



Title	Technical Note: Performance evaluation of volumetric imaging based on motion modeling by principal component analysis
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1 **Title:**

2 Technical Note: Performance evaluation of volumetric imaging based on motion modeling by principal  
3 component analysis

4

5 **Running title:**

6 Volumetric imaging based on PCA

7

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## 27 **Abstract**

28 **Purpose:** To quantitatively evaluate the achievable performance of volumetric imaging based on lung motion  
29 modeling by principal component analysis (PCA).

30 **Methods:** In volumetric imaging based on PCA, internal deformation was represented as a linear combination  
31 of the eigenvectors derived by PCA of the deformation vector fields evaluated from patient-specific four-  
32 dimensional-computed tomography (4DCT) datasets. The volumetric image was synthesized by warping the  
33 reference CT image with a deformation vector field which was evaluated using optimal principal component  
34 coefficients (PCs). Larger PCs were hypothesized to reproduce deformations larger than those included in the  
35 original 4DCT dataset. To evaluate the reproducibility of PCA-reconstructed volumetric images synthesized to  
36 be close to the ground truth as possible, mean absolute error (MAE), structure similarity index measure (SSIM)  
37 and discrepancy of diaphragm position were evaluated using 22 4DCT datasets of nine patients.

38 **Results:** Mean MAE and SSIM values for the PCA-reconstructed volumetric images were approximately  
39 80 HU and 0.88, respectively, regardless of the respiratory phase. In most test cases including the data of which  
40 motion range was exceeding that of the modeling data, the positional error of diaphragm was less than 5 mm.  
41 The results suggested that large deformations not included in the modeling 4DCT dataset could be reproduced.  
42 Furthermore, since the first PC correlated with the displacement of the diaphragm position, the first eigenvector  
43 became the dominant factor representing the respiration-associated deformations. However, other PCs did not  
44 necessarily change with the same trend as the first PC, and no correlation was observed between the coefficients.  
45 Hence, randomly allocating or sampling these PCs in expanded ranges may be applicable to reasonably generate  
46 an augmented dataset with various deformations.

47 **Conclusions:** Reasonable accuracy of image synthesis comparable to those in the previous research were shown  
48 by using clinical data. These results indicate the potential of PCA-based volumetric imaging for clinical  
49 applications.

50

## 51 **KEYWORDS**

52 Volumetric imaging, principal component analysis, motion modeling, data augmentation, respiratory motion

## 53 **1 INTRODUCTION**

54 Volumetric imaging<sup>1-13</sup>, which can visualize three-dimensional (3D) anatomical structures during treatment,  
55 is expected to be clinically practical as a motion management technique in radiation therapy. Some studies  
56 regarding volumetric imaging are based on motion modeling with principal component analysis (PCA). In PCA-  
57 based motion modeling<sup>2-4,7,9,12,14</sup>, internal deformation is represented as a linear combination of the eigenvectors  
58 derived by the PCA of the deformation vector field evaluated from patient-specific four-dimensional-computed  
59 tomography (4DCT) datasets. The volumetric image can be synthesized by warping the reference computed  
60 tomography (CT) image with a deformation vector field evaluated with optimal principal component  
61 coefficients (PCs), serving as eigenvector weights. Some techniques to estimate optimum PCs during treatment  
62 have been reported. One is based on minimizing the difference between the digitally reconstructed radiographs  
63 created from the synthesized CT and actual fluoroscopic images<sup>4</sup>. Another one is based on the correlation model  
64 between PCs and external surrogate information<sup>2</sup>. Recently, a method using convolutional neural networks  
65 (CNNs) has also been proposed<sup>7</sup>. In this approach, PCA was also applied for data augmentation to generate the  
66 training dataset, including various deformations.

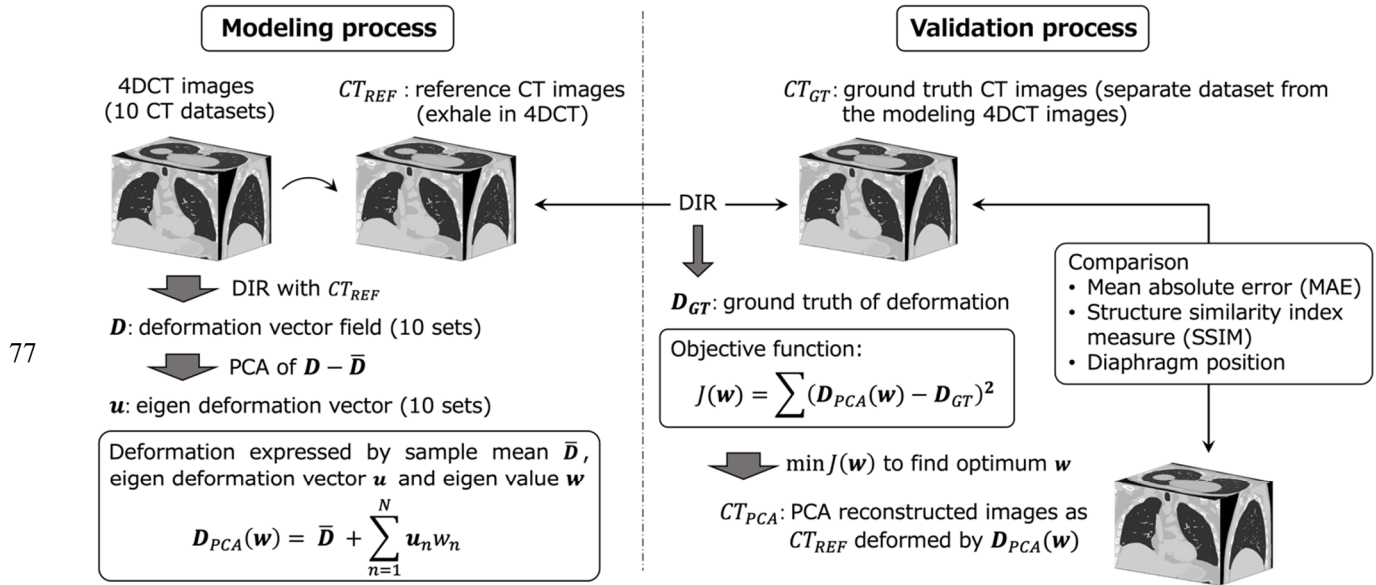
67 PCA has been applied for volumetric imaging and data augmentation in deep learning, as described in the  
68 last paragraph. Although, it is crucial to quantitatively evaluate the achievable performances of volumetric  
69 imaging based on PCA to support clinical feasibility, only a few reports on validation with clinical datasets  
70 simulating actual clinical situations such as the motion difference between treatment and 4DCT acquisition.  
71 Therefore, this study quantitatively evaluated the performance of PCA-based volumetric imaging using multiple  
72 clinical 4DCT datasets.

73

## 74 **2 MATERIALS AND METHODS**

### 75 **2.1 PCA-based motion modeling**

76



78 **FIGURE 1** Schematic showing the PCA-based motion modeling and validation processes in this study.

79

80 The PCA-based motion modeling process is shown in Fig. 1. First, the deformation vector field ( $\mathbf{D}$ ) was

81 evaluated using the deformable image registration (DIR) with each CT data. The CT data at the expiratory phase

82 of the 4DCT dataset (10 CT datasets for one respiratory cycle) were the reference ( $CT_{Ref}$ ). Furthermore, the

83 number of rows and columns of  $\mathbf{D}$  was the number of voxels multiplied 3 (# of deformation directions) and 10

84 (# of respiratory phase bins), respectively. Subsequently, the column vector ( $\bar{\mathbf{D}}$ ) was evaluated as the sample

85 mean of  $\mathbf{D}$ . Then, eigenvectors  $\mathbf{u}_1, \mathbf{u}_2, \dots, \mathbf{u}_{10}$  were obtained using the PCA of  $\mathbf{D} - \bar{\mathbf{D}}$ . Finally, using  $N$

86 principal eigenvectors, the internal deformation was expressed as follows.

87

$$\mathbf{D}_{PCA}(\mathbf{w}) = \bar{\mathbf{D}} + \sum_{n=1}^N \mathbf{u}_n w_n$$

88 where  $\mathbf{w} = (w_1, w_2, \dots, w_n)$  is the principal component coefficient (PC). By warping  $CT_{Ref}$  with  $\mathbf{D}_{PCA}(\mathbf{w})$ , a

89 volumetric image can be generated as a CT image. Larger PCs can then reproduce internal deformations larger

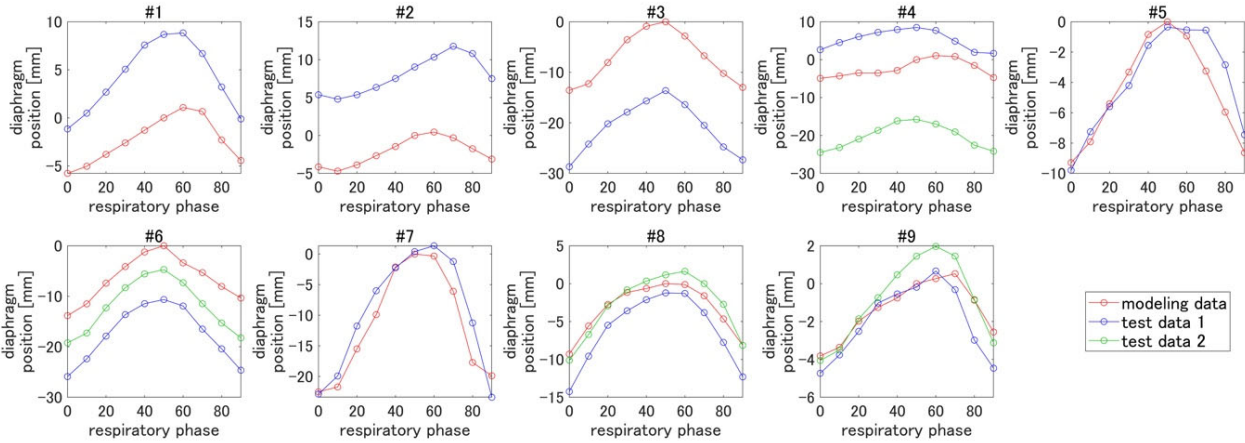
90 than those not included in the original 4DCT dataset.

91

92 **2.2 Patient data**

93 Twenty-two 4DCT datasets of nine patients with relatively small motion artifacts from The Cancer Image  
94 Archive<sup>15,16</sup> were used. This study assumed that these 4DCT datasets had been acquired during normal breathing  
95 at rest because the motion artifacts were small. Two or three 4DCT datasets were included for each patient. The  
96 displacement of the right diaphragm position for each 4DCT dataset is shown in Fig. 2, indicating the respiratory  
97 motion range. To evaluate the performance of PCA-based motion modeling in case of the larger deformations  
98 not included in the modeling data, the 4DCT dataset with smaller diaphragm displacements and the other 4DCT  
99 datasets were used as modeling data to derive eigenvectors and validation data, respectively. Hence, PCA-based  
100 motion model is created for each patient. The resolution of the CT data was 0.98 mm/pixel. The slice thickness  
101 was resampled from the original 3 mm to 1 mm. In the DIR function used in this study, one smoothing factor is  
102 applied to all three axes. Hence, slice thickness was resampled to 1 mm which was same as pixel size in order  
103 to equalize the smoothing effect to all axes. To avoid the influence of anatomical changes that eigenvectors  
104 could not reproduce, such as weight changes during the treatment course, the 4DCT datasets for modeling and  
105 validation were selected within 1 month. Additionally, because the patient setup position in each 4DCT  
106 acquisition was different, six-axis rigid image registration was performed in the spinal cord region, which was  
107 considered rigid, using the 4DCT dataset on the oldest date as a reference. Based on visual inspection of the  
108 registered images, it was confirmed that the anatomical variation between the 4DCT images acquired on  
109 different days was mainly induced by the respiration.

110



112 **FIGURE 2** Displacement of the diaphragm position for each respiratory phase in nine patients. The  
 113 displacement was evaluated on the basis of the phase 50 (expiration) in the modeling data.

114

### 115 **2.3 Evaluation of PCA-based lung deformation modeling**

116 The validation process is shown on the right side of Fig. 1. In this study, MATLAB (MathWorks Inc, USA)  
 117 was used for processing the DICOM (Digital Imaging and Communications in Medicine) format image, DIR,  
 118 and quasi-Newton method to find the optimal PCs. The deformation vector field obtained by DIR between the  
 119 CT image (defined as the ground truth:  $CT_{GT}$ ) obtained on a different date from the modeling 4DCT dataset and  
 120 the reference CT image ( $CT_{Ref}$ ) included in the modeling 4DCT dataset was defined as the ground truth of  
 121 deformation ( $D_{GT}$ ). In this study, the number of PCs was set to three as in previous studies (i.e.  $\mathbf{w} =$   
 122 [ $w_1, w_2, w_3$ ]), to consider the modeling accuracy and overfitting balance. It has been confirmed that using three  
 123 or more principal components resulted in an accumulated contribution rate more than 80% for each patient.  
 124 Then, the objective function was defined as the sum of the absolute differences between  $D_{GT}$  and  $D_{PCA}(\mathbf{w})$ :

$$125 \quad J(\mathbf{w}) = \sum (D_{PCA}(\mathbf{w}) - D_{GT})^2$$

126 After the PCs ( $\mathbf{w}$ ) that minimize  $J(\mathbf{w})$  were obtained using the quasi-Newton method, the CT image ( $CT_{PCA}$ )  
 127 was synthesized by warping the reference image ( $CT_{REF}$ ) by the deformation  $D_{PCA}(\mathbf{w})$ , followed by  
 128 evaluation with the optimum coefficient. In this way,  $CT_{PCA}$  could be synthesized using the deformation closest  
 129 to the ground truth.

130 This study evaluated the performance of PCA-based volumetric imaging by comparing  $CT_{PCA}$  with  $CT_{GT}$ .

131 The reproducibility of CT values and anatomical structures were evaluated using mean absolute error (MAE)

132 and structure similarity index measure (SSIM), respectively. MAE was evaluated as:

$$133 \quad MAE = \frac{1}{n} \sum_{i=1}^n |I_i - I_i^*| ,$$

134 where  $I_i^*$  is the actual CT value at voxel  $i$  in the ground truth image,  $I_i$  is the CT value at voxel  $i$  in the

135 synthesized image, and  $n$  is voxel number. SSIM which is commonly used in pattern matching as a measure  
 136 of the similarity of image structures was evaluated as:

$$137 \quad \text{SSIM} = \frac{(2\mu_x\mu_y + C_1)(2\sigma_{xy} + C_2)}{(\mu_x^2 + \mu_y^2 + C_1)(\sigma_x^2 + \sigma_y^2 + C_2)},$$

138 where  $\mu_x$  and  $\mu_y$  are the average CT values in ground truth image and synthesized image respectively,  $\sigma_x$   
 139 and  $\sigma_y$  are variance of CT value in ground truth image and synthesized image respectively, and  $\sigma_{xy}$  is a  
 140 covariance of ground truth image and synthesized image.  $C_1$  and  $C_2$  were defined as  $C_1 = (0.01 \times L)^2$   
 141 and  $C_2 = (0.03 \times L)^2$ , respectively.  $L$  was dynamic range of the image and was defined as the maximum CT  
 142 value in the ground truth image.

143 In addition, discrepancy of the diaphragm position between ground truth image and PCA-reconstructed  
 144 image was evaluated as positional accuracy. The diaphragm position was evaluated with the same area with  
 145 motion range evaluation shown in Fig.2.

146

## 147 **3 RESULTS**

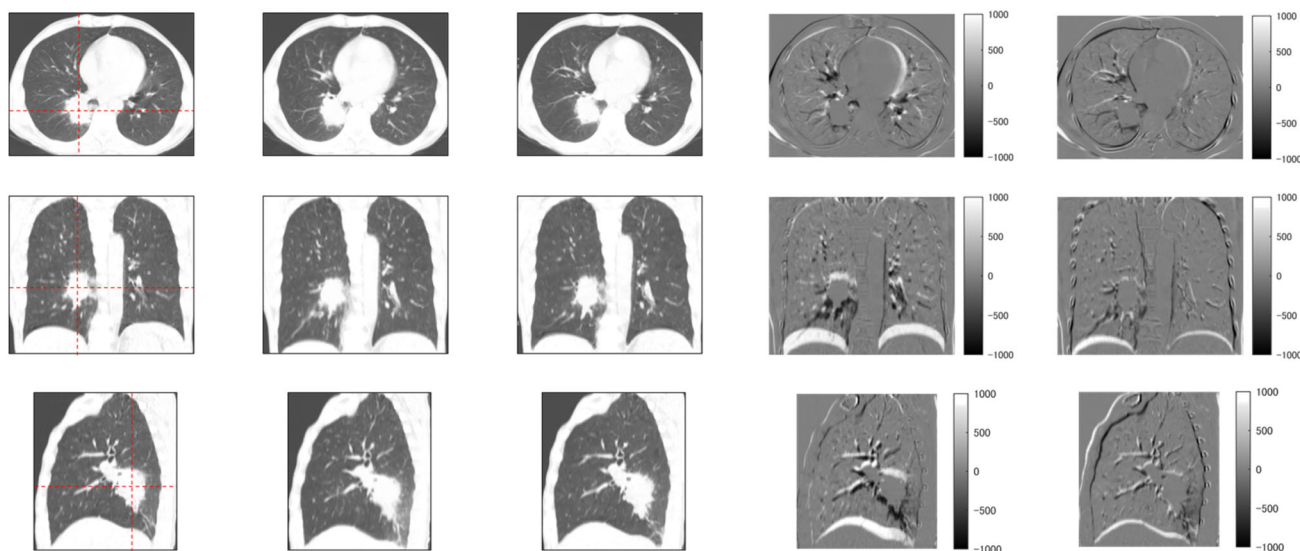
### 148 **3.1 MAE of PCA-reconstructed volumetric image**

149 An example of PCA-reconstructed volumetric images with assuming CT data at respiratory phase 0 in test  
 150 data 2 of patient 6 as the ground truth are shown in Fig. 3. We observed that the difference in diaphragm  
 151 positions between the reference and ground truth images was approximately 20 mm (see the second column  
 152 from the right in Fig. 3). As shown in Fig. 2, the diaphragm position at respiratory phase 0 in test data 2 of  
 153 patient 6 exceeded 5 mm from that in the modeling data. MAE and SSIM, in this case, were 89.0 HU and 0.85,  
 154 respectively, approximately an average of all evaluated cases. Although there was a discrepancy around the  
 155 diaphragm dome, the overall synthesized image was close to the actual, including that of the tumor, position  
 156 and shape.

157



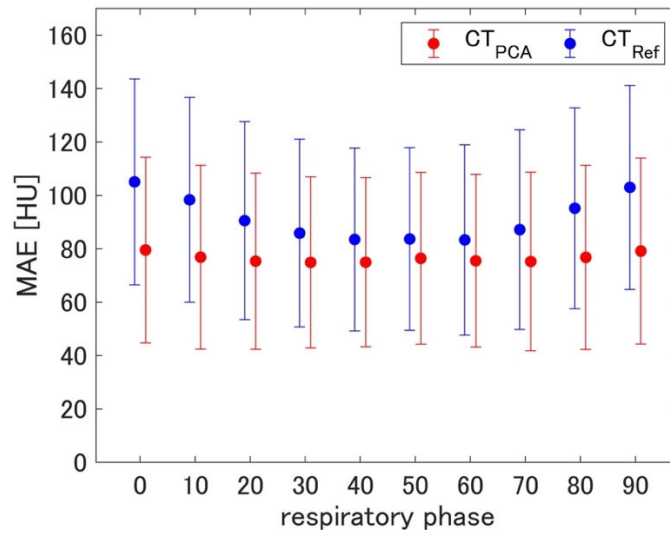
158



159 **FIGURE 3** From the left row: reference image (image to be deformed), ground truth image (respiratory phase  
 160 0 in test data 2 of patient 6), PCA-reconstructed volumetric image, difference between reference and ground  
 161 truth images, and difference between PCA-reconstructed volumetric and ground truth images. From top to  
 162 bottom: axial, coronal, and sagittal images. The dashed line in the reference image indicates the slice position  
 163 at the tumor center.

164

165 The MAE between PCA-reconstructed volumetric image and ground truth images for each respiratory phase  
 166 is shown in Fig. 4. Subsequently, the MAE between the reference and ground truth images was also evaluated  
 167 to show the difference between the original nondeformed reference and the ground truth. Since the expiratory  
 168 phase was used as the reference image, we observed that the MAE of the reference image was larger in the  
 169 inspiratory phase, whereas the deformation was relatively large. The mean MAE of the PCA-reconstructed  
 170 volumetric images for each respiratory phase was approximately 80 HU, and its accuracy was maintained even  
 171 in the inspiratory phase. These results suggest that PCA could reproduce large deformations not included in the  
 172 modeling data during normal breathing at rest. Moreover, the MAE appeared large in the validation data  
 173 containing deformations that were difficult to model with PCA, for example the deformations were different in  
 174 the left and right lungs.



175

176 **FIGURE 4** MAE of PCA-reconstructed volumetric image and reference image for the 13 cases from nine

177 patients at each respiratory phase.

178

### 179 3.2 SSIM of PCA-reconstructed volumetric image

180

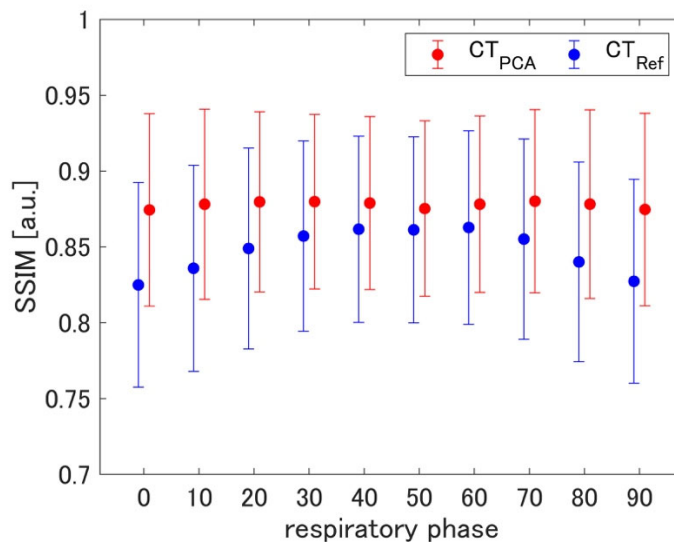
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184

The SSIM at each respiratory phase is shown in Fig. 5. As in the evaluation of the MAE, the SSIM between the reference and ground truth images was also evaluated. Since the expiratory phase was used as a reference, the SSIM of the reference image was decreased on the inspiratory phase. Alternatively, the mean SSIM of the PCA-reconstructed volumetric images was approximately 0.88 for each respiratory phase, maintaining a high structural reproducibility, even in the inspiratory phase.



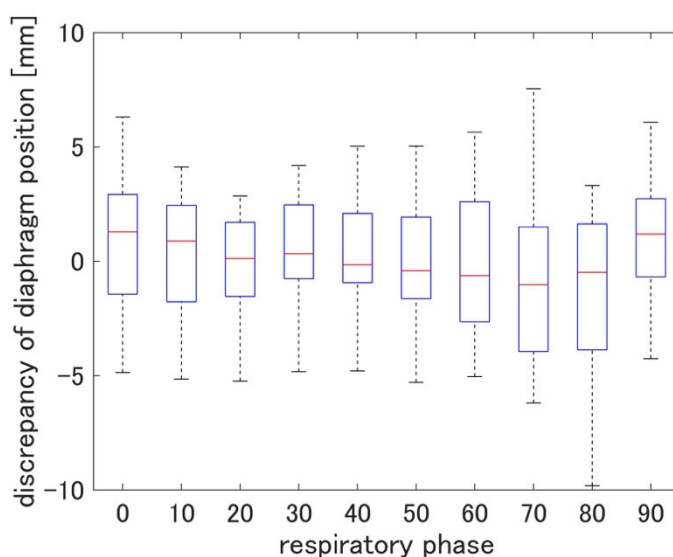
185

186 **FIGURE 5** SSIM of PCA-reconstructed volumetric image and reference image for the 13 cases from nine  
 187 patients at each respiratory phase.

188

### 189 **3.3 Positional accuracy of PCA-reconstructed volumetric image**

190 Discrepancy of the diaphragm position between ground truth image and PCA-reconstructed image is shown  
 191 in Fig.6. In most cases, the positional error of diaphragm was less than 5 mm. As shown in #1, #2, #3, #4, and  
 192 #6 in Fig.2, the motion range of half the test data exceeded that of the modeling data. Therefore, these results  
 193 suggested the possibility that PCA-based volumetric imaging could be applied to synthesize images even  
 194 when the motion is exceeded from the modeling data. In addition, since the diaphragm is the region that  
 195 moves the most due to breathing, the positional error in the lung region is expected to be smaller than that in  
 196 the diaphragm.



197

198 **FIGURE 6** Discrepancy of the diaphragm position between ground truth image and PCA-reconstructed image  
 199 for the 13 cases from nine patients at each respiratory phase.

200

## 201 **4 DISCUSSION**

202 This study quantitatively evaluated the achievable reproducibility of PCA-based volumetric imaging. The  
 203 mean values of MAE and SSIM of the PCA-reconstructed volumetric images were approximately 80 HU and  
 204 0.88, respectively, regardless of the respiratory phase, and were comparable with those evaluated in previous

205 studies<sup>5,8</sup>, using the same 4DCT dataset or digital phantoms. These results suggest that volume images could be  
206 synthesized with reasonable accuracy if the optimal PCs could be estimated even when the treatment motion  
207 differs from that observed during 4DCT acquisition.

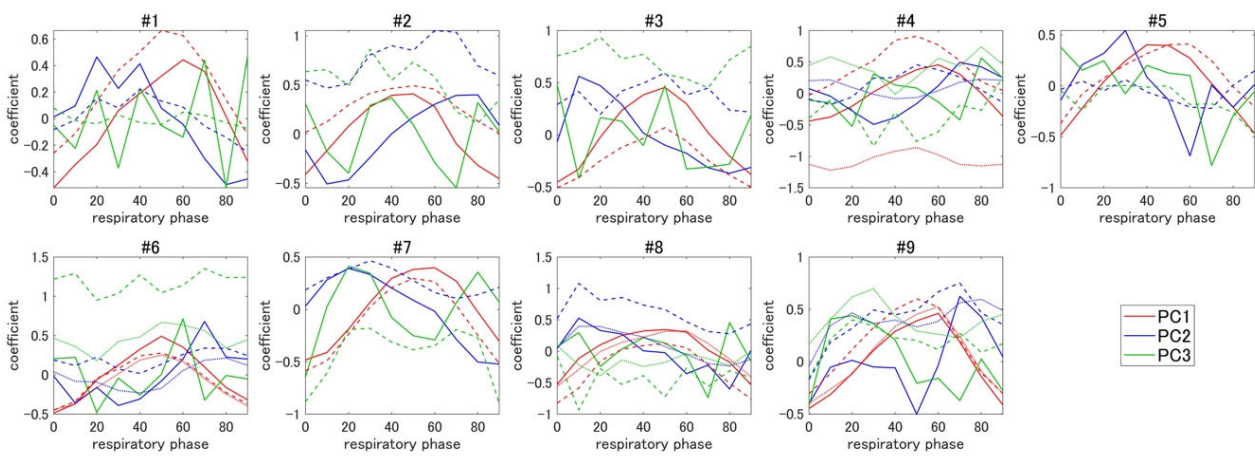
208 In deep learning-based techniques, which is based on a CNN to estimate PCs from the X-ray fluoroscopic  
209 images, training data is generated by data augmentation with applying various PCs. The quality of the training  
210 data is one of the most important factors that determine the performance of the volumetric imaging. That is, in  
211 the data augmentation, the data which could be clinically observed should be included for the effective training  
212 of CNN. In order to understand actual distribution of PCs in clinical cases, the three PCs that reproduced  
213 deformation closest to the ground truth were evaluated as shown in Fig. 7. Because the first PC (PC1) correlated  
214 with the displacement of the diaphragm position (Fig. 2), the first eigenvector was proposed as the dominant  
215 factor representing the deformation associated with respiration. However, the second and third PCs did not  
216 necessarily change with the same trend as PC1, and no correlation was observed between the coefficients. This  
217 result suggests that equally scaling all coefficients alone does not necessarily reproduce clinical data with large  
218 deformation beyond the original modeling data. Considering that no clear correlation existed between PCs,  
219 randomly allocating PCs<sup>7</sup> or sampling PCs in expanded ranges to generate various deformations could be a  
220 solution for data augmentation.

221 This study evaluated optimal PCs as the coefficients that minimize the difference between the internal  
222 deformations represented as the linear combination of eigenvectors and the ground truth of deformation.  
223 Although PC estimation methods are different in clinical practice, PC1 with the largest contribution is expected  
224 to be similarly estimated because it strongly correlates with respiratory motion. Therefore, the synthesized  
225 volume images could be applied to confirm the target location and evaluate the consistency of the internal  
226 structures between the planned and synthesized CT images as a motion management technique.

227 There were some error sources in this PCA-based volumetric imaging. One error source was the variation in  
228 the patient's breathing patterns. Assuming that the 4DCT data were acquired during normal breathing at rest, it  
229 could be challenging to reproduce deformation patterns different from those obtained during 4DCT acquisition,  
230 such as during forced breathing using additional muscles. Motion artifacts in 4DCT may also be an error source,

231 although the reconstruction algorithm could compensate for it<sup>17,18</sup>. The anatomical variation during the treatment  
 232 course, which cannot be evaluated from the 4DCT dataset, is also an error source. Therefore, it may be useful  
 233 to evaluate body shape changes with a 3D body surface measurement system and retake a 4DCT/four-  
 234 dimensional cone beam CT image to update the model. Tumor shrinkage or growth is also challenging to  
 235 reproduce with the PCA of the 4DCT dataset. Nevertheless, a method to simulate the tumor shape variation  
 236 based on image warping could be applicable<sup>5</sup>.

237



238

239 **FIGURE 7** Three principal component coefficients (PCs) that reproduced the deformation closest to the  
 240 ground truth. Solid, dashed, and dotted lines represent evaluations of the modeling test data 1 and 2.

241

## 242 5 CONCLUSIONS

243 This study quantitatively evaluated the achievable performance of volumetric imaging based on PCA using  
 244 multiple patient 4DCT datasets acquired on different dates. The mean MAE and SSIM of the PCA-reconstructed  
 245 volumetric images were approximately 80 HU and 0.88, respectively, regardless of the respiratory phase. In  
 246 most test cases including the data of which motion range was exceeding that of the modeling data, the positional  
 247 error of diaphragm was less than 5 mm. These results suggest that volume images could be synthesized with  
 248 reasonable accuracy for clinical applications by estimating the optimal PCs.

249

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