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Abdominal organ motion

Abdominal organ motion during inhalation and exhalation breath-holds: pancreatic motion at different lung volumes compared

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ABSTRACT

Purpose: Contrary to what is commonly assumed, organs continue to move during breath-holding. We investigated the influence of lung volume on motion magnitude during breath-holding and changes in velocity over the duration of breath-holding.

Materials and methods: Sixteen healthy subjects performed 60-second inhalation breath-holds in room-air, with lung volumes of ~100% and ~70% of the inspiratory capacity, and exhalation breath-holds, with lung volumes of ~30% and ~0% of the inspiratory capacity. During breath-holding, we obtained dynamic single-slice magnetic-resonance images with a time-resolution of 0.6 s. We used 2-dimensional image correlation to obtain the diaphragmatic and pancreatic velocity and displacement during breath-holding.

Results: Organ velocity was largest in the inferior–superior direction and was greatest during the first 10 s of breath-holding, with diaphragm velocities of 0.41 mm/s, 0.29 mm/s, 0.16 mm/s and 0.15 mm/s during $BH_{100\%}$, $BH_{70\%}$, $BH_{30\%}$ and $BH_{0\%}$, respectively. Organ motion magnitudes were larger during inhalation breath-holds (diaphragm moved 9.8 and 9.0 mm during $BH_{100\%}$ and $BH_{70\%}$, respectively) than during exhalation breath-holds (5.6 and 4.3 mm during $BH_{30\%}$ and $BH_{0\%}$, respectively).

Conclusion: Using exhalation breath-holds rather than inhalation breath-holds and delaying irradiation until after the first 10 s of breath-holding may be advantageous for irradiation of abdominal tumors.

Respiratory-induced motion of upper abdominal tumors during radiotherapy is often accounted for by using an internal target volume based on a pre-treatment 4-dimensional CT (4DCT), resulting in large treatment volumes and high dose values to surrounding healthy tissues [1]. However, several groups have shown that the respiratory motion of pancreatic tumors measured on a single pre-treatment 4DCT is not representative for daily tumor motion [2–4]. This discrepancy could limit the benefit of all 4DCT-based respiratory motion management techniques, such as using mid-ventilation [5].

Breath-holding can be used to reduce tumor motion during radiotherapy. Either inhalation or exhalation breath-holds are used in this technique, which is increasingly employed in many clinical applications in radiotherapy, including during irradiation of abdominal tumors [6–11]. Whether inhalation or exhalation breath-holding is used currently depends on the radiation technique and tumor type. For example, when using stereotactic body radiotherapy for pancreatic cancer, the planned dose to surrounding organs at risk was reduced when treatments were planned with the tumor at the exhalation rather than the inhalation position [12]. However, this was under the assumption that during breath-holding only minimal geometrical uncertainties remained.

The position variation of the tumor between multiple consecutive breath-holds, both inhalation and exhalation, has already been thoroughly determined for abdominal tumors [6,7,9,10,13,14]; mean variations of 1.2 and 2.3 mm were reported in the inferior–superior (IS) direction for inhalation and exhalation breath-holds, respectively [6,7]. The interfractional tumor position variation is similar for inhalation and exhalation breath-holds [15]. Preliminary results on abdominal tumor stability *during* exhalation breath-holds show good stability, but these studies also reported individual cases in which motion of up to 5 mm was observed during breath-holding [6,9]. Also, exhalation breath-holds are more challenging to perform and therefore often result in shorter breath-hold durations than inhalation breath-holds [6,9,16]. The

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generally good organ stability during exhalation breath-holds is in great contrast with the large organ drifts that have been observed during inhalation breath-holds in healthy subjects and patients [13,14,17,18]. In addition, it was observed that the motion during inhalation breath-holds was more pronounced at the beginning of the breath-hold [17,18].

Even though both inhalation and exhalation breath-holds are being used for radiotherapy of abdominal cancer, the difference in organ motion during both breath-hold types has not previously been investigated [7,9,10,19]. However, to determine the optimal breath-holding procedure in terms of organ stability and feasibility, this difference must be known. Also, if the velocity of organ motion changes during breath-holding [17,18], the irradiation must be applied when the velocity is least.

In this study, we obtained magnetic resonance (MR) images at a high frequency during 60-second breath-holds with four different lung volumes in a group of 16 healthy subjects. We compared pancreatic and diaphragmatic motion magnitude and velocity during breath-holding between the different lung volumes. We determined which lung volume resulted in the most stable anatomy during breath-holding and whether the velocity changed during breath-holding.

Materials and methods

Subjects and measurement protocol

We studied 16 healthy subjects with a mean age of 32 years and no history of pulmonary disease (more characteristics in Supplementary Table E1). All subjects consented to participation in the study and abstained from eating and drinking in the two hours prior to the measurement. Each subject was instructed to perform twelve 60-second inhalation breath-holds; six with fully inflated lungs ($BH_{100\%}$) and six with a lung volume of ~70% of $BH_{100\%}$ ($BH_{70\%}$). In addition, each subject was instructed to perform twelve 60-second exhalation breath-holds; six with a lung volume of ~30% of $BH_{100\%}$ ($BH_{30\%}$) and six with fully deflated lungs ($BH_{0\%}$). All breath-holds were performed in room-air and the subjects did not receive any visual or mechanical guidance on their voluntary breath-holds. So, the lung volumes of 30% and 70% were based upon the subjects' perception and might differ between the three repeated breath-holds for each subject and lung volume. Simple audial instructions were given before the start of each breath-hold. The start of the breath-hold was defined when there was no more visible chest surface movement. Subjects were given a minute of free breathing between breath-holds. To avoid any order effect, half of the subjects performed the inhalation breath-holds prior to performing the exhalation breath-holds and the other half performed the breath-holds vice versa.

MRI measurement and motion acquisition

MR scans were obtained with an Ingenia 3T MR scanner (Philips Healthcare, Best, the Netherlands). During each breath-hold, we obtained images (one image every 0.6 s) using a fast single-slice steady-state free precession sequence (bandwidth = 538 Hz/voxel), resulting in 100 images per breath-hold. For each lung volume, we obtained coronal slices during the first three breath-holds and sagittal slices during the last three breath-holds. The slices (thickness, 8 mm; pixel size, 0.93×0.93 mm^2) were positioned such that both the diaphragm and the pancreatic head were in the field of view.

Within each scan, the rigid pancreatic head and diaphragm displacements relative to the position at the start of breath-holding were obtained using a 2-dimensional image correlation algorithm, as used previously [13,20]. Displacements were determined by matching of a pre-determined template, containing the structure of interest (i.e. top of the right diaphragmatic dome or complete pancreatic head), to all images obtained during a single breath-hold. No deformable registration was used since only planar imaging was obtained and small organ displacements out of this plane could give a false representation of the organ deformation during breath-holding. To decrease the effects of small motion artifacts due to template mismatching, imaging artifacts or small organ deformations, we determined the pancreatic motion during breath-holding three times with different templates and averaged the results. Details about the algorithm can be found in the Supplementary material.

Data analysis

We measured the motion magnitude of the pancreatic head over time in the IS and left–right (LR) direction (coronal scans) and in the IS and anterior–posterior (AP) direction (sagittal scans). The inferior, left and anterior directions were defined as the negative directions. In each direction, the motion magnitude of the pancreatic head during breath-holding was defined as the maximum difference in position in the respective direction within a single breath-hold. For the diaphragm, we only determined the motion magnitude in the IS direction. Before determining the motion magnitude, the motion data were smoothed using a moving average filter with a width of five data points to remove residual motion artifacts due to template mismatching and displacements due to cardiac motion.

We investigated whether it would be beneficial, in terms of organ stability, to delay irradiation of a patient for a certain amount of time after the start of breath-holding. To do so, we used a sliding time-frame of 20 s to determine the motion magnitude during 20 s of breath-holding, resulting in a simulated delay of 0–40 s. The differences in motion magnitude after a simulated delay of 0 s and 10 s were tested using the Wilcoxon signed-rank test. The cut off of 10 s was chosen to maintain potentially manageable breath-holding durations of 30 s.

To investigate the change in velocity during breath-holding, we calculated and compared the mean velocity of the pancreatic and diaphragmatic motion during the first 10 s of breath-holding and during the remainder of the breath-hold. The velocity was defined as the motion magnitude divided by the time over which it was measured. By using organ velocity, we excluded any effects of breath-hold duration (i.e. when there is a drift, longer breath-hold durations result in larger motion magnitudes). The differences in velocity were tested using the Wilcoxon signed-rank test.

In some cases the diaphragm is used as a surrogate for tumor motion while the patient is breathing freely [21]. We determined whether diaphragm motion can be used as a surrogate for pancreatic motion during breath-holding. This was done by determining the slope and strength of the linear association between the motion of the two structures. The unsmoothed motion of the pancreatic head and of the diaphragm during all breath-holds was plotted. For each breath-hold, a correlation plot of the motion of the pancreatic head in the IS or LR direction versus the motion of the diaphragm in the IS direction was created and their relation was analyzed by simple linear regression. In addition, we calculated the coefficient of determination (r^2) and distinguished between weak ($r^2 < 0.6$) and a strong ($0.6 \leqslant r^2 < 0.8$) to very strong linear associations ($r^2 \geqslant 0.8$). For the breath-holds for which we observed at least a strong association ($r^2 \geqslant 0.6$), we determined the mean slope of the linear fits, as this describes the relation between pancreatic and diaphragmatic motion.

The lateral location of the sagittal slice was based on the location of the pancreatic head, which resulted in a lateral location of the slice through the heart and the mediastinum. At this location,