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Measurement of diaphragmatic length during the breathing cycle by dynamic MRI: comparison between healthy adults and patients with an intrathoracic tumor

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Abstract The purpose of this study was to assess diaphragmatic length and shortening during the breathing cycle in healthy volunteers and patients with a lung tumor using dynamic MRI (dMRI). In 15 healthy volunteers and 28 patients with a solitary lung tumor, diaphragmatic motion and length were measured during the breathing cycle using a trueFISP sequence (three images per second in the coronal and sagittal plane). Time-distance curves and maximal length reduction (= shortening) of the diaphragm were calculated. The influence of tumor localization on diaphragmatic shortening was examined. In healthy volunteers maximal diaphragmatic shortening was 30% in the coronal and 34% in the sagittal orientation, with no difference between both hemithoraces. Tumors of the upper and middle lung region did not affect diaphragmatic shortening. In contrast, tumors of the lower lung region changed shortening significantly ($P<0.05$). In hemithoraces with a tumor in the lower region, shortening was 18% in the coronal and 19% in the sagittal plane. The ratio of diaphragmatic length change from inspiration to expiration changed significantly from healthy subjects (inspiration length ≫ expiratory length, $P<0.05$) to patients with a tumor in the lower lung region (inspiratory length = expiratory length). dMRI is a simple, non-invasive method to evaluate diaphragmatic motion and shortening in volunteers and patients during the breathing cycle. Tumors of the lower lung region have a significant influence on shortening of the diaphragm.

Keywords Diaphragmatic function · Dynamic MRI · Tumor · Lung · Breathing cycle

Introduction

So far, impaired mechanics of the inspiratory pump (= diaphragm) have been investigated by respiratory inductive plethysmography, spirometry, transdiaphragmatic pressures and magnetometer [1]. Especially mild diaphragmatic weakness can hardly be detected by these techniques [2], and changes in diaphragmatic shortening, mobility and local changes, which are often the pathophysiologic correlate of dyspnea and impaired respiratory mechanics [1, 3, 4], cannot be examined. Imaging techniques are a major tool to describe the geometri-cal changes corresponding to the actions of the diaphragm and can be useful to understand various mechanical aspects of the respiratory system in normal conditions and disease and establish structure-function relationship [5].

Magnetic resonance imaging (MRI) has been shown to visualize the diaphragm in three dimensions in steady state [4, 6, 7]. In these studies, the shape of the diaphragm changed markedly along the sagittal plane with lung inflation, but there were no major changes in the coronal plane. Recently, ultra-fast MR acquisition techniques have permitted direct dynamic visualization of
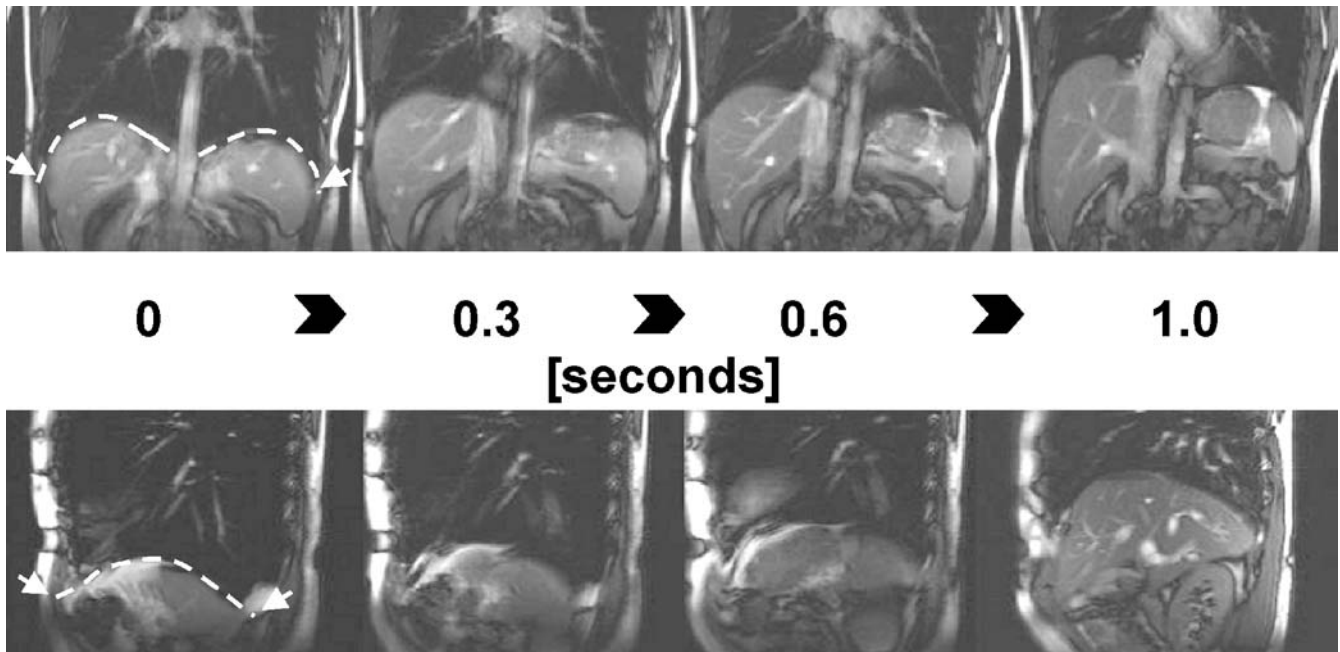
Fig. 1 Cineloop sequence of a subject during 1 s from maximal inspiration to maximal expiration. Coronal and a representative sagittal plane (right hemithorax) is shown. *Dotted* line exemplifies the line of the measurement of diaphragmatic length. Diaphragmatic lateral as well as anterior and posterior chest wall attachment is shown by the *arrows*

respiratory motion, including assessment of the parenchyma, chest wall and diaphragm, within high spatial and temporal resolution [8–11]. Continuous multiplanar documentation and measurement of the diaphragmatic length, shortening and mobility in healthy subjects and the influence of a solitary lung lesion on the diaphragmatic length during the breathing cycle using dynamic MRI has not been performed so far.

The aim of the study was to analyze continuous changes and mobility of the diaphragm during the breathing cycle in the coronal and sagittal orientation. The influence of intrathoracic tumor and its localization on diaphragmatic length and shortening was investigated in patients with a solitary lung tumor.

Materials and methods

Fifteen healthy volunteers (14 males; 1 female; mean age 28 years, range 21–35 years) without any evidence or history of pulmonary disease were included in this study. Also, to examine the influence of a solitary lesion on diaphragmatic shortening, 28 patients with a histologically proven intrathoracic solitary tumor (18 males; 10 females; mean age 48 years, range 41–74 years; maximal diameter of the tumor less than 5 cm) were included in this study. All patients were in good clinical condition, had no clinical or radiological signs of obstructive lung disease and were referred for potentially curative therapy, e.g., high-dose radiother-

apy. After the nature of the procedure had been fully explained, informed consent was signed by all participants under an institutionally approved subject research protocol. Tumor fixation to the chest wall or pleura was excluded in all patients using fast imaging with steady precession (trueFISP) MRI sequence in coronal, transversal and sagittal orientation. In all patients, no tumor treatment had been performed before MRI.

Magnetic resonance imaging (MRI)

MRI was carried out on a clinical 1.5-T whole-body scanner (Magnetom Symphony, Siemens Medical Solutions, Erlangen, Germany) equipped with eight receiver channels and a high performance gradient system (30 mT/m).

For the assessment of the diaphragmatic motion, dynamic MRI was acquired in a mid-coronal plane and two mid-sagittal planes over the right and left hemithorax using a trueFISP sequence [TE/TR: 1.7/37.3 ms; flip angle: 65°; receiver bandwidth: 977 Hz/pixel; field of view (FOV): 375×400; matrix 149×256; slice thickness: 10 mm; voxel size: 2.5×1.6×10 mm³]. These planes were chosen to correspond roughly to the orientations of diaphragmatic fibers, which radiate from the central tendon. The coronal plane was positioned through the trachea. The sagittal planes were placed through the most posterior part of the ribs [3]. Total acquisition time was 30 s for each slice, acquiring three frames per second (Fig. 1). All volunteers and patients were instructed to change from quiet tidal breathing to maximal inspiration followed by maximal expiration with as much effort as possible (Fig. 1). This procedure was rehearsed several times to ensure constant conditions and a constant frequency in breathing (about 2.5 s for tidal breathing from inspiration to expiration). Because of the interindividual differences of the duration of the maximal inspiration plateau, two bars were inserted in the figures and held prior to forced expiration, and measurement of the diaphragmatic length to maximal expiration was continued afterwards (Figs. 2, 3).
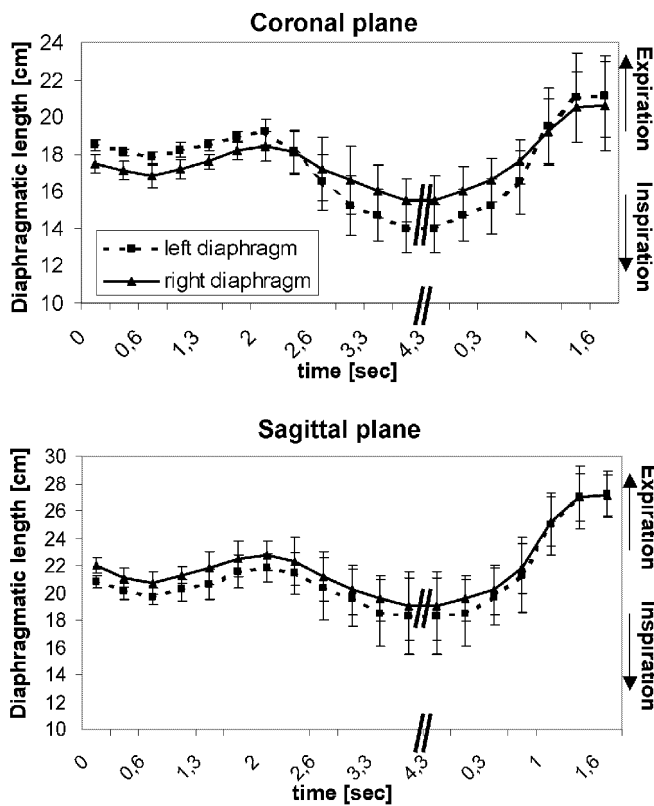
Coronal plane

Sagittal plane

Fig. 2 Continuous measurement of diaphragmatic length beginning with baseline position (mean length of the diaphragm in quiet breathing) followed by tidal inspiration and expiration and forced inspiration and expiration. Measurements of the diaphragmatic length in coronal and sagittal planes were not significantly different between the right and left hemithorax

Measurement of diaphragmatic length and shortening

The diaphragm can be divided into three areas [12]: the sternal part of the diaphragm is attached to the back of the xyphoid process. The costal part is attached to the internal surfaces of the lower six costal ribs and their cartilages. The lumbar part is fixed to the aponeurotic medial and lateral arcuate ligaments and to some lumbar vertebrae by means of the crura. Diaphragmatic lengths were calculated on three different planes: along the coronal and two sagittal planes we calculated total diaphragmatic length during the breathing cycle. Using a workstation (CHILI, CHILI GmbH, Heidelberg, Germany [13]) several representative points (10–20) were set along the diaphragmatic dome and connected, and the distance was measured (Fig. 1). Time-distance curves were performed on this basis. At constant breathing conditions (constant frequency in breathing), right and left hemithoraces were measured separately (separated by the spine and/or aorta descendens in the coronal plane). Maximum diaphragmatic length changes were defined as the maximum difference between deep inspiration and deep expiration. To investigate diaphragmatic length changes in respiration, mean diaphragmatic length in quiet breathing served as the baseline, and maximal length changes in inspiration and expiration were documented; a box-whisker Plot was calculated. To calculate shortening of the diaphragm, maximal length in expiration was subtracted from maximal length in inspiration, and relative length reduction was calculated.

Patients with a solitary tumor were divided into three groups according to Giraud et al. [14] to investigate the influence of a lesion on diaphragmatic length change and shortening: patients with a tumor cranial of the T (= thoracic) 3/T4 disk space belonged to the group of patients with tumors of the upper region, patients with tumors cranial of the T6/T7 disk space to the middle region, and patients with tumors cranial of the T9/T10 disk space belonged to the lower region group. Diaphragmatic length of the tumor-bearing hemithorax was compared with the non tumor-bearing hemithorax.

Statistical analysis

The statistical analysis of the data was performed with SAS software (SAS Institute, Inc., Cary, NC). To obtain simultaneous tests for mean comparisons, the Duncan's multiple-range test of ANOVA using a significance level of $P=0.05$ was used. Mean and standard deviation were calculated. In addition, a t-test for paired samples and box-whisker plots (demonstrating mean, standard deviation and double standard deviation) were performed.

Results

Dynamic MRI showed diagnostic image quality and regular synchronous diaphragmatic motions in all volunteers and patients. The diaphragm showed upward deflections during expiration (= relaxation) and downward deflections during inspiration (= contraction) (Fig. 1). The acquisition of three images per second allowed for continuous recording during the breathing cycle, even in forced respiration.

Measurement of diaphragmatic length in volunteers

Continuous imaging of the diaphragmatic length of a healthy volunteer from maximal inspiration to expiration is shown in Fig. 1. Continuous measurement of diaphragmatic length beginning with baseline position (mean length of the diaphragm in quiet breathing) followed by tidal inspiration and expiration and forced inspiration and expiration is shown in Fig. 2. A high correlation between the length of the right and left diaphragm is demonstrated in coronal and sagittal planes. The mean values of the minimum and maximum length of the diaphragm in the coronal plane were 15.5±1.3 cm in inspiration and 20.7±2.4 cm in expiration on the right and 14.0±1.3 cm in inspiration and 21±2.4 cm in expiration on the left (Fig. 2). The right and left diaphragmatic length was not significantly different in the coronal plane. There was also no significant difference between right and left diaphragmatic length in the sagittal plane (19±1.7 cm in inspiration vs. 27±2.5 cm in expiration on the right; 18.3±2.3 cm in inspiration vs. 27±2.8 cm in expiration on the left). The difference between coronal and sagittal diaphragmatic length changes was significant ($P<0.05$).
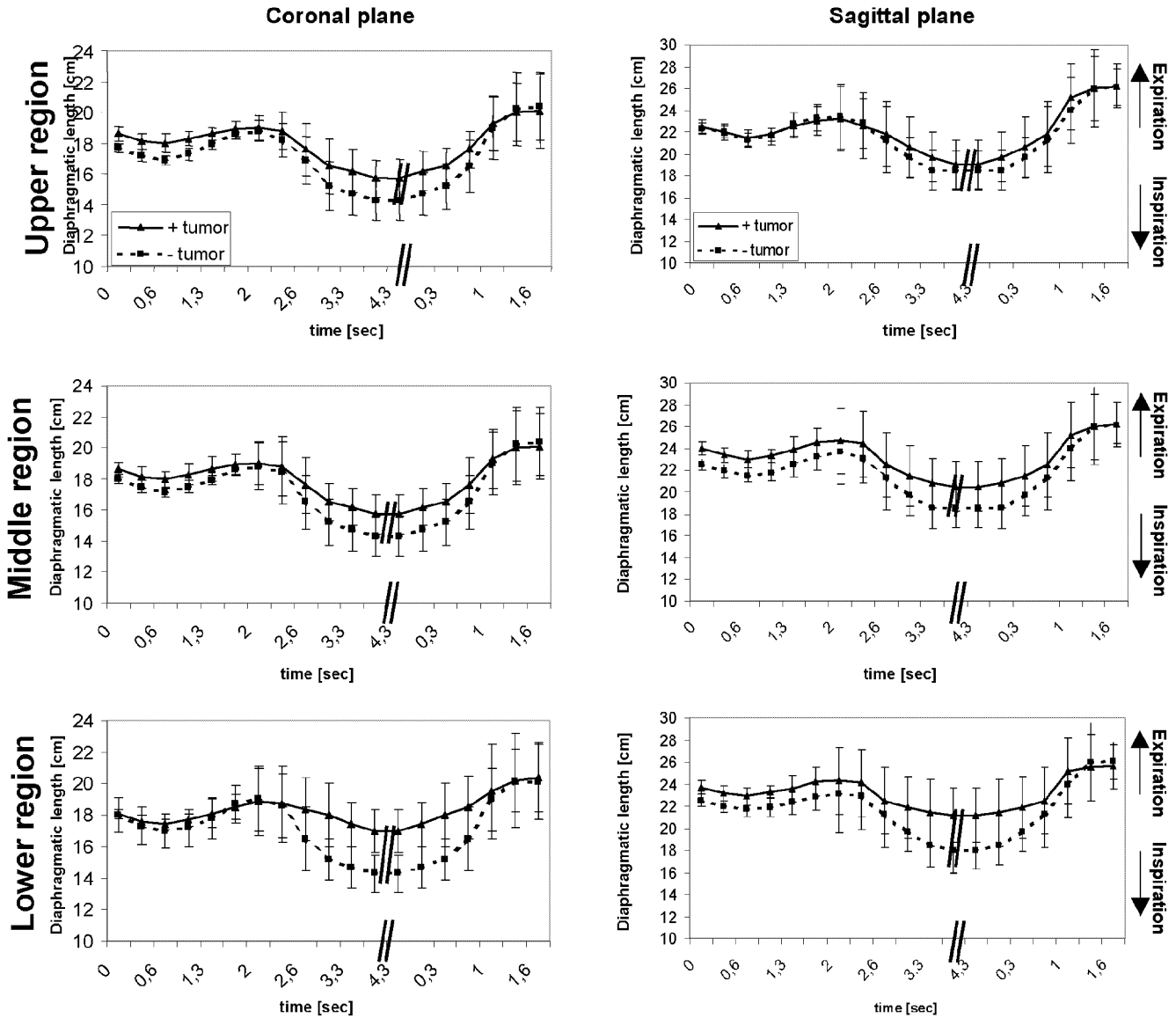
Fig. 3 Continuous measurement of diaphragmatic length beginning with baseline position (mean length of the diaphragm in quiet breathing) followed by tidal inspiration and expiration and forced inspiration and expiration. The tumor-bearing hemithorax was compared with the non-tumor-bearing hemithorax

Measurement of diaphragmatic length in patients with an intrathoracic tumor

A continuous measurement of the diaphragmatic length during the breathing cycle in patients with a solitary tumor is demonstrated in Fig. 3. Changes of diaphragmatic length of a tumor-bearing hemithorax (diaphragm of tumor-bearing hemithorax = DTBH) were compared with the contralateral, non-tumor-bearing hemithorax (DNTBH).

A tumor in the upper or middle region had no significant influence on diaphragmatic length compared with the non-tumor-bearing counterpart in both coronal and sagittal planes. A tumor in the lower region significantly influenced diaphragmatic length in the coronal plane (DTBH: 17.0±1.2 cm in inspiration vs. 20.2±2.0 cm in expiration; DNTBH: 14.3±1.4 cm in inspiration vs. 20.2±2.7 cm in expiration, P=0.04). In the sagittal plane, there was a substantial trend, but no significant difference (DTBH: 21.2±2 cm in inspiration vs. 25.5±3.1 cm in expiration; DNTBH: 18.0±2.5 cm in inspiration vs. 26.0±2.8 cm in expiration, P=0.06).

Box-whisker plots were performed using mean length of the diaphragm in quiet breathing as baseline (Fig. 4). The positive values represent relaxation in expiration, the negative values shortening in inspiration. In volunteers the coronal diaphragmatic length changed signifi-
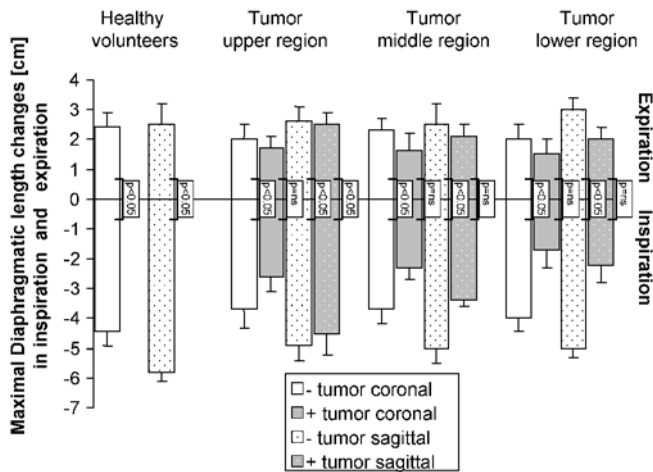
Fig. 4 Box-whisker plot of volunteers and patients with an intra-thoracic tumor. Baseline is the mean diaphragmatic length in quiet breathing. The area over the baseline represents maximal dia-phragmatic length change in expiration (= relaxation), the area be-low the baseline represents maximal diaphragmatic length change in inspiration (= contraction). In patients with a tumor, the more the tumor was close to the diaphragm the more equal the part of shortening and relaxation of the diaphragm proved to be in the forced breathing cycle, and shortening decreased
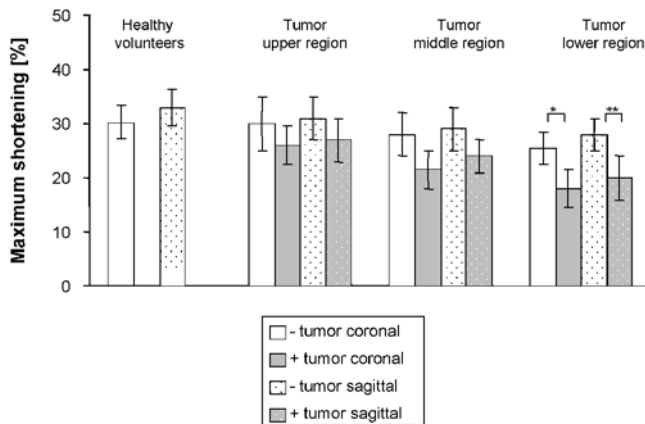

Fig. 5 Maximum shortening of the diaphragm of volunteers and patients with an intrathoracic tumor. In volunteers mean measure-ments of the diaphragmatic shortening in coronal (*left bar*) and sagittal (*right bar*) planes are demonstrated. In patients, diaphrag-matic shortening of the non-tumor-bearing hemithorax is com-pared with the tumor-bearing hemithorax. The closer the tumor was to the diaphragm, the less contractile the diaphragm proved to be. (*$P<0.05$, **$P<0.01$)

cantly more in deep inspiration than in forced expiration (4.5±0.5 cm in inspiration vs. 2.5±0.5 cm in expiration, coronal plane, $P<0.05$) and 5.8±0.6 vs. 2.6±0.6 cm (sagittal, $P<0.05$). In patients with a tumor in the upper region, diaphragmatic length changed also significantly more in deep inspiration than in forced expiration in the sagittal plane ($P<0.05$). In patients with a tumor in the

middle region, diaphragmatic length changed substan-tially more in deep inspiration than in forced expiration, but this was not significant. In patients with a tumor in the lower region length changes in inspiration and expi-ration were almost identical (1.7±0.6 vs. 1.5±0.5 cm in the coronal and 2.2±0.6 vs. 2.0±0.4 cm in the sagittal plane).

The shortening of the diaphragm was calculated by subtracting maximal diaphragmatic length in expiration from length in inspiration and calculating the relative length reduction. In healthy volunteers coronal shorten-ing was 30%. Sagittal shortening was 34%, respectively, (Fig. 5).

In patients with an intrathoracic tumor, diaphragmatic shortening was dependent on tumor localization. With tumors in the upper and middle region shortening was not significantly different with regard to non-tumor-bearing hemithorax. In the lower region, shortening was significantly reduced in both coronal (18 vs. 25% in DNTBH, $P<0.05$) and sagittal planes (19 vs. 28% in DNTBH, $P<0.01$).

Discussion

Our results indicate that MRI using trueFISP sequences is a feasible technique to directly and non-invasively vi-sualize and measure dynamic respiratory motions and shortening of the diaphragm. Intrathoracic tumors in the lower lung region have a significantly negative impact on diaphragmatic length changes and mobility.

In the past, diaphragmatic motion was investigated using a number of radiological and non-radiological techniques [1, 15–17]. Results were compared with a spectrum of expected values accounting for age, gender and body habitus and were classified as normal if they fell within 20% of the predicted mean. Thus, localized and early pathological changes of the diaphragm may not be detected by currently available techniques [18].

Imaging techniques are a major tool to describe local geometric changes reflecting the actions of the dia-phragm [5, 19]. They can be useful to understand various mechanical aspects of the diaphragm in physiological, but also pathological situations [20, 21]. In cardiological, pulmonological, neurological and oncological diseases, reduced diaphragmatic shortening was shown to corre-late with dyspnea and poor clinical outcome [4, 22–24]. In oncology, diaphragmatic shortening is of high impor-tance for radiotherapy planning because of its influence on tumor mobility [25].

Spiral CT has been proposed to image the diaphragm [26]. Cassart et al. [27] were able to study the effect of chronic hyperinflation on diaphragmatic length and sur-face area in patients with chronic obstructive pulmonary disease using CT. The inherent limitation of CT tech-nique is radiation exposure. Thus, especially in follow-

up controls, young patients and benign diseases, the application of CT is problematic.

As a consequence, we investigated the feasibility of MRI in measuring the diaphragm. In the study from Cluzel et al. [6], static MR imaging was proposed to investigate diaphragmatic motion in three dimensions with a good correlation to spirometry. Another group reported data on the diaphragm at three different lung volumes. Four healthy males were studied, and three sets of six slices, one in the coronal plane and one in the sagittal plane for each hemithorax, were performed [9]. All these techniques of chest imaging were static [14, 28–30].

Dynamic MRI is a new technique to measure mobility of the chest wall and the diaphragm. Up to now, only few reports have described the use of dynamic MRI during the breathing cycle [5, 8, 31]. MRI has the obvious advantage of lack of superimposition and irradiation [8, 32] and permits simultaneous assessment of respiratory motions of the lungs and chest wall and surrounding structures in multiple dimensions [11] such as the abdominal structures, muscles and organs as the liver or kidney and tumors. Suga et al. [5] applied a FLASH sequence in 6 healthy volunteers and 28 patients with pulmonary emphysema to measure maximal inspiratory and expiratory dimensions of the chest. The diaphragmatic dome has a different shape when viewed from the side or the front. It flattens and tilts as the lung volume increases. We found few studies that provided quantitative data for the human diaphragm in vivo [4, 21, 22]. In these studies, the shape of the diaphragm changed markedly along the sagittal plane with lung inflation, but there were no major changes in the coronal plane. The potential overestimation of total diaphragmatic length choosing an external costal marker has already been mentioned by Cluzel et al. [6]. In our study diaphragmatic length also changed more significantly in the sagittal plane, but changes in the coronal plane were also substantial. We used anatomic landmarks and the same loci of diaphragmatic insertion as proposed by Cluzel et al. [6]. In our study, diaphragmatic shortening was about 30% in the coronal and 34% in the sagittal plane. Other groups published data between 25 and 37% [7, 33]. In the group of volunteers, inspiratory changes of diaphragmatic length proved to be significantly more prominent than expiratory changes, which means that the diaphragm has a higher capacity to shorten than to relax. This is in good correlation with data from spirometry where inspiration leads to more prominent changes in lung volume than expiration [34].

In the next step, diaphragmatic shortening of patients with a solitary tumor was investigated to analyze the potential influence of a solitary lesion. It has been published that age is a significant parameter, which influences diaphragmatic shortening negatively [35]. In our study age was substantially different between volunteers and patients, but as diaphragmatic length changes and shortening were compared with the healthy contralateral hemithorax intra-individually the calculation of significance was independent from the age of the patient. A potential limitation of this study is the fact that diaphragmatic length is certainly influenced by both abdominal muscles and accessory respiratory muscles. Thus, contraction of the abdominal muscles will push the diaphragm upward and relaxation will displace the diaphragm downward. But as the standard deviation of shortening of the diaphragm was low and diaphragmatic shortening itself was similar to other studies [7, 33] we propose this method to be adequate.

The aim of the study was not to measure tumor mobility, but in contrast to some data [36, 37], the more distant the tumor was from the diaphragm, the more mobile the diaphragm proved to be both in deep inspiration and expiration. So the distance of a lesion to the diaphragm has a significant influence on shortening and finally on respiration. Only tumors of the lower region influenced diaphragmatic length and shortening significantly. One reason might be the tumor itself, but also the potentially reduced compliance of the tissue surrounding the tumor, which themselves influence the surrounding tissue. Thus, tumors of the lower lung region—because of their proximity to the diaphragm—might influence the diaphragmatic capability to shorten more significantly than tumors of the upper lung region.

Frequently, quiet respiration is the basis for investigations of diaphragmatic motion. For a given patient, the inspiration and expiration length of the diaphragm are randomly distributed around quiet respiration positions, with large differences, depending on the structure under scrutiny and tumor localization. This is in agreement with Giraud et al. [14], who suggested that the positions of the various thoracic structures observed on a quiet respiration acquisition should not generally be considered representative of an intermediate position between deep inspiration and deep expiration.

In radiotherapy planning of solitary intrathoracic tumors [25], quiet respiration baseline often is calculated as the mean between deep inspiratory and expiratory positions. In tumor-bearing patients, the closer the tumor was to the diaphragm, the more similar shortening and relaxation of the diaphragm proved to be, and overall shortening decreased. In patients with tumors of the lower region, changes of the diaphragmatic length were almost identical in inspiration and expiration, and shortening was reduced from 31 to 18% in the coronal plane. This might also be interpreted as a sign of the reduced compliance of the tumor surrounding tissue, reducing the shortening of the diaphragm. Thus, in patients with a solitary tumor in the lower lung region, the calculation of the quiet respiration baseline as the mean between deep inspiration and expiration is correct. However, it is valid for healthy people and patients with

a tumor in the upper and middle lung region since short-ening is much more prominent than relaxation of the diaphragm.

Conclusion

Dynamic MRI using a trueFISP sequence is a feasible technique to document diaphragmatic motion and short-ening. It allows for direct and quantitative evaluation of diaphragmatic mechanics and widens the repertoire of tools to examine lung function with high temporal reso-lution. The closer tumors are to the diaphragm, the more they reduce shortening. Even small changes in shorten-ing are measurable by this technique.

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