HOSTED BY
ELSEVIER
CrossMark
Available online at www.sciencedirect.com
ScienceDirect
Radiology of Infectious Diseases 3 (2016) 109–113
www.elsevier.com/locate/jrid

Research article

# Evaluation the activity of alveolar echinococcosis: A comparison between $^{18}$F-FDG PET and spectral CT

Jing Wang [a], Yi Jiang [a], Hao Wen [b], Hu Xiao [a], Ting-ting Li [a], Wenya Liu [a,*]

[a] Imaging Center, The First Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang 830011, China
[b] The First Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang 830011, China

Received 25 November 2015; revised 3 December 2015; accepted 4 December 2015
Available online 12 December 2015

**Abstract**

*Purpose*: To assess the iodine concentration of hepatic alveolar echinococcosis (HAE) using spectral computed tomography (CT) with comparison of [$^{18}$F] fluorodeoxyglucose positron-emission tomography ($^{18}$F-FDG PET), and to estimate the value of spectral CT for evaluation of HAE activity.
*Materials and methods*: 18 patients with histologically confirmed or clinically proved HAE underwent spectral CT and $^{18}$F-FDG PET examinations. After three-phase scanning, the quantitative iodine-based material decomposition images and optimal monochromatic image of spectral CT were reconstructed and iodine concentration (IC) was measured in different organizational structures.
*Results*: $^{18}$F-FDG PET identified increased metabolic activity in the corresponding lesions in 13 patients (13/18, 72.2%). The iodine concentration in marginal zone of lesion were significantly higher than in solid component of lesion and normal liver parenchyma during PVP and VP. The iodine value of edge tissue of the lesion and normal liver and iodine value of normal liver tissues showed statistically significant difference ($P < 0.001$). There was correlation between IC and $SUV_{max}$ in marginal zone of HAE lesion, it was highest during PVP ($r = 0.873$, $p < 0.001$). There was low correlation between CT values and $SUV_{max}$.
*Conclusion*: There was good correlation between spectral CT and $^{18}$F-FDG PET. Spectral CT could be recommended as a more practical tool in the clinical routine.


*Keywords:* Spectral CT imaging; Iodine-based material decomposition; $^{18}$F-FDG PET; Hepatic alveolar echinococcosis; Activity

## 1. Introduction

Hepatic alveolar echinococcosis (HAE) grows in the similar way to malignant tumors [1]. Moreover, it can metastasize through the blood and lymphatic system. Therefore, it brings great harm to human health. Although the traditional imaging for the qualitative diagnosis of HAE is quite valuable, it could not quantitatively evaluate the biological activity of the lesion [2]. Though CT perfusion imaging could better evaluate the blood-supply characteristics of alveolar echinococcosis (AE), it is not suitable for routine examinations due to the high radiation dose and poor reproducibility [3]. Currently, $^{18}$F-FDG PET-CT could be used clinically to directly display the lesion boundaries of AE and evaluate AE's biological activity according to the increased and concentrated radioactive uptake of the lesion [4]. However, PET is not a widely used method in clinical routine in our country since the high cost of patients. Therefore, this study tries using the technique of spectral CT iodine imaging to compare the differences of the iodine values in the solid portion, edge tissue, marginal zone of the lesion and normal liver. Through quantitatively analyzing the iodine concentration of hepatic alveolar echinococcosis. Furthermore, to assess

* Corresponding author. Tel.: +86 13999202977.
*E-mail address:* wenyaliu2002@163.com (W. Liu).
Peer review under responsibility of Beijing You'an Hospital affiliated to Capital Medical University.

http://dx.doi.org/10.1016/j.jrid.2015.12.001

the value of spectral CT for evaluation of HAE activity through comparing with the SUV max values of PET-CT.

## 2. Materials and methods

### 2.1. Subjects

This study was carried out after getting the approval of the Hospital Ethics Committee. Prospective research methods were adopted in this study. From January, 2013 to March, 2014, 33 cases of hepatic alveolar echinococcosis highly suspected patients were prospectively enrolled. These patients should not have any drug treatment experiences, in need of PET-CT and spectral CT, and all patients were pathologically or clinically confirmed to be HAE.18 patients were included in final analysis, which aged between 17 and 59 (an average of $42 \pm 9$,12 men and 6 women). They were from different ethnic groups including Han, Uygur, Kazak and Tibetan. Their disease duration ranged differently from three months to two years.

### 2.2. Methods and scanning parameters

#### 2.2.1. Spectral CT imaging

GE Company's Spectral CT (Discovery CT750HD, GE Healthcare, Mliwaukee, USA) was adopted. All the patients had upper-abdomen routine scan and three-phase enhanced scan (arterial phase (AP), portal venous phase (PVP) and phase (VP)). Scan voltage was 120 kV. The scan voltage was instantaneously switched between high energy (140 kVp) and low energy (80 kVp) at a high speed. Tube current was 600 mA, Tube speed 0.6—0.8 s/r, pitch 0.984, collimating 0.625 mm × 64, Two groups of images were reconstructed. The first group were the images of conventionally mixed energy, whose layer thickness and interval were both 5.00 mm. The other group was the 70 keV monoergic images, whose layer thickness and interval were both 1.25 mm. All the images were reconstructed using the standard algorithm. Enhanced Scan: Lopromide, the iodine contrast agent (300 mgI/mL) 80—100 mL, was injected into the peripheral vein using the pressure injector (3~4 mL/s). The scanning start time of the arterial phase was monitored (SmartPrep technique) and stimulated by the CT values within the hilus hepatis abdominal aorta. The monitoring threshold was 100HU. And it was monitored every two seconds. The scanning would start as soon as the threshold value was reached. The scanning duration for the portal phase was 50—52 s, with a delay period of 90 s.

#### 2.2.2. PET/CT imaging methods

$^{18}$F-FDG was manufactured by the QILING rotary accelerator of the US GE Company, whose radiochemical purity was >95%. The imaging instrument was Discovery VCT PET/CT, which provided by the US GE Company. All the patients investigated fasted 4—6 h before the examination with the peripheral fasting blood-glucose <7 mmol/L. Then 7.4 MBq/kg $^{18}$F-FDG was injected into the peripheral vein using the intravenous bolus injecting technique in a calm state. The patients were asked to drink 800—1000 ml water after the injection 20—30 min. Urinating completely, they drank 300 ml water in order to fully fill their gastrointestinal tracts 1 h later, then PET/CT imaging was carried out. CT Image-acquisition Parameters: Scan voltage was 120 kV, Tube current was 350 mA, the collimation was 0.625 mm × 64, layer thickness was 3.75 mm, interval was 3.75 mm, the tube speed was 0.6 ms/r, pitch 0.983, the scan time was 20—30 s, and the patients examined respired normally. The three-dimensional PET acquisition was performed in the same area that had been scanned by CT. Images were collected from 6 to 8 beds for 2—3 mins for each bed. After the completion of image acquisition, attenuation correction was conducted to PET images using CT data. OSEM was reconstructed to obtain the images of the cross sections, coronal sections, sagittal sections and the integrated images of PET/CT.

### 2.3. Image measurement and analysis

CT spectral image analysis and measurement were both completed on the workstation AW4.6 (GE Healthcare, USA). The dual-energy data were input into GSI Viewer software for analysis. The centre and edge tissue of the lesion, marginal zone of lesion and normal liver (region of interest, ROI) were chosen respectively. All the measuring points should be kept, to the greatest extent, in a straight line. And the calcification that could be distinguished by naked eyes should be avoided. The great vessels, the bile ducts and the areas with obvious hardening artifacts should be avoided as much as possible when measuring the hepatic tissue and the liver parenchyma around the lesion. The size as well as the shape of the region of interest was normalized to be a fixed value. The measuring positions should be as consistent as possible in the three-phase scanning. The CT values as well as the concentration of iodine (water) and water (iodine) of aforesaid four points were measured respectively. All the data were measured three times to obtain the mean values. And the $SUV_{max}$ values of the same areas were also measured (Fig. 1).

Patients' early images and delayed images of PET/CT were collected respectively. Physicians from the Nuclear Medicine Department with PET/CT diagnostic experience were responsible for finding out the normal physiological uptake, the normal variation, artifacts, etc., observing whether there were abnormal FDG concentrated lesiones, sketching the biological boundaries of the lesion and measuring the $SUV_{max}$ of corresponding positions as per the information provided by the energy spectrum CT.

### 2.4. Statistical methods

SPSS 16.0 statistical software and independent-sample t-test were adopted to compare the three-phase iodine values and the CT values of hydatid tissues, edge tissue of the lesion, marginal zone of lesion and normal liver of the three phases.

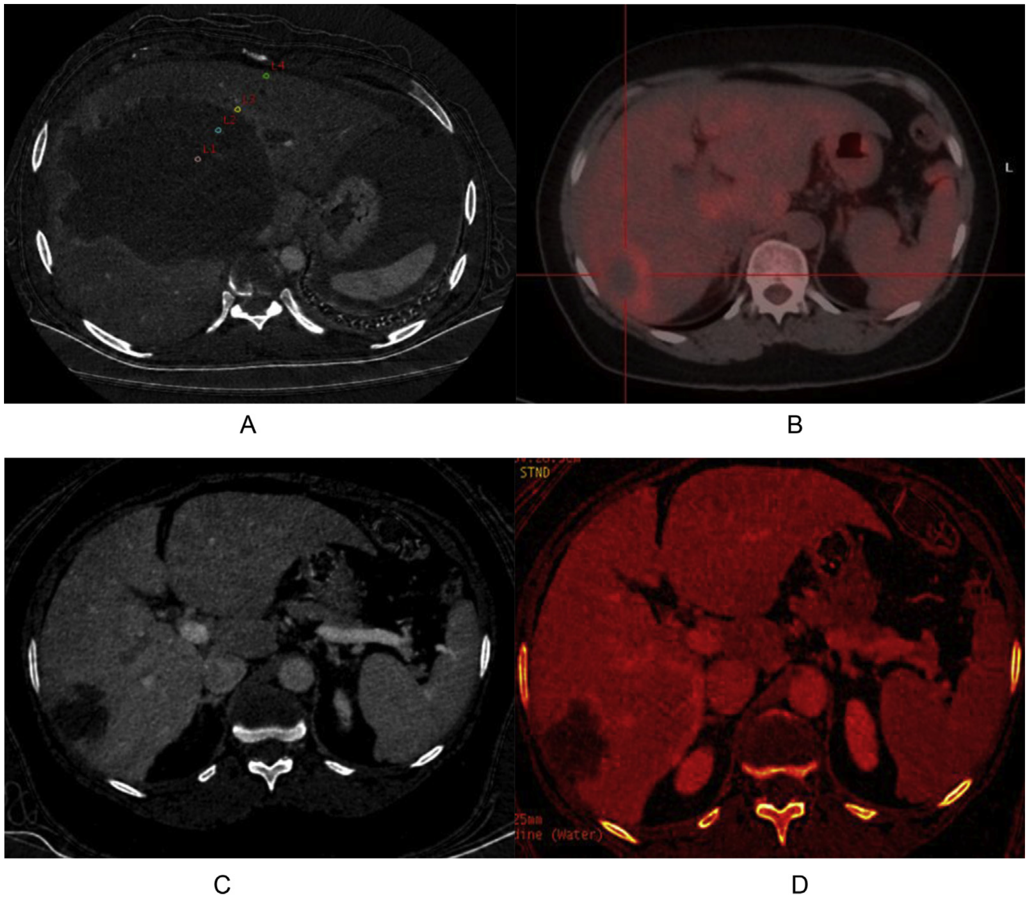


Fig. 1. A: The ROI measure in Iodine-based material decomposition. The centre and edge tissue of the lesion, marginal zone of lesion and normal live ROI were chosen respectively. All the measuring points should be kept, to the greatest extent, in a straight line; B: Positive $^{18}$F-FDG PET findings with "hot pot" were also positive at spectral CT images; C: $^{18}$F-FDG PET findings with "hot pot" were also displayed as continuous or discontinuous ring-like enhancement with the 5–10 mm thickness. The iodine concentration in marginal zone of lesion were significantly higher than in solid component of lesion and normal liver parenchyma; D: Pseudo-color image, abnormal reinforcement ring in marginal zone of lesion shows more clearly.

And $P < 0.05$ indicated that the difference was statistically significant. Sperarman method was used to analyze the correlation between the iodine values and the $SUV_{max}$ values of marginal zone of lesion obtained through the three-phase scanning of HAE.

## 3. Results

### 3.1. The expression of spectral CT and FDG-PTE

$^{18}$F-FDG PET identified increased metabolic activity in the corresponding lesions in 13 patients (13/18, 72.2%). The technique of energy spectral CT iodine imaging could directly reflect the blood-supply characteristics of 11 AE lesions, accounting for 61.1% of the total number of the lesions. Positive $^{18}$F-FDG PET findings with "hot pot" were also positive at spectral CT images which displayed as continuous or discontinuous ring-like enhancement with the 5–10 mm thickness. The extent to which the iodine was concentrated in edge tissue of the lesion in the portal and the venous phases was significantly higher than that in the solid portion of the lesion and the normal hepatic tissue.

### 3.2. Quantitative analysis

The iodine values of the four measuring points including hydatid tissues, edge tissue of the lesion, marginal zone of lesion and normal liver by the three-phase dual-energy enhanced scan were compared. The total iodine values of the four measuring points were all statistically significant. The differences in the iodine values of the lesion center by the three-phase enhanced scan were, however, not statistically significant. The differences in the iodine values of the lesion' edges, marginal zone of lesion and normal liver were of statistical significance in the arterial, portal and venous phases (Table 1).

### 3.3. The correlation

Sperarman was used to compare the correlation between the three-phase iodine values, CT values and $SUV_{max}$ values in marginal zone of lesion. The three-phase iodine values of the lesion's edges were found to be correlated to $SUV_{max}$ values, and the correlation was much higher in the portal phase than in the other two phases (Table 2).

Table 1
The iodine values of different position by the three-phase enhanced scan (mg/ml, $\bar{x}\pm s$).

| Position | N | $\bar{x}\pm s$ | | | F | *P* |
|---|---|---|---|---|---|---|
| | | Arterial phase | Portal venous phase | Venous phase | | |
| Hydatid tissues | 18 | 7.97 ± 1.95 | 11.39 ± 1.39 | 11.8 ± 1.52 | 4.758 | 0.17 |
| Edge tissue of the lesion | 18 | 5.37 ± 4.28 | 13.40 ± 4.70 | 12.29 ± 3.76 | 14.639 | ≤0.01 |
| Marginal zone of lesion | 18 | 8.26 ± 4.48 | 30.82 ± 1.32 | 27.74 ± 1.45 | 158.399 | ≤0.01 |
| Normal liver | 18 | 6.28 ± 2.77 | 26.16 ± 1.43 | 24.16 ± 1.44 | 446.025 | ≤0.01 |

## 4. Discussion

Clinically, hepatic alveolar echinococcosis develops latently and grows in a way similar to liver cancer. The patients clinically treated were mostly in the middle or advanced stage, so they had already lost the opportunity for excision. Anti-hydatid medicine is generally used in clinical treatment. Since there've been no clinical provisions on the period of medication so far, patients usually need long-term or even lifelong medication. Additionally, many patients may have fatigue, leucopenia and other complications, bringing about new clinical problems to patients. Therefore, examining the therapeutic effectiveness of the HAE medicine has become an urgent clinical problem to be solved. Since the advent of PET-CT and its applications in the efficacy evaluation of the radiotherapy and/or chemotherapy of tumors, some scholars have used it to examine the efficacy of the HAE medicine, and received positive results. However, under the basic condition of China, PET equipment has not been widely used yet [5]. Moreover, the examination fees are also too high, especially to those HAE patients living in the agricultural and pasturing areas. Hence, trying using the new technique of energy spectrum CT which is more popular could compensate for or partially replace the functions of PET-CT. This is where the significance of this study lies.

Jing Wang et al. [6] studied the relationship between CTP and MVD of the lesion and found that CTP and MVD were highly correlated to each other, and according to the CTP characteristics of the lesion, HAE's lesions could be divided into the two different types of hypermetabolic and low-metabolic ones, representing the activity within the lesion. However, CTP is not widely used for clinical applications because of its higher radiation dose. Therefore, based on the features of the energy spectrum CT, this study tries using the technique of energy spectrum CT iodine imaging whose radiation dose is similar to that of conventional scanning [7]. Through quantitatively analyzing the measured HAE lesion iodine, the differences of the iodine values in the solid portion of the lesion, edge tissue of the lesion, marginal zone of lesion and normal liver were compared. Furthermore, through comparing with the $SUV_{max}$ values of PET-CT, the significance of energy spectrum CT iodine imaging in evaluating the biological activity of AE is also explored.

The results of this study showed that in the three-phase dual-energy enhanced scan, hydatid tissues, edge tissue of the lesion, marginal zone of lesion and normal liver were statistical significance; The differences of the iodine values in edge tissue of the lesion, marginal zone of lesion and normal liver in the arterial, portal and venous phases were all statistically significant, while the CT values in the same phase and at the same position were of no statistical significance. Furthermore, the blood supply of the fringing tissue in the portal and venous phases was significantly higher than that of all the other three positions, of which the differences were statistically significant. Above mentioned results indicated that the blood supply in the fringing tissue was the most abundant and that the iodine images could reflect the blood-supply characteristics of HAE in the fringing tissue to some extent. Positive $^{18}$F-FDG PET findings with “hot pot” were also positive at spectral CT images which displayed as continuous or discontinuous ring-like enhancement with the 5–10 mm thickness. Compared with evaluating AE's biological activity as per the increased radioactive uptake of the lesion, the results of both methods were highly consistent with each other. The three-phase iodine values, CT values and $SUV_{max}$ values of marginal zone of lesion were measured, and their correlation were compared using the S method. It was found that they were correlated to each other in all of these three phases. And the correlation of iodine values in the portal phase was correlated well. The specific blood-supply features of HAE's fringing tissue were basically consistent with the research outcomes of Jiaqi Li et al. [8] who believed that the iodine distribution in the portal phase could, to some extent, reflect the perfusion features of HAE's blood volume. Its results were compared with MVD. Moreover, PET-CT was considered as the single-phase scan, whose time phase was similar to the portal phase. The differences of the iodine values in the center of the lesion by the three-phase enhanced scan were of no statistical significance, indicating that there was no significant blood supply within HAE's lesion. In combination with HAE's specific histopathological features, the iodine values were thought to be from the microcalcification within the lesion that could not be observed by naked eyes.

Table 2
The correlation between the three-phase iodine values, CT values and $SUV_{max}$ values in the marginal zone of lesion.

| Scan phase | The correlation between the iodine values, and $SUV_{max}$ | | The correlation between the CT values and $SUV_{max}$ | |
|---|---|---|---|---|
| | *r* | *P* | *r* | *P* |
| AP | 0.644 | <0.01 | 0.484 | <0.01 |
| PVP | 0.873 | <0.01 | 0.495 | <0.01 |
| VP | 0.697 | <0.01 | 0.526 | <0.01 |

### *4.1. Limitations of the study*

The deficiency of this study lies in the small sample size which could be enlarged for further research.

## 5. Conclusion

Afore mentioned results indicate that the biological activity of HAE revealed by spectral CT iodine imaging is highly consistent with that of PET-CT, indicating that when PET-CT examination is unavailable to evaluate the activity of the lesion, spectral CT iodine imaging would be a good option for clinical treatment to evaluate the activity of the lesion and the therapeutic effect of the medicine.

## References

[1] Charbonnet PL, Bühler L, Sagnak E, Villiger P, Morel P, Mentha G. Long-term followup of patients with alveolar echinococcosis. Ann Chir 2004;129:337−42.

[2] Reuter SL, Nüssle K, Kolokythas O, Haug U, Rieber A, Kern P, et al. Alveolar liver echinococcosis: a comparative study of three imaging techniques. Infection 2001;29(3):119−25.

[3] Goh V, Dattani M, Farwell J, Shekhdar J, Tam E, Patel S, et al. Radiation dose from volumetric helical perfusion CT of the thorax, abdomen or pelvis. Eur Radiol 2011;21:974−81.

[4] Rolle AM, Soboslay PT, Reischl G, Hoffmann WH, Pichler BJ, Wiehr S. Evaluation of the metabolic activity of Echinococcus multilocularis in rodents using positron emission tomography tracers. Mol Imaging Biol 2015;1:1536−632.

[5] Caoduro Cécile, Porot Clémence, Vuitton Dominique A, Bresson-Hadni Solange, Grenouillet Frédéric, Richou Carine, et al. The role of delayed $^{18}$F-FDG PET imaging in the follow-up of patients with alveolar Echinococcosis. J Nucl Med 2013;54:358−63.

[6] Jing WANG, Bo REN, Wen-ya LIU, Hao WEN, Song QING, Wei-dong XIE, et al. The correlation of CT perfusion imaging with microvessel density and vascular endothelial growth factor in hepatic alveolar Echinococcosis. Chin J Radiol 2011;45:1036−9.

[7] Ming-liang WANG, Xiao-zhu LIN, Fei MIAO, Ke-min CHEN, Xiang-peng ZHENG, Yan-qing HUA, et al. The value of gemstone spectral imaging in analysis of the content of iodine: phantom study. Chin Comput Med Imaging 2011;17:172−5.

[8] LI Jia-qi, JING Yi, LIU Wen-ya, YANG Wen, WANG Hai-tao, GAO Xiao-yan, et al. Dual source CT energy imaging evaluation of liver alveolar hydatid on blood flow imaging and pathologic features. Chin J Radiol, 8: 563−566.