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Attenuation correction of PET images with interpolated average CT for thoracic tumors

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Abstract

To reduce positron emission tomography (PET) and computed tomography (CT) misalignments and standardized uptake value (SUV) errors, cine average CT (CACT) has been proposed to replace helical CT (HCT) for attenuation correction (AC). A new method using interpolated average CT (IACT) for AC is introduced to further reduce radiation dose with similar image quality. Six patients were recruited in this study. The end-inspiration and -expiration phases from cine CT were used as the two original phases. Deformable image registration was used to generate the interpolated phases. The IACT was calculated by averaging the original and interpolated phases. The PET images were then reconstructed with AC using CACT, HCT and IACT, respectively. Their misalignments were compared by visual assessment, mutual information, correlation coefficient and SUV. The doses from different CT maps were analyzed. The misalignments were reduced for CACT and IACT as compared to HCT. The maximum SUV difference between the use of IACT and CACT was ∼3%, and it was ∼20% between the use of HCT and CACT. The estimated dose for IACT was 0.38 mSv. The radiation dose using IACT could be reduced by 85% compared to the use of CACT. IACT is a good low-dose approximation of CACT for AC.

(Some figures in this article are in colour only in the electronic version)

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Introduction

In modern positron emission tomography (PET) imaging, computed tomography (CT) has replaced Ge-68 for the transmission scan. The increased use of CT escalates the risk of radiation exposure for patients (Einstein *et al* [2007\)](#page-10-0), and acquisition protocols need to be optimized according to the as low as reasonably achievable philosophy. The drawback of the helical CT (HCT) is the higher radiation dose as compared to Ge-68. Additionally, CT images are usually a snapshot of a respiration cycle, while PET scans are the results of the average of respiratory cycles. The temporal difference between the scans often introduces misalignment artifacts in PET images.

These misalignments especially introduce misleading tumor locations, volumes and standardized uptake values (SUVs) in diagnosing thoracic cancer and in radiation treatment planning (Beyer *et al* [2004,](#page-9-0) Charron *et al* [2000](#page-9-0), Chin *et al* 2003, Kinahan *et al* [2003,](#page-10-0) Lardinois *et al* [2003](#page-10-0), Schöder *et al* 2003, Schwaiger *et al* [2005,](#page-10-0) Townsend *et al* [2004,](#page-10-0) Zaidi and Hasegawa [2003\)](#page-10-0). Reducing the mismatch between HCT and PET in PET*/*CT via the cine average CT (CACT) technique has been proposed (Cook *et al* [2007,](#page-10-0) Dawood *et al* [2009](#page-10-0), Pan *et al* [2005\)](#page-10-0). One concern is that its radiation dose is relatively high.

We previously described the use of the optical flow method (OFM), a deformable image registration algorithm, to register the CT pairs from different time phases and to provide a tissue motion map (Guerrero *et al* [2004](#page-10-0), Zhang *et al* [2008\)](#page-10-0). With this motion map, CT images representing the mid-phases of a respiratory cycle can be obtained by interpolation.

In this study, we develop and evaluate the feasibility of using interpolated average CT (IACT), generated from the end-expiration and -inspiration phases of cine CT and interpolated phases using deformable image registration, for the purpose of attenuation correction (AC). We also assess the potential dose reduction by using IACT.

Materials and methods

PET/CT data acquisition

Six cancer patients were recruited for this study. The tumor locations include left lower lobe, left anterior chest wall, right lower lobe, distal esophagus, right upper lobe, anterior mediastinum and right hilum. Images were acquired using a PET*/*CT scanner (Discovery VCT, GE Medical Systems, Milwaukee, WI, USA). All patients were injected with 298–458 MBq of 18F-FDG and scanned 1 h after injection. The default acquisition settings of HCT data were as follows: 120 kV, smart mA (range 40–210 mA) (Kalra *et al* [2004](#page-10-0)), i.e. automatic tube current modulation to maintain constant image quality at the lowest dose for a different body anatomy, 1.375:1 pitch, 8×2.5 mm x-ray collimation, and 0.5 s CT gantry rotation. Cine CT data were acquired at 120 kV, 10 mA, 8×2.5 mm x-ray collimation, 0.5 s CT gantry rotation and 5.9 s cine CT duration which covers at least one breath cycle. A total of 13 phases in a respiratory cycle from the cine CT were averaged to generate the CACT (Pan *et al* [2005\)](#page-10-0). PET data were acquired at the 3 min per 15 cm bed position. Our protocol was approved by the local ethics committee and the subject number was kept to be minimal, while still showing the significance of the proposed method, to avoid unnecessary radiation exposure. Written informed consents were obtained from all patients.

Deformable image registration

The OFM (Guerrero *et al* [2004](#page-10-0), Zhang *et al* [2008\)](#page-10-0) was applied to calculate the velocity matrix on two successive CT images in cine CT. The velocity matrix includes lateral,

Figure 1. The generation of IACT. The two extreme phases in cine CT, end-inspiration and -expiration, are registered using the OFM. The resultant deformation matrix is then used to interpolate the phases in between with equal temporal intervals. IACT_{2011i}, used for AC in PET reconstruction, is the average of the 2 original phases and the interpolated 11 phases.

anterior–posterior and inferior–superior displacements for each voxel, respectively. The OFM calculation equation is as follows:

$$
v^{(n+1)} = v^{(n)} + \nabla f\left(\frac{\nabla f \cdot v^{(n)} + \frac{\partial f}{\partial t}}{\alpha^2 + \|\nabla f\|^2}\right),\tag{1}
$$

where *n* is the number of iterations, $v^{(n)}$ is the average velocity driven from the surrounding voxels, f is the image intensity, and α is the weighting factor whose value is empirically set at 5 for the OFM in CT (Huang *et al* [2010,](#page-10-0) Zhang *et al* [2008](#page-10-0)).

Interpolated average CT

For IACT calculated from 2 original phases + 11 interpolated phases (IACT_{2o11i}), two extreme phases in cine CT, i.e. normal end-inspiration and -expiration, are used to generate the motion maps via the OFM. The total motion range for each voxel in the forward motion map is equally spaced into six intervals, resulting in five sets of interpolated CT images as the mid-phases from inspiration to expiration. Similarly, the backward motion map is used to calculate the five mid-phases from expiration to inspiration (figure 1). The ten interpolated phases together with the two original phases, plus the next inhalation compose a complete respiratory cycle. These 13 phases are averaged to generate the $IACT_{2011i}$.

To study the reliability of the proposed IACT technique, different numbers of original phases in the cine CT are used in calculating IACT. Other configurations of the IACTs include 4 original phases + 9 interpolated phases ($IACT_{409i}$), 6 original phases + 7 interpolated phases $(IACT_{607i})$, and 8 original phases + 5 interpolated phases (IACT_{805i}).

Image reconstruction

All PET images were reconstructed using the OS-EM reconstruction method with 2 iterations and 28 subsets. AC were conducted using the obtained CT maps: HCT, CACT, IACT $(IACT_{2011i}, IACT_{409i}, IACT_{607i}, IACT_{805i}),$ and average CT was obtained from two extreme phases (ACT). Their reconstructed PET images were compared and their differences in image quality and associated radiation dose were quantified.

Data analysis

Mutual information. In order to provide the overlap invariance, normalized mutual information (MI) was utilized (Studholme *et al* [1999\)](#page-10-0). The normalized MI between *X* and *Y*, denoted as *I*(*X*, *Y*), is a measure of the statistical dependence between both variables, defined as in equation (2). In this study, normalized MI was applied to estimate the nonlinear image intensity distribution between IACT*/*HCT*/*ACT and CACT:

$$
I(X, Y) = \frac{P(X) + P(Y)}{P(X, Y)},
$$
\n(2)

where $P(X)$ is the histogram of *X*, $P(Y)$ is the histogram of *Y* and $P(X, Y)$ is the joint histogram of *X* and *Y*. MI represents how much the knowledge of *X* decreases the uncertainty of *Y*. Therefore, *I*(*X*, *Y*) is a measure of the shared information between *X* and *Y*. The larger the normalized MI values, the more similar two images are (Studholme *et al* [1999](#page-10-0), Zhang *et al* [2008\)](#page-10-0).

Correlation coefficient. The correlation coefficient (CC) was applied to calculate the linear intensity relationship point by point between IACT*/*HCT*/*ACT and CACT. The CC value represents the total intensity difference between two image sets, i.e. the summation of the intensity difference for all *n* voxels. The equation defining the CC is

$$
CC = \frac{S_{u,v}}{S_u \times S_v} = \frac{\sum_{i=1}^{n} (u_i - \overline{u}) \times (v_i - \overline{v})}{\sqrt{\sum_{i=1}^{n} (u_i - \overline{u})^2} \times \sqrt{\sum_{i=1}^{n} (v_i - \overline{v})^2}}
$$
(3)

where S_u is the standard deviation of object *u*, S_v is the standard deviation of object *v*, and $S_{u,v}$ is the covariance of objects *u* and *v*. The value of the CC is between -1 and 1, indicating negatively correlated to positively correlated, respectively.

Both MI and CC methods are capable of giving a quantitative measure of similarity between CT images. Since they have different sensitivities to different components of differences, both are included in this study to demonstrate their usage in similarity comparison.

Standardized uptake value. The PET images reconstructed using HCT, CACT and IACT for AC were compared by visual assessment. The same volumes-of-interest (VOIs) were delineated at the same location around the tumor and the average SUVs in the VOI were obtained. The average SUVs were compared using the following equation:

$$
\text{diff}_{\text{IACT-CACT}} = \frac{|\text{SUV}_{\text{IACT}} - \text{SUV}_{\text{CACT}}|}{\text{SUV}_{\text{CACT}}} \times 100\%.
$$
 (4)

The differences between the HCT/ACT and CACT techniques, diff_{HCT–CACT} and diff_{ACT–CACT}, were also calculated by replacing IACT with HCT*/*ACT in the above equation. Smaller values of diff_{IACT}-CACT, diff_{HCT}-CACT and diff_{ACT}-CACT indicate better estimations of the CACT technique, i.e. less misalignment errors between the associated CT and PET images.

Figure 2. (A) Values of normalized MI between HCT, ACT, CACT and IACT with different configurations. (B) Values of CC between HCT, ACT, CACT and IACT with different configurations.

Radiation dose

Radiation dose was expressed using the volume CT dose index (CTDIvol) in Gy, and effective dose in mSv. The dose–length product is defined as the $CTDI_{vol}$ multiplied by the scan length, and is an indicator of the integrated radiation dose of an entire CT examination. An approximation of the effective dose was obtained by multiplying the dose–length product by a conversion factor, *k* (equal to $0.017 \text{ mSv mGy}^{-1} \text{ cm}^{-1}$) (ICRP [2007\)](#page-10-0).

Results

The MI and CC results showed that as the number of original phases in IACT increases, IACT and CACT become more relevant, while $IACT_{2011i}$ performs better than ACT (figure 2). Figure [3](#page-7-0) shows the sample reconstructed images of HCT, CACT and $IACT_{2011i}$, their associated PET images and the fused PET*/*CT images. The only noticeable difference between CACT and $IACT_{2011i}$ is the higher noise level in $IACT_{2011i}$ as compared to CACT. This is expected as CACT is an average of all 13 original phases from cine CT, while $IACT_{2011i}$ uses only 2 original phases. On the other hand, PET images using HCT for AC demonstrate noticeable artifacts in the diaphragm region. The SUV analysis for HCT, CACT, different IACTs and ACT is shown in figure [4.](#page-8-0) For tumor nos 1 through 7, the difference from the one using CACT is smallest when $IACT_{805i}$ is used, and it is largest when HCT is used. However, even with IACT_{2011i} where the difference is the largest among all IACT configurations, it is $\leq 3\%$ as compared to CACT, while the difference was ≥10% with the maximum difference of ~20%, between the use of HCT and CACT, consistent with the reported values (Pan *et al* [2005\)](#page-10-0). The results of ACT are generally inferior to those of $IACT_{2011i}$ except for tumor no 4.

The effective radiation doses (and CTD_{Vol}) from the CT scans are listed in table [1.](#page-7-0) The higher dose from HCT, 5.28 mSv (11.18 mGy), is due to the clinical setting of smart mA. In cine CT, the current is set at 10 mA ; thus the effective dose is 2.46 mSy (5.17 mGy). If the two original phases in the $IACT_{2011i}$ are replaced by two breath-hold CT scans with the same tube current as of cine CT, the effective dose would be 0.38 mSv (0.79 mGy) , i.e. an 85% reduction from cine CT and a 93% reduction from HCT. In addition, the typical effective

Figure 3. (A) Sample reconstructed images of HCT, CACT and IACT_{2011i}, (B) their associated attenuation-corrected PET images and (C) PET*/*CT fused images. Noticeable misalignment artifacts in the diaphragm region (arrow) can be found in the HCT-corrected PET.

	HCT	CACT	$IACT2$ -breath-hold CT
Scan mode	Helical mode	Axial cine mode	Helical mode
Tube voltage (kVp)	120	120	120
Tube current (mA)	$40 - 210$	10	10
Number of phases		13	2
$CTDI_{vol}$ (mGy)	11.18	5.17	0.79
Scan coverage (cm)	28	28	28
Dose-length product $(mGy cm)$	310.49	144.62	22.25
Effective dose (mSv)	5.28	2.46	0.38

Table 1. HCT, CACT and IACT scanning parameters and doses estimation.

dose from 18F-FDG PET imaging is about 10.73 mSv which is invariant with the AC method (Deloar *et al* [1998,](#page-10-0) Wu *et al* [2005\)](#page-10-0).

Discussion

The OFM establishes the link between two extreme respiratory phases. With the interpolated phases added, the whole respiratory cycle is constructed. Our results showed that $IACT_{2011i}$

Figure 4. (A) SUV difference between PET images corrected by HCT, ACT, CACT and IACT with different configurations. (B) Transaxial PET images at the lesion level corrected by (left) HCT images, (middle) CACT images and (right) $IACT_{2011i}$ images.

generally outperforms ACT, demonstrating the effectiveness of this method. The little difference in the SUV for PET using IACT and CACT for AC also indicates that IACT is a good approximation of CACT, with the advantage of less radiation dose. For gated PET studies, other approaches for AC are proposed. For example, respiratory gated CT corresponding to the gated PET frames are acquired for phase-dependent AC. Other methods include transforming a single CT image to match the associated PET frames through tracking the diaphragm motions in PET (McQuaid *et al* [2009](#page-10-0)). These methods require manual segmentation of the diaphragm and their accuracy highly depends on the motion model.

The motion amplitude may impact the accuracy of the motion maps. Zhong *et al* [\(2010](#page-10-0)) showed that the average error in deformable image registration in thoracic regions was around 0.7 mm for a diaphragm motion of 2.6 cm. This accuracy is sufficient for PET AC as PET resolution is much coarser.

The selected lesions located in diversified thoracic regions are representative of general clinical scenarios. Chi *et al* [\(2008](#page-9-0)) reported that out of 216 lung cancer patients, 68% had mis-registration and only 10% had an SUV change of *>*25% at the tumor location. Four out of seven lesions in our study showed *>*10% SUV difference between the use of CACT and HCT, with the maximum SUV difference of ∼20% for the esophageal lesion which is closest to the diaphragm among all cases.

The drawback of the very low dose setting (10 mA) in both CACT and IACT methods is the increased noise in the CT images. Noisy AC data can introduce noise into the PET emission images. As shown in figure $3(B)$ $3(B)$, the emission data for CACT and IACT appear noisier than the images corrected with HCT data because of the higher quantum noise in the AC data in CACT and IACT. If the same signal-to-noise ratio in the emission images of the HCT method is desired, the current setting in CACT and IACT has to be the same as that in the HCT method. The dose to the patient would be higher for the IACT method as compared with HCT, but still much lower than that in CACT. As the purpose of the PET images is to obtain accurate SUV and tumor location and shape, as long as the noise in PET does not affect the extraction of such information, the very low dose setting should be sufficient for a reasonable AC CT quality.

It should be noted that the proposed method may not produce better PET image quality as compared with CACT either. The quality of each phase CT in a low-dose 4DCT set is sufficient for clinicians to read. The very low dose breath-hold CT should possess at least the same quality of each phase of the CT in the 4DCT as the current and voltage settings are the same, with the residual motion, which often exists in each phase of 4DCT, not present in the breath-hold CT. The major advantage of the proposed IACT method is less dose to the patient and yet a good approximation of the CACT method in the SUV and tumor location.

Clinically, two extreme phases in cine CT can be replaced by two separate CT scans, one at normal end-inspiration and the other at end-expiration. Since breath-hold CTs are likely different from the phases in free-breathing cine CT, an active breath control (ABC) system, originally developed by Wong *et al* [\(1999](#page-10-0)) for clinical radiotherapy, can be used to ensure breath-hold CTs being taken at desired phases. This non-invasive device integrates a spirometer with a personal computer to control the flow meters and scissor valves. A nose clip is used to ensure that the patients only breathe via the mouthpiece. Patients can be trained using this device prior to the actual CT scanning, and CT images can then be taken at desirable lung volume, i.e. a particular phase of the breathing cycle. Partridge *et al* [\(2009](#page-10-0) showed that a breath-holding time of 15–30 s can be achieved for patients with lung cancer. Further study with real breath-hold CT data using ABC is warranted.

Conclusion

The application of IACT for PET AC reduces misalignment artifacts and SUV quantification errors for thoracic tumors as compared to that of HCT. The radiation dose using IACT could be reduced by 85% compared to that of CACT. It serves as a low-dose alternative to CACT. Further study with separate CT scans placed at end-expiration and -inspiration phases is needed.

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教師出席國際學術會議報告

98 年 7 月 17 日

報告內容應包括下列各項:

一、參加會議經過

張貼海報並與國際學者互相討論各自研究心得,會中聆聽國際學者的口頭報告。於會議 餐會,結識外國學者,邀請國外學者有機會至我們學校演講並分享相關研究心得。,

二、與會心得

影像處理技術在放射科學應用為目前非常熱門的題目,在目前幾個大型研討會,皆有專 門的 SECTION,參與發表與討論者很多,應用技術減少病人對放射性的吸收,減低併發 症機率提升醫療治癒率,是全世界上醫事放射人員的目標。

三、考察參觀活動(無是項活動者省略)

四、建議

放射照影與治療技術一日千里,每隔一段時間就有新技術與儀器出來,新的技術與儀器 對病人都有實質上的幫助,希望學校或附設醫院,能多補助老師與醫事人員進修或參與 研討會,以期增進學校與附設醫院的競爭力。

五、攜回資料名稱及內容

1. 參與海報(附件一)

2. 研討會論文集

六、其他

附件一

Three-dimensional Dose Verification Using Normoxic Polymer Gel Dosimeters for Tomotherapy

im of this study is to

RESULTS & Discussion

CONCLUSIONS

INTRODUCTION

matherapy delivers radiation using a
aing intensity-modulated fan bonm
amelry, and the modulation varies
hi gantry -angle. -Because -the
allant-dase-dichibulions -comprise gennety, and the modulision varies raised and the modulisian varies raised and the second field denotes a modulision from a angles. He system has the polential to deliver highly centernal resoluted to be a grappene. Fighty **HEBULIB & DISEUSSION**

MAGAT gel dosimeter has the schemes and the schemes optical

from exploration and the monomental from exploration by the schemes and the schemes and proportion steps and approximation of the content

in this work, we have to panse curves for
gel doctueler
py as the dose do tils MACT as it -30_d stady is the
se polented
reading de
The dose a final al In applies the
MACT as a reducinglers \mathbf{u} öπ ionnoatc polymer
ibined with MVCT ar co as a m

ACKNOWLEDGEMENTS

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by the National Science Council of
Takem. NSC 99-2221-E-039-010

METHODS AND MATERIALS

The dirical helical tomotherapy unit
(TamoTherapy Inc., Madison, The chircal helical isomolectory will (Then Chirchary Inc., MacDon, 1994)

(Wiscomia, USA) convision of a GAIN finese accelerate with a binary multi-

[lead collinator and a second control of a second collinator and a sec

parent masses are constructed in the electronic part integrals of electronic period. The distribution sching of evidence conditions away appear on the electronic condition and only and distribution and only and a series of

Figure 1. Figure 1. Dos response curves of rest-
time reading (@) and 12 hours delay reading ()
The horizontal axis is the had does in cOu aha and the vertical
the MMCT the sion

Figure 2. Dose n curves for 12 hours delayed
reading with no filter() and pao (), Gauss (x). in (@). mean (+), max (*) and min () libers. The antal. acus is the
dose in cGy, and
all acús is the varical a

BONABI

國科會補助計畫衍生研發成果推廣資料表

日期:2011/08/08

99 年度專題研究計畫研究成果彙整表

國科會補助專題研究計畫成果報告自評表

請就研究內容與原計畫相符程度、達成預期目標情況、研究成果之學術或應用價 值(簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性)、是否適 合在學術期刊發表或申請專利、主要發現或其他有關價值等,作一綜合評估。

