water = 0 HU, air = -1000 HU and bone = 1000 HU [11,12], the HU values in the CT-scan were measured for each CT exam at all times by placing a region of interest in the brain, heart, liver, and kidney.

RESULTS AND DISCUSSION

In the current study, the rabbits were used in the computed tomography (CT-scan) examination, the iodine solution, and the iodine nanoparticles contrast media to compare the effectiveness of nanoparticles within its survival in the different organs during the examination by comparing with time remaining in the organ.

The study included different organs of rabbits such as the heart, kidney, liver, bladder, and brain using iodine and iodine nanoparticles as contrast media to monitoring the [13] contrast media in 0, 5, 10, 20, 30, and 60 minutes as shown in table 1.

Study the Heart Organ

Table 1 illustrated the HU values of the heart

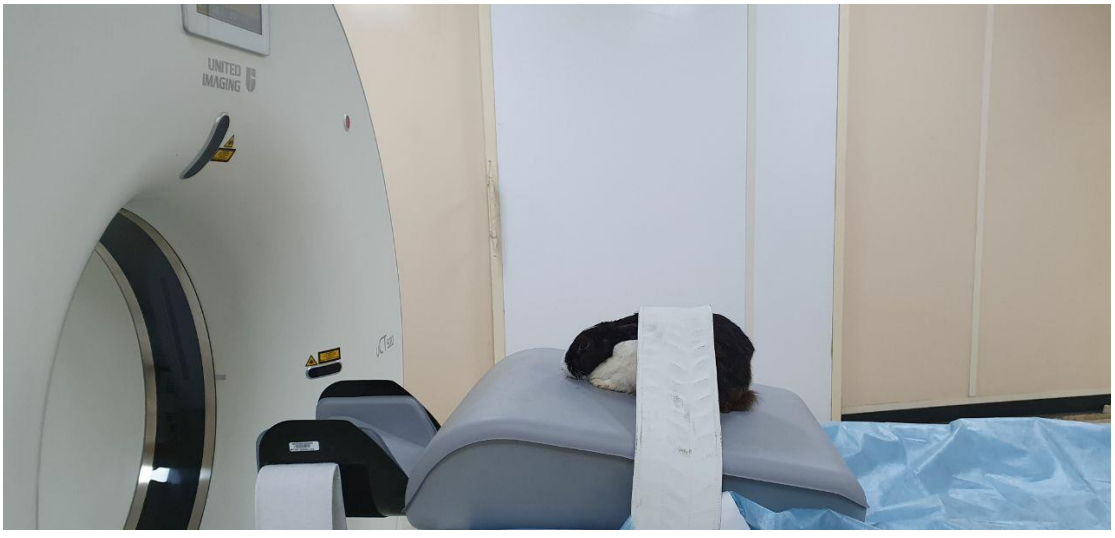

Fig. 2. Preparation the rabbit in the spiral CT-Scan.

Table 1. iodine micro and nanoparticles as contrast media of CT-scan imaging for the heart of rabbit in different doses after different times.

		Heart imaging HU values in Time					
Contrast dose	Control HU	0min	5min	10min	20min	30min	1hr
1ml lohexol	31	165	141	139	130	98	72
0.5ml Nano- lohexol	29	90	100	120	118	120	64
2ml lohexol	43	135	156	119	136	115	90
1ml Nano- lohexol	52	130	131	130	128	122	88
3ml lohexol	53	316	259	206	206	142	144
1.5ml Nano- lohexol	50	215	134	119	108	102	92
4ml lohexol	56	204	144	155	102	74	73
2ml Nano- lohexol	106	107	74	110	111	95	180
5ml lohexol	43	137	126	123	122	112	110
2.5ml Nano- lohexol	54	180	179	164	137	125	114

organ after injected with each of iodine and iodine nanoparticles in the same concentration (1.5 ml of 350 mg/ml) after different times, 0, 5, 10, 30, and 60 minutes which find the high HU values in the iodine NPs comparing with the iodine micro particles, addition to the remaining the nano contrast medium in the heart organ for longer time (HU value at 0 minute has 215 after 30 minutes has 120) while the iodine micro particles decreased in the HU values in the same time (HU value at 0 minute has 204 after 30 minutes has 74) as shown in tabl1 and Fig. 3, these phenomena of using the nano iodine contrast medium is very important for monitoring the heart and the vessels imaging by CT-Scan technique for easy diagnostic method.

Study the Brain organ

Another study for using nano iodine contrast medium is monitoring the CT-scan imaging of the brain organ of rabbit the value of HU is 54 after 0 minutes and the contrast still remaining in the brain after one hour with 50 HU value as shown in table 2, also iodine NPs can be used as a good contrast medium for diagnostic the brain problems with easy method.

Study the Kidney Organ

There are two positions in the CT-scan imaging of kidney organ of the rabbit was studied in this work, cortex kidney imaging and medulla kidney imaging. The results were found after using iodine nanoparticles as a contrast medium, and comparing with iodine micro particles as in the following:

In the cortex kidney organ, the HU value in iodine NPs after 0 minutes has 275 and after 60 minutes has 378 which still in the kidney with more resolution in a long time, which enhanced the resolution of the image. While, the HU value in iodine micro particles when using in the cortex kidney has 278 after 0 minutes and decreased to 125 after 60 minutes, the resolution of kidney image has low clearness comparing with the using iodine NPs, these results can see in table 3 and Fig. 4.

In the medulla kidney image can be seen the same phenomena as in the cortex kidney, it was found that the values of HU in the medulla kidney of the rabbit when using iodine nanoparticles has 222 after 0 minutes and enhanced the resolution of imaging to 437 after 60 minutes, this jump of the resolution means that nanoparticles of iodine set in the kidney for a long time because the nano size of the iodine particles [14]. While the iodine micro particles were decreased the HU value after 60 minutes from 1145 to 271, the resolution of medulla kidney imaging has a lower value after passing the time, so using iodine NPs in diagnostic kidney diseases is more efficient than using iodine micro particles in CT-scan [15].

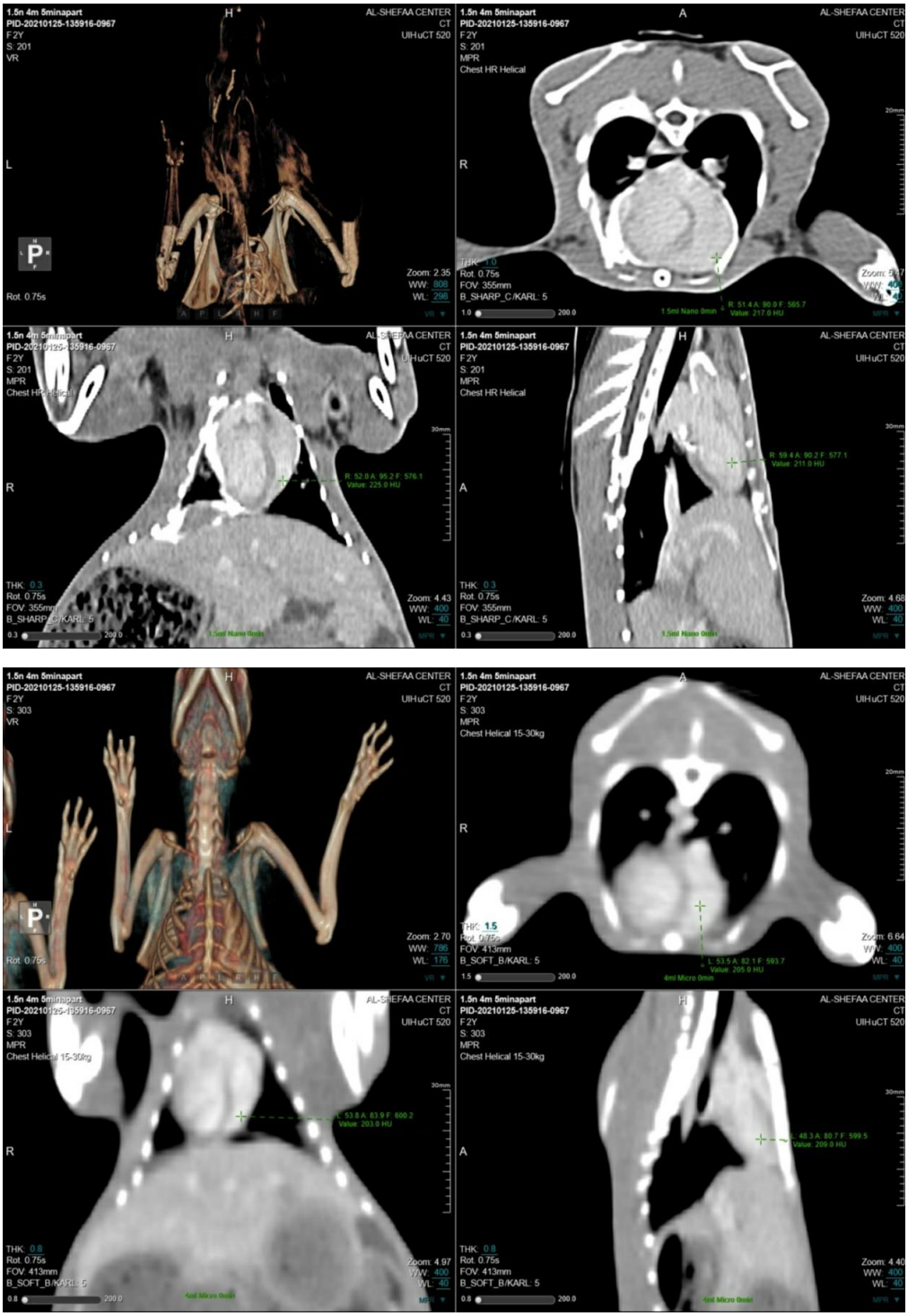

Fig. 3. comparison between the hearts immediatlely post injection of 4ml of iohexol and 1.5 ml of nano iohexol.

Study the Liver Organ

The liver organ of the rabbit was studied for both iodine and iodine NPs which have good results through using iodine NPs comparing the iodine micro particles.

The resolution of the liver image was studied by

Table 2. Iodine micro and nanoparticles as contrast media of CT-scan imaging for the brain of rabbit in different doses after different times.

Contrast dose	Control HU	Brain imaging HU values in Time 0min	5min	10min	20min	30min	1hr
1ml lohexol	41	56	53	52	50	46	48
0.5ml Nano- lohexol	36	44	43	40	44	41	40
2ml lohexol	41	45	35	61	50	51	50
1ml Nano- lohexol	40	56	52	57	42	40	44
3ml lohexol	30	45	38	40	44	40	48
1.5ml Nano- lohexol	36	54	59	37	48	45	44
4ml lohexol	43	51	53	40	32	40	48
2ml Nano- lohexol	28	27	57	50	52	41	60
5ml lohexol	45	65	55	53	51	51	48
2.5ml Nano- lohexol	44	66	62	53	52	55	51

using iodine NPs in CT-scan technique has HU value after 0 minutes 121 and still remaining with the same value 122 after 60 minutes, the resolution of CT scan image is to save in the value for a longer time. But, iodine micro particles cannot save the contrast medium of iodine for loge time in the organ because the size of the particles has bigger than nanoparticles. The HU values of the liver after 0 minute has 182 decreased to 95 after 60 minutes, so the liver cannot save with the micro iodine contrast medium for a long time as shown in table 4 and Fig. 5.

Study the Bladder Organ

In the same CT-scan examination of bladder organ by using iodine in micro and nanoparticles

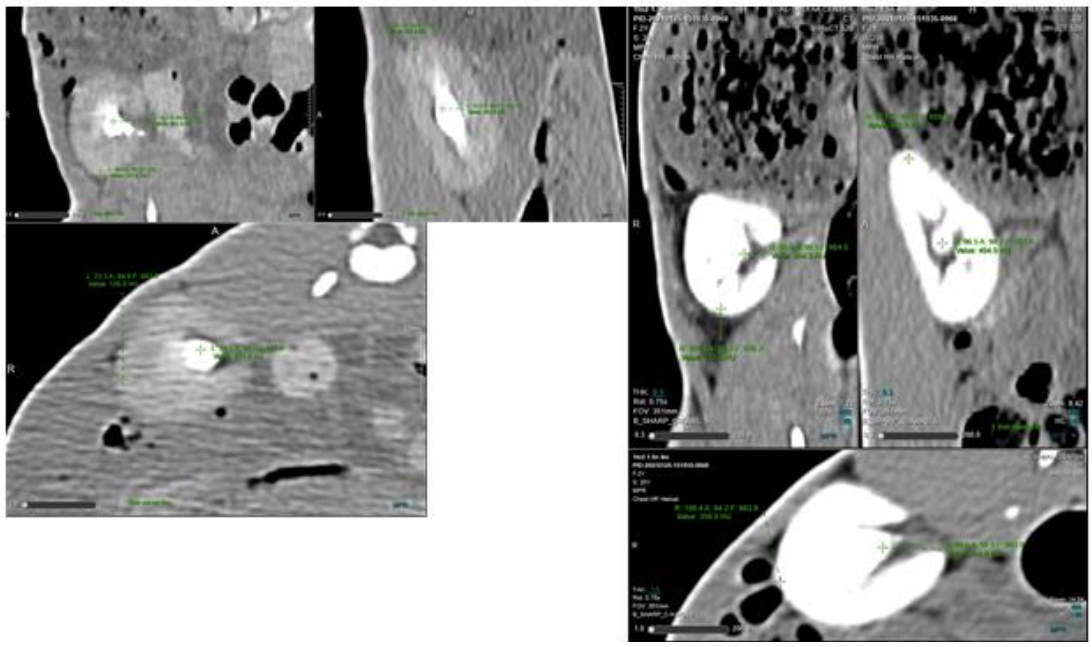

Fig. 4. Comparison between the kidneys after 1 hr post injection of 4ml of iohexol and 1.5 ml of nano iohexol.

Table 3. Iodine micro and nanoparticles as contrast media of CT-scan imaging for the kidney of rabbit in different doses after different times.

		Kidney cortex imaging HU values in Time					
Contrast dose	Control HU	0min	5min	10min	20min	30min	1hr
1ml lohexol	49	103	100	91	90	89	70
0.5ml Nano- lohexol	53	202	30	227	314	239	313
2ml lohexol	48	142	141	127	90	226	180
1ml Nano- lohexol	47	79	85	49	77	73	143
3ml lohexol	45	118	163	179	239	212	224
1.5ml Nano- lohexol	49	275	229	279	379	414	378
4ml lohexol	43	278	224	188	168	164	125
2ml Nano- lohexol	53	62	91	141	127	90	99
5ml lohexol	51	239	232	223	216	224	239
2.5ml Nano- lohexol	52	50	64	98	103	110	50
		Kidney medulla imaging HU values in Time					
Contrast dose	Control HU	0min	5min	10min	20min	30min	1hr
1ml lohexol	49	128	236	107	105	93	90
0.5ml Nano- lohexol	53	566	456	432	463	353	354
2ml lohexol	48	106	130	458	155	256	417
1ml Nano- lohexol	47	87	119	120	174	311	390
3ml lohexol	45	280	288	404	353	454	442
1.5ml Nano- lohexol	49	222	425	538	701	667	437
4ml lohexol	43	1145	560	774	591	601	274
2ml Nano- lohexol	53	106	159	317	458	156	232
5ml lohexol	51	229	603	704	171	169	162
2.5ml Nano- lohexol	52	146	447	465	400	423	432

at different times to monitoring the resolution of the imaging by HU values, it was found that iodine NPs contrast medium plays an important role for using as alternative contrast medium from the iodine micro particles, the HU value of bladder organ has 1284 after 5 minutes and 2650 after 60 minutes which has a good resolution of the imaging for the bladder organ, so, iodine NPs contrast medium can be used with safety way to monitoring the working of this organ by CT-scan examination as shown in table 5.

Cyclic voltammetry study

Iodine nanoparticles can be used as an alternative contrast method in a CT scan to diagnose tumors and abdominal organs safely and with good visualization, which helps the doctor give more brightness and high resolution to the image, in addition to the long time remaining in the organs, which gives the doctor the correct

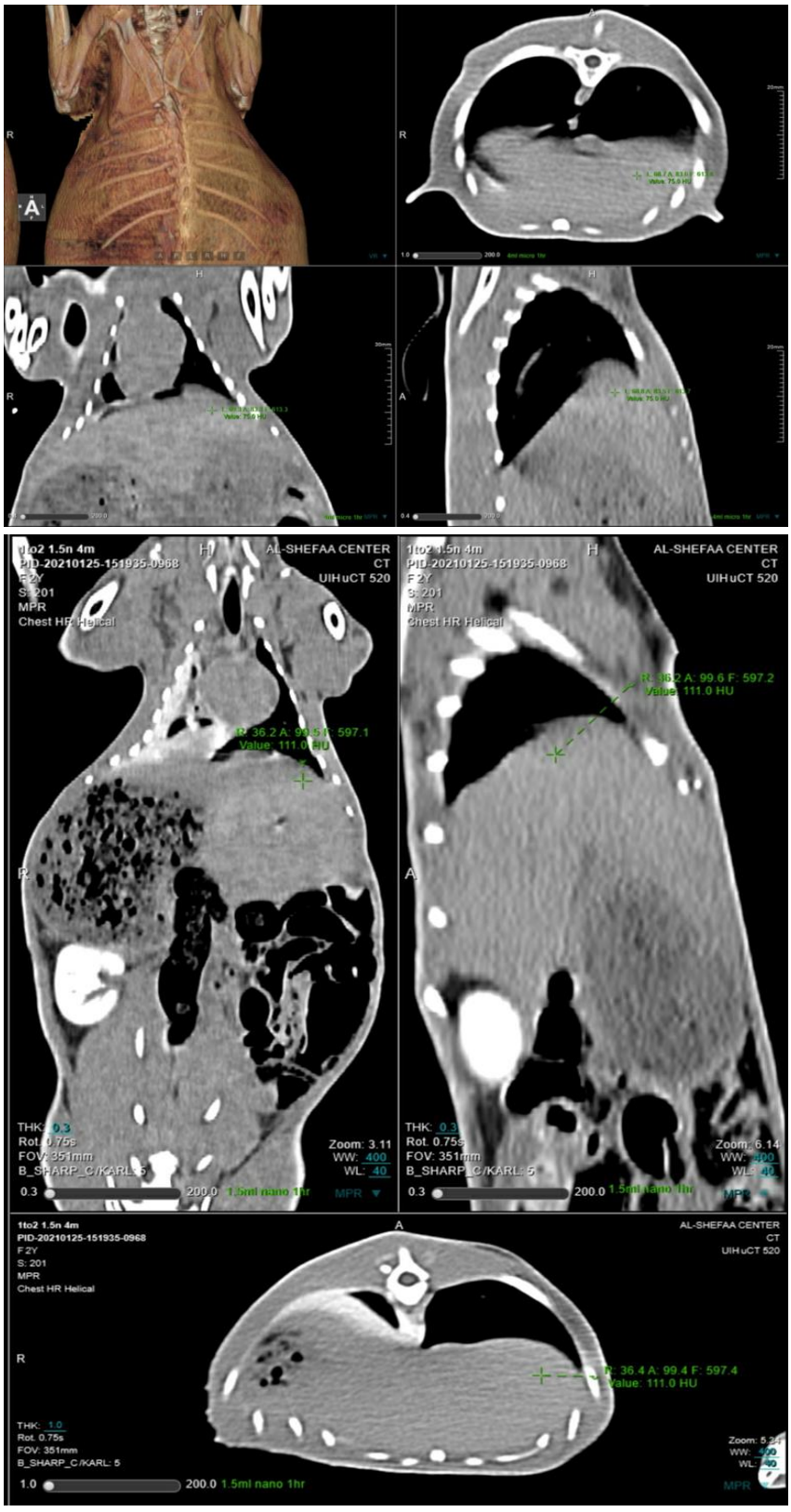

Fig. 5. Comparison between the liver after 1 hr post injection of 4ml of iohexol and 1.5 ml of nano iohexol.

Table 4. Iodine micro and nanoparticles as contrast media of CT-scan imaging for the heart of rabbit in different doses after different times.

		liver imaging HU values in Time					
Contrast dose	Control HU	0min	5min	10min	20min	30min	1hr
1ml lohexol	49	56	53	52	50	46	48
0.5ml Nano- lohexol	50	44	43	40	44	41	40
2ml lohexol	53	102	99	119	108	87	93
1ml Nano- lohexol	48	99	123	140	146	154	155
3ml lohexol	47	81	95	85	107	112	106
1.5ml Nano- lohexol	45	121	108	95	112	123	122
4ml lohexol	49	182	107	123	95	85	93
2ml Nano- lohexol	53	102	81	82	99	108	59
5ml lohexol	51	121	101	111	104	130	109
2.5ml Nano- lohexol	52	121	105	72	80	87	104

Table 5. Iodine micro and nanoparticles as contrast media of CT-scan imaging for the heart of rabbit in different doses after different times.

		Bladder imaging HU values in Time					
Contrast dose	Control HU	0min	5min	10min	20min	30min	1hr
1ml lohexol	44	825	573	631	341	331	3712
0.5ml Nano- lohexol	34	45	2062	2099	447	1095	663
2ml lohexol	37	285	417	522	187	417	838
1ml Nano- lohexol	41	45	135	135	683	942	856
3ml lohexol	23	22	27	22	2098	2354	1821
1.5ml Nano- lohexol	17	22	1284	2016	2203	2439	2650
4ml lohexol	32	3881	2467	2518	3025	4242	3047
2ml Nano- lohexol	35	187	695	417	522	286	232
5ml lohexol	40	45	47	44	2666	2840	2430
2.5ml Nano- lohexol	45	45	1074	1220	1472	1475	1555

decision to give a good diagnosis.

Fig. 6 shows the periodic graph of iodine in a healthy blood medium that found an oxidation capacity of a peak current of -0.8 V, so iodine acts as an oxidizing reagent [16].

Fig. 7 illustrated the cyclic voltammogram of iodine nanoparticles in blood medium to fine the effect of nanoparticles on the blood components of rabbit

In this study, the rabbit was used in vivo study by CT-Scan with iodine nanoparticles of contrast medium as an alternative of iodine solution, the

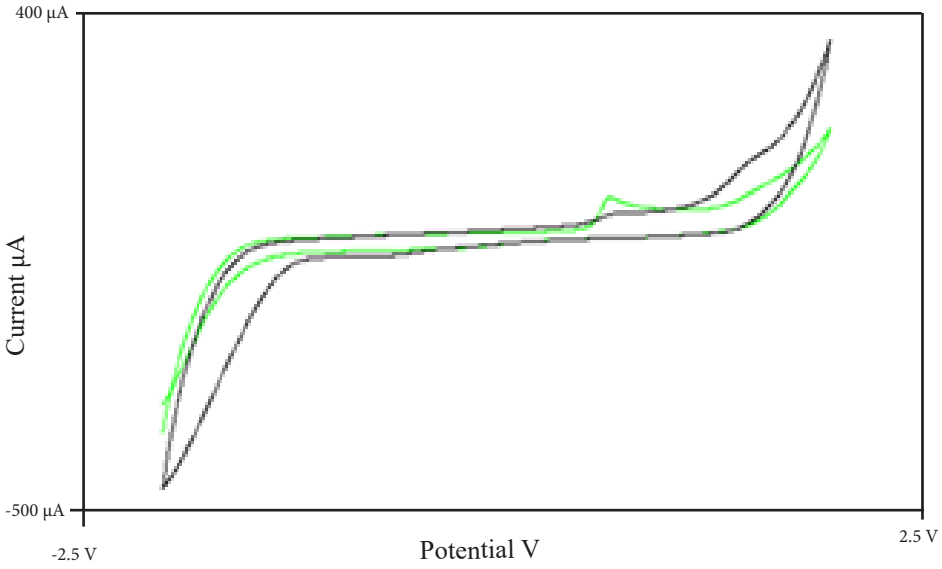

Fig. 6. Cyclic voltammogram of iodine solution in blood medium on glassy carbon electrode as working electrode versus Ag/AgCl as reference electrode at 0.1 Vsec-1

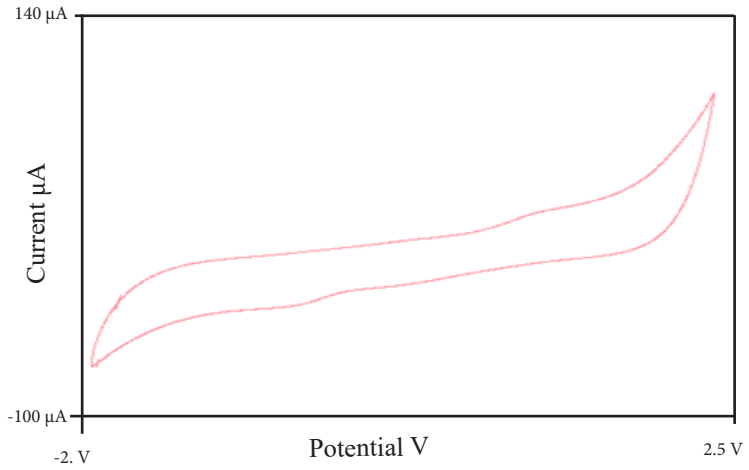

Fig. 7. Cyclic voltammogram of iodine nanoparticles solution in blood medium on glassy carbon electrode as working electrode versus Ag/AgCl as reference electrode at 0.1 Vsec-1

imaging of CT for the different rabbit organs.

CONCLUSION

Through the study of the contrast media which used in the CT-Scan device and comparing them to the nano contrast media that given them some physical and chemical properties, it can be concluded that:

1. The results showed by using nanoparticle of iodine, it gives high resolution images with a lower concentration than using in micro-iodine

2. The half-life of the nano iodine in different organs is more than the period in which it remains, which gives a distinctive feature in facilitating the follow-up of important organs such as the heart and blood vessels to identify the problems that afflict them.

3. The nano contrast media are characterized by their ability to give high-definition images without side effects compared to micro-contrast media as

in the iodine solution.

4. The electrochemical study showed that nano iodine solution is an antioxidant compound, as there are no oxidation current peaks in its cyclic voltammogram, but rather reduction current peaks in it, while in the micro-iodine composition, oxidation current peaks appear in the cyclic voltammogram of the iodine in blood medium, which causes blood oxidation, and gives a dangerous toxicity.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

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