MRI for the diagnosis of pulmonary embolism

Van Beek, E. J.R.; Oudkerk, M.

Published in:
Imaging Decisions MRI

DOI:
10.1046/j.1617-0830.2002.60304.x

Publication date:
2002

MRI for the Diagnosis of Pulmonary Embolism

E. J. R. van Beek[1], M. Oudkerk[2]
[1]*Unit of Academic Radiology, Royal Hallamshire Hospital, Sheffield, UK;* [2]*Department of Radiology, State University Hospital Groningen, Groningen, The Netherlands*

Correspondence to:
Edwin J. R. van Beek, MD PhD FRCR
Unit of Academic Radiology, Royal Hallamshire Hospital, Floor C
Glossop Road, Sheffield S10 2JF, UK
Tel: +44 114 2712487; Fax: +44 114 2724760; E-mail: e.vanbeek@sheffield.ac.uk

Key words: pulmonary embolism, diagnosis, MRI, MR angiography, MR perfusion, 3-Helium, Ventilation MR

.

Introduction

Magnetic resonance imaging (MRI) is a highly versatile technology, incorporating proton imaging, contrast-enhanced MR angiography (MRA) and imaging using new ventilation agents. Although the use of MRI in the diagnosis of pulmonary embolism (PE) is still in infancy, there are huge gains to be made in terms of its noninvasive nature, safe contrast agents and (maybe most importantly) its inherent lack of ionizing radiation. As a result of these advantages, developments are ongoing to make MRI an integral part of imaging of the chest and pulmonary arteries.

Until relatively recently, MRI of the chest was virtually unheard of. This was owing to the lack of protons within the chest, motion of both heart and lungs, and the susceptibility artefacts due to the interfaces between air and soft tissues. However, with the development of contrast-enhanced MRA, it became possible to image the large vessels in the chest. Newer sequences also improved other lung imaging parameters, such as perfusion imaging, direct thrombus visualization techniques and, more recently, the use of hyperpolarized noble gases for imaging of the air spaces. The use of faster imaging sequences has made it feasible to image even breathless patients.

The availability of MRI remains problematic in most hospitals. Thus, extension of services to include an acute disease such as venous thromboembolic disease will be difficult. However, as more systems are coming on line and with new laws on the medical use of ionizing radiation, it seems essential to develop this technology for use in the short term for those that have adequate MR resources and in the longer term for those that will have more MR capacity later. It should be emphasized that all work thus far has been performed on high gradient, high field-strength (1.5 T) systems. It seems unlikely that this requirement will change in the foreseeable future.

MRA

Gadolinium (Gd)-enhanced MRA is now the standard technique for many body areas. For imaging in the chest, the use of fast sequences has allowed imaging during a single breath-hold, using 3-D gradient echo sequences and the first pass effect on T1 relaxation by the gadolinium bolus (1–4). The breath-hold time has slowly decreased from nearly 30 s to less than 10 s with the introduction of newer sequences and better software (1–7). Most recently, a sequence has been described that decreases the breath-hold requirements for pulmonary MRA. This sequence obtains dynamic 3-D information on the entire pulmonary arterial tree in less than 4 s (7). Thus, the sequence almost omits the necessity for breath-holding and enhances the feasibility of MRA in patients with suspected pulmonary embolism who are more likely to be breathless. The initial results were encouraging, with visibility to subsegmental level and accurate diagnosis of PE in four patients. However, further validation of this technique is still required.

Other fast imaging sequences, such as dynamic 2-D MR digital subtraction angiography (DSA), are sequences that use thick slabs and maximum intensity projection. Although they have increasingly good temporal resolution, this is at the cost of signal-to-noise ratio and spatial resolution in the third dimension. However, they may be useful as they are directly comparable to standard DSA and they also show the dynamics of blood flow into the pulmonary arterial tree.

Only few published reports have assessed the value of contrast-enhanced MRA in reasonable numbers of patients. The first series in 13 patients was published by Isoda et al., but these patients had a variety of lung diseases other than pulmonary embolism (1).

The study by Meaney et al. investigated the performance of contrast-enhanced 3-D angiography in 30 patients with proven pulmonary embolism (5). The im-

ages were reported independently by three radiologists. In 10% of the patients, the images were of insufficient quality to be diagnostic. The sensitivity and specificity of MRA for PE for the remaining 27 patients varied between 75% and 100%, and 95% and 100%, respectively (5). Some of the criticisms of this study were the inherent selection bias and the fact that many patients with suspected PE would not be able to hold their breath for 27 s.

When considering the optimal use of MRA in a diagnostic strategy, one has to consider the role of perfusion lung scintigraphy, as this is capable of safely excluding PE in up to 50% of outpatients. Therefore, a more recent study performed contrast-enhanced 3-D MR pulmonary angiography in patients with an abnormal perfusion lung scintigram (6).

This study was performed in a consecutive series of 141 patients, and pulmonary angiography was performed as reference standard. The MR sequence used consisted of a double contrast injection and independent imaging using thick slabs of the two lungs. The sequence is described in more detail in Table 1 (6). The use of a biphasic injection of gadolinium chelate contrast agent has the advantage of obtaining greater signal-to-noise ratio, as the bolus will be optimal during data acquisition in the centre of k-space.

In this consecutive series of patients, MRA was contraindicated in 13 patients (9%), while images were not interpretable in eight patients (6%). MRA was performed in two patients in whom conventional pulmonary angiography was contraindicated. Thus, MRA and DSA were available in 118 patients (84%). The prevalence of PE was 30%, which can be attributed to the exclusion of patients with normal findings by performing perfusion scintigraphy prior to MRA. Some examples of MRA and correlating DSA images are shown in Figures 1 and 2, which demonstrate PE in both instances. Images were read independently in 115 patients, and agreement was obtained in 105 cases (91%), with a kappa value of 0.75. MRA demonstrated 27 of 35 patients with proven PE (overall sensitivity, 77%; 95% CI 61–90%). The sensitivity for isolated subsegmental, segmental and central/lobar PE was 40%, 84% and 100%, respectively ($P<0.01$ for isolated subsegmental vs. segmental or larger PE). Figure 3 demonstrates a normal MRA, but isolated subsegmental PE on DSA. However, these subgroups contained relatively small numbers. MRA demonstrated PE in two patients with normal angiogram at a specificity of 98% (95% CI 92–100%). Thus, it would seem that MRA is sensitive for segmental or larger PE and highly specific. These results are comparable to helical computed tomography (CT) literature data.

As demonstrated in Figures 4 and 5, one of the advantages of MRA is the capability to assess clot resolution. As there is no radiation involved, it is a good way of performing follow-up studies in patients at increased risk of developing chronic thromboembolic hypertension, such as those with relatively extensive PE.

More recently, the use of a very fast imaging technique with the newest gradient systems (1.5 T, ampli-

Table 1: Contrast-enhanced 3-D MR pulmonary angiography technique as used on a 1.5 T unit with enhanced gradients (Vision, Siemens Medical Systems).

Scan parameter	Value
Field-of-view (minimum)	200 × 320 mm
Matrix	90–106 × 512
Flow compensation	no
Breath-hold	yes, two separate breath-holds of 15 s
Slab thickness	125 mm for each lung in sagittal orientation
Encoded partitions	44
Reconstructed images	100
Slice thickness	1.25 mm
Coil	phased array body coil
Scan mode	3-D
Scan technique	Fast Low Angle Single Shot
TE	1.6 ms
TR	3.65 ms
Flip angle	25°
Bandwidth readout	390 Hz/pixel
Encoding	centre of data at half scan time
Test bolus	4 mL
Contrast total volume	20 mL for each lung
Contrast injection	2 mL/s, 10-s injection time for each lung
Mode of injection	biphasic: 1 mL/s for 5 s, 2 mL/s for remainder
Scan duration	40 s

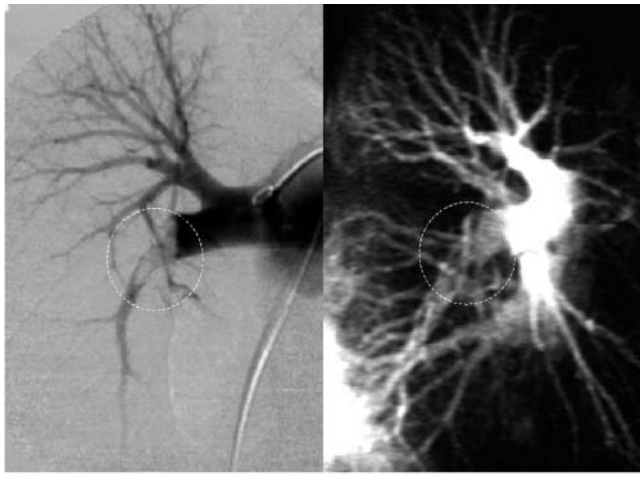

Fig. 1. Patient with a massive thrombus in the right descending pulmonary artery. The conventional pulmonary angiogram **(A)** compares closely to the projection obtained with contrast-enhanced 3D MRPA **(B)**. Circular dashed regions demonstrate the location of the embolus.

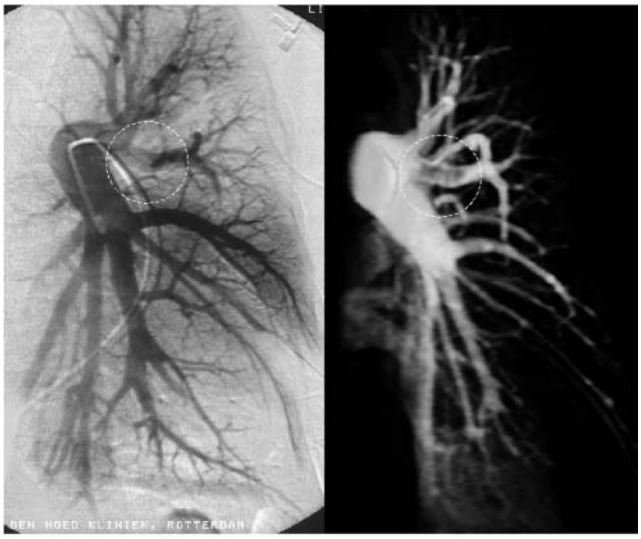

Fig. 2. Initial contrast-enhanced 3D MRPA on a patient with multiple emboli lodged in both lungs. A nice correlation is possible on the left lung between the conventional pulmonary angiogram **(C)** and the volume-rendered MRPA acquisition **(D)**. A double sagittal slab contrast-enhanced 3D MRPA protocol was performed.

tude 40 mT/m, slew rate 200 mT/m/ms) has resulted in a gadolinium-enhanced 3-D MRA sequence that can be performed in under 4 s per image dataset, with 5 datasets acquired within a 19-s breath-hold (7). A summary of the MRI parameters is shown in Table 2. The sequence has been tested in three healthy volunteers and eight dyspnoeic patients in whom a diagnosis of pulmonary embolism was contemplated. Pulmonary embolism was demonstrated in four patients and this was confirmed by CT or scintigraphy in all cases. In the other four patients pulmonary embolism was deemed absent, and this was also corroborated by noninvasive diagnostic tests. Only two of the eight patients could hold their breath for 19 s, while all patients could hold their breath for 8 s, during which time two datasets were acquired. It is concluded that this technique may offer a fast, reliable test for the diagnosis of pulmonary embolism, but further studies will be required to confirm this.

Direct thrombus imaging

Another concept is to develop sequences that do not require gadolinium contrast and directly image thrombus (8). The huge advantage of this technique is that it is fast and can be employed as a single-stop assessment of the entire deep venous system and the pulmonary arterial system, similar to that advocated for CT pulmonary angiography combined with venography (9). The technique proved highly accurate for the diagnosis of deep vein thrombosis, as was demonstrated in a study in 101 patients with suspected DVT in whom contrast venography was also performed (10). Although the cohort was not a consecutive group of patients, the authors prevented selection bias by including all patients with a positive venogram and randomly selecting 25% of patients who had a normal venogram result. Two independent reviewers reported sensitivity and specificity ranging from 94% to 96% and from 90% to 92%, respectively. As could be expected, the diagnostic accuracy for isolated calf vein thrombosis was slightly lower than for ileofemoral thrombosis, but nevertheless remained high (10). Furthermore, the interobserver variability was greater than 0.8, suggesting excellent robustness of interpretation for this technique.

Currently, this technique is being investigated in a large randomized clinical management trial and compared with three other management strategies: 1) lung scintigraphy followed by ultrasonography of the deep venous system of the leg if the lung scan is nondiagnostic; 2) same as strategy 1, but with pulmonary angiography as final diagnostic test if ultrasonography is normal; 3) helical CT pulmonary angiography (10).The initial results of the first 45 patients managed by MRI alone showed venous thromboembolic disease in 12 patients; these were treated with anticoagulant therapy. An example of a patient with central pulmonary embolism and concurrent deep vein thrombosis is shown in Figure 6. In the remaining 33 patients, in whom thrombosis was excluded by MR thrombus imaging, anticoagulants were withheld and patients were followed for 3 months. In the 33 patients with complete follow-up, two patients died from unrelated causes (one due to disseminated malignancy and one due to renal failure)

Table 2: Contrast-enhanced 3-D MR pulmonary angiography technique as used on a 1.5 T unit with high-performance three-axial gradients (Sonata, Siemens Medical Systems)

Scan parameter	Value
Field-of-view (minimum)	360 mm
Matrix	140×256
Flow compensation	no
Breath-hold	yes, 19 s for 5 image sets acquisitions
Slab thickness	110 mm
Encoded partitions	40
Reconstructed images	100
Slice thickness	2.75 mm
Coil	phased array body coil
Scan mode	3-D
TE	0.6 ms
TR	1.64 ms
Flip angle	15°
Bandwidth readout	1295 Hz/pixel
Test bolus	no
Contrast total volume	20 mL
Contrast injection	3 mL/s followed by saline flush
Scan duration	3.74 s per data set (5 image data sets required)

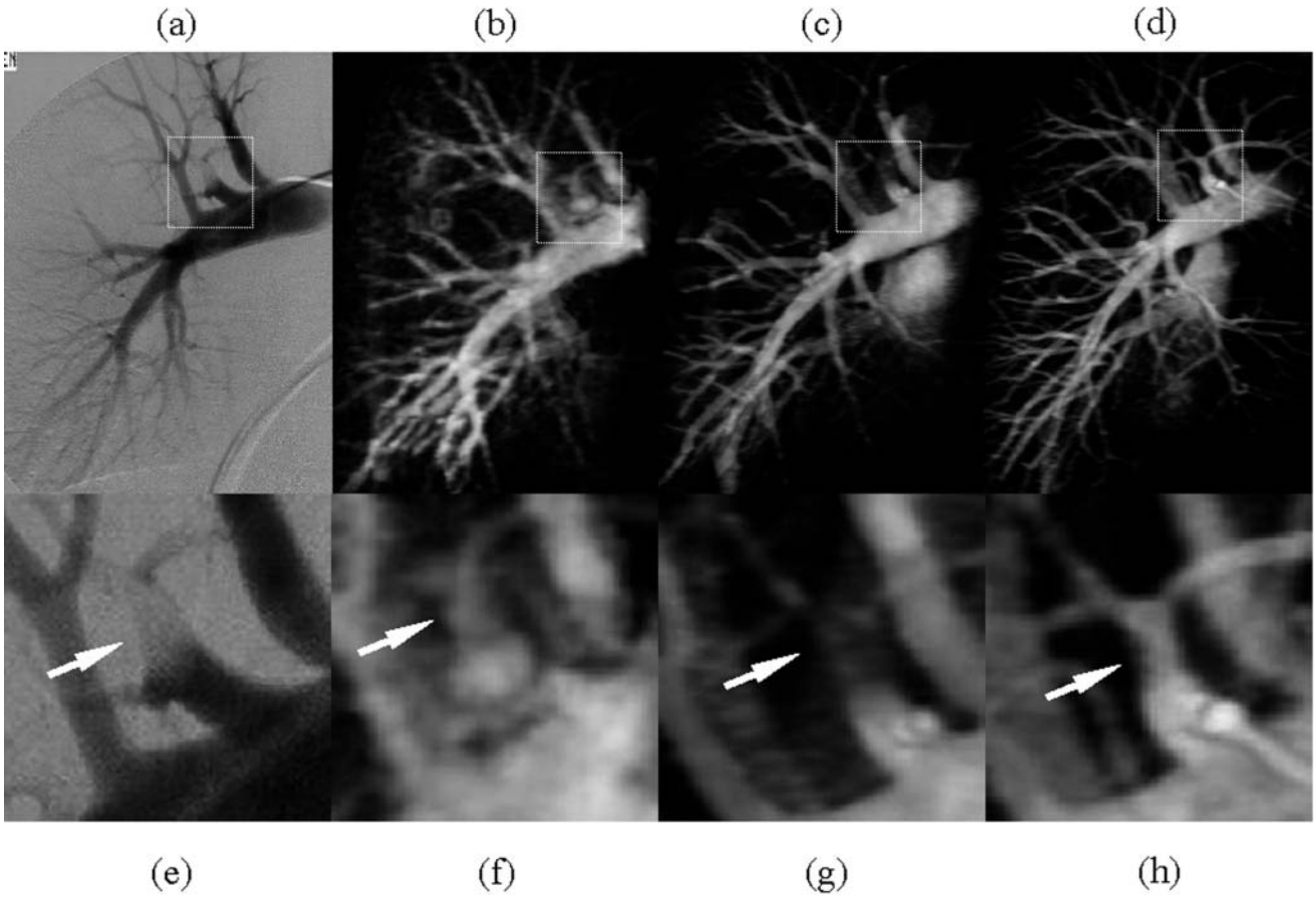

Fig. 3. Comparison between conventional and contrast-enhanced 3D MRPA on a patient with a small pulmonary embolus in the middle right pulmonary artery. **(A)** Conventional pulmonary angiogram. **(B)**. The magnified views of **(E-H)** correspond to the rectangular view (white dashed square) in **(A-D)** with arrows pointing at the vessel containing the small thrombus. Note that in conventional MRPA the contrast between thrombus and blood does not permit good differentiation **(F)**, better seen on the contrast-enhanced scan **(G)**. **(D)** and **(H)** illustrate the 3D MRPA acquisition after anticoagulant therapy (3 months after first examination) with complete clearance of the blood clot. For the conventional 3D MRPA scan, a sagittal acquisition was performed using FLASH 3D with TR/TE=3.5/1.4msec, α=5°, 110 mm, 44 sections (2.5mm), 96 × 256 matrix, FOV=220 = 340 mm^2, 15 sec breath-hold. Volume rendering was used for **(B-D)** after manual segmentation of the thorax.

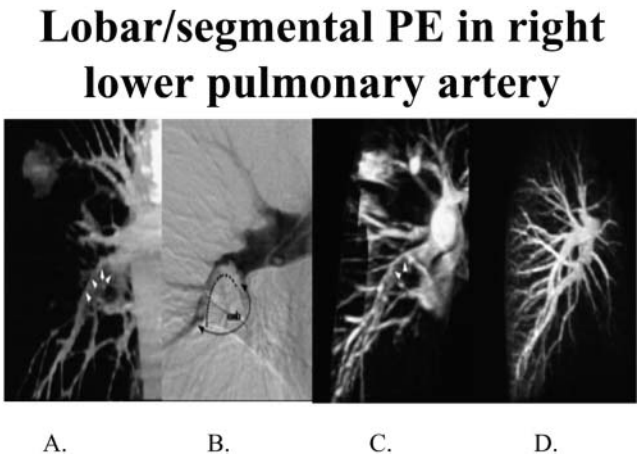

Fig. 4. Corresponding images of CTA **(A)**, DSA **(B)**, MRA **(C)** and follow-up MRA after treatment for PE **(D)**.

(10).There were no symptomatic thromboembolic events during this period. The outcome of the MR thrombus imaging management protocol was similar to that of the other management strategies. If these results could be replicated in additional patient numbers, this would show that MR thrombus imaging could replace other technologies in the management of venous thromboembolic diseases. The MR time availability remains a problem at present. However, the lack of ionizing radiation and the absence of (nephrotoxic) contrast agents, combined with the high reproducibility and diagnostic accuracy of this technique, make it a very promising method.

Perfusion imaging

Lung perfusion imaging is being developed using a variety of sequences (1, 5, 7, 8). One can use the so-called first pass effect of gadolinium-based contrast agents

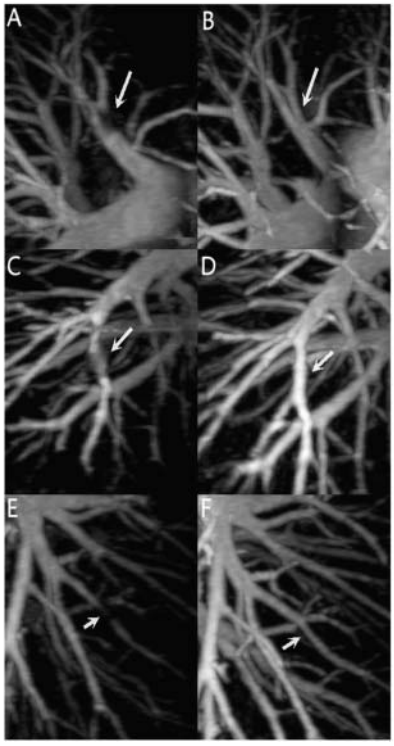

Fig. 5. Corresponding detailed images of pulmonary arterial MRA pre- and post-anticoagulant therapy. The images were obtained 1 week following a course of heparin/oral anticoagulants. From: Oudkerk M et al. Lancet 2002;359:1643–1647, Figure 2.

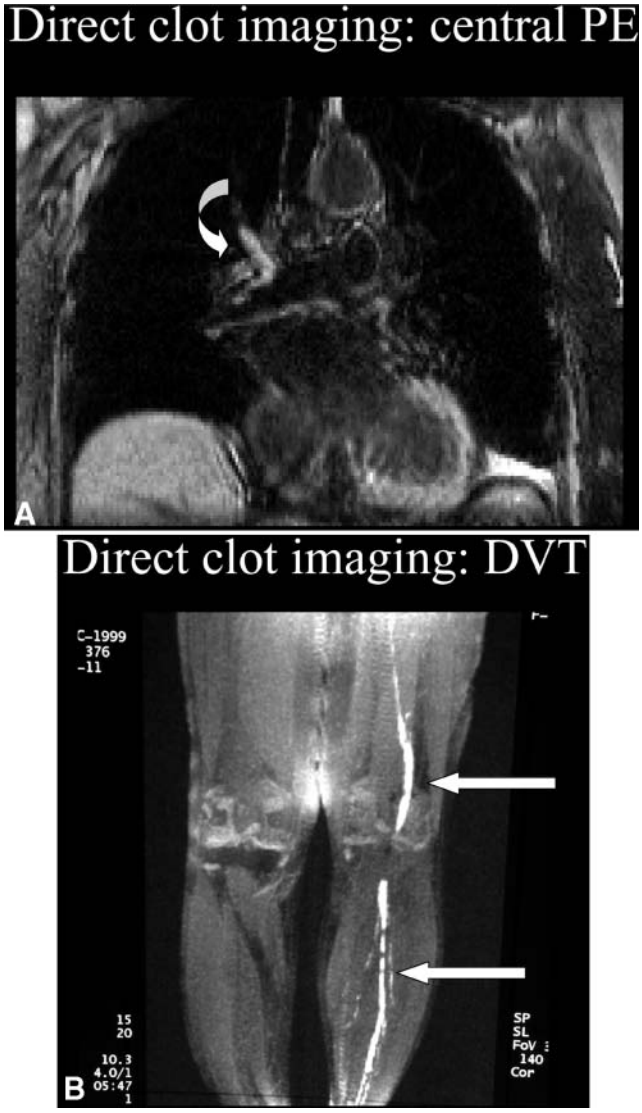

Fig. 6. Direct thrombus imaging sequence, demonstrating central pulmonary embolism **(A)** and deep vein thrombosis **(B)** in the same patient (images courtesy of Prof. Alan Moody, Nottingham, UK).

(similar to other techniques such as helical CT), but it is also possible to obtain perfusion information without contrast agents.

The contrast-based perfusion technique is usually combined with 3-D MRA, giving a dynamic enhancement of the pulmonary vascular tree similar to pulmonary angiography. Thus, perfusion-deficient areas can be shown and this can aid in the visualization of PE after reconstruction of the pulmonary arterial tree.

A recent publication using gadolinium-enhanced perfusion MR of the lung showed that semiquantitative evaluation of regional pulmonary perfusion can be achieved (11). This technique used consisted of a 5 mL bolus injection followed by saline flush at a rate of 3 mL/s. Three dynamic imaging sets of 6–7 s each were obtained during a single breath-hold. The initial imaging set was obtained prior to contrast injection, while the following two were obtained 7 s after start of bolus injection (pulmonary arterial phase) and 13 s after start of bolus injection (aortic phase). The technique was applied in 20 patients with potentially surgically resectable lung cancer (11). For comparison, pulmonary perfusion scintigraphy and pulmonary function tests were obtained and the patients' outcome was observed. The results showed good correlation between MR perfusion and lung scintigraphy, while MR perfusion also seemed able to predict postoperative outcome.

Arterial spin-labelling techniques are capable of using the red blood cells as magnetic particles. Thus the inflowing red blood cells can be visualized, giving information on lung perfusion. The technique has been under development and has recently been used in human lung experiments (12).

Perfusion-ventilation imaging

Ventilation lung MRI has become feasible using two techniques: subtraction MRI using oxygen enhancement and hyperpolarized noble gases. Recently, the

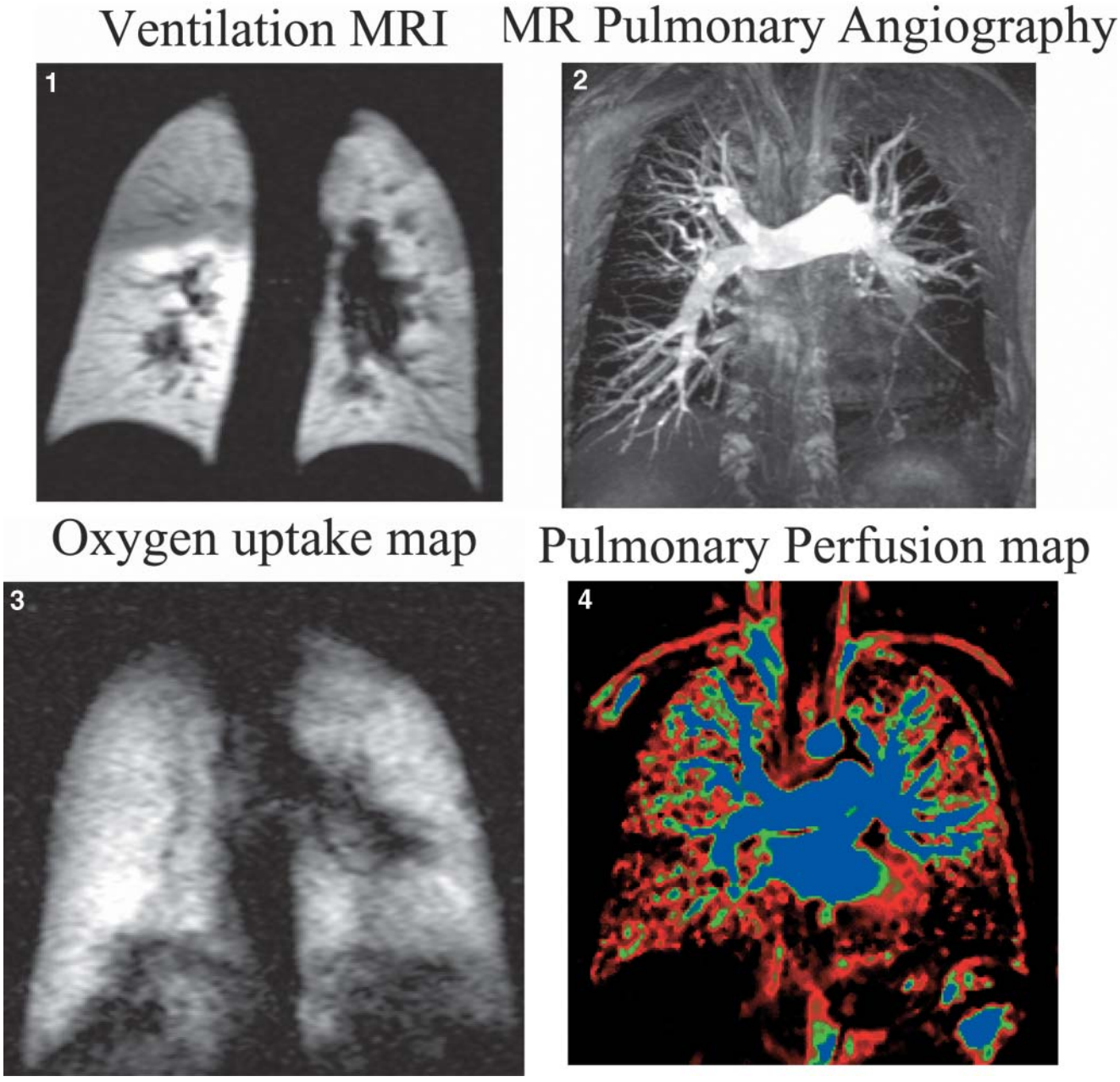

Fig. 7. Combination of hyperpolarized helium-3, Gd-enhanced perfusion MR and Gd-enhanced 3-D MRA will result in overall assessment of lung function. This example shows the results in a patient with chronic thromboembolic pulmonary hypertension (images courtesy of Dr Hans-Ulrich Kauczor, Mainz, Germany).

first human volunteers were imaged using this technology. These results were encouraging, and studies in patients with pulmonary embolism are currently in progress (13).

The introduction of ventilation imaging using hyperpolarized noble gases, such as helium-3, has introduced another method to perform perfusion/ventilation imaging. One recent overview gives a good outline of technical requirements and the initial results in animals and human studies (14). Another overview focuses on the potential role within the field of lung functional imaging. For an overview of helium-3 MRI, the reader is referred to the literature (15).

No human studies have been performed assessing the feasibility of perfusion/ventilation imaging. However, initial results of rat experiments have demonstrated that this technique may have potential (this could be even more relevant in pulmonary hypertension assessment) (16).

Figure 7 shows what is feasible for imaging of human pulmonary function. This patient was known to suffer from chronic thromboembolic pulmonary hypertension. The patient underwent pulmonary perfusion studies with the aid of gadolinium, pulmonary MRA and hyperpolarized helium-3 imaging for assessing ventilation homogeneity and oxygen uptake mapping.

Thus, an entirely noninvasive, nonionizing radiation protocol can now be used to assess parameters such as ventilation/perfusion mismatch, extent of disease in terms of oxygen uptake and direct visualization of the pulmonary vascular tree. It is this development of MRI of the chest that will ultimately be required for full implementation in the management of patients with both acute and chronic pulmonary embolism.

Conclusions

MRI of the chest is rapidly evolving and the inherent advantages of noninvasiveness, the nonionizing radiation requirement, the use of safer contrast agents and the versatile sequences employed to assess various tissues in the chest render it of potential value for the future. However, more investigations are needed to demonstrate clinical applicability in a setting of acute pulmonary embolism. As demonstrated above, it seems highly likely that MRI will play a major role in the diagnosis of venous thromboembolic diseases in the future.

References

1. Isoda H, Ushimi T, Masui T, et al. Clinical evaluation of pulmonary 3D time-of-flight MRA with breath-holding using contrast media.. J Comput Assist Tomogr 1995; 19: 911–919.
2. Wielopolski P, Hicks S, Obdeijn AIM, Oudkerk M.. PE detection using contrast-enhanced breathhold 3D Magnetic Resonance Angiography. Preliminary experience.. Proc ISMRM 1996; 2: 705.
3. Steiner P, McKinnon GC, Romanowski B, Goehde SC, Hany T, Debatin F. Contrast-enhanced, ultrafast 3D pulmonary MR angiography in a single breathhold: initial assessment of imaging performance.. J Magn Reson Imaging 1997; 7: 177–182.
4. Leung DA, Debatin JF. Three-dimensional contrast-enhanced magnetic resonance angiography of the thoracic vasculature.. Eur Radiol 1997; 7: 981–989.
5. Meaney JFM, Weg JG, Chenevert TL, et al. Diagnosis of pulmonary embolism with magnetic resonance angiography.. N Engl J Med 1997; 336: 1422–1427.
6. Oudkerk M, Van Beek EJR, Wielopolski P, et al. Comparison of contrast-enhanced MRA and DSA for the diagnosis of pulmonary embolism: results of a prospective study in 141 consecutive patients with an abnormal perfusion lung scan.. Lancet 2002; 359: 1643–1647.
7. Goyen M, Laub G, Ladd ME, et al. Dynamic 3D MR angiography of the pulmonary arteries in under four seconds.. J Magn Reson Imaging 2001; 13: 372–377.
8. Crossley I, Moorby S, Macdonald I, Delay S, Moody AR. Magnetic resonance direct clot imaging as a first line test in the evaluation of patients with suspected pulmonary embolism.. Radiology 2001; 221(P): 257.
9. Ghaye B, Dondelinger RF. Non-traumatic thoracic emergencies: CT venography in an integrated diagnostic strategy of acute pulmonary embolism and venous thrombosis.. Eur Radiol 2002; 12: 1906–1921.
10. Fraser DG, Moody AR, Morgan PS, Martel AL, Davidson I. Diagnosis of lower-limb deep venous thrombosis: a prospective blinded study of magnetic resonance direct thrombus imaging.. Ann Intern Med 2002; 36: 89–98.
11. Iwasawa T, Saito K, Ogawa N, Ishiwa N, Kurihara H. Prediction of postoperative pulmonary function using perfusion Magnetic Resonance Imaging of the lung.. J Magn Reson Imaging 2002; 16: 685–692.
12. Mai VM, Chen Q, Bankier AA, et al. Effect of lung inflation on arterial spin labelling signal in MR perfusion imaging of human lung.. J MRI 2001; 13: 954–959.
13. Mai VM, Bankier AA, Prasad PV, et al. MR ventilation-perfusion imaging of human lung using oxygen-enhanced and arterial spin labelling techniques.. J MRI 2001; 14: 574–579.
14. Möller HE, Chen XJ, Saam B, et al. MRI of the lungs using hyperpolarized noble gases.. Magn Reson Med 2002; 47: 1029–1051.
15. Kauczor H-U, Chen XJ, van Beek EJR, Schreiber WG. Pulmonary ventilation imaged by magnetic resonance: at the doorstep of clinical application.. Eur Respir J 2001; 17: 1–16.
16. Viallon M, Berthezene Y, Decorps M, et al. Laser polarized 3-Helium as a probe for dynamic regional measurements of lung perfusion and ventilation using magnetic resonance imaging.. Magn Res Med 2000; 44: 1–4.