

• Clinical Research •

Analysis of abdominal organ motion using four-dimensional CT

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[Abstract] **Background and Objective:** Accurate individualized measurement of organ motion is the premise of defining internal margin (IM) for abdominal malignancies. This study was to assess the three-dimensional abdominal organ motion caused by respiration using four-dimensional computed tomography (4DCT), and to analyze the association between the movement of diaphragm and abdominal organs. **Methods:** The 4DCT scans of 13 patients with hepatocellular carcinoma were analyzed, five of whom had para-aortic lymph node metastases. The liver, kidneys, pancreas, spleen, and para-aortic lymph nodes were contoured in all 10 respiratory phases of 4DCT scans. The 3D movement of diaphragm and organs was calculated and the relationship between the movement of diaphragm and abdominal organs was analyzed. **Results:** The average diaphragmatic movement was (10.3±4.0) mm with wide interpatient variations. Analysis of the center of the mass of abdominal organs revealed predominant cranio-caudal (CC) movement, with a mean of (10.1±3.9) mm for liver, (9.3±2.9) mm for left kidney, (9.6±4.1) mm for right kidney, (7.6±3.0) mm for pancreas, (10.6±3.3) mm for spleen, and (5.7±1.8) mm for para-aortic lymph nodes. The CC movement of the liver and the right kidney correlated well with the diaphragmatic movement, and no significant differences were observed. There was no significant correlation of the diaphragmatic movement to the CC movement of left kidney, pancreas and spleen. The movement of both kidneys was comparable, however, the movement of one kidney did not predict the movement of the contralateral one. **Conclusions:** The 4DCT scanning can accurately measure abdominal organ motion during whole respiration. The diaphragmatic mobility can approximate the CC movement of liver and right kidney, and the movement amplitude of para-aortic lymph nodes is much smaller than diaphragmatic mobility.

Key words: four-dimensional computed tomography, respiratory mobility, abdominal malignancy, radiotherapy

Accurate target location and reducing the radiation dose to normal tissue is the key issue of precise radiation therapy. According to ICRU 62 Report,¹ the safe border should be expanded based on the clinical target volume (CTV), including the internal margin (IM) and setup margin (SM), to form the planning target volume (PTV). For abdominal tumors, physical exercise such as respiratory, gastrointestinal peristalsis, heart and vascular pulsatility, can cause significant deviation of actual dose comparing with the plan for targets and normal organs, and the impact of the respiratory movement is particularly significant. In radiotherapy of abdominal

tumors, accurately measuring respiratory mobility of abdominal organs individually is the premise to determine the degree of IM. So far, X-ray, ultrasound, repeated CT scans, dynamic magnetic resonance (MRI) and other methods have been reported to measure the mobility of abdominal organs, but have their own shortcomings.

Four-dimensional computed tomography (4DCT) is a new technology emerging in recent years, which applies respiratory phase registration techniques to collect CT images, design plans and perform radiotherapy. It can get CT images containing respiratory motion information, reflecting the movement of organs with different locations and different breathing phases.^{2,5} In this study, three-dimensional mobility of abdominal organs caused by respiratory was measured by 4DCT, and the relationship between diaphragm and the mobility of other organs was further analyzed, which may provide a reference to determine the target for the design of radiotherapy plans.

Materials and Methods

Clinical data. From October 2006 to December 2008, a total of 13 cases diagnosed as primary liver cancer at Sun Yat-sen University Cancer Center were enrolled, five of which had para-aortic lymph node metastasis. In the group there were nine males, four females, with a median age of 43 years old (33-69 years).

Position fixed and 4DCT scanning. Equipments: Discovery ST 16 slice PET / CT and 4D software produced by GE company (Advantage 4D, GE Medical Systems, WI), and real-time positioning management system produced by Varian company.

Position fixed: The patients were in a supine position, with both hands above holding their head, and fixed by a vacuum bag. Before CT positioning, patients received simple respiratory training to keep calm, even breath.

Scanning process: At the upper abdomen, a plastic marker was placed at the midline site with obvious respiratory motion (between xiphoid and navel), and its movement was monitored and

marked by infra-red camera, then transformed into a curve of respiratory rhythm by computer software. After the respiratory curve became smooth, the 4DCT movie mode, i.e. axial continuous, rapid scanning in the same bed position, was used to acquire different respiratory phase CT.^{6,7} The CT scan ranged from 3-4cm above diaphragm to the 4th lumbar spine, with enhancement and slice thickness of 2.5mm. The total scan time was about 90-120s.

4DCT sequencing. After the CT scan, 4D software was used to sequence and reorganize a large number of CT data with different positions and different respiratory phases, and 10 CT sequences of different respiratory phases were obtained, named as CT0% (end of aspiration), CT10%, CT20% (middle of aspiration), CT30%, CT40%, CT50% (end of expiration) .. CT90%. All the CT sequences were transmitted through computer networks to 3DTPS (Philips ADAC Pinnacle3 8.0d) workstation for image registration.

Measurement of respiratory mobility.
Measurement of diaphragmatic mobility. The maximum cranio-caudal displacements of the top right side of diaphragm in respiratory cycles were measured in each case at A-W workstation (Advantage Workstation 4.2).

Measurement of organs respiratory mobility. Normal organs were delineated in CT images of 10 respiratory phases, including liver, bilateral kidneys, pancreas, and spleen, as shown in Fig. 1. Para-aortic lymph node was also delineated to analyze its mobility. In order to ensure the accuracy and repeatability of delineation, all organs were delineated by a doctor at the same window width and level (L=40Hu, W=250Hu). The three-dimensional coordinates of organs geometric centers at different phases were available in the TPS workstation, and the maximum displacements in left-right (LR), anterior-posterior (AP), cranio-caudal (CC) direction of centers in the respiratory cycle were calculated.

Statistical methods. SPSS 12.0 statistical software was used for analysis. One-way ANOVA was used to compare respiratory mobility of different organs. Linear correlation was

performed to analyze the relationship between diaphragm mobility and organs mobility. A p value of less than 0.05 was considered statistically significant.

Results

The mobility of diaphragm and organs.

The average respiratory mobility of diaphragm, liver, kidney, pancreas, spleen and para-aortic lymph node are shown in Table 1. The average cranio-caudal mobility of the top right side of diaphragm was (10.3 ± 4.0) mm (6.1-20.5 mm), with marked individual differences. The mobility of abdominal organs in the CC direction was significantly greater than that in the LR and AP directions. The mobility of liver, kidney and spleen in the CC direction had no significant difference comparing with that of diaphragm ($p = 0.086, 0.525, 0.066, 0.820$). The mobility of pancreas and para-aortic lymph node was less than that of diaphragm ($p = 0.025, 0.042$). The mobility of bilateral kidneys had no significant difference in three-dimensional directions.

The correlation between mobility of diaphragm and organs. Scatter diagram of liver

and diaphragm mobility in the CC direction showed a line trend (Fig.2). Linear correlation analysis showed a high degree of linearity between them ($r = 0.996, p = 0.000$). Similar to liver, right kidney ($r = 0.741, p = 0.004$) and para-aortic lymph node ($r = 0.983, p = 0.003$) also had positive correlation with diaphragm for mobility. Figure 3 shows mobility and correlation of diaphragm, liver, right kidney of all cases. There was no significant correlation of the mobility among left kidney, pancreas, spleen and diaphragm. In addition, the mobility of bilateral kidneys had no correlation ($r = 0.015, p = 0.962$), which suggests that the mobility of one side kidney could not predict that of the other one (Fig. 4).

Table 1 The mean mobility of diaphragm and abdominal organs

Item	LR (mm)	AP (mm)	CC (mm)
Diaphragm	–	–	10.3 ± 4.0
Liver	1.3 ± 0.5	1.2 ± 1.0	10.1 ± 3.9
Left kidney	0.8 ± 0.4	2.1 ± 1.7	9.3 ± 2.9
Right kidney	0.8 ± 0.6	1.7 ± 1.5	9.6 ± 4.1
Pancreas	2.3 ± 1.0	2.2 ± 1.3	7.6 ± 3.0
Spleen	1.2 ± 0.8	1.1 ± 1.4	10.6 ± 3.3
Para-aortic lymph nodes	1.7 ± 0.6	1.8 ± 0.5	5.7 ± 1.8

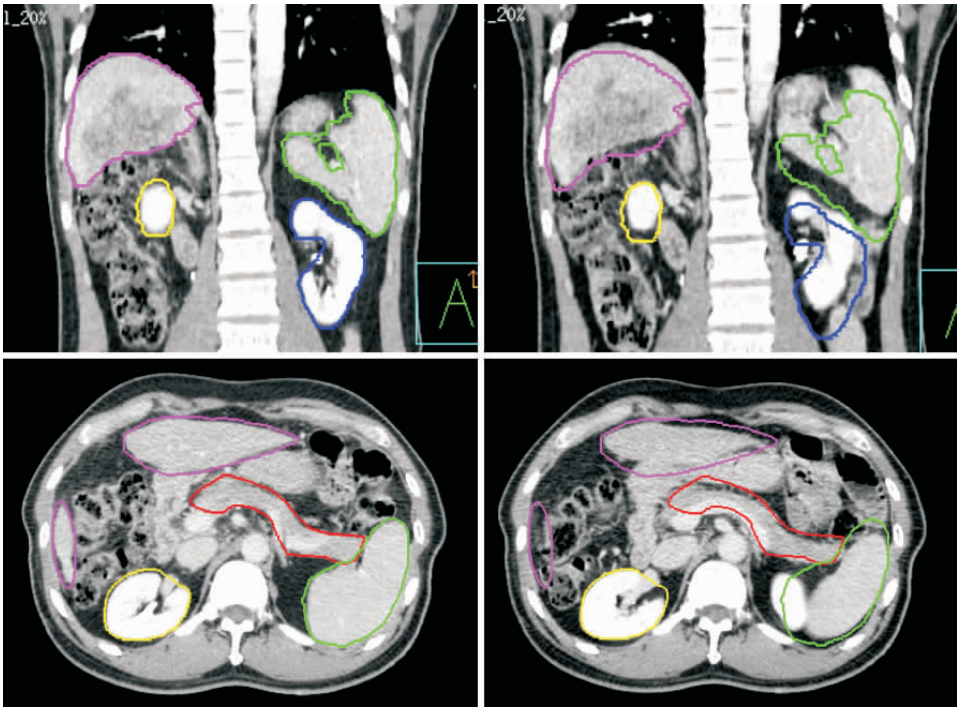


Figure 1 Contouring of abdominal organs on 4DCT scans (Left, 0 phase; Right, 50% phase)

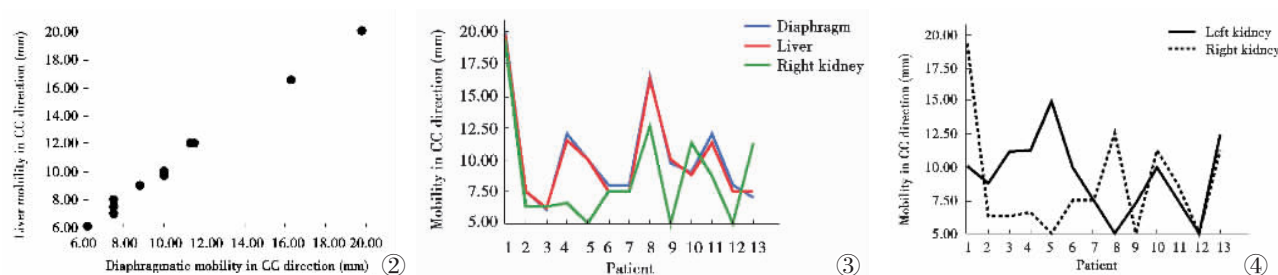


Figure 2 Scatter plot of diaphragmatic movement and liver movement in the CC direction

Figure 3 Movement in the CC direction and relationship of diaphragm, liver, and right kidney

Figure 4 Movement in the CC direction of bilateral kidneys

Discussion

In order to avoid missing the radiation target, positioning error, target mobility, changes in the tumor size through the treatment and other factors must be taken full account. At the same time, the ICRU 62 report recommended expanding outside borders of endangered organs to form PRV, to compensate for the physical movement and positioning error affecting the dose to endangered organs. Therefore, accurate individualized measurement of organs respiratory mobility is a key step in determining PTV and PRV in the conformal radiotherapy plan, which is difficult to be performed using conventional methods, such as X-ray, B-ultrasound. X-ray can only detect displacement of diaphragm in the CC direction, and it is difficult to measure the displacement of liver and other abdominal organs such as kidneys, pancreas, and spleen in three-dimensional direction.⁸ Although B-ultrasound has been used to measure respiratory mobility, studies have shown that the repeatability of ultrasound measurements is poor, it is susceptible to interference caused by intestinal gas, and the selected location and section would seriously affect the measurement. 911 Aruga et al.¹² reported that repeated breath-hold CT scan at end-aspiratory and end-expiratory phases could calculate the displacement of organs between two respiratory phases. This method is relatively simple, but breath-hold CT can not represent the state of free end-aspiratory and end-expiratory phases, and ignores the hysteresis of respiratory

movement. Bussels et al.¹³ used dynamic MRI scan to measure respiratory mobility of abdomen organs, and found that the mobility of pancreas was similar to that of liver in the CC direction, which was (23.7 ± 15.9) mm and (24.4 ± 16.4) mm respectively, and the mobility of left and right kidney was (16.9 ± 6.7) mm and (16.1 ± 7.9) mm respectively. The method has higher accuracy, but can be influenced by the selected central slice, and is also expensive to be commonly used in clinical practice.

Comparing with conventional spiral CT, 4DCT contains CT data from a complete respiratory cycle, and can reflect the respiratory movement of thoracic and abdominal organs as well as targets trajectory. At present, in radiotherapy of thoracic and abdominal tumors, 4DCT is mainly used in mobility measurements of target and / or normal organ, determining individual target volume, respiratory-gated radiotherapy and beam follow-up treatment.¹⁴⁻¹⁶ Based on 4DCT, studies of esophagus, lung tumor, mediastinal lymph nodes and bifurcation of the trachea are more common,¹⁷⁻¹⁹ while studies of abdominal organs are relatively fewer. Brandner et al.²⁰ measured abdominal respiratory mobility in 13 patients using 4DCT, and revealed that mobility of liver, spleen, left and right kidney was 1.3cm, 1.3cm, 1.1cm and 1.3cm, respectively in the CC direction, which were slightly larger than the results of our study. This may be related to the lack of audio-visual feedback device in the scanning process of our study and the differences in East-West groups.

Clinically, the safe border of the liver tumor in the CC direction is usually determined by the

diaphragm movement, but some studies indicated that the movements of diaphragm and liver tumors were not perfectly aligned.⁸ This study showed that there was no significant difference in the mobility of diaphragm with liver and the right kidney, indicating a high degree of positive linear correlation. Therefore, we suggest that the diaphragmatic mobility can represent those of liver and the right kidney. Mobility of diaphragm can be measured using a simple method, such as X-ray, which may be a good alternative for hospitals without 4DCT. Pancreas is located in retroperitoneal space adjacent to many organs, and its anatomical location is relatively fixed with relatively small mobility. Thus, the narrow safe border of PTV can be assigned for pancreatic tumors. For all cases, left kidney, spleen and diaphragm had no significant difference with mobility, so diaphragm can not predict the mobility of left kidney and spleen except for individual cases. In addition, bilateral kidneys had no related mobility in three-dimensional directions, so mobility of one side kidney could not predict the other side, which was in line with Kostas report.²¹

Radiotherapy is the main method of local treatment for upper abdominal tumors such as liver, stomach and other abdominal lymph node metastasis. To date, no literature reported mobility of para-aortic lymph node. Generally, clinicians determine the safe border for intra-abdominal lymph node metastases based on their clinical experience. Because tumor mobility is not measured individually, missed or over-expanded target is bound to present. In this study, the movement of para-aortic lymph node was less than 3mm (0.6-2.8mm) in LR, AP directions and (5.7 ± 1.8) mm (4.5-8.6 mm) in the CC direction, which were significantly smaller than those of diaphragm. This may be related to the anatomical location of retroperitoneal space, and can provide some references to determine the safe border in patients without 4DCT. However, in this group, only five cases with liver cancer had para-aortic lymph node metastasis, and the location, size of lymph nodes were not uniform, which could not represent the overall mobility of intra-abdominal lymph nodes. Therefore, more cases and further

in-depth studies are needed.

In this study, the mobility of abdominal organs varied greatly, which was consistent with other studies.^{13,20,21} Therefore, measuring the mobility of the tumor and endangered organs individually is necessary in setting PTV or PRV, rather than a simple expansion of outer "group" safe borders, in order to avoid missing the target or excessive irradiation to normal tissue. For patients with greater respiratory mobility, respiratory-gated therapy based on 4DCT can be implemented, which gives repeated short-term radiation therapy in a specific period of respiratory cycle to reduce the expanded safe border in accordance with respiration, thereby narrows the target to reduce the exposure of normal tissue surrounding the tumor and may increase the radiation dose. The technology has been initially carried out internationally and shown a good application prospect.¹⁶

In summary, 4DCT can accurately measure respiratory mobility of abdominal organs in three-dimensional directions, which would help physicians determine individual PTV and PRV. Mobility of diaphragm can represent those of liver and right kidney in the CC direction, and the mobility of para-aortic lymph node is relatively small. In addition, mobility of diaphragmatic can not represent those of left kidney, pancreas and spleen.

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