The differentiation between solitary pulmonary inflammatory lesion and solitary cancer using gemstone spectral imaging (GSI): the correlation with lesion size

LiuHong Zhu

Radiology Department, Xiamen Branch, Zhongshan Hospital, Fudan University

Funan Wang

Radiology department, Xiamen Branch, Zhongshan Hospital, Fudan University

Yanwei Wang

Radiology Department, the Second Affiliated Hospital of Xiamen Medical College

Qihua Cheng

Radiology Department, the Second Affiliated Hospital of Xiamen Medical College

Jianjun Zhou (✉ zsxmfskz@163.com)

Zhongshan Hospital Fudan University

Research

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Abstract

Background: There were still nonnegligible overlaps between lung inflammatory and malignant lesions in morphologic appearance and enhancement pattern using conventional computed tomography (CT) especially when the lesion size was smaller than 3cm, which made misdiagnosis often happen in clinical practice. The study was to verify whether spectral CT parameters can differentiate solitary lung cancer from solitary inflammatory lesions or not, and to find the correlation between GSI parameters and lesion size.

Methods: 102 patients with solitary inflammatory or lung cancer lesions underwent enhanced CT scans with GSI mode. While total of 78 ROIs (region of interest) were finally collected and divided into inflammatory group (group I: $\leq 3\text{cm}$, IA; $>3\text{cm}$, IB) and cancer group (group II: $\leq 3\text{cm}$, IIA; $>3\text{cm}$, IIB) according to their maximum diameter (D_{max}). CT values measured on 40keV and 70 keV monochromatic images ($\text{HU}_{40\text{keV}}$, $\text{HU}_{70\text{keV}}$), effective atomic number (Z_{eff}), iodine concentration (IC), normalized IC (NIC) and slopes of spectral curve (λ_{30} , λ_{40}) were calculated. Intergroup and intragroup comparisons were made using Mann-Whitney U test, and receiver operating characteristic curve (ROC) analysis were done. Correlation analysis was used to find the relationship between D_{max} and GSI parameters.

Results: NIC and λ_{30} under venous phase could distinguish general solitary inflammatory from cancer group. No significant correlation was found between GSI parameters and D_{max} in inflammatory group, while negative correlations were found between them in cancer group. The GSI parameters (except $\text{HU}_{70\text{keV}}$) of group IIA were significantly higher than those of group IIB. When D_{max} was larger than 3cm, there were significant differences between solitary inflammatory group and cancer group in $\text{HU}_{40\text{keV}}$, IC, NIC, λ_{30} and λ_{40} , under both AP and VP, while the AUC for λ_{30} under VP was largest, and the corresponding sensitivity and specificity were 96.32% and 85.71% respectively. However, only the $\text{HU}_{40\text{keV}}$ and $\text{HU}_{70\text{keV}}$ under arterial phase of IIA were significantly higher than those of IA.

Conclusions: Most of quantitative parameters of GSI can contribute to the differentiation between solitary lung cancer from solitary inflammatory lesions when D_{max} is larger than 3cm, while only few parameters are meaningful when D_{max} is smaller than 3cm.

Background

Up to 2.1 million new cases of lung cancer occurred globally in 2018, ranking first among all cancer types. Although the survival rates for all cancers have improved in recent years, lung cancer survival remains at a relatively low level, which in men was about 16.8% and 25.1% in women [1–3]. Early surgery and chemotherapy, which were based on accurate diagnosis, have been shown to be effective treatment techniques in most patients with lung cancer. However, the misdiagnosis rate of solitary pulmonary lesions was relatively high in clinical practice, and remained a hot topic among researchers.

Evaluation of the solitary pulmonary lesions remains a challenge in clinical. Among all imaging examination tools, conventional contrast-enhanced CT scan is still the most important one for the patient with solitary pulmonary lesion [4]. It can offer the morphological signs, inner densities and enhancement patterns to characterize pulmonary lesions. However, there is considerable overlap between inflammatory and malignant masses in morphologic appearance and enhancement pattern, especially when the size of lesion is less than 3 cm, making it difficult to produce an accurate diagnosis in clinical practice.

With the rapid development of dual-energy spectral CT imaging, the researchers turned to explore its potential in the diagnosis of solitary pulmonary lesions. As one of dual-energy spectral CT imaging techniques [5], GSI was based on rapid switching between high and low voltage (80kVp and 140kVp) during a single rotation of the tube. It can acquire multiple parameters, such as monochromatic spectral images at energy levels ranging from 40 to 140 keV, material decomposition images, effective atomic number and spectral HU curve [6, 7]. Specially, iodine concentration measured on iodine-enhanced images, which is considered to be comparable to the real value of enhancement, could reflect the blood supply of pulmonary lesions, and is essential for differential diagnosis [8, 9]. The spectral CT imaging has been applied to multiple studies, such as non-small cell lung cancer (NSCLC) subtype differentiation [9, 10], gastric cancer evaluation [11, 12] and hepatocellular cancer differentiation [13–15], evaluation of lymph nodes preoperatively [16] and differentiation between benign and malignant solitary pulmonary nodules (SPNs) [17], etc.. Several researchers reported that spectral CT imaging with quantitative parameters may be useful in the differentiation of solitary lung cancer from solitary inflammatory lesions [18–19], however, they haven't taken the lesion size into account. Therefore, the aim of our study was to verify whether spectral CT parameters under GSI mode can differentiate solitary lung cancer from solitary inflammatory lesions, and clarify the correlation between GSI parameters and the lesion size.

Methods

Study population and groups

This prospective study was reviewed and approved by the Medical Ethics Committee of the Second Affiliated Hospital of Xiamen Medical College (approval No. 2016011) and written informed consent was obtained from all subjects prior to the examination. A total of 102 patients with suspected solitary pulmonary lesions were enrolled in our study during past eight months.

Patients were selected according to the following inclusion criteria: (a) presence of a solitary pulmonary lesion, (b) no contraindications to the administration of iodinated contrast material, and (c) were able to finish the procedures cooperatively. They were underwent dual-phase CT scanning under GSI mode. And seventeen patients were excluded due to : (a) the lesion was combined with cavitation and significant calcification (n = 8), (b) absence or inadequate pathologic diagnosis (n = 9), (c) unsatisfactory image quality because of artifacts caused by contrast material (n = 3), and (d) ground glass nodules and /or nonsolid nodules (n = 4). Thus, 78 patients (49 men, 28 women, average age, 59.1 ± 7.3 years) were finally included in our study.

Seventy-eight lesions in all patients were divided into two groups based on the pathologic results. Lung cancer group (n = 47) was composed of adenocancer (n = 28) and squamous cell cancer (n = 19). Lung inflammatory group (n = 31) was composed of granuloma (n = 9) and pneumonia (n = 22). Taking 3 centimeter as the cutoff value for the maximum diameter of lesions, the above each group can be divided into two subgroups respectively (Table 1).

Table 1. Characteristics of lesions

Diagnosis	D _{max} ≤3cm	D _{max} >3cm
Lung inflammatory (Group I, n=31)	Group <i>IA</i> (n=17, 55%, $\overline{D_{max}}$:1.87±0.61cm) Granuloma (n=11) Pneumonia (n=6)	Group <i>IB</i> (n=14, 45%, $\overline{D_{max}}$: 4.83±1.12 cm) Granuloma (n=10) Pneumonia (n=4)
Lung cancer (Group II, n=47)	Group <i>IIA</i> (n=20, 43%, $\overline{D_{max}}$: 2.13±0.28 cm) Adenocancer (n=12) Squamous cell cancer (n=8)	Group <i>IIB</i> (n=27, 57%, $\overline{D_{max}}$: 5.31±1.55 cm) Adenocancer (n=16) Squamous cell cancer (n=11)

Note: $\overline{D_{max}}$ means the average value of D_{max} of a specific group.

Imaging techniques

Computed tomography examinations were performed using two-phase enhanced CT scanning on a spectral CT scanner (GE Discovery 750HD CT ; GE Healthcare, Milwaukee, WI, USA) under GSI mode. Patients were injected with the given volume (1.1 ml/kg of body weight) of nonionic contrast media named loversol (320 mg I/ml, GE healthcare) through venous access. The injection flow rate was 3-3.5 ml/s, followed by 30 ml saline with same rate. When the net CT value of descending aorta increased by 100HU, the arterial phase (AP) scanning was triggered (about 22 ~ 28 s after the start of contrast medium injection). The venous phase (VP) scanning was 40 s delay after the AP. The GSI scanning parameters were: scan range including the entire chest, helical tube rotation time 0.8 seconds, helical pitch 1.375:1, tube current of 260 mA, slice thickness of 1.25 mm and spacing of 1.25 mm. The CT dose index volume (CTDI_{vol}) for each phase under GSI mode was 7.37 mGy. A dataset of monochromatic images at energies ranging from 40 to 140 keV was generated, which can be analyzed with GSI Volume Viewer software package at AW4.6 workstation (GE Healthcare).

Images analysis

Two radiologists (YW.W and QH.C with 7 and 22 years of experience in chest CT diagnosis respectively), who were blinded to pathologic diagnosis, interpreted and analyzed the images independent of each

other.

(a). Firstly, raw data containing both AP and VP of each patient were loaded using GSI Volume Viewer software simultaneously to ensure the size, shape and location of regions of interest (ROIs) afterwards were the same on both AP and VP to the greatest extent.

(b). After reviewing the lesion manifestations, three ROIs were placed at the upper, middle (maximum section) and lower slices of the lesion respectively. The ROIs were outlined as large as possible on the condition of avoiding necrosis, vessels and bronchi. And the average values of the three represented the measurement.

(c). Outline a round ROI on descending aorta at the carina level.

(d). Measured the maximum diameter ($D_{\max}$) of each lesion to represent the lesion size.

For each ROI, CT values measured on 40 keV and 70 keV monochromatic images ($HU_{40\text{keV}}$, $HU_{70\text{keV}}$), effective atomic number (Z_{eff}) and iodine concentration (IC) measured on iodine/water based material decomposition image under two phases were obtained. Normalized iodine concentration (NIC) and slopes of the spectral HU curve (λ_{30} , λ_{40}) under two phases were calculated. The NIC was defined as the IC ratio between lesion and descending aorta ($\text{NIC} = \text{IC}_{\text{lesion}} / \text{IC}_{\text{aortic}}$). The λ_{30} and λ_{40} were calculated as $|HU_{40\text{keV}} - HU_{70\text{keV}}|/30$, and $|HU_{40\text{keV}} - HU_{80\text{keV}}|/40$ respectively. Above seven parameters of each phase were used in our study.

Statistical analysis

The parameters were expressed as mean $\pm$ standard deviation. All the data were test for the normality before two sample t-test comparisons. When the data did not meet the normality, Mann-Whitney U test was used to statistically compare these parameters between groups. Group I and II were compared to find out whether the GSI parameters were useful in their differentiation diagnosis. To test the influence of lesion size to the GSI parameters, group IA and IB, IIA and IIB were compared, and the correlation between $D_{\max}$ and GSI parameters were done. Also, we compared group IA and IIA, IB and IIB to verify the performance of GSI parameters in the distinguishing lung cancer and lung inflammatory when the lesion size was lower and higher than 3 cm respectively. ROC analysis about the performance of these parameters were done. P value < 0.05 was considered to indicate a significant difference. All statistical analyses were performed using SPSS (Version 25.0; Chicago, IL, USA) and Prism (Version 8.3; Graphpad Software; San Diego, CA, USA) software.

Results

General comparison

The solitary lung inflammatory group and lung cancer group were compared in Table 2. There were no significant differences in $HU_{40\text{keV}}$, $HU_{70\text{keV}}$, Z_{eff} at both AP and VP between general solitary inflammatory

group and lung cancer group. While the IC, NIC λ_{30} , λ_{40} under VP and λ_{30} under AP of lung cancer group were significantly lower than those of inflammatory group. The ROC curves for predicting solitary inflammatory from cancer based on these indices were compared (Fig. 1), and the AUC of λ_{30} under VP were highest (AUC = 0.74).

Table 2

The GSI parameters for differentiating general solitary lung inflammatory and lung cancer lesions

Group		HU _{40kev} (HU)	HU _{70kev} (HU)	Z _{eff}	IC (*100 µg/ml)	NIC	λ_{30}	λ_{40}
AP	Inflammatory	108.36 ± 43.84	49.42 ± 10.94	8.22 ± 0.3	10.49 ± 5.38	0.11 ± 0.05	1.89 ± 1.07	1.67 ± 0.87
	Cancer	104.24 ± 33.76	53.53 ± 12.96	8.14 ± 0.22	9.18 ± 3.87	0.10 ± 0.03	1.34 ± 0.53	1.46 ± 0.59
	<i>P value</i>	<i>0.834</i>	<i>0.122</i>	<i>0.279</i>	<i>0.385</i>	<i>0.294</i>	<i>0.030*</i>	<i>0.377</i>
	<i>AUC</i>	/	/	/	/	/	<i>0.65</i>	/
VP	Inflammatory	123.46 ± 43.10	55.16 ± 22.53	8.28 ± 0.29	12.47 ± 4.88	0.48 ± 0.24	2.13 ± 0.85	1.97 ± 0.72
	Cancer	114.38 ± 30.26	57.24 ± 10.99	8.17 ± 0.20	10.16 ± 3.33	0.33 ± 0.10	1.45 ± 0.49	1.59 ± 0.54
	<i>P value</i>	<i>0.242</i>	<i>0.523</i>	<i>0.09</i>	<i>0.035*</i>	<i>0.011*</i>	<i>< 0.01*</i>	<i>0.012*</i>
	<i>AUC</i>	/	/	/	<i>0.64</i>	<i>0.67</i>	<i>0.74</i>	<i>0.67</i>
<i>Note: AP, arterial phase; VP, venous phase; HU_{40kev}/ HU_{70kev}, the CT number on the 40kev/70kev monochromatic image; Z_{eff}, effective atomic number; IC, iodine concentration; NIC, normalized iodine concentration; λ_{30} / λ_{40}, the slope of spectral curve; * means $p < 0.05$.</i>								

The intra-group comparison of GSI parameters and correlation analysis between D_{max} and GSI parameter

The inflammatory group (group I) was divided into two subgroups (group IA: D_{max} ≤ 3 cm) and (group IB: D_{max} > 3 cm). No significant differences were found between the GSI parameters of group IA and IB under both AP and VP (Table 3). The Pearson correlation between D_{max} and GSI parameters of solitary inflammatory group were also done. No significant correlation between D_{max} and any GSI parameters were found (p (two tailed) > 0.05) under both AP and VP, and Fig. 2 showed the scatter chart of GSI parameters plotted with D_{max} under VP.

Table 3

The difference between subgroup IA ($D_{\max} \leq 3$ cm) and subgroup IB ($D_{\max} > 3$ cm) in GSI parameters of solitary lung inflammatory

Group		HU _{40kev} (HU)	HU _{70kev} (HU)	Z _{eff}	IC (*100 µg/ml)	NIC	λ_{30}	λ_{40}
AP	IA (n = 17)	94.81 ± 41.06	46.66 ± 10.81	8.19 ± 0.31	9.67 ± 4.95	0.10 ± 0.05	1.79 ± 0.99	1.51 ± 0.77
	IB (n = 14)	124.81 ± 42.77	52.78 ± 10.52	8.26 ± 0.33	11.48 ± 5.88	0.13 ± 0.05	2.01 ± 1.19	1.88 ± 0.97
	<i>P value</i>	<i>0.53</i>	<i>0.059</i>	<i>0.92</i>	<i>0.625</i>	<i>0.297</i>	<i>0.681</i>	<i>0.336</i>
VP	IA (n = 17)	113.44 ± 43.70	50.50 ± 27.75	8.28 ± 0.24	11.42 ± 3.96	0.40 ± 0.16	1.91 ± 0.78	1.81 ± 0.63
	IB (n = 14)	135.62 ± 40.58	60.82 ± 12.68	8.28 ± 0.36	13.76 ± 5.68	0.59 ± 0.29	2.39 ± 0.88	2.16 ± 0.79
	<i>P value</i>	<i>0.100</i>	<i>0.161</i>	<i>0.860</i>	<i>0.186</i>	<i>0.064</i>	<i>0.084</i>	<i>0.100</i>

For the cancer group (group II), it was also divided into two subgroups (group IIA: $D_{\max} \leq 3$ cm) and (group IIB: $D_{\max} > 3$ cm). Significant differences were found between GSI parameters of group IIA and IIB under both AP and VP except parameter HU_{70kev} (Table 4). The Pearson correlation between $D_{\max}$ and GSI parameters of solitary cancer group were also done. Significantly negative correlation between $D_{\max}$ and any GSI parameters (except HU_{70kev}) were found (p (two tailed) < 0.05) under both AP and VP, and Fig. 3 showed the scatter chart of GSI parameters changed with $D_{\max}$ under VP.

Table 4

The difference between subgroup IIA (≤ 3 cm) and subgroup IIB (> 3 cm) in GSI parameters of solitary lung cancer

Group		HU _{40kev} (HU)	HU _{70kev} (HU)	Z _{eff}	IC (*100 µg/ml)	NIC	λ_{30}	λ_{40}
AP	IIA (n = 20)	120.38 ± 30.32	56.60 ± 12.17	8.25 ± 0.22	10.97 ± 3.94	0.11 ± 0.03	1.57 ± 0.56	1.73 ± 0.61
	IIB (n = 27)	92.29 ± 31.55	51.26 ± 13.27	8.06 ± 0.19	7.86 ± 3.29	0.09 ± 0.03	1.16 ± 0.44	1.26 ± 0.49
	<i>P value</i>	0.003*	0.149	0.002*	0.009*	0.022*	0.011*	0.009*
VP	IIA (n = 20)	133.07 ± 25.57	59.58 ± 7.66	8.27 ± 0.21	12.13 ± 3.30	0.39 ± 0.09	1.76 ± 0.48	1.94 ± 0.53
	IIB (n = 27)	100.54 ± 25.97	54.02 ± 10.93	8.09 ± 0.16	8.70 ± 2.55	0.29 ± 0.08	1.22 ± 0.35	1.33 ± 0.39
	<i>P value</i>	< 0.001*	0.093	< 0.004*	< 0.001*	< 0.001*	< 0.001*	< 0.001*
<i>Note: * means $p < 0.05$.</i>								

The inter-group comparisons between subgroup IA and IB, IIA and IIB under two phases

Significant differences can be found in HU_{40kev} and HU_{70kev} under AP between lung inflammatory and cancer when the D_{max} of a solitary lesion was no larger than 3 cm (Table 5, Fig. 4, Fig. 5). The AUC, sensitivity and specificity were 0.72, 95.0% and 58.8% for HU_{40kev} under AP, and 0.74, 75.0%, 82.4% for HU_{70kev} under AP. When the D_{max} of a solitary lesion was larger than 3 cm, the HU_{40kev}, IC, NIC, λ_{30} and λ_{40} under both AP and VP of the inflammatory group were significantly higher than those of the cancer group (Table 5, Fig. 4, Fig. 6). The ROC analysis (Fig. 7) showed that the AUC, sensitivity and specificity for λ_{30} under VP performed best (AUC 0.90, sensitivity 96.32% and specificity 85.71%).

Table 5
The comparison of GSI parameters between group IA and IB, group IIA and IIB

Group		HU _{40kev} (HU)	HU _{70kev} (HU)	Z _{eff}	IC (*100 µg/ml)	NIC	λ ₃₀	λ ₄₀
AP	IA (n = 17)	90.69 ± 43.25	46.66 ± 10.81	8.19 ± 0.31	9.67 ± 4.95	0.10 ± 0.05	1.79 ± 0.99	1.51 ± 0.77
	IIA (n = 20)	120.38 ± 30.32	56.60 ± 12.17	8.25 ± 0.22	10.97 ± 3.94	0.11 ± 0.03	1.57 ± 0.56	1.73 ± 0.61
	<i>P value</i>	0.026*	0.011*	0.517	0.326	0.557	0.752	0.297
	<i>AUC</i>	0.71	0.74	/	/	/	/	/
	IB (n = 14)	124.81 ± 42.77	52.78 ± 10.52	8.26 ± 0.33	11.48 ± 5.88	0.13 ± 0.05	2.01 ± 1.19	1.88 ± 0.97
	IIB (n = 27)	92.29 ± 31.55	51.26 ± 13.27	8.06 ± 0.19	7.86 ± 3.29	0.09 ± 0.03	1.16 ± 0.44	1.26 ± 0.49
	<i>P value</i>	0.014*	0.734	0.037*	0.042*	0.045*	0.007*	0.026*
	<i>AUC</i>	0.74	/	0.70	0.70	0.69	0.75	0.71
VP	IA (n = 17)	113.44 ± 43.70	50.50 ± 27.75	8.28 ± 0.24	11.42 ± 3.96	0.40 ± 0.16	1.91 ± 0.78	1.81 ± 0.63
	IIA (n = 20)	133.07 ± 25.57	59.58 ± 7.66	8.27 ± 0.21	12.13 ± 3.30	0.39 ± 0.09	1.76 ± 0.48	1.94 ± 0.53
	<i>P value</i>	0.074	0.244	0.892	0.341	0.598	0.869	0.311
	IB (n = 14)	135.62 ± 40.58	60.82 ± 12.68	8.28 ± 0.36	13.76 ± 5.68	0.59 ± 0.29	2.39 ± 0.88	2.16 ± 0.79
	IIB (n = 27)	100.54 ± 25.97	54.02 ± 10.93	8.09 ± 0.16	8.70 ± 2.55	0.29 ± 0.08	1.22 ± 0.35	1.33 ± 0.39
	<i>P value</i>	0.001*	0.026*	0.067	0.002*	0.001*	< 0.001*	< 0.001*
<i>AUC</i>		0.82	0.71	/	0.79	0.81	0.90	0.85
Note, IA: lung inflammatory ≤ 3 cm; IB: lung inflammatory > 3 cm; IIA: lung cancer ≤ 3 cm; IIB: lung cancer > 3 cm; * means p < 0.05.								

Discussion

The solitary inflammatory and cancer were two common kinds of lung lesions in the clinical practice. However, due to the similarity of their manifestations in conventional CT, the differentiation between them was difficult for radiologists. In our study, we investigated the potential of quantitative parameters derived from monochromatic images and material decomposition images (water-iodine) provided by gemstone

spectral CT imaging in this field. As we all known, iodine was the main ingredient of contrast medium, which could directly reflect the blood flow and distribution in the intravascular and extracellular spaces of the tissue [18]. The spectral CT can provide both the monochromatic image series from 40 to 140 keV and the material decomposition images. Multiple parameters could derive from spectral CT, such as iodine concentration, spectral curve, effective atomic number and CT value under different keV maps. The iodine concentration or normalized iodine concentration reflects the blood supply of the masses. Spectral curve reflected the dynamic change of measured CT numbers of ROIs against increasing keV values. Each tissue had its characteristic HU curve. The slope is used to evaluate the attenuation characteristics in different tissues.

According to our analysis above, IC, NIC, λ_{30} , λ_{40} under venous phase and λ_{30} under arterial phase of general solitary inflammatory group were significantly higher than solitary lung cancer group, although their AUCs (Table.2) under the ROC curves were not high. The findings were partly consistent with some previous studies [19, 20] about the differences of NIC and λ_{30} between inflammatory and cancer lesions. However, there were no significant differences between these two groups when using the parameters under the arterial phase except λ_{30} . Some reasons could be used to explained this finding. Firstly, the injection flow rate used in our study was 3-3.5 ml/s, while some previous studies [17, 19, 20] set this value to 4–5 ml/s or even higher 6 ml/s. Secondly, the timings for AP and VP were different. We applied the triggering technology in our study to minimize the impact of individual differences instead of the experienced values, and the VP was set 40 s delay after the AP. The scan timing may cause the finding differences among previous studies.

When we took the D_{max} into account, the study revealed some interesting results. In clinical, we usually classified lung lesions less than 3 cm in maximum diameter as nodules, and larger than 3 cm as masses. The inflammatory and cancer groups in our study were also classified into two subgroups respectively. No significant differences were found between the GSI parameters of group IA ($D_{max} \leq 3$ cm) and IB ($D_{max} > 3$ cm) of the inflammatory under both AP and VP. Also, there was no significant correlation between D_{max} and any GSI parameters. Therefore, this may not only indicate that the value of GSI parameters will not change with the lesion size, but also the structure tends to be homogeneous in the solitary lung inflammatory lesion. Proliferation of inflammatory granulation tissue or residual of acute inflammation will form granulomatous inflammation and organizing pneumonia, and the rich and dilatate capillaries of masses are stimulated by inflammation gradually [22, 23]. Our finding was in line with the growth characteristics of lung inflammatory.

For lung cancer group, significant differences were found between GSI parameters of group IIA and IIB under both AP and VP except parameter HU_{70keV} (Table 4). Significantly negative correlation between D_{max} and GSI parameters (except HU_{70keV}) were also found. That was to say, the larger the cancer lesions were, the lower the GSI parameters were. This finding indicated that the structure of solitary lung cancer lesion tends to be inhomogeneous. This finding was in line with the lung malignant tumor growth characteristics. As we all know, malignant tumors tended to grow towards the blood vessels to find

nutrition [24]. In malignant tumors, the establishment of angiogenesis and irregular vascular networks usually appeared, which could not support the rapid growth of tumor. Subsequently, the delivery of oxygen reduced, hypoxic in lung cancer occurred. With the continuous hypoxic, the necrosis might appear, which resulted in the tumor inhomogeneous.

The distinction between solitary lung inflammatory and cancer when the $D_{\max}$ were not larger than 3 cm confused radiologists much using the conventional CT in practice. In our study, $HU_{40\text{kev}}$ and $HU_{70\text{kev}}$ under AP of solitary cancer were significantly higher than those of solitary inflammatory when the $D_{\max}$ was no larger than 3 cm, and the sensitivity and specificity for $HU_{40\text{kev}}$ and $HU_{70\text{kev}}$ under AP were 95.0%, 58.8% and 75.0%, 82.45% respectively. However, significant differences were not found in iodine concentration and the slope of spectral curve between above two groups, which indicated that the blood supplies of solitary lung inflammatory and cancer were close when the $D_{\max}$ were not larger than 3 cm. Nevertheless, our finding showed that GSI parameter might be a new way to distinguish them despite our finding might be affected by several possible factors, such as the subject number, scanning protocol, injection flow rate etc.. When the $D_{\max}$ were larger than 3 cm, the $HU_{40\text{kev}}$, IC, NIC, λ_{30} and λ_{40} under both AP and VP, Z_{eff} under AP and $HU_{70\text{kev}}$ under VP of the inflammatory group were significantly higher than those of the cancer group. And the λ_{30} under VP performed the best (AUC 0.90, sensitivity 96.30% and specificity 85.71%).

This study also had some limitations. First, the number of subjects in subgroups was small. Further collection needs to be performed in the future. Second, we divided the groups using 3 cm as a $D_{\max}$ cutoff, more cutoffs should be used to reveal more findings about the differentiation, especially the characteristics of lesion when their $D_{\max}$ was between 2 cm and 3 cm. We will do more research with a larger number of lesions in the future.

Conclusions

In conclusion, most of quantitative parameters of GSI can contribute to the differentiation between solitary lung cancer from solitary inflammatory lesions when $D_{\max}$ is larger than 3 cm, while only few parameters are meaningful when $D_{\max}$ is smaller than 3 cm .

Abbreviations

GSI, gemstone spectral imaging; CT, computed tomography; Z_{eff} , effective atomic number; IC, iodine concentration; NIC, normalized IC; AP, arterial phase; VP, venous phase; $HU_{40\text{kev}}$, the CT number on the 40kev monochromatic image; $HU_{70\text{kev}}$, the CT number on the 70kev monochromatic image; λ_{30} , $|HU_{40\text{kev}} - HU_{70\text{kev}}|/30$; λ_{40} , $|HU_{40\text{kev}} - HU_{80\text{kev}}|/40$; CTDI_{vol}, CT dose index volume; ROI, region of interest; ROC, receiver operating characteristic curve; NSCLC, non-small cell lung cancer; SPN, solitary pulmonary nodule.

Declarations

Ethics approval and consent to participate

This study was approved by the academic committee at The Second Affiliated Hospital of Xiamen Medical College and written informed consent has been obtained from each patient.

Consent for publication

Not applicable.

Availability of data and materials

Materials are available upon request.

Competing interests

All authors declared that they had no conflicts of interest to disclose.

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Authors' contributions

LiuHong Zhu, Funan Wang: conceptualization, methodology, data acquisition, data analysis and interpretation, writing original draft preparation; Yanwei Wang: data curation, visualization, investigation; Jianjun Zhou and Qihua Cheng: Study supervision, review and revision of manuscript. All authors read and approved the final manuscript.

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Figures

Figure 1

Receive operating characteristic (ROC) curves by using IC, NIC, λ_{30} , λ_{40} under VP and λ_{30} under AP to differentiate solitary inflammatory from cancer.

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Receive operating characteristic (ROC) curves by using IC, NIC, λ_{30} , λ_{40} under VP and λ_{30} under AP to differentiate solitary inflammatory from cancer.

Figure 2

The scatter chart of GSI parameters of the solitary inflammatory group changed with Dmax under VP. Analysis about Pearson linear correlation between Dmax and GSI parameters were done. And p values of all parameters were larger than 0.05, which means the GSI parameters under VP of the solitary inflammatory group will not change with Dmax.

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Figure 3

The scatter chart of GSI parameters of the solitary lung cancer group changed with Dmax under VP. Analysis about Pearson linear correlation between Dmax and GSI parameters were also done. All the parameters except HU70kev had significantly negative correlation with Dmax, which meant that the larger Dmax was, the smaller GSI parameters will be.

Figure 3

The scatter chart of GSI parameters of the solitary lung cancer group changed with Dmax under VP. Analysis about Pearson linear correlation between Dmax and GSI parameters were also done. All the parameters except HU70kev had significantly negative correlation with Dmax, which meant that the larger Dmax was, the smaller GSI parameters will be.

Figure 4

The box-whisker plots for comparisons of GSI parameters of four subgroups under both AP and VP (* means 0.001<p<0.05, **means p<0.001).

Figure 4

The box-whisker plots for comparisons of GSI parameters of four subgroups under both AP and VP (* means $0.001 < p < 0.05$, ** means $p < 0.001$).

Figure 5

Lung CT Images of inflammatory and cancer lesions with Dmax less than 3cm. Plain and spectral CT images under AP from a 74-year-old male with pneumonia (Fig. 1-3, Dmax=1.5cm) which was misdiagnosed as malignant tumor due to its slight lobulated manifestation, and 56-year-old female with adenocarcinoma (Fig. 4-6, Dmax=3.4cm) : axial and coronal or CPR images with pulmonary window (Fig. 7, 8), iodine-based images (Fig. 9, 10) and spectral curves (Fig. 11, 12). HU40kev=68.44HU vs. 168.08HU, IC=9.47 vs. 10.57 (*100 μ g/ml), NIC=0.11 vs. 0.13, λ_{30} =1.85 vs. 2.12.

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Lung CT Images of inflammatory and cancer lesions with Dmax less than 3cm. Plain and spectral CT images under AP from a 74-year-old male with pneumonia (Fig. 1-3, Dmax=1.5cm) which was misdiagnosed as malignant tumor due to its slight lobulated manifestation, and 56-year-old female with adenocancer (Fig. 4-6, Dmax=3.4cm) : axial and coronal or CPR images with pulmonary window (Fig. 1, 4), iodine-based images (Fig. 2, 5) and spectral curves (Fig. 3, 6). HU40kev=68.44HU vs. 168.08HU, IC=9.47 vs. 10.57 (*100 μ g/ml), NIC=0.11 vs. 0.13, λ_{30} =1.85 vs. 2.12.

Figure 6

Lung CT Images of inflammatory and cancer lesions with Dmax larger than 3cm. Plain and spectral CT images under AP from a 35-year-old female suffering from inflammatory granuloma with local fibrosis (1-2, Dmax=3.9cm), which was also misdiagnosed as malignant tumor, and 48-year-old female with adenocancer (5-6, Dmax=3.4cm) : axial and coronal or curved planar reconstruction (CPR) images with pulmonary window (1, 5), iodine-based images (3, 7) and spectral curves (4, 8). HU40kev=121.34HU vs. 59.25HU, IC=17.67 vs. 4.75 (*100µg/ml), NIC=1.03 vs. 0.17, λ_{30} =3.14 vs. 0.75, and λ_{40} =2.80 vs. 0.74.

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Lung CT Images of inflammatory and cancer lesions with Dmax larger than 3cm. Plain and spectral CT images under AP from a 35-year-old female suffering from inflammatory granuloma with local fibrosis (Fig. 1, Dmax=3.9cm), which was also misdiagnosed as malignant tumor, and 48-year-old female with adenocarcinoma (Fig. 2, Dmax=3.4cm) : axial and coronal or curved planar reconstruction (CPR) images with pulmonary window (Fig. 1a, 1b), iodine-based images (Fig. 1c, 1d) and spectral curves (Fig. 1e, 1f). HU40keV=121.34HU vs. 59.25HU, IC=17.67 vs. 4.75 (*100 μ g/ml), NIC=1.03 vs. 0.17, λ_{30} =3.14 vs. 0.75, and λ_{40} =2.80 vs. 0.74.

Figure 7

Receive operating characteristic (ROC) curves by using HU40kev, IC, NIC, λ_{30} , λ_{40} under both AP and VP, Zeff under AP and HU70kev under VP to differentiate solitary inflammatory from cancer when Dmax larger than 3cm. The AUC for λ_{30} under VP was largest, and the corresponding sensitivity and specificity were 96.32% and 85.71% respectively.

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Receive operating characteristic (ROC) curves by using HU40kev, IC, NIC, λ_{30} , λ_{40} under both AP and VP, Zeff under AP and HU70kev under VP to differentiate solitary inflammatory from cancer when Dmax larger than 3cm. The AUC for λ_{30} under VP was largest, and the corresponding sensitivity and specificity were 96.32% and 85.71% respectively.