12

Computer-Assisted Visualization of Central Lung Tumours Based on 3-Dimensional Reconstruction

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1. Introduction

Each year, lung cancer is diagnosed in approximately 1.4 million people world-wide. There are approx. 205,000 new cases in the USA and approx. 345,000 in Europe [Cancer Atlas of the Federal Republic of Germany]. US researchers at the Centers for Disease Control and Prevention [CDC] expect the number of deaths to continue to rise as an immediate consequence of smoking. During the 20th Century, tobacco consumption caused about 100 million deaths, and this number is estimated at about one billion deaths world—wide for the 21st Century [CDC].

Axial 2-D computed tomography (CT) of the thorax is the accepted and established standard method used in pre-operative morphological imaging diagnosis in patients with central benign or malignant lung tumours. Tumour size, infiltration of central structures or segmental relatedness are the decisive parameters that the surgeon can derive in variable quality from 2-dimensional images, in order to assess the technical operability and the extent of the resection. However, the availability and quality of CTs vary greatly from one hospital to the next. The surgeon is thus often given print-outs on paper of a CT with 5 mm slices. Comprehensive coverage across the board with multi-slice detector CT (MSDCT) with 1mm slices and the possibility of interactive observation by the operator is, however, not yet available. Improved imaging and image-processing is crucial to the further optimization of pre-operative risk assessment, especially with reference to population development in industrialized nations. Multimorbid patients, patients with severe obstructive or restrictive diseases of the respiratory tract, as well as patients of advanced age, often limit the – actually required – tactical oncological extent of resection due to a post-operative lung function that is too low. Demands must therefore be made for a best-possible pre-operative localization and functional diagnostics, also with reference to the constant rise in patient age for the corresponding co-morbidities.

2. 3-D visualization in modern clinical practice

The pre-operative assessment of a malignant lung tumour, its anatomical and topographical position, the final extent of the tumour and the possibility of infiltration of central mediastinal structures or of the thoracic wall are of central importance to the thoracic surgeon undertaking the treatment. The (technical) operability of a patient is ultimately determined to a large degree based on the imaging, in combination with the lung capacity and the concomitant co-morbidities (functional operability).

Based on digital CT data, a precise 3-dimensional reconstruction of lung tumours, the tumour position, blood supply and the relationship to the bronchial system was developed within an research project of Fraunhofer MEVIS together with about 20 german hospitals for lung surgery (funded by the german society for research, DFG PE 199/20-1) and could serve as a new basis for pre-operative risk assessment. Different approaches for computer assistance in image based surgery planning were assessed within that large research cooperation. Can an improved pre-operative risk assessment be achieved through animated 3-D imaging, analogous to cardiac surgery? And how can the high-risk group of patients with a central lung tumour benefit from this? The following question were focus of that part of research, that was conducted at the University Hospital Lübeck: The aims of our research were to evaluate the use of computer-assisted reformatting and visualization using specially adapted software with reference to risk assessment and surgical strategy in patients with a central lung tumour [Limmer et al. 2010].

Within the framework of pre-operative imaging, two main application areas make use of in this computer-assisted approach: On the one hand, the computer-assisted extraction of quantitative diagnostic parameters, such as the estimation of lung emphysema portions which help to make predictions of post-operative lung function impairment possible through objectivation and expansion of the pre-operative imaging diagnostics. On the other hand, the computer-assisted approach should help the surgeon to plan surgery as precisely as is possible [Huenerbein M et al. 2003]. Computer-assisted planning based on images is the clinical standard today in the areas of neurosurgery as well as in operations on the locomotor apparatus [Tormenti MJ et al. 2010]. Radiation therapy also uses a computer-assisted approach with specially adapted software to achieve a precise radiation localization and optimized doses during stereotactic irradiation of tumours – under suppression of respiratory excursions [Alexander E 2001; Jolesz FA 2005]. The computer-assisted approach during surgical interventions on parenchymatous organs is currently the focus of interdisciplinary research conducted by collaboration between the fields of surgery, radiology and information technology. A central problem is that the pre-operative data cannot simply be transferred to the site of the operation due to organ movement and deformation. Furthermore, the pre-operative diagnostic data cannot be matched to the intra-operative situation using osseous landmarks [Grenacher L et al. 2005]. Concepts in the computer-assisted planning of surgery have been successfully driven forward in recent years, especially in the field of hepatic surgery [Lang H et al. 2005; Oldhafer KJ et al. 1999; Bornik A. et al. 2006]. The aims were to reduce the risks of surgery through pre-operative identification of structures that are at risk, as well as through predictions and minimization of the functional impairment to portions of tissue due to inadequate blood supply or backflow in the case of surgically induced disorders in the vascular system. The development of computer-assisted intra-operative support through suitable navigation systems and recording procedures for soft tissue surgery has been a focus of research for many years (BMBF funded project FUSION - Future Environment for Gentle Liver Surgery Using Image-Guided Planning and Intra-Operative Navigation [FUSION]). The research conducted by the University Hospital Luebeck in the field of navigated hepatic surgery is worthy of particular mention here [Hildebrand et al. 2007 und 2009].

3. Computer assistance for thoracic surgery planning

Standard risk assessment in thoracic surgery is based on conventional imaging techniques like x-ray and CT. In exceptional cases, additional examinations are carried out using, e.g., MRT, PET, SPECT or US. The oncological requirements (curative therapeutic approach), on the one hand, and the patient's technical and functional prerequisites, on the other, must be balanced individually for each patient. While the computer-assisted approach to the planning of thoracic surgical interventions is the aim of the current research, other questions pertaining to CT-assisted pulmonary diagnostics have already been answered. Rigorous quantification and visualization methods already exist for screening and early recognition of bronchial carcinomas, planning of biopsies, radiological monitoring of chemotherapy for lung metastases, quantification of parenchyma in lung function disorders, or embolism diagnostics. The researchers that specialize in medical applications at Fraunhofer MEVIS - Institute for Medical Image Computing, Bremen, develop prototypic software applications for the reconstruction, quantification and visualization of thoracic CT data, with the aim of supporting the planning of thoracic surgery in cases where complex resections are required in oncological lung patients [Dicken et al. 2005, Stoecker et al. 2009]. Methods and algorithms have been developed in close collaboration with about 20 german hospitals for lung surgery, to facilitate the delimitation of anatomical structures and pathologies in high-resolution CT data on the lungs.

Results, conducted by the University Hospital Luebeck from a 3-D reconstruction dating from 2005 revealed reformatting and visualization that was still highly simplified and the user modules for interactive use had also not yet been developed. The technical feasibility and a 3-dimensional reconstruction were initially evaluated and validated on 9 patients in a first exploratory phase between December 2005 and February 2006. These patients were characterized by a great diversity as possible with reference to age, tumour genesis, primary tumour/relapse, tumour localization or infiltration of extra-thoracic / mediastinal structures. The original CT and the reconstructed data sets for a 54-year-old patient with bilateral lung metastases derived from a uterine leiomyosarcoma are shown below as an example (Fig. 3.1 and Fig. 3.2). In addition to the simplified screen shots, the coarse grid of the reformatting is of particular note.

Over the course of the years, a computer-assisted approach was developed that allowed automatic segmentation of the lungs, the branching structures of the bronchial tree as far as the subsegmental level and interactive segmentation of the pulmonary blood supply. The method of reformatting and 3-D visualization has also proved to be robust in cases of central tumour localization with potential tumour invasion of larger vessels or central mediastinal structures. The differentiation of the lobes of the lungs is carried out automatically, the approximation of the individual lung segments is also possible with some manual interaction. The segmentation masks of the delimited regions form the basis for a quantitative analysis of functional CT data, such as lung volumes, emphysema index or mean lung density. The portion of the lung requiring resection can be calculated prior to surgery using this instrument and the expected post-operative loss of function can be approximated.

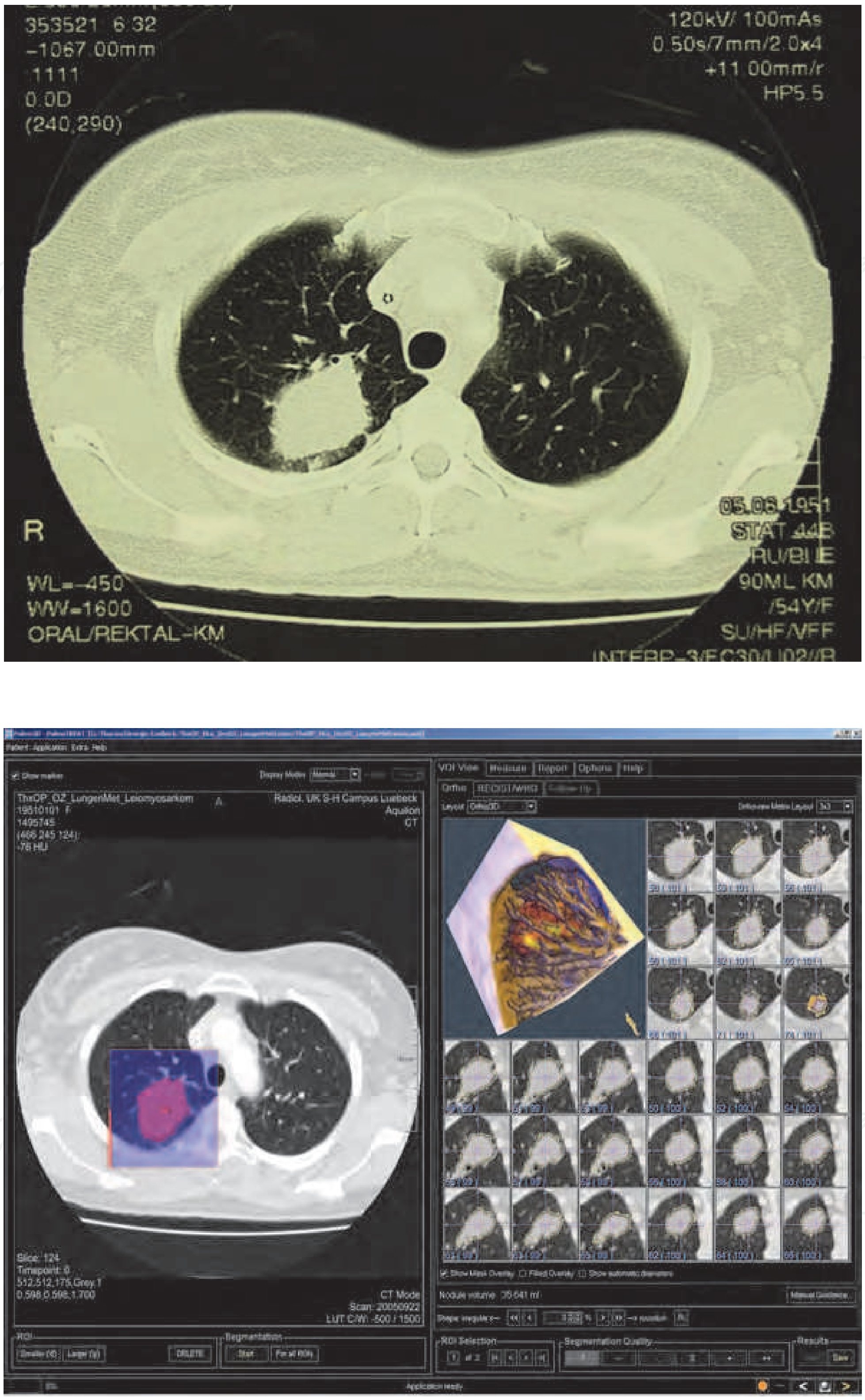

Fig. 3.1 Axial CT of a 54-year-old patient with bilateral lung metastases. As an example, the largest metastasis is shown in the right left upper lobe of the lung (left). Reformatting and volumetric evaluation of the metastasis (right image).

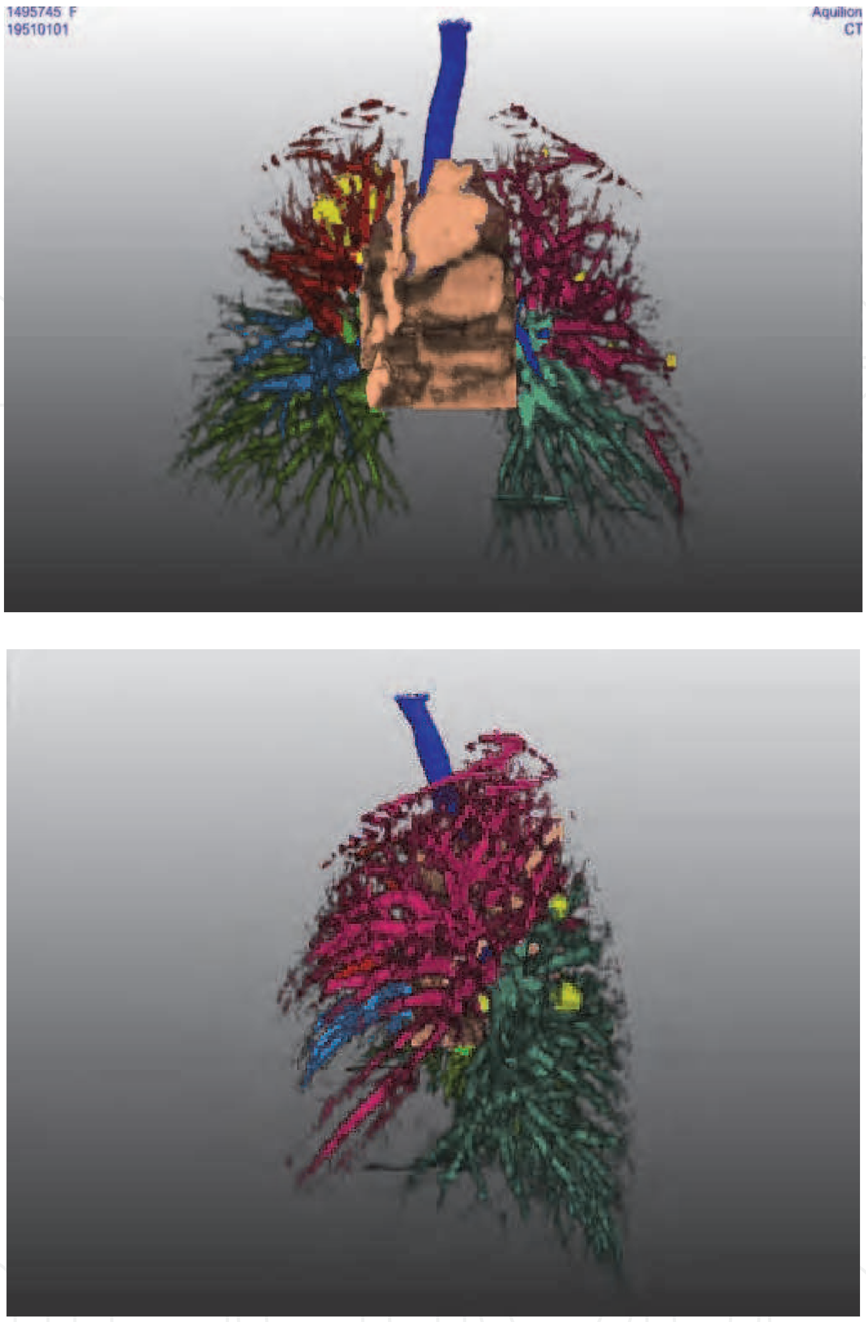

Fig. 3.2 Animated 3-D reconstruction of the axial CT images (3.1). Ventral (left) and left-lateral (right) view. The lobes of the lungs are coloured selectively, the bronchial tree is blue, lung metastases are coloured yellow.

Conventional methods (multiplanar reformatting, volume rendering) can be complemented by colour coding and anatomical reformatting of the data [Dicken et al. 2003], i.e., the data are not depicted on flat sections, but based on their distance to the pleura. This means that more superficial changes, e.g., pleural mesotheliomas, defects in the thoracic wall or osseous changes in the bony thorax can be depicted in a way that resembles the surgical situation (Fig. 3.3). Volumetric and metric calculations permit a precise statement on tumour thickness or distance of the tumour from its surrounding structures (thoracic wall). Furthermore, 3-D visualizations of the hilum of the lung or of regions around the lesions can be produced, in order to depict the morphological and topographical relationship of the tumour to the bronchial and vascular tree with colour coding. All pulmonary areas, including emphysematous portions, can be depicted separately in three dimensions in variable detail and resolution. All 3-D scenes can be interactively rotated or enlarged by the observer and set to obtain an optimum view.

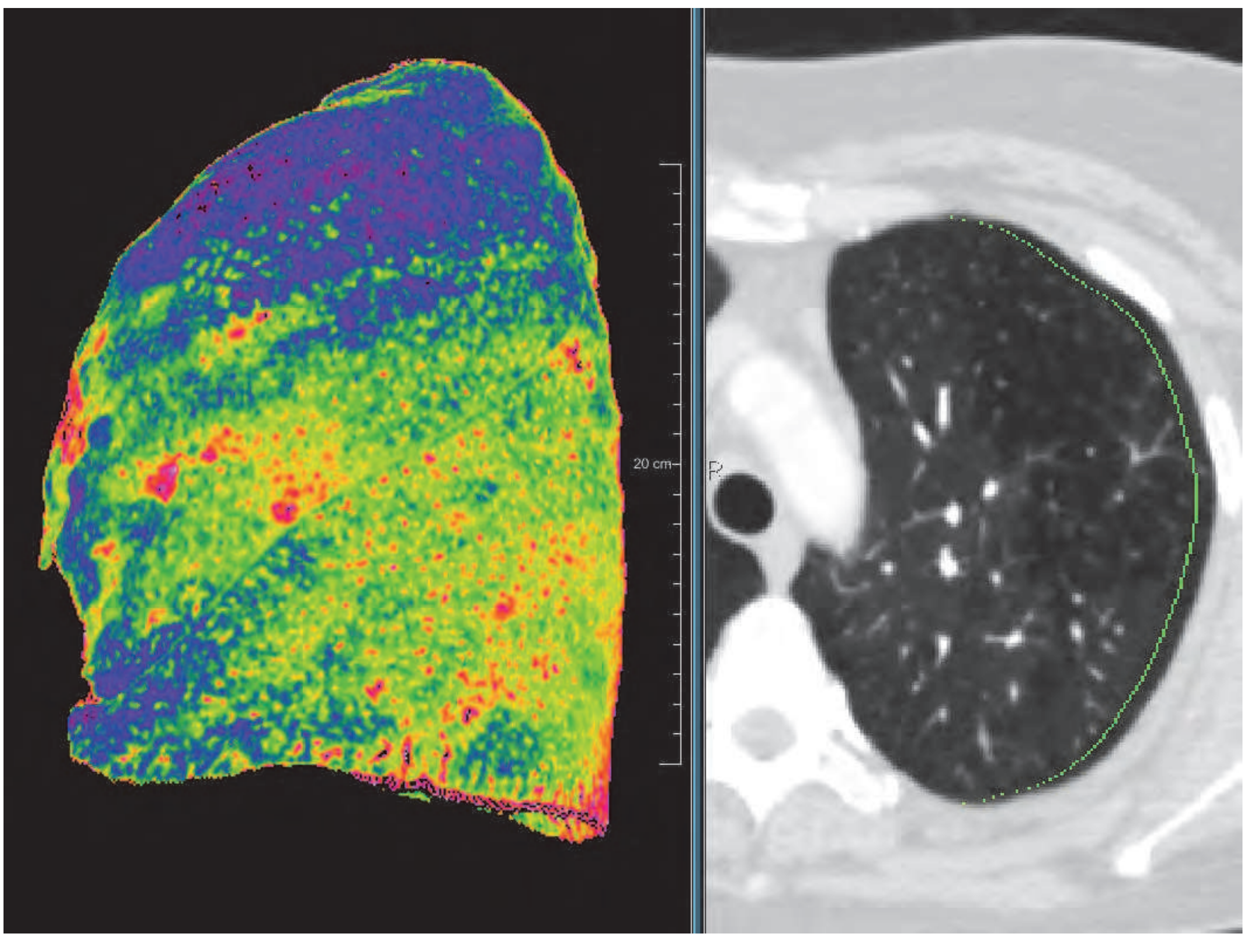

Fig. 3.3 The conventional display of CT data on flat sections provided by the data set is complemented here by the depiction of all image points that, similar to the layers in an onion, are all at a constant distance to the surface of the organ. On the left, you can see a superficial depiction of such a layer, located at approx. 10 mm from the internal thoracic wall. Lung density is colour coded. On the right, you can see the corresponding conventional view.

4. The 3-D reconstruction and visualization techniques

4.1 Lungs, lobes, segments and the bronchial system

The number of publications on the identification of anatomical lung structures rose dramatically after the introduction of MSDCT. Examples of bronchial tree segmentation and analytical methods are found as early on as 1999 in a publication by Preteux and later on in publications by Aykac and Tschirren [Preteux F et al. 1999, Aykac D et al. 2003, Tschirren J et al. 2002]. A variety of algorithms for the automatic segmentation of the lung have been published by Kitasaka, Hu, Leader, Kuhnigk and Sluimer [Kitasaka T et al. 1999, Hu S et al.

2001, Leader JK et al. 2003, Kuhnigk JM et al. 2003, Sluimer I et al. 2005]. A first method on the segmentation of the lobes of the lungs, an algorithm based on fissure detection and knowledge from anatomical atlases, was presented by Zhang [Zhang L et al. 2003]. An alternative method used the Voronoi division of the lung starting at the lobar bronchi for a coarse estimate of the lobes [Zhou et al. 2003]. A method that includes both the areas of vascular and bronchial supply and fissure formations, and thus permits a more rapid interactive refinement of the results, is an integral part of a software solution for parenchyma analysis, developed by Fraunhofer MEVIS [Kuhnigk JM et al. 2005]. Furthermore, also a method for the approximation of lung segments which are not delimited by fissures is available. It was introduced by Krass in 2000 [Krass S et al. 2000] and is based on a similar approach to Zhou's lung lobe segmentation algorithm. The method has currently been further refined which is described in [Welter et al. 2011]. An expanded variant of the lobe segmentation approach developed by Kuhnigk was introduced by Ukill [Ukil S et al. 2005 and 2006]. Methods for the qualitative and quantitative analysis of the lung parenchyma had already been developed in the 1990’s by Kalender, Uppaluri and Coxson [Kalender WA et al. 1990, Uppaluri R et al. 1997, Coxson HO et al. 1999] and were further developed over the course of the years [Blechschmidt RA et al. 2001, Hara T et al. 2003, Xu Y et al. 2006]. A first system for quantitative analysis under inclusion of a regional division of the lung, previously achieved through segmentation, was presented by Reinhardt in 2001, whereby Zhou’s fissure-based lobe segmentation was used and no further division into subsegments could be undertaken [Reinhardt JM et al. 2001]. There is currently no generally available software for CT-based division of the lung into lobes and segments. There are the following additional challenges when segmenting the supply systems, especially in the case of the lungs: In the segmentation of the bronchial tree, on the one hand, the structures that take a horizontal course in the internal regions are rendered very bright and, on the other hand, the centres of the thinner bronchi that take a diagonal course through the volume are no longer coherent within the meaning of neighbouring relationships in the voxel grid in the discrete reconstruction [Park W et al. 1998, Prêteux F et al. 1999, Ley S et al. 2002]. The focus of current research is the stabilization of automatic segmentation methods that produce a satisfactory segmentation result without interaction from the user [Tschirren J et al. 2005b, Schalthölter T et al. 2002, Hoffmann EA et al. 2003].

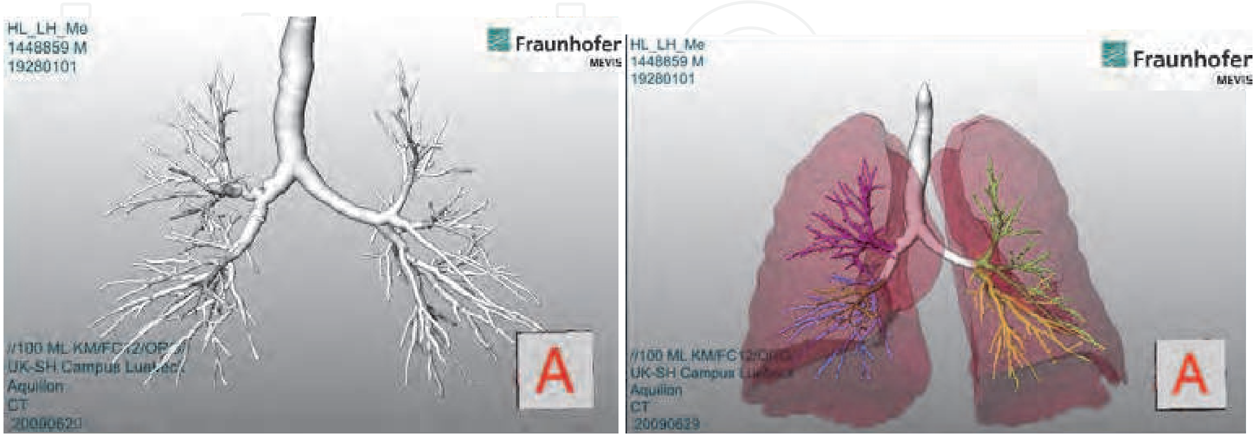

Fig. 4.1.1 Visualization of the segmented bronchial tree (left) and additional colour-coded lobe segmentation (right). Coronary view.

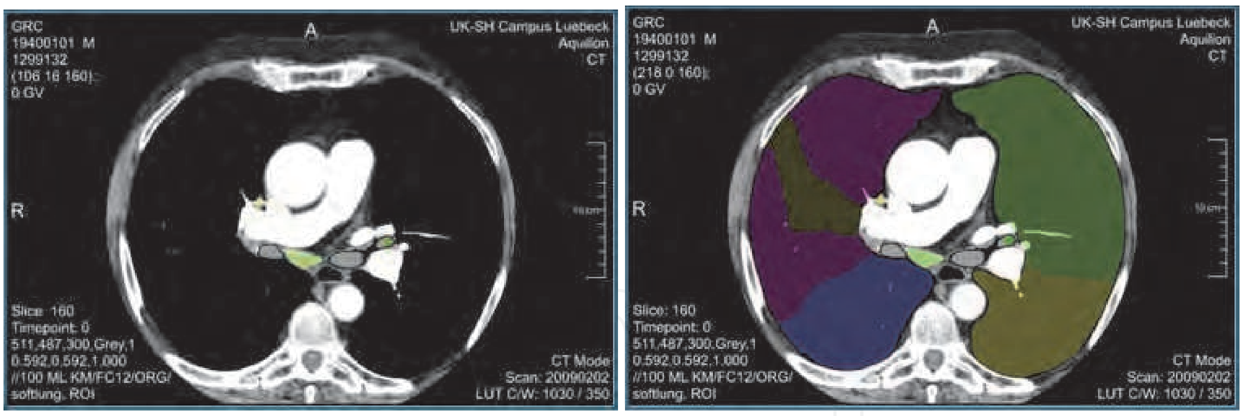

Fig. 4.1.2 Colour-coding of the central vessels and the bronchial system (left). Axial computed tomographic scan of the thorax with colour-coding of the lung lobes. (right)

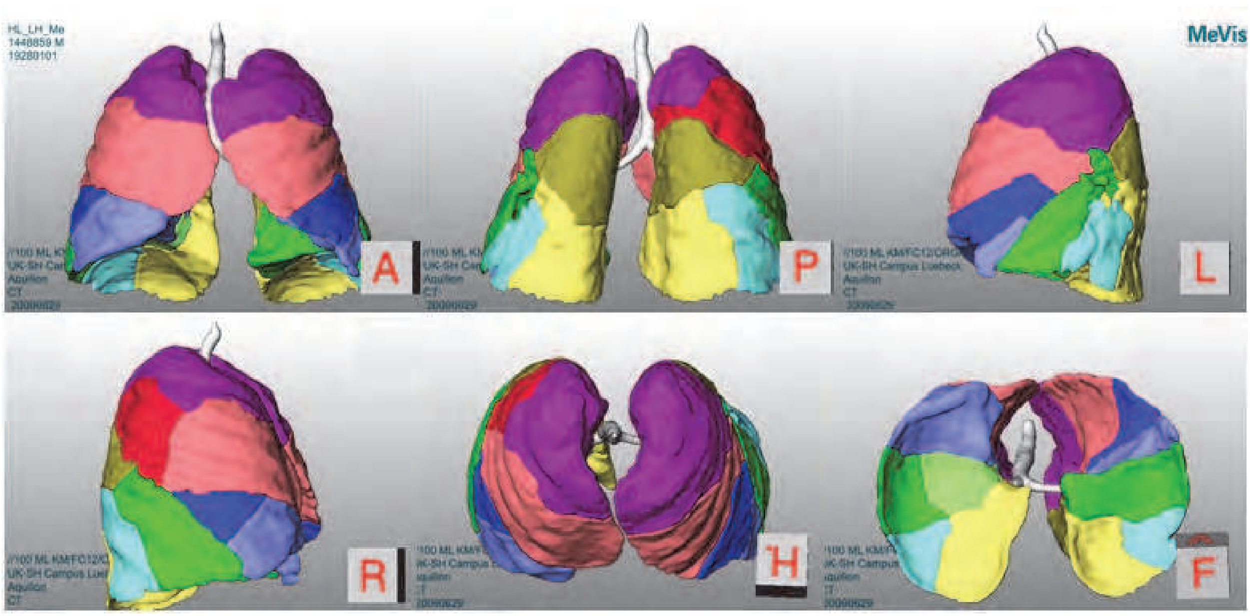

Fig. 4.1.3 3-D visualization of the lungs with colour-coded lung segment analysis.

4.2 Vascular system

The segmentation of pulmonary arteries and veins plays an important role in pre-operative image analysis, in addition to segmentation and the functional units of the lung. This also permits the quantitative determination of morphological parameters for these tree-like supply systems, such as, e.g., diameter and cross-sectional area of vessels, curvature, as well as length or volume of a section. Methods for the segmentation of tubular structures can be broadly divided into two categories. The methods in the first category are based on the determination of the path between two pre-determined end points and subsequently carry out the segmentation on reformatted layers orthogonal to the course of the path [Frangi AF et al. 1999, Hernandez-Hoyos M et al. 2002]. During this process, the calculation of the path results from the minimization of a cost functional, into which, on the one hand, external parameters, such as, e.g. voxel intensity or local contrast, and on the other hand, internal parameters such as, e.g., path length or curvature are fed. This "functional" approach can be efficiently realized and has the advantage that the segmentation of the cross-sections is mainly

carried out in 2-D layers. On the other hand, there is no guarantee that the resultant path actually runs parallel to the structure, as length and curvature are taken into consideration in path minimization, which results in non-orthogonal cross-sections in the region of branching and strong curvature, in particular, and thus in erroneous values for diameter and cross-sectional area. Furthermore, these methods are often not suitable for interactive expansions aimed at the improvement or correction of an initial segmentation result.
In contrast, the methods in the second category largely take a 'geometric' approach, i.e., first a 3-D segmentation is carried out on the structure of interest, then its mid-line is determined and, finally, the vessel is measured on reformatted layers that are orthogonal to the mid-line. In this procedure, the mid-line is determined with the aid of skeletonization algorithms that can achieve high levels of accuracy [Lam L et al 1992, Selle D 1999, Borgefors G et al. 2001]. An advantage of this approach is that the user can verify and, if necessary, interactively modify the 3-D segmentation result, prior to calculating the mid-lines. Both approaches can, of course, be combined. For example, it may be meaningful to conduct another, further refined 2-D segmentation of the lumen based on the vascular cross-sections obtained using a geometric approach. During segmentation of the vascular systems, no satisfactory solution has been found to date for the automatic separation of the venous and arterial trees, in particular, which is, however, a prerequisite to producing 3-D depictions that have been coloured in analogous to illustrations in textbooks for each patient for the planning of surgery.

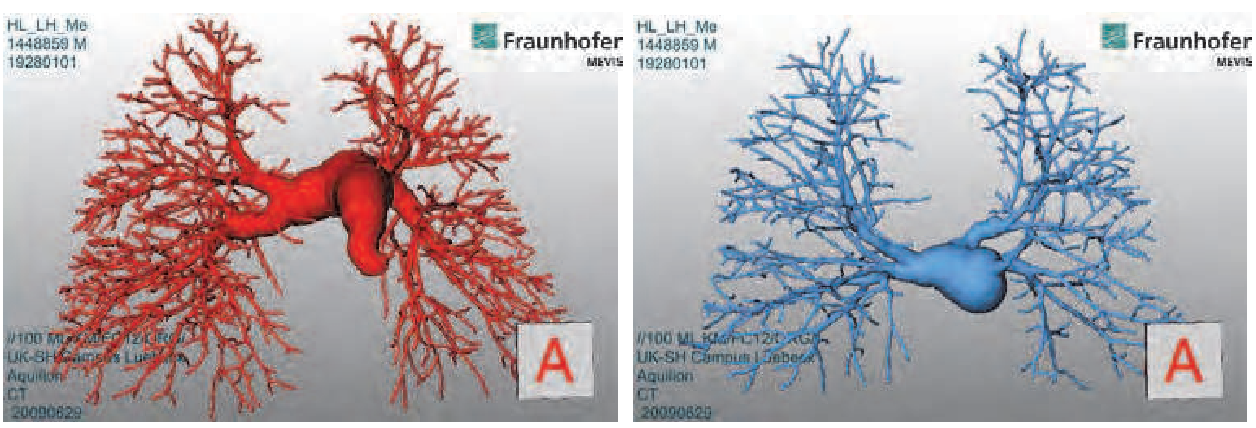

Fig. 4.2.1 Isolated 3-D reconstruction of the pulmonary arterial (left) and the pulmonary venous (right) systems. Anterior view.

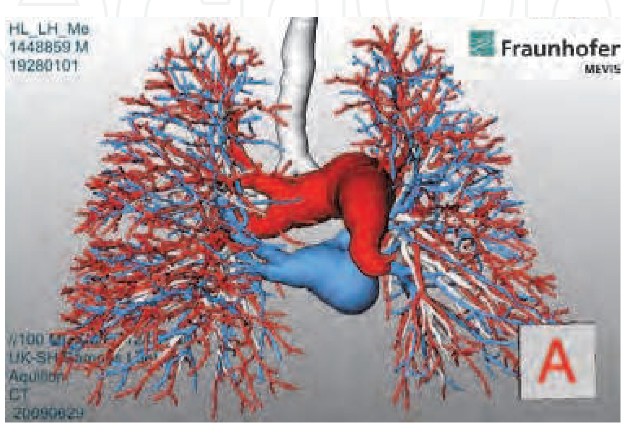

Fig. 4.2.2 Combined depiction of the vascular and bronchial systems. Anterior view.

4.3 Lung tumors and mediastinal lymph nodes

The assessment of the size, shape, location and number of lung tumours plays a substantial role in radiological diagnostics and in the planning of surgical interventions. The locational relationship to structures in lung, in particular, can provide important information on whether a tumorous process is locally restricted to an individual lobe or segment of the lung or whether it extends across multiple lobes or segments, which has a decisive effect on the extent of the resection. In this case, the most important tasks to be fulfilled by the algorithm are the segmentation and the quantification of such masses in the lungs. Research into the segmentation and volumetry of round lung lesions in CT data has, to date, been mainly motivated by CT screening studies for the early recognition of lung cancer. A corresponding emphasis has been placed on the reproducibility of the quantification of small round lesions in the algorithms developed to date. In many cases, these have an almost spherical shape and are generally only in slight contact with the pleura or the vessels. In the approach taken by Kostis [Kostis et al. 2003], a semi-automatic classification into one of very few round lesion models (isolated, close to pleura, with connection to vessels) is made prior to segmentation. After the subsequent initial segmentation with fixed threshold values, the connected, highly dense structures are severed by morphological operations. In 2005, Okada introduced an automated method for the approximation of so-called ’ground glass opacities’ (GGO) to ellipsoids [Okada K et al. 2005]. Fetita also used an approach involving an initial segmentation with fixed threshold values and the subsequent application of morphological procedures [Fetita et al. 2003]. However, in this case, global information was also used, while the other methods only based their calculations on a section of the data set. The first commercial software packages that are intended for lung-screening examinations have been introduced on to the market since 2002 (R2, Siemens, GE, Philips). What these tools have in common is that the segmentation of larger and/or more complex tumors with substantial contact to the pleura or vessels is inadequate in many cases and there are often no options available to the user for making corrections, or these options are difficult to operate, as all methods to date for segmentation have been primarily developed for small round lesions.

4.4 Quantitative analysis of lung parenchyma

The standard method for functional lung parenchyma analysis is the selective perfusion scintigraphy. Computed tomography has gained in importance in emphysema diagnostics due to the low sensitivity of conventional x-rays for the detection of emphysema and the low sensitivity of lung function tests for the detection and quantification of early forms of emphysema, in particular [Grosse C and Bankier A 2007]. In addition to the quantification of emphysematous changes in lung parenchyma, computer tomographic scans (CT) also permit determination of the severity of the disease. Recognized standard parameters are the mean lung density (MLD) and the pixel index (PI) or – a synonym – also the emphysema index (EI). The EI can be determined globally or regionally [Blechschmidt, Achenbach]. Thin layer images (1 – 2 mm layer thickness) and the use of a high-resolution algorithm are prerequisites to optimum radiological evaluation. However, constantly improving technologies (4-, 16-, 64-slice CT) also require a large number of images. A data set comprising 300 – 600 images is usually produced, depending on the size of the patient’s thorax, which corresponds to 150 - 300 MB storage capacity. However, this quantity of data is of limited practicality to routine clinical use. There are different research software application for quantitative analysis of parenchyma, e. g. MeVisPulmo3D [Kuhnigk JM et al.

2005, Heußel CP et al. 2006], that allows the depiction of emphysematous pulmonary areas, separated into lung, lobe or segment regions. Absolute and relative volumes, MLD and EI can be calculated and quantified selectively. The time-consuming part of the calculation is outsourced to a fully automated pre-processing procedure. The text report that is generated is complemented by two- or three-dimensional results.

Pre-operative 3-D visualization in combination with quantitative analysis of the parenchyma is greatly superior to a conventional CT analysis with a lung function test, especially in the case of extensive pulmonary emphysema (Fig. 4.4.1).

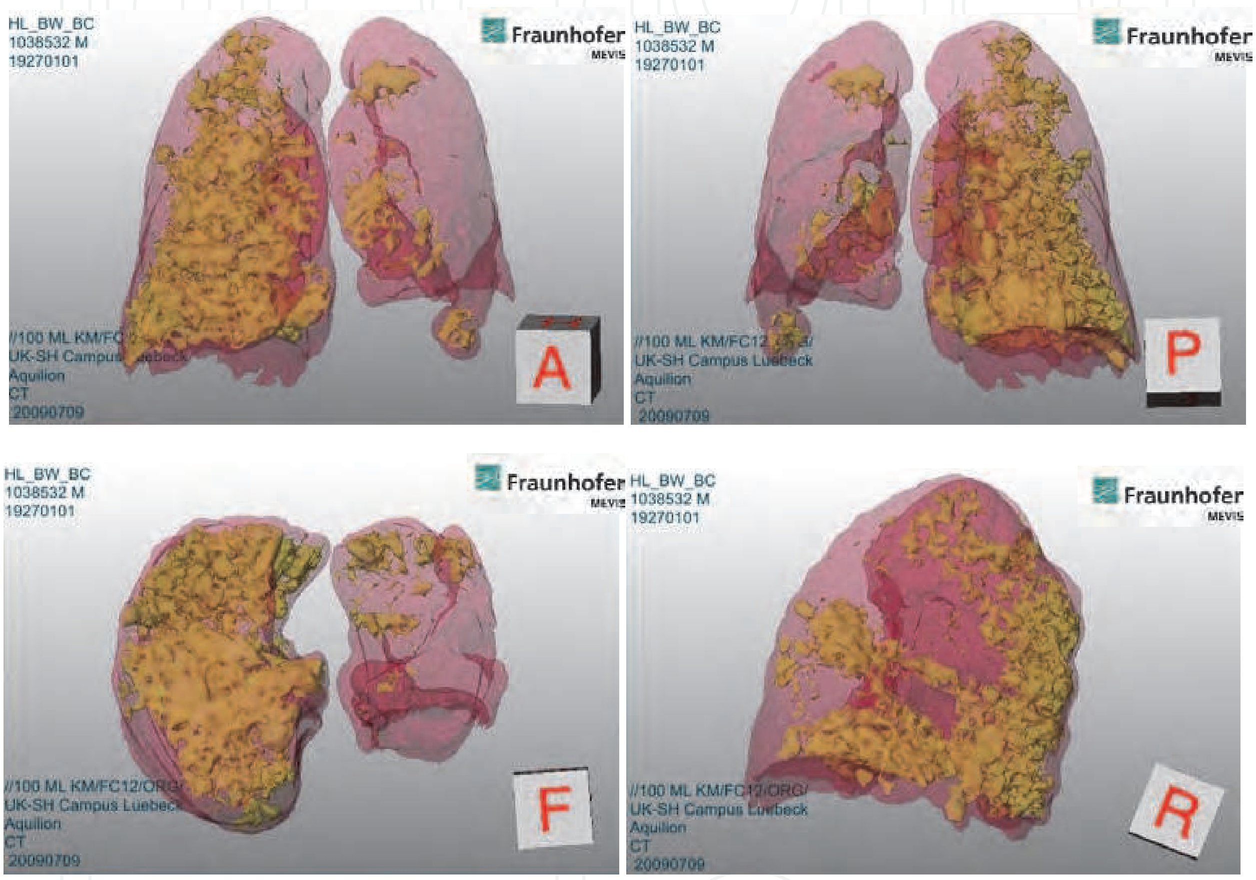

Fig. 4.4.1 Pre-operative 3-D visualization of a patient with extensive lung emphysema in addition to lung cancer of the left lower lobe. View from anterior (A), posterior (P), feet (F) and right side (R).

4.5 Visualization

The visualization of complex medical structures is a current challenge in the field of computer graphics. While algorithms for rapid volume rendering are now part of the functional scope of modern radiological units, to date, special methods for the accentuation of relevant information in the image data generally only exist in the context of prototypic research applications. The depiction of spatially complex anatomical situations that include a variety of diagnostic parameters and can be evaluated intuitively by the surgeon using it must be realized if a precise reproduction of the acquired image data is to be central to the purpose of radiological diagnostics. In the case of spatial visualizations, in particular, the targeted exploration of individual structures, i.e., the furtherance of visibility and recognition of individual partial objects in a complex spatial scene, generally requires the use of special image-enhancement techniques. Above all, the development of non-photorealistic enhancement techniques that support an intuitive assessment of complex spatial scenes, has a high potential for the efficient implementation of such visualization tasks [Strothotte T et al. 2002, Ibanez L et al. 2005]. For example, the targeted use of contour lines, transparency and shadow projections can substantially improve the visibility of the enhanced objects and the recognition of the shape of the object [Preim B et al. 2002]. The targeted use, focused on specific tasks, of such enhancement techniques for the visualization of medical data is a topic in current research [Ibanez L et al. 2005].

The analysis and visualization of CT data and the production of dynamic image sequences was carried out by Fraunhofer MEVIS, Bremen. In connection with the tasks of planning a lung intervention, the visualization of bronchial and vascular trees is of particular importance. A correct illustration of the branching structure and the spatial relationships between vessels and supplied parenchyma is also important in this case, as is the accentuation of the decrease in vascular diameter towards the periphery.

Conventional visualization techniques, such as volume or surface rendering, reach their limits of applicability in this case, partially due to the fact that the resolution of the image data is too low and partially because of interference from artefacts due to noise and other distortions. Specially developed software permits a rapid and robust visualization of the vascular and bronchial trees. This is based on a surface depiction of the vessels through geometric filtration based on their mid-lines and radii [Ritter et al. 2006, Hahn et al. 2001]. The bronchial tree and the pulmonary vascular trees can be clearly illustrated with a very smooth and natural appearance using these methods. Triangulated surface models are often used for the visualization of segmented objects, where the surface of an object that is to be depicted is approximated using a network composed of triangles. This type of visualization provides a diversity of options, such as, for example, the transparent depiction of surfaces or the simultaneous illustration of multiple objects that penetrate each other, and has a long tradition of use in the field of 3-D computer graphics. For the purposes of surface visualization, Fraunhofer MEVIS has developed a flexible and modular library for the production, modification and visualization of surface models based on so-called winged edge meshes (WEM), that is characterized by a high efficiency and quality and is particularly well suited to interactive applications. The speed at which a surface model can be depicted is essentially determined by the number of triangles used. Although the quality of the visualization increases with the number of triangles, it can become so slow that smooth interactions are no longer possible. The number of triangles can be drastically reduced using a special, locally adapted filtering algorithm, without the quality deteriorating to any great extent. It is even possible to obtain a faster and also more precise visualization by simultaneously increasing the sampling rate.

Besides isosurface representation methods, also (direct) volume rendering is used for 3-D visualization. Volume rendering is the visualization of a three-dimensional data set through the projection of the individual voxels on to an image plane. In this process, the transparency and coloration of the voxels is determined by the grey values and a transfer function. Volume rendering is a reliable and established technique for the depiction of radiological images as this type of visualization does not require segmentation. An illumination model and a multi-dimensional transfer function are often used in modern volume rendering, which include additional attributes for the depiction of the voxel grey values on to colours and transparencies and thus make special effects possible. For example, vessels or tumours can be highlighted using this technique, with the surrounding areas of the image being illustrated as a transparent silhouette.

5. 3-D reconstruction for the planning of interventions on central tumours

To evaluate the potential of the CT based segmentation and 3-D reconstructions of morphological structures of the lung for thoracic surgery planning 40 cases were analysed. The surgical approach was decided on by the thoracic surgeon undertaking the treatment, while the pre-operative tumour classification was mainly carried out by colleagues in radiology. All 40 CT examinations were initially evaluated without knowledge of the 3-D reconstruction analysis, which is the common procedure in clinical routine. The optimal, oncologically correct surgical intervention was planned. The peri-operative risk assessment with reference to the selected intervention was carried out, also taking into consideration the patient's pulmonary reserve and the general condition. Finally, the oncological approach to resection and the extent of resection were determined individually for each patient. 17 patients were staged as inoperable and not scheduled for surgery. The scheduled surgical strategy which was based on 2-D slices only was documented. In a second step, the 3-D reconstruction analysis was taken into consideration as an additional information and assessment device. In some cases the knowledge of the 3-D analysis lead to a change of the planned surgical procedure. The planned surgical procedure based on the 3-D reconstruction as an additional planning device was documented. The scheduled procedures were then compared to the actually carried out surgical intervention respectively. The assumption of a primary inoperable situation (n = 17 patients) based on the 2-D slices was confirmed by the 3-D reconstruction analysis only in 10 of 17 cases. Finally, 30 patients were scheduled for surgery.
The surgical approach in the 30 patients with operative treatment, selected based on the 2-D slices, corresponded to the therapy that was ultimately carried out in 14 patients (46.7 %, Table 5.1). Ultimately, the final surgical approach was only predicted in just under half of the patients based on the usual 2-D analysis. The risk analysis after the 3-D reconstruction had been viewed revealed a correct predictive outlook in 25 cases (83.3 %) (Table 5.2).
We were not able to classify the operability in 3 patients neither in the 2D nor in the 3D analysis, so we decided to perform a surgical exploration. 4 of the 17 patients – not resectable after 2D analysis - were predicted to be resectable in a curative intention after using the 3D based analysis. In 3 of these 4 patients a curative resection could be performed, the 4th patient turned out to be not resectable despite the 3D analysis.
After neo-adjuvant therapy (stage IIIB), 3 patients became operable (stage IIIA). This stage improvement with a corresponding surgical approach was correctly predicted both based on the 2-D and on the 3-D analysis. No advantage of the 3-D reconstruction was determined in patients after neo-adjuvant therapy with reference to the risk analysis.

		Frequency	Percentage
Valid	Incorrect	16	53.3
	Correct	**14**	**46.7**
	Total	30	100.0

Table 5.1 **Decision based on** 2-D CT slices only (all cases operated on)

		Frequency	Percentage
Valid	Incorrect	5	16.7
	Correct	**25**	**83.3**
	Total	30	100.0

Tab. 5.2 **Decision with** 3-D analysis (all cases operated on)

A comparison of the 2-D and 3-D proposals for surgery reveals 25 congruent and 15 divergent results for all cases (n = 40) and 15 congruent and 15 divergent cases, respectively, for those patients operated on. The analysis of the divergent results (n = 15) revealed the following constellation: out of 15 divergent results, 13 (87 %) had been properly corrected by the 3-D analysis, i.e., the initially incorrect prediction was improved to a correct prediction through the pre-operative use of the 3-D depiction in 13/15 cases. In only 2 cases was the 2-D analysis found to be correct, compared with a subsequent incorrect 3-D analysis. In these cases, the correct 2-D analysis was erroneously changed by the 3-D reconstruction. Patient 1 exhibited status post atypical resection of the left upper lobe with pulmonary metastasis. Given a metastatic relapse in the left lower lobe, the probable operation was regarded as pneumonectomy of the residual lung based on 2-D CT slices. The 3-D representation favoured a lower lobe resection under retention of the partially remaining upper lobe. Pneumonectomy of the residual lung had to be carried out intra-operatively, such that the initial 2-D assessment was confirmed. Patient 2 exhibited a left-central, small-cell bronchial carcinoma with broad-based contact to the aortic arch. While the 2-D analysis indicated inoperability due to a suspected infiltration of the aortic arch, based on the 3-D analysis, the observers thought it would be possible to conduct a resection just within healthy tissue. However, intra-operatively, the tumour infiltration was revealed as even more extensive than on the pre-operative images. The intervention had to be abandoned as an exploration.
In 3 patients, neither the 2-D, nor the 3-D analysis produced a correct analysis of the final surgical strategy. The extent of the resection was underestimated in 2 patients, while it was possible to spare more parenchyma during surgery in 1 patient, when compared with what had been planned based on the analyses.

6. Outlook: Fusion of different modalities

In this outlook we discuss the potential of combining CT information with modalities from nuclear medicine. This discussion is kind of a roadmap of upcoming research in the area of image based preoperative risk assessment and planning of surgical interventions in the lung.

6.1 Functional imaging (SPECT) and data fusion SPECT/3-D

In addition to the depiction of the morphology, the functionality of the original and remaining residual lung tissue is of central interest for a large thoracic resective intervention. The functionality of the lung parenchyma can be assessed with lung function or exercise tests (spirometry, spiroergometry or body plethysmography). At the university hospital Lübeck, selective digital perfusion scintigraphy SPECT (Fig. 6.1.3) is used as the functional imaging method. The examination technique permits a graphic illustration of functional aspects in individual organs. Based on the principle of scintigraphy, a radiotracer is administered intravenously to the patient. The tracer used in lunge perfusion exams is constructed to be fixed in the lung capillaries during first pass. The radionuclides - (Tc99m) -

that are used emit gamma radiation that can be detected and measured with using gamma cameras. One or more gamma cameras rotate around the body and detect the emitted radiation from different directions in space. The distribution of the radiotracer in the lung depends on the amount of blood passing thought the different parts of the lungs. It can be deduced from these planar projections using inverse radon transformation and the distribution can then be depicted in the form of computed tomographic sections through the body. This allows the production of a three-dimensional image of lung function. The substance, Tc-99m-labeled macroaggregated albumin, that is used for perfusion scans has no medicinal effects or side effects as it is used in tiny quantities that produce only small doses of gamma radiation. After about 36 h, 99 % of the material has decayed or been excreted. The levels of radiation exposure are substantially smaller than for an x-ray examination. Beside perfusion scans ventilation scans could be performed using radioisotops of noble gases. As handling of radioactive gases is demanding perfusion scans are preferred at many sites.

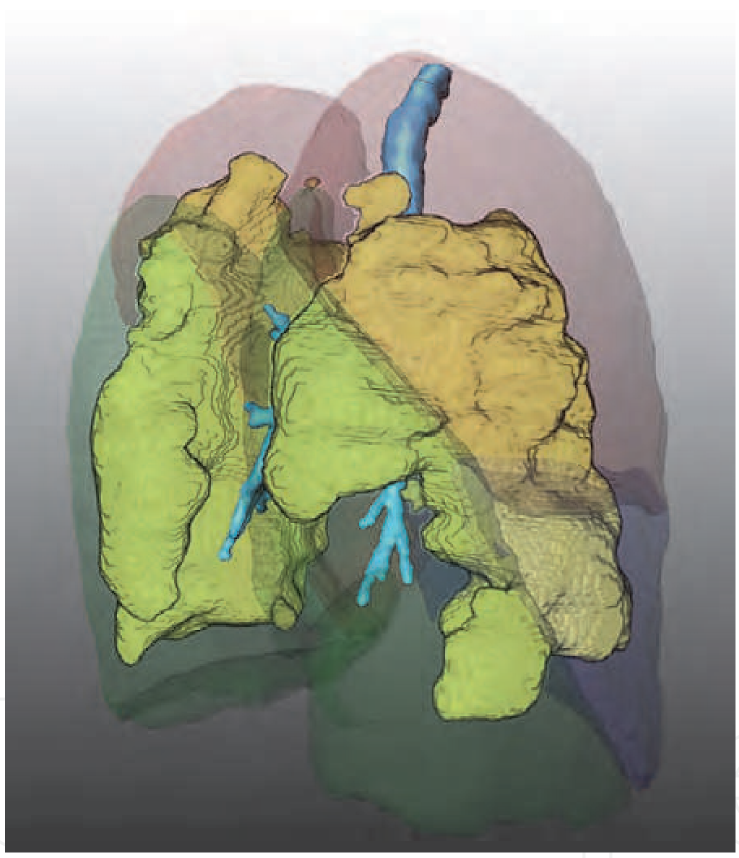

Fig. 6.1.1 Three-dimensional visualization for a patient with severe lung emphysema. Software fusion of SPECT data set with CT data using ManualRegistration in MeVisLab. Ventilated areas are highlighted in colour, non-ventilated areas are depicted semitransparently.

A relatively novel technique is the combination of SPECT and CT to obtain SPECT quantification on a lobar basis. Both scans are therefore used during the examination: CT produces images of the body's morphology, SPECT depicts the perfusion. Superimposed SPECT and CT images then permit a precise local determination of ill perfused areas. As CT data cannot be acquired in the available SPECT scanner we undertook an external fusion of the available image data and subsequent 3-D visualization. In a feasibility experiment, a CT dataset (Clinic for Radiology, University Hospital Schleswig-Holstein (UKSH) , Campus Luebeck) and the tomographic SPECT perfusion data (Clinic for Nuclear Medicine, UKSH, Campus Luebeck) were fused using user guided registration (rigid + scale) (Fig. 6.2) and visualized in 3D externally (Fraunhofer MEVIS /Bremen), and sent back online. Along with the renderings, a quantitative relative and absolute measurement of lung perfusion per lobe and emphysema scores based on the CT data was computed, employing the lung lobe segmentation performed at MEVIS (see Section 5.4). Figure 6.1 shows the corresponding visualization.

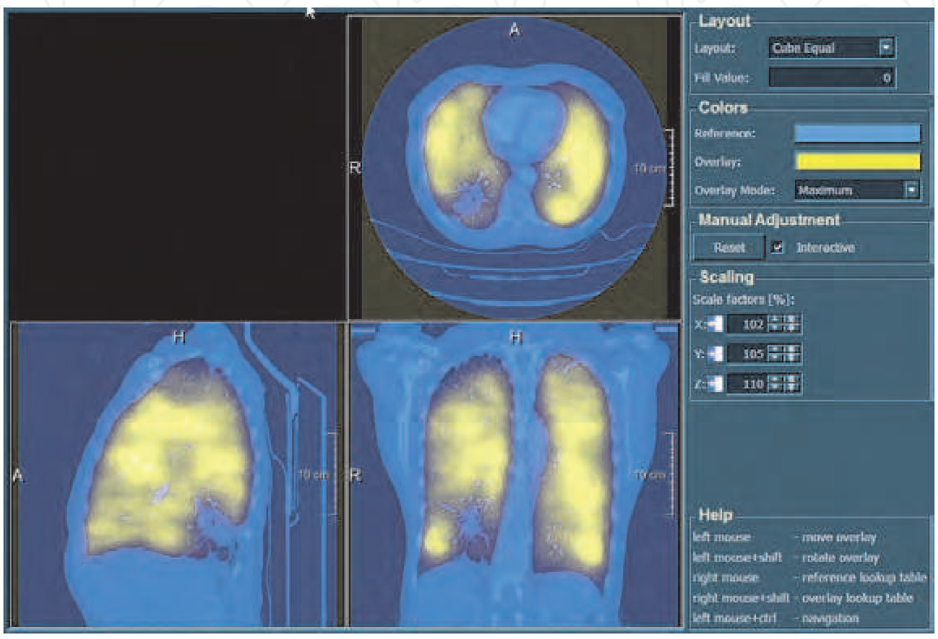

Fig 6.1.2 Reformatted data after fusion with SPECT. Graduated illustration of the ventilation density (dark = reduced ventilation, light = good ventilation).

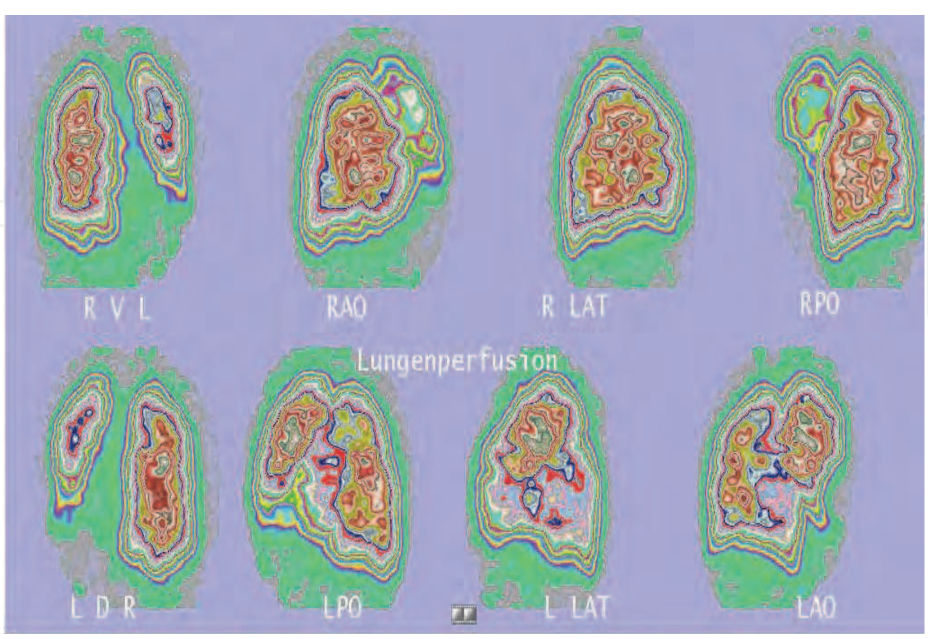

Fig. 6.1.3 Scintigram of the lungs after i.v. administration of a radionuclide (^{99m}Tc). From a higher number of such projection images a 3D-SPECT perfusion image can be reconstructed.

6.2 Fusion of 18-F FDG- PET with 3-D CT

Until recently mostly only anatomy and topography has been illustrated prior to thoracic surgery using MSDCT. In addition to this, the depiction of functional aspects also plays an important role in the planning of surgery. So far scintigraphy of the lungs to illustrate perfusion and, if necessary, ventilation, has been established in clinical routine, as the determination of vessel diameters or the distribution of pulmonary density using CT does not permit secure conclusions with reference to perfusion or ventilation. More recently, positron emission tomography (PET) has become more and more established as an additional diagnostic tool in everyday clinical routine. PET is an imaging method used in nuclear medicine to study the distribution of small doses of radioactively labelled substances in the organism and to thus depict biochemical and physiological functions. In this context, particular interest is in its use in investigating the activity of a suspected tumorous structure, in order to differentiate between scar tissue, artelectasis (non ventilated lung appearing in similar density as the tumor in CT) and tumour tissue in the search for tumour extends, metastases, or within the framework of a staging examination following on from (neo-)adjuvant therapy to assess tumour response to chemotherapy. The fusion of an individual PET finding with 2-dimensional CT images on a light box is difficult and a task that is almost impossible to accomplish for a non-radiologist or nuclear medic, in particular. Therefore most recent PET installations combine a PET an a CT scanner. The CT images from a PET/CT however are commonly not of diagnostic quality. The option of fusing FDG-PET and diagnostic CT images with high 3D resolution was also assessed within the framework of the current study.
For the PET scan a radiopharmaceutical is administered intravenously to the patient at the start of a PET examination. For oncology application mostly 18-FDG is used, a radiolabeled sugar, that has high uptake in tumours and other metabolic highly active areas (e.g. the brain or inflammation areas). In contrast to SPECT, PET uses radionuclides that emit positrons (β^+ rays). The spatial distribution of 18FDG within the body can be deduced from the temporal and spatial distribution of the recorded decay events and a series of cross-sectional images can be calculated. Furthermore, the distribution of the tracer in the volume under investigation can be precisely quantified – which is not as well possible with SPECT - as the absorption of the photons being measured depends only on the thickness of the irradiated tissue and not on the origin of the photons. Oncological PET uses metabolically active glucose as the radionuclide (also called radiopharmaceutical or tracer), in which a hydroxyl group on C6 of the sugar molecule is replaced by the radionuclide F18. FDG-6-phosphate cannot undergo any further metabolism after phosphorylation and accumulates in tissue (‘metabolic trapping’). Metabolically active processes taking place in tumours and metastases can thus be depicted and distinguished from non-metabolically active structures like scar tissue. In PET-CT, the patient is passed through the two detector rings for CT and PET, one after the other (in housing for the equipment). The images that are produced are automatically fused in the computer. In contrast to a conventional thoracic CT, a so-called low-dose CT scan is sufficient for a PET-CT. The exposure to radiation for a pure PET examination using F-18 is about 4mSv and is thus in the range of a computed tomography on the thorax. For a feasibility study the digital PET images were fused to the high resolution diagnostic CT data externally (Fraunhofer MEVIS, Bremen) in order to create 3D visualization incorporating the functional PET information. The CT data (Clinic for Radiology, University Hospital Schleswig-Holstein (UKSH) , Campus Lübeck) and digital

PET images (Clinic for Nuclear Medicine, UKSH, Campus Luebeck) were sent separately online, fused with user guidance in dedicated MeVisLab software prototypes (Figs. 6.2.1 and 6.2.2) and rendered in 3D externally (Fraunhofer MeVis, Bremen), the data structures allowing interactive 3D visualizations were then sent back to Lübeck online. The advantages of a high-dose CT became clear: only with high resolution CT data an acceptable image quality will be feasible for 3D visualizations. They provide a greatly improved fused image quality when compared with a low-dose CT image. However, as PET-CT is a rather expensive imaging method, it is not currently available across the board in Germany.

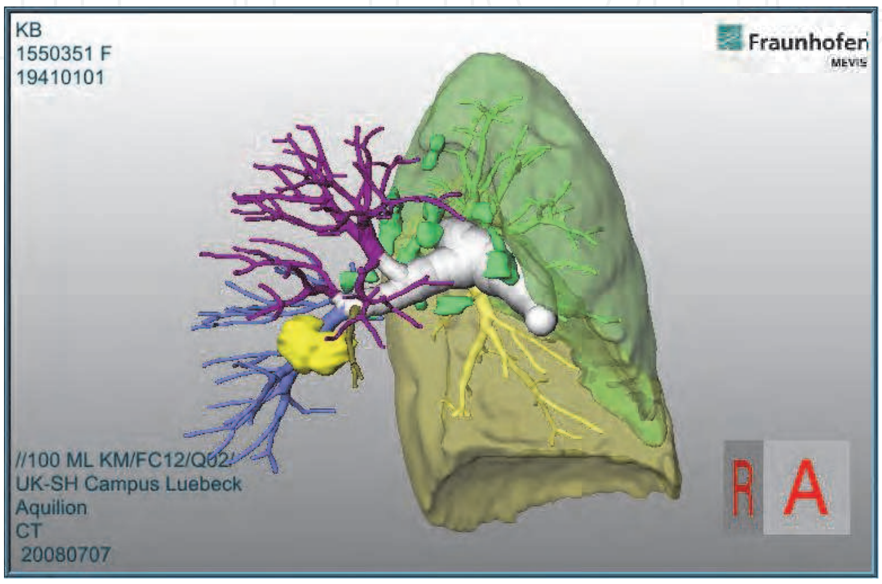

Fig. 6.2.1 67-year-old patient with a suspected local relapse of an adenocarcinoma in the right lower lobe. Status post primary transthoracic radiation therapy with initial functional inoperability (tumor highlighted in yellow).

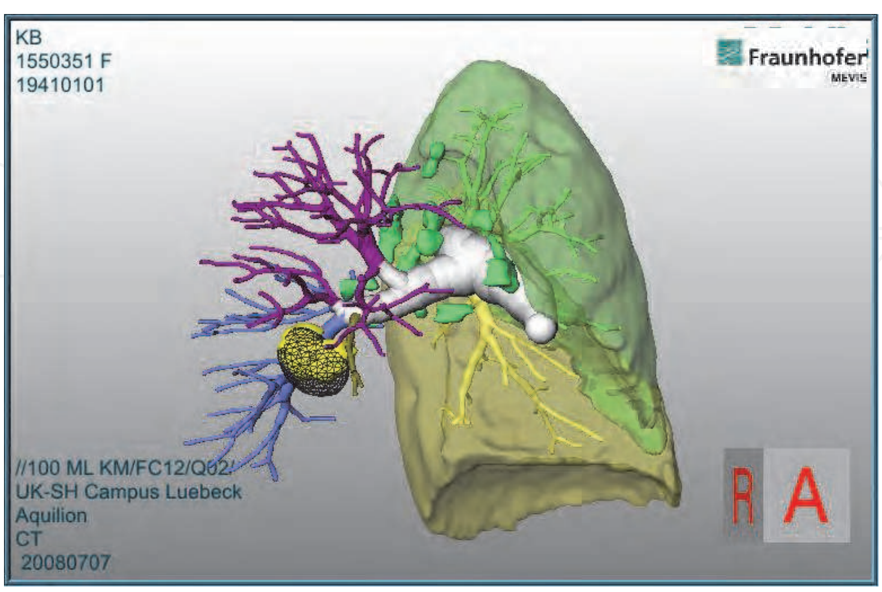

Fig. 6.2.2 PET-CT image fusion. Clear superimposition of metabolically active areas on the F18-PET (black grid lines) with the tumor (yellow).

7. Limits of 3-D reconstruction

The basic prerequisite for a subsequent optimal and meaningful 3-D reconstruction is the initial CT. Standard CT quality (5mm sections) does not permit adequate 3-D reconstruction. Distances between layers that are too great or CT layers that are too thick result in 3D-images of poor quality containing little information and possibly in inaccurate results of software based segmentations. In turn, if no, or too little, contrast agent is administered, this results in a deficient depiction of the intra-thoracic vascular supply. The initial CT must therefore fulfil the following requirements: }{Hochauflösendes Computertomogramm (mindestens 4-Zeiler), maximale Schichtdicke 2 mm, maximaler Schichtabstand 1,5mm undKontrastmittelgabe zur Gefäßdarstellung.|high-resolution computed tomography scan (minimum 4-slice), maximum layer thickness 2 mm, maximum distance between layers 1.5 mm and administration of contrast agent for vascular depiction.}

The thresholds for 3-D imaging are identical to those for an axial 2-D CT: The differentiation between a solid tumour and a post-stenotic atelectasis is just as impossible as the secure delimitation of a point of contact between a tumour and a potential infiltration of a vascular wall or solid mediastinal organs.

Even so, the image analysis and 3-D reconstruction constitutes an enormous gain in quantitative and qualitative information for the surgeon. In addition to the quantitative depiction and calculation of tumour size and tumour volume, the lobe volumes and calculations of distances, it is mainly the qualitative advance that is of importance when compared with an axial 2-D CT. The possibility of segmentation permits the selective observation of tumour, vascular system or bronchial tree and is vastly superior to the visual depiction in 2 planes. The method of anatomical 3-D reformatting currently provides the best possible imaging for pre-operative risk analysis in complex thoracic interventions.

In the medium term, computer analysis should also be used for intra-operative detection of lung tumours and for navigation during VATS. However, prior to this, the problem that is specific to the lungs, e.g. changes in locational anatomy due to the peri-operative atelectasis, must be clarified and a full understanding must be gained.

8. Summary

The segmentation and 3-dimenstional visualization of thoracic morphology based on CT is a novel and highly promising method for pre-operative imaging and risk analysis for central lung tumours. This allows a visualization of the tumour in combination with colour-coded lobe and segment association and the anatomical relationship to neighbouring structures. Furthermore, the depiction and calculation of lung volumes and emphysematous portions permits estimates of the expected residual functionality of the lung. The 3-dimensional image that can be moved in all planes, in combination with the possibility of anatomical segmentation, is easier and more simple for the observer to understand than the 2-D scans used to date with/without the associated radiological information.

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researchers at Fraunhofer MEVIS. It is also a result of a lot of fruitful discussions with a variety of thoracic surgeons throughout Germany within and beyond the frame of the ongoing project.

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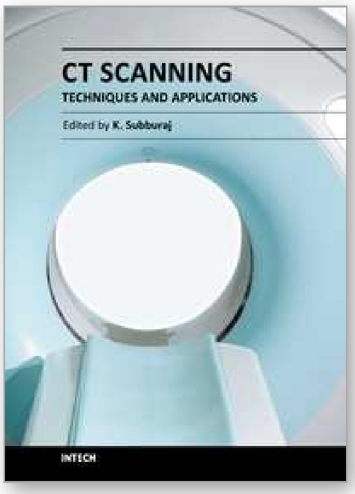

CT Scanning - Techniques and Applications

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Since its introduction in 1972, X-ray computed tomography (CT) has evolved into an essential diagnostic imaging tool for a continually increasing variety of clinical applications. The goal of this book was not simply to summarize currently available CT imaging techniques but also to provide clinical perspectives, advances in hybrid technologies, new applications other than medicine and an outlook on future developments. Major experts in this growing field contributed to this book, which is geared to radiologists, orthopedic surgeons, engineers, and clinical and basic researchers. We believe that CT scanning is an effective and essential tools in treatment planning, basic understanding of physiology, and and tackling the ever-increasing challenge of diagnosis in our society.