Cancer Imaging (2006) **6,** S140–S144
DOI: 10.1102/1470-7330.2006.9027

CI

e-med
www.e-med.org.uk

FOCUS ON: TREATMENT PLANNING

Wednesday 18 October 2006, 09:30–11:00

Imaging tumour motion for radiotherapy planning using MRI

Hans-Ulrich Kauczor* **and Christian Plathow*†**

**Department of Radiology, German Cancer Research Center, Heidelberg, Germany; †Department of Diagnostic Radiology, Eberhard-Karls-University, Tuebingen, Germany*

Corresponding address: Prof. Hans-Ulrich Kauczor, MD, Department of Radiology, Innovative Cancer Diagnostics and Therapy, German Cancer Research Center, Im Neuenheimer Feld 280, 69120 Heidelberg, Germany
E-mail: hu.kauczor@dkfz.de

Abstract

Novel technology has made dynamic magnetic resonance imaging (MRI) of lung motion and lung tumour mobility during continuous respiration feasible. This might be beneficial for planning of radiotherapy of lung tumours, especially when using high precision techniques. This paper describes the recent developments to analyze and visualize pulmonary nodules during continuous respiration using MRI. Besides recent dynamic two-dimensional approaches to quantify motion of pulmonary nodules during respiration novel three-dimensional techniques are presented. Beyond good correlation to pulmonary function tests MRI also provides regional information about differences between tumour-bearing and non-tumour bearing lung and the restrictive effects of radiotherapy as well as the compensation by the contralateral lung.

Keywords: *Lung tumour; lung cancer; dynamic MRI; lung motion; tumour motion; radiotherapy planning.*

Introduction

Pulmonary nodules and lung tumours move substantially during respiration with significant differences according to the tumour localization. Respiratory tumour motion is a big challenge for radiotherapy, especially for high precision techniques. An additional target dose escalation which is deemed necessary for a curative approach of lung cancer is limited as so far as tumour motion is not sufficiently quantified and integrated into modern treatment planning. Thus, the risk of side effects within the surrounding normal tissue is unacceptably high. Radiation pneumonitis and the development of lung fibrosis are the physiological reactions of the lung which are not acceptable in severely ill patients. Thus modern techniques of adaptive radiotherapy will greatly benefit from devices which take lung and tumour motion into account in radiotherapy planning. The final objective is an additional increase in the radiation dose within the tumour volume together with maximum protection of the adjacent normal lung parenchyma[1]. A basic requirement is the accurate measurement and quantification of the mobility of pulmonary tumours. But also for follow-up examinations of patients with pulmonary tumours, a confident registration of the respiratory level is important in order to achieve easy identification and valid measurements.

Integration of the knowledge about lung and lung tumour motion is essential for planning of high precision radiotherapy. Four-dimensional imaging using computed tomography (4D-CT) is under development for optimization of radiotherapy by integration of motion[2–4]. These developments also include online imaging with a linac-integrated cone beam CT[5]. The particular advantages of magnetic resonance imaging (MRI) are the high soft-tissue contrast, differentiation of tumour and atelectasis, the possibility to choose the optimal plane for motion quantification and the possibility to integrate further dynamic parameters, e.g. lung perfusion or O_2 quantification, into one imaging session. The temporal resolution is already reasonably high for monitoring lung tumour motion in real-time[6].

1470-7330/06/020140 + 05

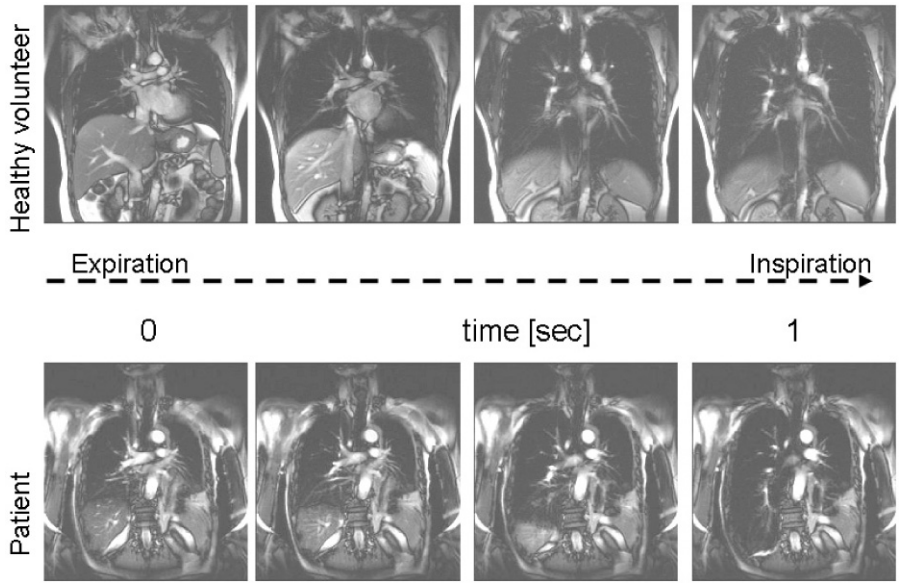

Figure 1 **Respiratory cycle from maximum expiration to maximum inspiration within 1 s. Top row shows a healthy volunteer with synchronous movement of both lungs. Bottom row shows a patient with lung cancer on the left and subsequently reduced motion range of the left lung.**

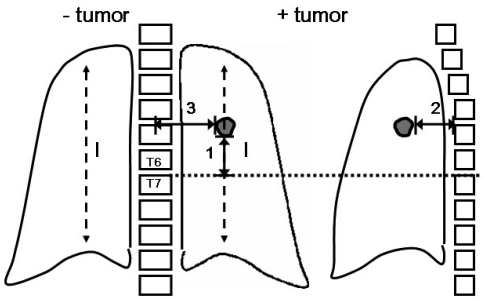

Figure 2 **Schematic drawing of possible measurements of lung and tumour motion during the respiratory cycle. Lung motion is reflected by measuring the distance from the apex to the top of the diaphragm (l). Cranio-caudal lung tumour motion is measured with regard to the intervertebral space T 6/7 (1); antero-posterior motion with regard central anterior margin of the spine (2); and medio-lateral motion with regard to the centre line of the spinal processus (3).**

MRI techniques

Novel MRI techniques allow for non-invasive acquisition of the motion of lung and pulmonary tumours[7] during the respiratory cycle with high spatial and temporal resolution[8,9]. Continuous improvements and new developments in MR scanner technology, such as high performance gradient systems and pulse sequences, have made this possible and address the inherent challenges of MRI of the chest, such as low proton density with an unfavourable signal to noise ratio and short T2* relaxation times with substantial susceptibility artefacts. Parallel imaging techniques make use of the different spatial sensitivities for the receiver coils in order to employ them for the simultaneous acquisition of image data, significantly reduce the phase encoding steps and achieve a marked improvement in spatial and temporal resolution. Thus, important requirements were met to measure the respiratory movement of the lung quantitatively. Established clinical methods, such as spirometry, are used for correlation and validation.

Fast-low-angle-shot (FLASH) sequences with a temporal resolution of one image per second demonstrate chest wall motion per se and postoperative changes of respiratory motion, i.e. changes of the cranio-caudal distance before and after lung volume reduction surgery[7]. The results exhibited a good correlation with spirometry. Modified true-fast-imaging-with-steady-state-precession (TrueFISP) sequences, widely used in cardiac MRI, were successfully applied in volunteers (Fig. 1). By adding a mathematical model, a continuous quantitative measurement of lung volume was achieved, which again showed a high correlation with spirometry[10].

Visualisation of lung tumour motion

After successful tests in volunteers, dynamic MRI was transferred to patients with solitary pulmonary tumours in order to visualise lung tumour motion by MRI in two dimensions (Fig. 1). Quantification was performed by measuring the cranio-caudal distance and the diaphragmatic length over time. Again, the results showed good correlations with the forced expiratory capacity in 1 s[11]. The diaphragmatic length was particularly useful in the assessment of respiratory

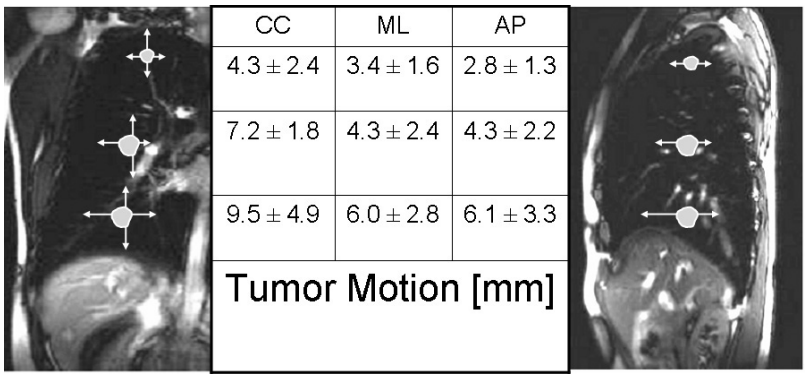

Figure 3 **Maximum lung tumour motion (mm) during shallow breathing in cranio-caudal (CC), medio-lateral (ML) and antero-posterior (AP) direction depending on tumour localization in the upper, middle or lower lung zone.**

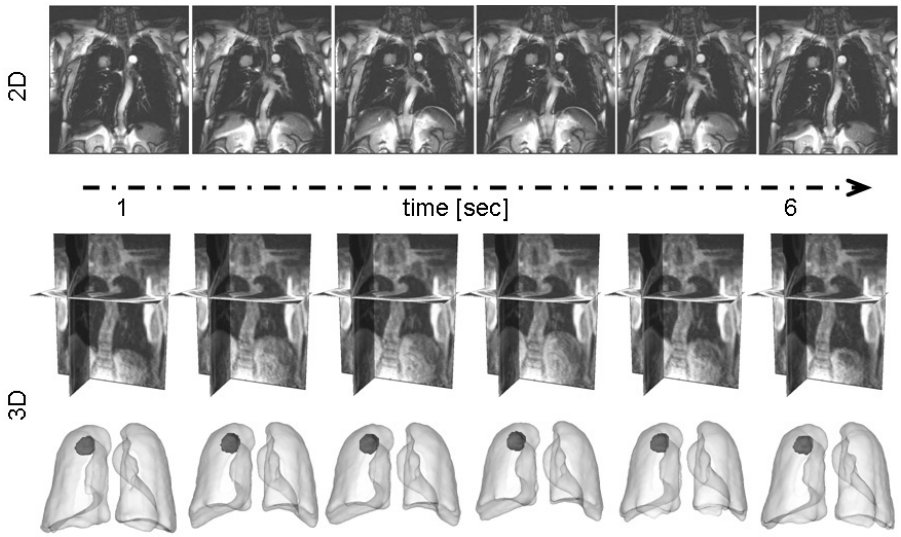

Figure 4 **Whole respiratory cycle from maximum inspiration to maximum expiration and back to maximum inspiration. Top row, 2D-TrueFISP sequence; middle row, 3D-FLASH sequence with a temporal resolution of one volume data set per second; bottom row, volume segmentation of lung and tumour from the 3D-FLASH data set.**

mechanics and the respective effects of pulmonary tumours[12]. In such studies the TrueFISP sequence was superior to a FLASH sequence due to its higher T2 signal[13]. Typical temporal resolution was three images per second. This allows for an almost continuous analysis of respiratory motion in two dimensions. The respiratory motion of patients with a pulmonary tumour showed a significant difference between the tumour bearing and the non-tumour bearing hemithorax. In addition, the location of the nodule had a marked effect on the regional mobility of the lung. Such regional differences are occult to global spirometric measurements. Thus, MRI is capable of providing important complementary quantitative regional information, which might be especially useful during follow-up.

Depending on size and location of the tumour, differences in motion were observed in the three axes (X-, Y- and Z-direction)[14]. For this assessment pulmonary nodules were grouped as cranial, middle and caudal according to Giraud *et al.*[15] (Fig. 2). Especially, the cranio-caudal motion (Y-direction) showed a significant dependence on tumour size and location. Small tumours in the caudal lung area can move up to 5 cm during maximum respiration. But also during shallow breathing, motion of nodules is considerable[16].

During shallow breathing, nodules in the lower lung zone exhibited a mean dislocation of 9.5 mm in the cranio-caudal direction and 6.6 mm in the anterior–posterior direction (Fig. 3). These results confirm similar publications using conventional radiological techniques. Theoretical calculations for 20 patients with pulmonary nodules demonstrated that this information for treatment planning might already lead to a marked increase of the target dose. A sufficient safety margin might not

be larger than 3.4 mm for the upper, 4.5 mm for the middle, and 7.2 mm for the lower lung zone. This is substantially smaller than the conventional safety margin of 5 or 10 mm, respectively, and might allow for an additional dose escalation especially in the upper lung zone. But it has to be mentioned that an individual quantification of the tumour motion is recommended as the interindividual differences in tumour motion are high. Simultaneous application of markers on the external chest wall demonstrated correlation and influencing factors between internal and external motion. Such knowledge is important to integrate triggering for radiotherapy [17].

Further developments in parallel imaging technology, especially view sharing techniques, have resulted in a further improvement in temporal resolution. This advantage can be applied to establish a three-dimensional FLASH sequence for a continuous volumetric visualisation of respiratory motion of lung and tumours [18]. In Fig. 4, the 3D-FLASH sequence is compared to the 2D-TrueFisp sequence. A 3D-FLASH data set contains 52 slices with isotropic 3 mm voxels and a temporal resolution of one data set per second. Motion of pulmonary nodules can be visualised and quantified in all three axes in order to be transferred in potential treatment concepts. Segmentation of such data sets, however, is still demanding and time-consuming and cannot be recommended for clinical use, yet.

Besides the mere information about tumour motion, three-dimensional techniques also allow for quantification of changes in tumour volume during the respiratory cycle. Changes in tumour volume are associated with deformations and changes of the main rotation axes of the nodules. Although this is not real rotation, the rotation of the axes can add up to 30° and impressively reflects the degree of deformation [19]. However, this information seems to be highly important, e.g. for further improvements in position and adaptation of collimators in radiotherapy. In addition, the knowledge about deformation of nodules and changes in volume during the respiratory cycle has substantial impact on the accuracy of volume measurement during the follow-up of pulmonary nodules and attempts to calculate nodule doubling times.

Therapy monitoring

Imaging of motion of lung tumours can also be used for therapy monitoring. Radiotherapy very quickly leads to a significant, often temporary reduction of motion of the treated hemithorax when compared to the situation prior to radiotherapy. This ipsilateral reduction is compensated for by an increased motion range of the contralateral lung [20]. Obviously, such changes between right and left lung cannot be detected by global lung function tests. Further studies are warranted to demonstrate which patients might benefit from preventive treatment, e.g. to prevent clinical aggravation.

Summary

Novel dynamic MRI techniques are capable of following respiratory motion in real-time. Surrogates derived from such series demonstrate good correlations with spirometry. Additional split lung analysis is feasible revealing important insights into differences between right and left lungs undetectable by global pulmonary function tests. Motion of pulmonary tumours can be measured in two or three dimensions, effects of respiration on volume and shape can be calculated. However, presently the evaluation of such data sets is extremely time-consuming.

Acknowledgement

Substantial portions of this paper and the figures were originally published in Plathow C, Meinzer HP, Kauczor H-U. Visualization of pulmonary nodules with magnetic resonance imaging (MRI). Radiologe 2006; 46: 260–6. Reproduce with kind permission from Springer Science and Business Media.

References

[1] Hof H, Herfarth K, Debus J. Stereotaktische Bestrahlung von Lungentumoren. Radiologe 2004; 44: 484–90.

[2] Hof H, Herfarth KK, Munter M, Essig M, Wannenmacher M, Debus J. The use of the multislice CT for the determination of respiratory lung tumor movement in stereotactic single dose irradiation. Strahlenther Onkol 2003; 179: 542–7.

[3] Leter EM, Cademartiri F, Levendag PC, Flohr T, Stam H, Nowak PJ. Four-dimensional multislice computed tomography for determination of respiratory lung tumor motion in conformal radiotherapy. Int J Radiat Oncol Biol Phys 2005; 62: 888–92.

[4] Alasti H, Cho YB, Vandermeer AD *et al*. A novel four-dimensional radiotherapy method for lung cancer: imaging, treatment planning and delivery. Phys Med Biol 2006; 51: 3251–67.

[5] Dietrich L, Jetter S, Tucking T, Nill S, Oelfke U. Linac-integrated 4D cone beam CT: first experimental results. Phys Med Biol 2006; 51: 2939–52.

[6] Lagerwaard FJ, Van Sornsen de Koste JR, Nijssen-Visser MR *et al*. Multiple slow CT scans for incorporating lung tumor mobility in radiotherapy planning. Int J Radiat Oncol Biol Phys 2001; 51: 932–7.

[7] Suga K, Tsukuda T, Awaya H *et al*. Impaired respiratory mechanics in pulmonary emphysema: evaluation with dynamic breathing MRI. J Magn Reson Imaging 1999; 10: 510–20.

[8] Gierada DS, Curtin JJ, Erickson SJ, Prost RW, Strandt JA, Goodman LR. Diaphragmatic motion: fast gradient-recalled-echo MR imaging in healthy subjects. Radiology 1995; 194: 879–84.

[9] Kondo T, Kobayashi I, Taguchi Y *et al*. A dynamic analysis of chest wall motions with MRI in healthy young subjects. Respirology 2000; 5: 19–25.

[10] Plathow C, Ley S, Fink C *et al*. Evaluation of chest motion and volumetry during the breathing cycle by dynamic MRI in healthy subjects: comparison with pulmonary function tests. Invest Radiol 2004; 39: 202–9.

[11] Plathow C, Fink C, Sandner A *et al*. Comparison of relative forced expiratory volume of one second with dynamic magnetic resonance imaging parameters in healthy subjects and patients with lung cancer. J Magn Reson Imaging 2005; 21: 212–8.

[12] Plathow C, Fink C, Ley S *et al*. Measurement of diaphragmatic length during the breathing cycle by dynamic MRI: comparison between healthy adults and patients with an intrathoracic tumor. Eur Radiol 2004; 14: 1392–9.

[13] Plathow C, Klopp M, Fink C *et al*. Quantitative analysis of lung and tumour mobility: comparison of two time-resolved MRI sequences. Br J Radiol 2005; 78: 836–40.

[14] Plathow C, Fink C, Ley S *et al*. Measurement of tumor diameter-dependent mobility of lung tumors by dynamic MRI. Radiother Oncol 2004; 73: 349–54.

[15] Giraud P, De Rycke Y, Dubray B *et al*. Conformal radiotherapy (CRT) planning for lung cancer: analysis of intrathoracic organ motion during extreme phases of breathing. Int J Radiat Oncol Biol Phys 2001; 51: 1081–92.

[16] Plathow C, Ley S, Fink C *et al*. Analysis of intrathoracic tumor mobility during whole breathing cycle by dynamic MRI. Int J Radiat Oncol Biol Phys 2004; 59: 952–9.

[17] Plathow C, Zimmermann H, Fink C *et al*. Influence of different breathing maneuvers on internal and external organ motion: use of fiducial markers in dynamic MRI. Int J Radiat Oncol Biol Phys 2005; 62: 238–45.

[18] Plathow C, Schoebinger M, Fink C *et al*. Evaluation of lung volumetry using dynamic three-dimensional magnetic resonance imaging. Invest Radiol 2005; 40: 173–9.

[19] Plathow C, Schoebinger M, Fink C *et al*. Quantification of lung tumor volume and rotation during respiration using 3D dynamic parallel MRI with view sharing – preliminary results. Radiology 2006; Jun 26 [Epub ahead of print].

[20] Plathow C, Hof H, Kuhn S *et al*. Therapy monitoring using dynamic MRI: analysis of lung motion and intrathoracic tumor mobility before and after radiotherapy. Eur Radiol 2006; Apr 21 [Epub ahead of print].

[21] Plathow C, Meinzer HP, Kauczor HU. Visualization of pulmonary nodules with magnetic resonance imaging (MRI). Radiologe 2006; 46: 260–6.