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# CT ventilation imaging derived from breath hold CT exhibits good regional accuracy with Galligas PET

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ABSTRACT

*Background and purpose:* CT ventilation imaging (CTVI) derived from four dimensional CT (4DCT) has shown only moderate spatial accuracy in humans due to 4DCT image artefacts. Here we assess the accuracy of an improved CTVI using high quality exhale/inhale breath-hold CT (BHCT).

*Materials and methods:* Eighteen lung cancer patients underwent exhale/inhale BHCT, 4DCT and Galligas PET ventilation scans in a single imaging session. For each BHCT and 4DCT scan, we performed deformable image registration (DIR) between the inhale and exhale phase images to quantify ventilation using three published metrics: (i) breathing induced lung density change, $CTVI_{DIR-HU}$ (ii) breathing induced volume change $CTVI_{DIR-Jac}$ and (iii) the regional air-tissue product, $CTVI_{HU}$ Spatial accuracy was reported as the voxel-wise Spearman correlation r between CTVI and Galligas PET.

*Results:* For BHCT-based CTVIs ($N = 16$), the $CTVI_{DIR-HU}$, $CTVI_{DIR-Jac}$ and $CTVI_{HU}$ methods yielded mean (range) $r$ values of 0.67 (0.52–0.87), 0.57 (0.18–0.77) and 0.49 (0.14–0.75) respectively. By comparison the 4DCT-based CTVIs ($n = 14$) had values of 0.32 (−0.04 to 0.51), 0.16 (−0.31 to 44) and 0.49 (0.20–0.77) respectively.

*Conclusions:* High quality CT imaging is a key requirement for accurate CT ventilation imaging. The use of exhale/inhale BHCT can improve the accuracy of CTVI for human subjects.



Ventilation imaging is extremely important in the planning of ablative pulmonary interventions in order to minimise treatment-induced parenchymal injury [1]. The last decade has seen several clinical investigations using computed tomography ventilation imaging (CTVI), which visualises air volume changes by analysing lung motion in respiratory-correlated four-dimensional CT (4DCT) [2–12]. Compared to the gold standard nuclear medicine ventilation imaging, CTVI offers the benefits of high resolution and high accessibility (especially in radiation oncology departments). Additionally CTVI is non-invasive and does not require the preparation of a radioaerosol or contrast agent.

Most CTVI implementations use deformable image registration (DIR) to calculate breathing induced air-volume changes in terms of regional lung density changes [2] or volume changes [3]. A major research focus for CTVI has been cross-modality validation in humans, that is, voxel-to-voxel comparisons of CTVI against a ground truth ventilation imaging modality such as $^{99m}$Tc-based (DTPA and "Technegas") single photon emission computed tomography (SPECT) [4,5,7,10,12] or $^{68}$Ga-based ("Galligas") positron emission tomography (PET) [8,11,13]. In particular for radiotherapy treatment planning it is desirable to demonstrate strong voxel-level accuracy using the Spearman correlation $r$. Early validation studies using DTPA-SPECT showed relatively poor correlations ($r < 0.2$) and this has been attributed mainly to radioaerosol clumping in the central airways [4]. Kida et al. [10] reported much improved correlations between CTVI and DTPA-SPECT ($\bar{r} \approx 0.4$) for 8 patients with non-severe clumping. The use of Galligas 4DPET/CT, which uses a smaller radioaerosol less prone to clumping and provides better co-registration between the 4DCT and nuclear medicine scans, has also lead to improved voxel-level correlations ($\bar{r} \approx 0.45$) [8,11].

Despite the improved results in recent CTVI validation studies, Hegi-Johnson et al. [12] found that the correlation between CTVI and ventilation SPECT was less than the agreement between ventilation SPECT and perfusion SPECT ($\bar{r} \approx 0.6$ for 11 patients) and suggested that poor image quality of clinical 4DCT remains the major

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limitation on CTVI accuracy. It is known that 90% of clinical 4DCT scans suffer image artefacts >4 mm due to irregular breathing which manifest as anatomic blurring, duplication and truncation [14]. As a result of these imaging errors, CTVIs can vary depending on the 4DCT slice sorting method [15]. For surgical applications and assessment of global lung function, it is acceptable to mitigate this by assessing ventilation over larger regions of interest, for example lung thirds ($\bar{r} \approx 0.45$) [6] or lung lobes ($\bar{r} = 0.96$) [13,16]. For lung cancer radiotherapy however, a strong level of voxel-level accuracy still needs to be demonstrated.

The purpose of this study is to investigate an improved CTVI derived from pairs of exhale/inhale breath-hold CT (BHCT) scans free of motion artefacts. We perform the first head-to-head comparisons of BHCT-based CTVIs and 4DCT-based CTVIs using best-practice validation methodology. In particular the BHCT, 4DCT and Galligas PET scan components are all acquired in a single session on a combined 4DPET/CT scanner to minimise time delays and/or patient setup differences between the scans. The voxel level accuracy of CTVI is reported in terms of the Spearman $r$ and compared against other CTVI validation studies. A schematic of the study design is shown in Fig. 1.

## Methods

### *Patients*

This study was a prospective single institution clinical trial approved by the health district ethics committee, (HREC/12/169) and registered with the Australian New Zealand Clinical Trials Registry (ACTRN12612000775819). The patient characteristics are described in (Table 1). A subset of this cohort was investigated in a previous CTVI study [13].

### *Image acquisitions*

All image acquisitions were performed on a Siemens Biograph mCT.S/64 PET/CT scanner (Siemens, Knoxville, USA) at the Royal North Shore Hospital between 2013 and 2015. A total of 14 4DCT scans, 16 inhale/exhale BHCT scans and 18 Galligas PET scans were successfully acquired for the 18 patients.

### *4DCT and Galligas PET acquisitions*

The 4DCT and Galligas PET scans were acquired with the use of a respiratory motion sensor, the Anzai AZ-733V system (Anzai

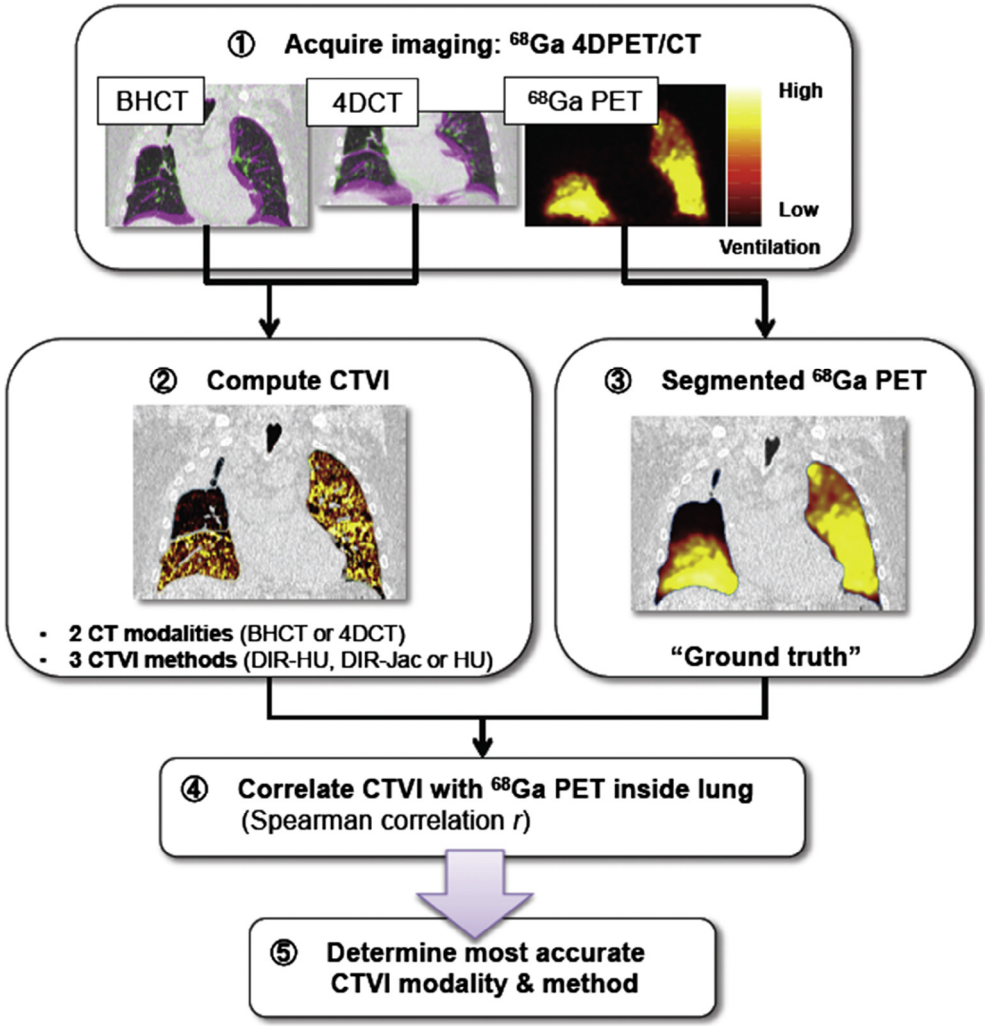


**Fig. 1.** Schematic of study design.

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