MRI proves clinical value in lung cancer

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Non-small cell lung cancer is the leading cause of cancer-related deaths in women and men in the Western Hemisphere. Surgical resection remains the mainstay of therapy in disease at stages I and II, and this treatment has an acceptable morbidity and mortality rate. Imaging is needed for effective treatment planning and accurate diagnosis, including preoperative assessment of resectability.

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MR imaging has failed to assume the same importance as CT in the radiological evaluation of lung cancer. It is usually considered as an alternative modality when CT findings are inconclusive or as a primary modality in cases of contraindication to iodinated contrast media. Key reasons for the limited role of MRI relate to technical limitations, including longer scan times, inferior spatial resolution, and low signal of the lung parenchyma. Unfavorable signal characteristics are due to the lungs' low proton density and high magnetic susceptibility.

MR offers several benefits over CT for assessing lung cancer, however. Its contrast media have lower toxicity than contrast used in CT scans, the examination involves no ionizing radiation, and resulting images provide much better soft-tissue contrast. MR also offers a variety of contrast options (T1 weighting, T2 weighting, fat saturation, etc.), which in practice facilitates differentiation of pathologic tissue growth. The modality allows imaging in any desired plane without further need for image processing.

Contrast-enhanced MR angiography has also proved valuable for evaluating the thoracic vascular system, allowing noninvasive assessments of tumor invasion. Continuous improvements in MR hardware, including high-performance gradient systems and new pulse sequences, are counteracting the modality's technical drawbacks. Improved triggering options and pulse sequence techniques, for example, reduce cardiac and/or respiratory motion artifacts. Use of fast MR sequences now enables the entire thorax to be imaged during a single breath-hold. Application of long-term averaging to conventional turbo spin-echo MRI produces high image quality with reduced motion artifacts. Single-shot pulse sequences, such as half-Fourier single-shot turbo spin-echo (HASTE), further decrease susceptibility to cardiac or respiratory motion, reducing scan times to below one second per image. Problems arising from T2*-related signal loss can be reduced by using short echo times, which allow improved visualization of lung parenchyma. Results can be improved by applying parallel imaging techniques.

MRI TUMOR STAGING

Pathologic changes to lung parenchyma, such as pulmonary nodules, show an increased T2* relaxation time of more than 140 msec. This results in high contrast to the surrounding normal lung, which has a T2* relaxation time of approximately five msec. Detection rate of solitary pulmonary nodules on MRI varies according to nodule size. MRI has a sensitivity of over 80% (compared with gold standard CT or surgery) for detection of nodules with diameter greater than 10 mm. Limited spatial resolution causes sensitivity to drop below 70% for nodules smaller than 10 mm in diameter. Introduction of new 3D pulse sequences with a higher spatial resolution and implementation of parallel imaging techniques should boost the accuracy of MRI further for the detection of solitary pulmonary nodules.

MRI can also be used to characterize lung nodules. Several studies using dynamic contrast-enhanced MRI have shown malignant nodules to have faster and stronger enhancement than benign lesions. Inflammatory lesions also show rapid and strong enhancement, however, and this overlap should be kept in mind.
Low soft-tissue contrast on CT images makes it difficult to differentiate secondary lung changes (i.e., atelectasis, postobstructive pneumonia) from the lung tumor. MRI offers much better soft-tissue contrast, which facilitates this identification. T2-weighted MRI characterizes postobstructive lung changes as having higher signal intensity than the tumor, owing to their retention of mucus and bronchial secretion (Figure 1). Differences in the magnitude and kinetics of contrast enhancement between the tumor and secondary lung changes can also be used for differentiation. Postobstructive lung changes typically show an increased and faster enhancement than tumors.

Knowledge of mediastinal tumor invasion (T3 and T4) is important when assessing the resectability of central lung tumors. Tumors exhibiting minimal invasion into mediastinal fat tissue, the parietal pleura, or the pericardium (T3), are still considered technically resectable. Tumor invasion can be assessed by examining continuity of mediastinal fat planes on T1-weighted MRI (Figure 2). This method offers some advantages over CT, including much better soft-tissue contrast, and choice of imaging plane. MRI makes it possible to acquire axial, coronal, sagittal, oblique, or double oblique images adapted to the structure of interest, providing the best image quality to, for example, evaluate tumor infiltration. Documented studies record a sensitivity of 75% to 80% for MR assessments of mediastinal invasion.

So-called black blood MR techniques have proved effective for assessment of vascular invasion. Contrast-enhanced 3D MR angiography could also be used in this role. MRA remains inferior to CT for assessments of segmental or subsegmental lung vessels, owing to its inferior spatial resolution. The accuracy of CT and MRI in assessments of mediastinal vessels, however, is similar. Application of parallel MR techniques promises improvement in the spatial and temporal resolution of MRA. Preoperative assessment of chest wall invasion by lung cancer remains a common clinical problem. The superior soft-tissue contrast of MR over CT again could be of benefit. Chest wall invasion should be suspected if T1-weighted MRI shows the usually continuous thin extrapleural fat layer invaded by tissue of medium signal intensity. These tumor infiltrations appear as high signal intensity on T2-weighted MRI.

Both fat-saturated T2-weighted MRI and fat-saturated contrast-enhanced T1-weighted MRI offer valuable alternatives for assessment of chest wall invasion. A number of studies have shown the advantages of MR in evaluations of Pancoast tumors. MRI provides an excellent delineation of important soft-tissue structures such as brachial plexus roots, neck blood vessels, and the arms, as well as important bone structures such as ribs and vertebral bodies. This is not the case on CT. The accuracy of MRI for detecting tumor infiltration in the brachial plexus, spine, or subclavian artery has been given as 94%, compared with 63% on CT.

**METASTATIC SPREAD**

Assessment of nodal metastasis is an important prognostic factor for patients with lung cancer. Nodal staging can also affect treatment choice. Ipsilateral hilar nodal spread (N1) reduces the overall prognosis but poses no contraindication for surgical therapy. Tumors with ipsilateral mediastinal nodal involvement (N2) can also be treated with surgery. Contralateral mediastinal nodal spread (N3), however, excludes the possibility of curative surgical resection.

MR-based lymph node evaluation is based mainly on an assessment of nodal size and shape, as with CT. Both T1- and T2-weighted pulse sequences can be used in the detection and morphologic evaluation of lymph nodes. T2-weighted fat-saturated pulse sequences such as STIR show lymph nodes with very high contrast. ECG triggering or single-shot sequences should be considered to reduce pulsation artifacts.

MRI has recorded a similar accuracy to CT in the assessment of nodal involvement. In comparative studies, the sensitivity of MRI and CT was between 48% and 90% and 52% and 82%, respectively. The specificity ranged from 64% to 93% and 69% to 88%, respectively. Attempts to increase the accuracy of MRI further, using measurements of signal intensity or contrast enhancement to differentiate between nodal hyperplasia and nodal metastasis, have proved disappointing. Use of lymphotropic MR contrast media holds promise as a new approach to nodal staging.

Dextran-coated ultrasmall superparamagnetic iron oxide particles (USPIO) developed for this purpose have already entered clinical trials. The mechanism of action is based on phagocytosis by nodal macrophages, causing signal loss on T2-weighted MRI. Cases of nodal metastasis, where nodal macrophages are replaced by tumor, reveal a similar signal on pre- and postcontrast images. One study for the assessment of mediastinal nodes in patients with lung cancer concluded that USPIO-enhanced MRI was equal to PET and superior to CT. Accuracy levels for PET, MRI, and CT
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(against the gold standard of surgical biopsy) were 84%, 83%, and 76% respectively. Another multicenter trial found the sensitivity, specificity, and accuracy of USPIO-enhanced MRI in the detection of nodal metastasis to be 92%, 80%, and 85%, respectively. Most false-positive results found on USPIO-enhanced MRI are due to follicular hyperplasia, which also replaces nodal macrophages.

The most frequent hematogenous sites of metastasis in patients with lung cancer are the brain, axial skeleton, adrenals, and lungs. The accuracy of CT and MRI is equal for the assessment of adrenal metastasis, but MRI offers superior performance for detecting brain or bone metastasis. New developments in MR technology, such as whole-body scans with automatic table movement, will further improve systemic assessments. Application of multiple coil arrays, using multiple receiver channel technology and fast pulse sequences with parallel MRI, can reduce imaging time considerably. This time saving will make whole-body acquisitions feasible in a clinical context.

Fat-saturated T2-weighted MRI or contrast-enhanced fat-saturated T1-weighted MRI are typically used to detect metastasis. Clinical studies show ventilation MRI agrees well with conventional bone scintigraphy, while additionally detecting metastases in soft tissue and organs (Figure 3).

FUNCTIONAL STUDIES

MRI can provide functional evaluations of lung cancer patients as well. These include time-resolved dynamic measurements of the tumor and chest wall mobility during the breathing cycle. Clinical studies have demonstrated the potential of this technique for assessing chest wall invasion (Figure 4). Knowledge of tumor motion can also help when optimizing target volume in radiotherapy planning.

Functional MRI studies can also assess lung perfusion, either through unenhanced arterial spin labeling, or dynamic contrast-enhanced MRI. Several studies have shown a high correlation of pulmonary perfusion MRI with conventional radionuclide lung perfusion scintigraphy (Figure 5). Parallel imaging techniques are improving temporal and spatial resolution of pulmonary perfusion MRI, enabling 3D acquisitions of the whole lung. Pulmonary perfusion MRI has been proposed as a viable method of assessing functional operability in lung cancer patients.

MR-based assessments of ventilation are also possible. Proposed techniques include inhalation of aerosolized gadolinium chelates, hyperpolarized noble gases (for example, He-3), or molecular oxygen. Clinical studies have shown that ventilation MRI correlates well with both conventional lung function tests and CT. Combined ventilation and pulmonary perfusion MRI studies will eventually permit comprehensive assessment of pulmonary gas exchange.

MRI is likely to play a greater role in assessment of lung cancer patients in the future. It is already the imaging modality of choice for certain clinical problems such as superior sulcus tumors. Combinations of sophisticated morphologic and functional imaging techniques-for example, whole-body MRI, perfusion MRI, and ventilation MRI-will provide a comprehensive evaluation of lung cancer within a single examination. This could make MRI even more cost-effective than a combination of conventional imaging modalities.

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