

# Advantages of CT nano-contrast agent in tumor diagnosis

## A retrospective study

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### Abstract

The purpose of this retrospective study was to explore the advantages of computed tomography (CT) nano-contrast agent in tumor diagnosis.

A total of 100 patients with malignant tumor who were diagnosed in Shaanxi Province Public Hospital between January 2018 and January 2019 were included in this retrospective study. They were randomly divided into observation and control groups with 50 patients in each group. The patients in the observation group used new type of nano-contrast agent for examination, and the patients in the control group used traditional iohexol contrast agent for examination. The detection rate, misdiagnosis rate, and incidence of adverse reactions were observed. In addition, single photon emission computed tomography or CT scan was performed on patients to observe the radioactive concentration.

The detection rate was 100% in the observation group and 84% in the control group, and the difference between the 2 groups was statistically significant ( $\chi^2=8.763$ ,  $P=.001$ ). The incidence of adverse reactions was 2% in the observation group and 30% in the control group, and the difference between the 2 groups was significantly different ( $\chi^2=12.683$ ,  $P=.000$ ). The radioactive concentration in the observation group was markedly higher than that in the control group ( $t=19.692$ ,  $P=.001$ ).

The use of CT nano-contrast agent in tumor diagnosis had higher detection rate of tumor and radioactive concentration, and it had lower misdiagnosis rate and adverse reaction rate than traditional iohexol contrast agent.

**Abbreviations:** CT = computed tomography, SPECT = single photon emission computed tomography, T/NT = tumor and nontumor.

**Keywords:** computed tomography nano-contrast agent, traditional iohexol contrast agent, tumor diagnosis

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YZ and YS contributed equally.

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This study was approved by the ethics committee of Shaanxi Province Public Hospital. Each patient signed an informed consent form. A total of 100 patients with malignant tumor who were diagnosed in our hospital between January 2018 and January 2019 were included in this study.

Consent for publication is not applicable.

Availability of data and material is not applicable.

The datasets generated during and/or analyzed during the current study are publicly available.

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## 1. Introduction

Computed tomography (CT) is one of the noninvasive clinical diagnostic methods, which has the advantages of wide application range, high efficiency and low cost.<sup>[1]</sup> In recent years, with the continuous advancement of medical standards, the application of CT enhanced examination has become more and more common. Many tumor diseases need to be diagnosed by enhanced examinations.<sup>[2]</sup>

In particular, exogenous CT contrast agents are required for CT enhanced examination. At present, iohexol is the most commonly used contrast agent in clinic.<sup>[3]</sup> However, the short circulating time of iodine contrast agent is not conducive to its wide application.<sup>[4]</sup> In addition, although iodides are usually safe, serious adverse reactions sometimes occur due to their high osmolality and viscosity.<sup>[5]</sup>

In order to reduce the occurrence of anaphylaxis, medical researchers have made continuous efforts to develop a new tungsten oxide nano-contrast agent.<sup>[6]</sup> Some studies have shown that it can effectively reduce the incidence of allergic reactions in patients.<sup>[7]</sup> The main purpose of this retrospective study was to explore the advantages of tungsten oxide nano-contrast agent in tumor diagnosis. We hypothesized that tungsten oxide nano-contrast agent could improve tumor detection rate and reduce the incidences of adverse reactions and misdiagnosis in comparison with traditional iohexol contrast agent.

## 2. Patients and methods

### 2.1. Patients

This study was approved by the ethics committee of Shaanxi Province Public Hospital. Each patient signed an informed consent form. A total of 100 patients with malignant tumor who were diagnosed in our hospital between January 2018 and January 2019 were included in this study. All the patients were diagnosed as tumor patients by pathology. Inclusion criteria<sup>[8,9]</sup>: all patients were confirmed to be malignant tumors by pathology; and all patients had no symptoms such as cold, fever, dizziness, and nausea within 2 weeks before the examination. Exclusion criteria<sup>[10,11]</sup>: patients with severe heart, liver and other important organ failure; patients with severe cognitive dysfunction, unable to cooperate with the examination; and patients with infectious diseases such as hepatitis B.

### 2.2. Diagnostic method

The patients were randomly divided into observation group and control group with 50 patients in each group. The patients in the observation group used new type of nano-contrast agent for examination, and those in the control group used traditional iohexol contrast agent for examination. All patients were scanned by 64-slice CT with the thickness of 1 mm.<sup>[12]</sup> When single photon emission computed tomography (SPECT)/CT scanning was performed, technetium salt solution<sup>[13]</sup> was injected into the new type of tungsten oxide nanoparticle contrast agent and iohexol contrast agent. After being thoroughly mixed, they were placed at 95°C and heated for 30 min, respectively. When the temperature drops to room temperature, they were injected into the patients.<sup>[14]</sup> After imaging, SPECT/CT postprocessing software was used to draw the region of interest. The total count of 4 pixels were taken to calculate the tumor and nontumor (T/NT) ratio,<sup>[15]</sup> so as to compare the radioactive concentration.

### 2.3. Evaluation standard

The detection rate, misdiagnosis rate, incidence of adverse reactions and radioactive concentration of the patients in the 2 groups were compared. Mild anaphylaxis<sup>[16]</sup>: pruritus, urticaria, dizziness, and nausea. Moderate anaphylaxis<sup>[17]</sup>: systemic skin redness, swelling, pruritus, and urticaria, and mild laryngeal edema. Severe anaphylaxis<sup>[18]</sup>: severe laryngeal edema, dyspnea, and shock. Detection rate: the positive rate of tumor examination. Different contrast agents have different development conditions and diagnosis conditions, so the detection rate is different.

### 2.4. Statistical analysis

Statistical analysis was made by software SPSS 20.0 (International Business Machines, corp., Armonk, NY). Count data were expressed as percentage (%), and  $\chi^2$  test was used to assess the differences between the 2 groups. Measurement data were expressed as means  $\pm$  standard deviation, and *t* test was used to assess the differences between the 2 groups. Five radiologists participated in the result analysis of detection rate. Differences were considered statistically significant when  $P < .05$ .

## 3. Results

### 3.1. The general clinical data

In this retrospective study, all participants concluded the study. There were 50 patients in the observation group, including 22 males and 28

females, with an average age of  $(56.85 \pm 16.23)$  years. Among them, there were 15 with lung cancer, 13 with liver cancer, 8 with prostate cancer and 14 with ovarian cancer. There were 50 patients in the control group, including 29 males and 21 females, with an average age of  $(58.62 \pm 15.69)$  years. Among them, there were 18 with lung cancer, 15 with liver cancer, 10 with prostate cancer and 7 with ovarian cancer. There was no statistical significance in age, gender, and tumor type between the 2 groups ( $P > .05$ ).

### 3.2. The detection rates and misdiagnosis rates

The detection rate was 100% (50/50) in the observation group and 84% (42/50) in the control group, and the difference between the 2 groups was statistically significant ( $\chi^2 = 8.763$ ,  $P = .001$ ). Furthermore, the misdiagnosis rate was 0% (0/50) in the observation group and 16% (8/50) in the control group, and the difference between the 2 groups was statistically significant ( $\chi^2 = 8.759$ ,  $P = .001$ ). The results were shown in Table 1.

### 3.3. The incidences of adverse reactions

The overall incidence of adverse reactions in the observation group was 2% (1/50), and only 1 patient had mild adverse reactions. The overall incidence of adverse reactions in the control group was 30% (15/50). Twelve patients had mild adverse reactions, 2 patients had moderate adverse reactions, and 1 patient had severe adverse reactions. The difference between the 2 groups was statistically significant ( $\chi^2 = 12.683$ ,  $P = .000$ ) (Table 2).

### 3.4. The radioactive concentration

The results showed that T/NT ratio in the observation group was  $3.26 \pm 0.27$ , and that in the control group was  $1.79 \pm 0.23$  (Table 3). The difference between the 2 groups was statistically significant ( $t = 19.692$ ,  $P = .001$ ).

## 4. Discussion

In recent years, the incidence of tumors has been increasing year by year, and the population is becoming younger and younger.<sup>[19]</sup> However, with the continuous advancement of medical standards, the tumor is not an incurable disease. If many malignant tumors are treated promptly, the 5-year survival rate is generally higher.<sup>[20]</sup> Therefore, early detection and diagnosis of tumors play very significant roles in the prognosis of patients.

CT enhanced examination is a noninvasive examination with a high detection rate for tumors, which is close to the detection rate of gold standard pathological examination.<sup>[21]</sup> CT enhanced examination is mainly through intravenous injection of contrast agent. The absorption of contrast agent by tumor tissue is higher than that by normal tissue. The tumor can be diagnosed by contrast imaging and accurately located. The accuracy of CT examination mainly depends on the absorption of contrast

**Table 1**

**The detection rate and misdiagnosis rate in the two groups.**

Groups	n	Detection rate (%)	Misdiagnosis rate (%)
Observation group	50	50 (100%)	0
Control group	50	42 (84%)	8 (16%)
$\chi^2$		8.763	8.759
<i>P</i>		.001	.001

**Table 2****The incidences of adverse reactions in the 2 groups.**

Groups	n	Incidence (%)			
		Mild adverse reactions	Moderate adverse reactions	Severe adverse reactions	Overall adverse reactions
Observation group	50	1 (2%)	0	0	1 (2%)
Control group	50	12 (24%)	2 (4%)	1 (2%)	15 (30%)
$\chi^2$		6.621	5.698	4.782	12.683
<i>P</i>		.007	.010	.016	.000

medium by tumor,<sup>[22]</sup> so the choice of contrast medium plays a crucial role in the diagnosis of tumor. As a new type of contrast agent, tungsten oxide nano-contrast agent has the characteristics of high sensitivity, high accuracy and low adverse reaction rate.<sup>[6]</sup> The purpose of this study is to compare the difference between tungsten oxide nano-contrast agent and traditional contrast agent in CT diagnosis for tumor. This study not only explores the detection rate, misdiagnosis rate and adverse reaction rate, but also explores the radioactive concentration of tungsten oxide nano-contrast agent and traditional iohexol contrast agent under SPECT/CT.

Our results show that the overall incidence of adverse reactions is 2% in the observation group and 30% in the control group. Tungsten oxide nanoparticles can be coupled with proteins or biologically active ligands, which can improve their stability and the effectiveness of cell absorption. Therefore, the tungsten oxide nano-contrast agent is more stable than that of iohexol, which is not easy to cause allergic reaction.

In addition, the detection rate is 100% in the observation group and 84% in the control group. The misdiagnosis rate is 0% in the observation group and 20% in the control group. We think that the main reason is that the tungsten oxide nano-contrast agent can be targeted to the tumor site, and the tumor cells have good absorption of tungsten oxide nano-contrast agent, so its detection rate is high, and misdiagnosis rate is low. On the contrary, the normal tissues can also absorb iohexol contrast agent, and the absorption rate of thyroid tumor cells for iohexol is not high, which is easy to be misdiagnosed as other diseases.<sup>[23]</sup> It is also a major reason for the high misdiagnosis rate in the control group.

Moreover, our results suggest that the T/NT value of the observation group is higher than that of the control group. It shows that the radioactive concentration in the observation group is significantly higher than that in the control group, which further explains the reason for the high detection rate of tungsten oxide nanoparticles, making the tumor imaging clearer and diagnosis more sensitive.

Our research filled a gap about new type of nano-contrast agent in domestic research. However, there are also some limitations. Firstly, there are several types of tumor diseases, which are different in the 2 groups. To some extent, it also has a

certain impact on the results. Besides, the evaluation of this study is still largely focused on rates and ignores the image. Furthermore, we have not collected the types of malignant tumors of the study population. The age, gender, and the types of tumors may affect the detection rate. Moreover, the sample size is small. In future, large sample size will be needed.

In conclusion, tungsten oxide nano-contrast agent had the advantages of high accuracy and high sensitivity. It can achieve targeted delivery, effectively reduce the incidence of adverse reactions, and can be widely used in clinical.

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Not applicable.

### Author contributions

YZ and YFZ are responsible for the guarantor of integrity of the entire study, study concepts & design, definition of intellectual content, literature research, clinical studies, experimental studies, data acquisition & analysis, statistical analysis, manuscript preparation & editing & review; JL is responsible for the guarantor of integrity of the entire study, study concepts & design, definition of intellectual content, literature research, clinical studies, experimental studies, data acquisition, statistical analysis, manuscript preparation & editing & review. All authors read and approved the final manuscript.

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**Table 3****The T/NT ratio in the 2 groups.**

Groups	n	T/NT ratio
Observation group	50	3.26 ± 0.27
Control group	50	1.79 ± 0.23
<i>t</i>		19.692
<i>P</i>		.001

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