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Signal quality of single dose gadobenate dimeglumine pulmonary MRA examinations exceeds quality of MRA performed with double dose gadopentetate dimeglumine

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Abstract

During a recent multi-center trial assessing gadolinium (Gd)-enhanced magnetic resonance angiography (MRA) for diagnosis of acute pulmonary embolism (PE), the Food and Drug Administration announced a risk of nephrogenic sclerosing fibrosis in patients with renal insufficiency who had received intravenous Gd-based MR contrast agents. Although no patients in this trial had renal insufficiency, in cautious response to this announcement, the trial protocol was changed from an intravenous administration of 0.2 mmol/Kg of a conventional Gd-based MR contrast agent to 0.1 mmol/Kg of gadobenate dimeglumine. The study described herein compares the signal quality of pulmonary MRA performed with double dose conventional agent to single dose gadobenate dimeglumine. This study is a retrospective analysis of data from a prospective, multicenter study in men and women ≥ 18 years with documented presence or absence of PE. The study was approved by the Institutional Review Board at all participating centers, and all patients provided written indication of informed consent. We performed both objective and subjective analysis of pulmonary artery image quality. Signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) in the main pulmonary artery were assessed in single and double dose protocols and compared. SNR and CNR of the main PA were correlated with subjective quality assessment of main/lobar, segmental and subsegmental pulmonary arteries. Although there were individual outliers, both SNR ($P = 0.01$) and CNR ($P = 0.008$) were higher in all quartiles for examinations using gadobenate dimeglumine than with gadopentetate dimeglumine. Subjective quality of vascular signal intensity at each vessel order was significantly better for gadobenate dimeglumine ($P < 0.0001$), and correlated well with SNR and CNR at each order (<0.001). Because of agent high relaxivity, a single dose of gadobenate dimeglumine provides better pulmonary MRA signal quality than double dose of a conventional Gd-based MR contrast agent.

Keywords

Pulmonary MR angiography; Contrast agents; Image quality; Pulmonary embolism

Introduction

The Prospective Investigation of Pulmonary Embolism Diagnosis-III (PIOPED III) is a prospective, NIH-funded, multicenter cohort trial performed to assess the accuracy of gadolinium (Gd)-enhanced magnetic resonance angiography (MRA) for the detection of acute pulmonary embolism (PE) [1]. During the performance of PIOPED III, the Food and Drug Administration (FDA) announced a risk of nephrogenic sclerosing fibrosis (NSF) for patients receiving gadolinium-based MR contrast agents [2, 3]. To date, NSF has occurred only in patients with renal insufficiency, usually on dialysis. It is a rare condition of skin thickening and tightening. In some cases, the skin thickening is so severe that it inhibits the flexion and extension of joints, resulting in contractures. Severely affected patients may be unable to walk, and in rare cases, internal organs may be affected, resulting in death [3].

While gadolinium-based intravenous MR contrast agents are contraindicated in patients with severe renal failure, patients with a glomerular filtration rate (GFR) above 30 but less than 60 ml/min/1.73 m² may still be candidates for MR angiography. In addition, a single dose of a gadolinium-based MR contrast agent is not nephrotoxic in comparison to the dose of iodinated CT contrast required for pulmonary CT angiograms [4–6].

Standard protocols for pulmonary MR angiography have suggested a double-dose (0.2 mmol/Kg) [7] and sometimes even a triple dose (0.3 mmol/Kg) [8, 9] of a gadolinium-based MR contrast agent in order to maintain adequate signal within the pulmonary arteries. At the time of the NSF risk announcement, per the request of our Data Safety and Monitoring

Board (DSMB), and in order to demonstrate feasibility of performing pulmonary MRA with a reduced contrast load, we changed our protocol from a double dose (0.2 mmol/Kg) conventional gadolinium-based MR contrast agent to a single dose (0.1 mmol/Kg) gadolinium based MR contrast agent of a higher relaxivity [10]. In the publication of the original trial data, it was noted that the SNR and CNR was better in the MRA examinations performed with gadobenate dimeglumine [1]. This manuscript is a formal analysis of the SNR and CNR data, and a description of the protocols used.

Methods

There were 450 patients examined by MRA in the PIOPED III study across all centers [1].

Pulmonary MRA protocol

All patients were examined in commercially available 1.5T whole body MR systems except 73 patients at one center who were examined in a 3.0 T MR unit. Patients examined in the 3.0T MR system were not included in this analysis. Most patients, 376 of 450 (84%), received 0.1 mmol/Kg body weight gadobenate dimeglumine (MultiHance, Bracco, Milan, Italy). Gadopentetate dimeglumine, 0.2 mmol/Kg body weight, (Magnevist, Bayer Healthcare, Morristown, NJ) was administered to 66 of 450 (15%) of patients. Only 8 patients received 0.2 mmol/Kg gadodiamide (Omniscan, GE Healthcare, Princeton, NJ) or gadoversetamide (OptimMARK, Covidien, St. Louis, MO). All patients receiving either gadobenate dimeglumine (MultiHance) or gadopentetate dimeglumine (Magnevist) and who underwent MR angiography on a 1.5T MR scanner (Table 1) were included in this study. Patients receiving gadodiamide or gadoversetamide were not included. The relaxivity and gadolinium concentration of gadobenate dimeglumine and gadopentetate dimeglumine is included in Table 2 [11].

The study was approved by the Institutional Review Board at all participating centers, and all patients provided written indication of informed consent. In all patients, pulmonary Gd-MRA was performed using a 3D gradient recalled echo (GRE) sequence in the coronal plane using the following parameters: minimum TR ($TR \leq 6.6$ ms), and minimum TE (≤ 2.3 ms), flip angle = 20° – 40° , approximately 384 by 288 matrix, 40 cm field of view, bandwidth 380–1,500 Hz/pixel, single acquisition/number of excitations (NEX), 3 mm slice thickness (interpolated to 1.5) and at least 44 (88 interpolated) slices or sufficient to cover the anatomy. Parallel imaging was used in most patients, with breath-hold ranging from 14 to 22 s.

In all patients receiving gadopentetate dimeglumine, contrast was administered intravenously at a rate of 3 ml/s via a commercially available MR-compatible power injector, and timed to enhance the main pulmonary artery. In patients receiving gadobenate dimeglumine, because of the lower contrast volume, contrast was administered intravenously at a rate of 2 ml/s. The contrast injection was followed by a flush of 15 ml normal saline injected at the same rate. The scan delay, allowing peak contrast enhancement at the center of K-space, was calculated using a test bolus.

SNR and CNR calculation

Signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) calculations were made using standard calculations [12]. Signal in the pulmonary arteries was determined by placement of a circular region of interest (ROI) of approximately 400 mm² placed in the main PA by the MR technologist or radiologist at the recruiting center. For the SNR, mean signal in the PA was divided by the standard deviation of signal in adjacent non-vascular lung. For CNR, mean signal in the adjacent non-vascular lung was subtracted from the signal in the main

PA. This difference was divided by the standard deviation of signal in adjacent non-vascular lung.

Subjective quality analysis by artery order

During the original PIOPED III central reader interpretation, central readers were asked to grade the quality of vascular opacification (i.e., signal intensity) in the main and lobar arteries, segmental arteries, and subsegmental arteries as either good, fair or poor. Good and fair were lumped together to allow the binary classifications of good/fair versus poor quality. The SNR and CNR of the main PA calculated was correlated to subjective quality assessment at each vessel order.

Statistical analysis

A non-parametric test was used to compare SNR and CNR measurements between 0.1 mmol/Kg gadobenate dimeglumine and 0.2 mmol/Kg Gadopentetate dimeglumine and the significance of any difference in SNR and CNR between the two contrast agents was calculated using a Wilcoxon two-sample test ($P < 0.05$) [13].

Results

Of the 442 patients receiving either gadobenate dimeglumine or gadopentetate dimeglumine, 438 had complete pulmonary MR angiography data sets for analysis.

SNR and CNR

Statistically significant differences in pulmonary SNR ($P = 0.01$) and CNR ($P = 0.008$) were found between gadobenate dimeglumine (MultiHance) and gadopentetate dimeglumine (Magnevist), with SNR and CNR higher in all quartiles for examinations using gadobenate dimeglumine than those using gadopentetate dimeglumine. The median SNR for gadopentetate dimeglumine was 30, and 38 for gadobenate dimeglumine ($P = 0.01$). The CNR median was 28 and 35 for gadopentetate dimeglumine and gadobenate dimeglumine, respectively, ($P = 0.008$). The distribution of SNR and CNR values for gadobenate dimeglumine and gadopentetate dimeglumine are shown in Fig. 1.

Although the examinations with the highest SNR and CNR values were performed with gadopentetate, SNR and CNR in each quartile were highest in pulmonary MRA examinations performed with gadobenate. In addition, the distribution of SNR and CNR was more extreme across examinations using gadopentetate and there was more SNR and CNR heterogeneity than among those examinations in which gadobenate was used. The examinations with the highest SNR and CNR values using gadopentetate were outliers.

Subjective quality analysis by artery order

Subjective quality at each vessel order was significantly better for gadobenate dimeglumine ($P < 0.0001$), and correlated with calculated SNR and CNR values $P < 0.001$ (Figs. 2, 3).

Discussion

Although most contrast-enhanced pulmonary MRA has been performed at 0.2 mmol/Kg contrast dosing [14, 15], this study demonstrates that 0.1 mmol/Kg gadobenate dimeglumine (MultiHance) performs at least as well as 0.2 mmol/Kg of gadopentetate dimeglumine (Magnevist), and that this lower contrast dosing of gadobenate dimeglumine can be used to obtain pulmonary MRA examinations when necessary.

Since MR angiography was first performed in the early 1990s, it has been routinely performed with twice and sometimes three times the Food and Drug Administration approved dose of gadolinium-based MR contrast agents, 0.2–0.3 mmol/Kg [14, 15]. It was felt that this dosing of contrast agent was necessary to maintain adequate SNR and CNR of the angiography images. Standard gadolinium-based MR contrast agents have relaxivities (r_1 and r_2) on the order of $3\text{--}4\text{ mmol}^{-1}\text{ s}^{-1}$ at pH and temperature plasma conditions similar to those in the human body (pH 7 and $39\text{ }^{\circ}\text{C}$) at 1.5T [11]. The longitudinal (r_1) and transverse (r_2) relaxivity of a complex are defined as the enhancement of the relaxation rates R_1 and R_2 , respectively, induced by 1 mmol of the paramagnetic center per liter. Usually, these relaxivities are measured over a range of concentrations and are defined as the slope of the regression line of relaxation rates R_1 and R_2 , respectively, against concentration [16].

Gadobenate dimeglumine differs from other available gadolinium agents in terms of relaxivity. The gadobenate dimeglumine molecule interacts weakly and transiently with serum albumin, resulting in a slowing of the tumbling rate of the Gd complex, which allows for a longer rotational correlation time with inner shell water protons [11, 16, 17]. This protein binding increases both r_1 and r_2 of gadobenate dimeglumine in normal blood serum at body pH and temperature nearly two times for r_1 and more than three times for r_2 the relaxivity of other gadolinium agents such as gadopentetate dimeglumine [11], likely allowing for the high SNR and CNR of gadobenate dimeglumine in pulmonary MR angiography despite the administration of half of the dose.

With the demonstration that higher doses of Gd-based MR contrast agents were associated with NSF in renal insufficiency patients [2], we sought to reduce the overall contrast dose administered to patients in the PIOPED III multicenter trial.

It should be noted that the entrance of gadofosveset trisodium, an even higher relaxivity agent, into the United States market in January, 2010, and unavailable to us during the PIOPED III trial, would have potentially permitted even lower contrast dosing. The r_1 and r_2 of gadofosveset trisodium is 8.9 ± 2.7 and $37.6 \pm 5.16\text{ mmol}^{-1} \times \text{s}^{-1}$, respectively and the agent has a Food and Drug Administration single dose recommendation of 0.03 mmol/Kg [18]. This agent may be useful in pulmonary MR angiography not only because of its increased relaxivity, but also because of its increased intravascular half life. Like gadobenate dimeglumine, it interacts with serum albumin, reversibly binding, but permits an intravascular half life of up to 1 h and optimal arterial imaging out to 20–30 min, with the potential for repeat imaging in patients with suboptimal breath-holds or in the instance of a mis-timed contrast bolus [18]. Its prolonged half life also would permit optimal imaging of the lower extremity deep venous system to assess deep venous thrombosis using the same contrast bolus administered for the pulmonary angiogram.

Other pulmonary MR angiography techniques with potential of reducing MR contrast agent dose include pulmonary time-resolved imaging [19, 20]. By utilizing a small dose of contrast material ($\sim 5\text{ ml}$), rapid serial scanning at reduced spatial resolution combined with subtraction of a pre-contrast mask allowed good visualization of important dynamic functional and morphological information of vasculature using an incremental dose of only 0.03–0.05 mmol/Kg of a conventional Gd-based MR contrast agent such as gadopentetate dimeglumine [19]. While this method was available at the time of the initiation of the PIOPED III trial (2005), the spatial resolution was relatively low and the sequence was considered unacceptable for use pulmonary embolism assessment. More recent advances in the technique permit in-plane spatial resolution on the order of $1.3 \times 1.8\text{ mm}^2$, and z-axis resolution of 3 mm [20].

An additional method yet to be assessed in the pulmonary embolism patient population is steady-state free precession MR angiography methods coupled to free breathing navigator techniques. This method has been used in aortic vascular imaging and has the potential to provide high SNR pulmonary artery images without the use of an intravenous Gd-based contrast agent [21].

Limitations of this study include the retrospective analysis, and the disparate sample size of the examinations performed with the agents (gadobenate dimeglumine n = 297; gadopentetate dimeglumine n = 63). The difference in sample size of the studies performed with the two agents, however, was unavoidable given the reason for the modification of dosing in the midst of an on-going multicenter trial.

The results of this study are supported by similar findings in prospective, cross-over comparison studies of gadobenate dimeglumine and gadopentetate dimeglumine for MR angiography of peripheral arteries [22, 23]. In one study [22], 0.1 mmol/Kg dosing of both agents, demonstrated significantly better contrast enhancement of MR angiograms performed with gadobenate dimeglumine. In the second study [23], 0.1 mmol/Kg dosing of gadobenate dimeglumine showed better SNR and CNR within the aorta in comparison to 0.2 mmol/Kg dosing of gadopentetate dimeglumine, however, higher SNR and CNR were not statistically significant at all measured levels.

In conclusion, because of agent high relaxivity, a single dose of gadobenate dimeglumine provides better pulmonary MRA signal quality than double dose of gadopentetate dimeglumine. This allows for lower dosing of a gadolinium-based MRI contrast agent with one of the better safety records in terms of NSF. This knowledge may be of significance in determining the contrast-enhancement protocol in patients at risk for NSF if MR angiography must be performed.

Acknowledgments

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References

1. Stein PD, Chenevert TL, Fowler SE, Goodman LR, Gottschalk A, Hales CA, Hull RD, Jablonski KA, Leeper KV, Naidich DP, Sak DJ, Sostman HD, Tapson VF, Weg JG, Woodard PK. Gadolinium-enhanced magnetic resonance angiography for pulmonary embolism: a multi-center prospective study (PIOPED III). *Annals Int Med*. 2010; 152(7):434–443.
2. US Food and Drug Administration. [24 Sep 2010] Information on gadolinium-containing contrast agents. 2010. <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm142882.htm>
3. Cowper, SE. International Center for Nephrogenic Fibrosing Dermopathy Research (ICNFDR). 2009. <http://www.pathmax.com/dermweb/> last updated 25 Oct 2009
4. Prince MR, Arnoldus C, Frisoli JK. Nephrotoxicity of high-dose gadolinium compared with iodinated contrast. *J Magn Reson Imaging*. 1996; 6(1):162–166. [PubMed: 8851422]
5. Ledneva E, Karie S, Launay-Vacher V, Janus N, Deray G. Renal safety of gadolinium-based contrast media in patients with chronic renal insufficiency. *Radiology*. 2009; 250(3):618–628. [PubMed: 19244037]
6. Sam AD II, Morasch MD, Collins H, Song G, Chen R, Pereles FS. Safety of gadolinium contrast angiography in patients with chronic renal insufficiency. *J Vasc Surg*. 2003; 38(2):313–318. [PubMed: 12891113]

7. Stein PD, Woodard PK, Hull RD, Kayali F, Weg JG, Olson RE, Fowler SE. Gadolinium-enhanced magnetic resonance angiography for detection of acute pulmonary embolism: an in-depth review. *Chest*. 2003; 124(6):2324–2328. [PubMed: 14665516]
8. Hany TF, Schmidt M, Hilfiker PR, Steiner P, Bachmann U, Debatin JF. Optimization of contrast dosage for gadolinium-enhanced 3D MRA of the pulmonary and renal arteries. *Magn Reson Imaging*. 1998; 16(8):901–906. [PubMed: 9814772]
9. Goyen M, Debatin JF. Gadopentetate dimeglumine-enhanced three-dimensional MR-angiography: dosing, safety, and efficacy. *J Magn Reson Imaging*. 2004; 19(3):261–273. [PubMed: 14994293]
10. Stein PD, Gottschalk A, Sostman HD, Chenevert TL, Fowler SE, Goodman LR, Hales CA, Hull RD, Kanal E, Leeper KV Jr, Nadich DP, Sak DJ, Tapson VF, Wakefield TW, Weg JG, Woodard PK. Methods of prospective investigation of pulmonary embolism diagnosis III (PIOPED III). *Semin Nucl Med*. 2008; 38(6):462–470. [PubMed: 19331840]
11. Pintaskse J, Martirosian P, Graf H, Erb G, Lodemann KP, Claussen CD, Schick F. Relaxivity of gadopentetate dimeglumine (Magnevist), gadobutrol (Gadovist), and gadobenate dimeglumine (MultiHance) in human blood plasma at 0.2, 1.5, and 3 tesla. *Invest Radiol*. 2006; 41(3):213–221. [PubMed: 16481903]
12. Murphy BW, Carson PL, Ellis JH, Zhang YT, Hyde RJ, Chenevert TL. SNR measures for MR imagers. *Magn Reson Imaging*. 1993; 11:425–428. [PubMed: 8505876]
13. Gibbons, JD.; Chakraborti, S. Nonparametric statistical inference. 4th. Marcel Dekker; New York: 2005. p. 314
14. Blum A, Bellou A, Guillemin F, Douek P, Laprévote-Heully MC, Wahl D. Performance of magnetic resonance angiography in suspected acute pulmonary embolism. *Thromb Haemost*. 2005; 93(3):503–511. [PubMed: 15735802]
15. Meaney JF, Weg JG, Chenevert TL, Stafford-Johnson D, Hamilton BH, Prince MR. Diagnosis of pulmonary embolism with magnetic resonance angiography. *N Engl J Med*. 1997; 336(20):1422–1427. [PubMed: 9145679]
16. De Haën C, Cabrini M, Akhnana L, et al. Gadobenate dimeglumine 0.5 mM solution for injection (Multi-Hance®): pharmaceutical formulation and physicochemical properties of a new magnetic resonance imaging contrast medium. *J Comput Assisted Tomogr*. 1999; 23(Suppl 1):S161–S168.
17. Aime S, Chiaussa M, Digilio G, et al. Contrast agents for magnetic resonance angiographic applications: ¹H and ¹⁷O NMR relaxometric investigations on two gadolinium(III) DPTA-like chelates endowed with high binding affinity to human serum albumin. *J Biol Inorg Chem*. 1999; 4:766–774. [PubMed: 10631608]
18. Blockley NP, Jiang L, Gardener AG, Ludman CN, Francis ST, Gowland PA. Field strength dependence of R1 and R2* relaxivities of human whole blood to ProHance, Vasovist, and deoxyhemoglobin. *Magn Reson Med*. 2008; 60(6):1313–1320. [PubMed: 19030165]
19. Krishnam MS, Tomasian A, Lohan DG, Tran L, Finn JP, Ruehm SG. Low-dose, time-resolved, contrast-enhanced 3D MR angiography in cardiac and vascular diseases: correlation to high spatial resolution 3D contrast-enhanced MRA. *Clin Radiol*. 2008; 63(7):744–755. [PubMed: 18555032]
20. Ersoy H, Goldhaber SZ, Cai T, Luu T, Rosebrook J, Mulkern R, Rybicki F. Time-resolved MR angiography: a primary screening examination of patients with suspected pulmonary embolism and contraindications to administration of iodinated contrast material. *AJR Am J Roentgenol*. 2007; 188(5):1246–1254. [PubMed: 17449767]
21. Krishnam MS, Tomasian A, Malik S, Desphande V, Laub G, Ruehm SG. Image quality and diagnostic accuracy of unenhanced SSFP MR angiography compared with conventional contrast-enhanced MR angiography for the assessment of thoracic aortic diseases. *Eur Radiol*. 2010; 20(6):1311–1320. [PubMed: 20013276]
22. Gerretsen SC, le Maire TF, Miller S, Thurnher SA, Herborn CU, Michaely HJ, Kramer h, Vanzulli A, Vymazal J, Wasser MN, Ballarati CE, Kirchin MA, Pirovano G, Leiner T. Multicenter, double-blind, randomized intraindividual crossover comparison of gadobenate dimeglumine and gadopentetate dimeglumine for MR angiography of peripheral arteries. *Radiology*. 2010; 255(3):988–1000. [PubMed: 20501735]
23. Prokop M, Schneider G, Vanzulli A, Goyen M, Ruehm SG, Douek P, Dapra M, Pirovano G, Kirchin MA, Spinazzi A. Contrast-enhanced MR angiography of the renal arteries: blinded

multicenter crossover comparison of gadobenate dimeglumine and gadopentetate dimeglumine. Radiology. 2005; 234:399–408. [PubMed: 15616119]

Fig. 1.

Box-and-whisker plots show the distribution of signal-to-noise (*SNR*) and contrast-to-noise (*CNR*) in pulmonary MR angiograms performed in PLOPED III. The *box* shows the 25th to the 75th percentile. The *top of the line* is the maximum and the *bottom line* is the minimum in the distribution. *SNR* and *CNR* values are unitless. The *P* values are from the non-parametric Wilcoxon two-sample test using the normal approximation

Fig. 2.

Box-and-whisker plots show SNR by subjective quality assessment of arterial phase opacification and vessel. The *box* shows the 25th to the 75th percentile. The *top of the line* is the maximum and the *bottom line* is the minimum in the distribution. SNR and CNR values are unitless. $P < 0.001$

Fig. 3.

Box-and-whisker plots show CNR by subjective quality assessment of arterial phase opacification and vessel. The *box* shows the 25th to the 75th percentile. The *top of the line* is the maximum and the *bottom line* is the minimum in the distribution. SNR and CNR values are unitless. $P < 0.001$

Table 1
MR scanners used in PIOPED III

Institution	MR scanner *
Clinic A	Siemens Sonata
Clinic B	Philips Intera GE Signa
Clinic C	GE Twinspeed
Clinic D	GE Signa
Clinic E	Siemens Avanto
Clinic F	GE Signa Toshiba Vantage
Clinic G	Siemens Avanto

* All scanners used in this analysis are 1.5T whole body MRI scanners

Table 2
Relaxivity of contrast agents assessed

Contrast agent	r_1 relaxivity* ($l \times mmol^{-1} \times s^{-1}$)	r_2 relaxivity* ($l \times mmol^{-1} \times s^{-1}$)
Gadobenate dimeglumine	8.1 ± 0.4	18.7 ± 0.5
Gadopentetate dimeglumine	3.9 ± 0.2	5.3 ± 0.2

* At body temperature and at pH 7.4, at [0.5] mM

Modified from reference [11]